

Annex K: Oral Hearing Transcripts

The oral hearings ran from November 2018 to May 2019. The transcripts are organised by date and session.

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* These Oral Hearings have an associated Right of Reply document, please see <https://www.immdsreview.org.uk/Evidence.html> to view the Rights of Reply.

20th November 2018

Session 1: FACSaware

START OF TRANSCRIPT

Julia Cumberlege: Right, well thank you so much for coming. We're very grateful for seeing you today and for the time that you've had to take to come here. I just want to say that, of course, we know, certainly, Emma very well. We've had a number of informal meetings across the country, in looking at three different areas, Primodos, sodium valproate, and surgical mesh. Those are the things we've been asked to review by the Secretary of State.

So, we've had a lot of informal meetings, which have been really helpful, and we've learned a lot from them. But now we are into our next stage, which is the oral hearings. It really is an opportunity for you to tell us more about what we need to know and what we need to think about. Today, of course, we're discussing with you sodium valproate.

So, I want to start by thanking you for your written submissions. They're really helpful and we've taken note of those. So, if I could just introduce the panel who is with me here today. I'm Julia Cumberlege and I have been commissioned to chair this review. On this side is my Vice Chairman, Sir Cyril Chantler. On this side is Simon Whale, who is also a member of the panel. Valerie Brasse, who is our secretary, and Sonia Macleod who is our researcher. We have got one or two other people in the room, just to make sure this event runs smoothly.

I just want to set the tone, to say that we're not a Select Committee. This isn't an inquisition. What we really want to do is to have a conversation and for you to tell us things that we haven't already read in your submission, in addition to, and some things you may want to just put greater emphasis on. We absolutely understand that.

I'd like to welcome your observer here today as well. Thank you very much for coming, for supporting this organisation.

So, just to set the scene, we are video recording these sessions because we want it to be transparent throughout the whole of our review, and this is part of that transparency. What is videoed today will be then posted on our website so everybody can see it in due course.

Perhaps, Carol, you may not want exactly what you're going to be saying to be made too public and we absolutely understand that because what

we have suggested is that, Emma, you should bring a patient experience - a person who has had experience to meet us. So, welcome today.

Perhaps, Emma, formally if you just introduce yourselves and your organisation.

Emma Friedman: I'm Emma Friedman. I have epilepsy and a son with Foetal Valproate Syndrome. I'm Campaign Director of FACSaware, which is an online awareness campaign to raise awareness of valproate, the effects of medicines during pregnancy, and the importance of reporting adverse drug reactions.

Here, I have Carol Short, who is also a woman with epilepsy...

Carol Short: I am also - yes.

Emma Friedman: ...and a son with Valproate Syndrome.

Carol Short: Yes, that's the same. Yeah.

Julia Cumberlege: So, Carol, I think it would be really good, perhaps, if you started, if that's alright...

Emma Friedman: May I...

Julia Cumberlege: ...and then Emma.

Emma Friedman: I've prepared my statement, with Carol coming in after me talking for six minutes. So, if I talk for six minutes, invite questions from you, and then introduce Carol for her statement, and then I'll come in with a list of suggestions of what we feel we need now and looking forward into the future regarding the regulatory aspects of this review. Is...

Julia Cumberlege: Yes.

Emma Friedman: Would that be okay for you?

Julia Cumberlege: Perfect, thank you.

Emma Friedman: Yeah? Lovely.

Well, thank you very much for inviting us here today. We're all very, very pleased to have taken part in this review and are very pleased with the way that you, as a panel, have conducted yourselves when you are dealing with us, as patients, and our very, very emotional stories. So, thank you.

There has been a lot of positivity. Things that we have been involved in over a period of time that have been positive things for us. So, we've been part of creating the 2016 Valproate Toolkit. We worked with the MHRA to produce this and it was - and here's the little pharmacy card. It was really nice to be involved in something so positive.

Along our journeys, we have met people from France, we've met people at the MHRA, who are the regulator in the UK. France puts out quite a lot of information. There's a charity here in the UK. ASSAC, who are the Swiss group. Association Belge are the Belgian group. Another little booklet that was OACS and the Fetal Anti-Convulsant Trust from a few years ago. The recent FACSaware leaflet. Most recently, what we have been involved in is the new Valproate Toolkit and the ban on the use of valproate in pregnancy, with a pregnancy prevention programme and a list for prescribers to go through.

We're, obviously, delighted that Jeremy Hunt announced that he would ask you to do this review. So, this statement is written by me based on the views from our Facebook page and our networks. We welcome the review and its independence as you will be able to give constructive critique on actions taken and not taken by successive governments.

We ask you to recommend a full compensation package for those affected by sodium valproate and their families. An end to cuts, and to introduce ring-fenced funding for the essential services that we rely on. A judge-led public inquiry into sodium valproate as an exemplar of the problems with medicine regulation and the licensing of medicines, devices, and products, to highlight the need to update consumer protection law here in the UK post-Brexit. A review of Legal Aid reforms and their impact on access to justice for those suspected of being harmed by pharmaceutical products and devices.

We expected Legal Aid to enable our disabled children to access justice. The Lord Chancellor to investigate the public interest element of Legal Aid and reinstate it in the group action to sue Sanofi. The Prime Minister to intervene, as he had a disabled child, had an understanding of epilepsy, and was Vice President of Epilepsy Society. The epilepsy charities to support us. Doctors to give us up to date information about risk. Doctors to have an understanding of Valproate Syndrome. Doctors to make referrals for diagnosis and necessary therapies.

We expected a national high-profile media coverage and campaign about valproate risk, the withdrawal of Legal Aid, inaction of politicians, fundraising for our legal costs, scrutiny of medicine regulation,

pharmaceutical accountability, and the impact on public services. We also expected politicians to act in the interests of their constituents and the public purse. We were wrong to expect anything.

Abuse. Our children are immensely vulnerable and remain so throughout their adult lives. Many children with FACS will have been taken into care if their mothers' epilepsy or mental health became unstable. Many of these children are at risk of being neglected, mistreated, and sexually abused whilst in the care of the State. Some parents have been accused of abuse because poorly educated clinicians have not recognised the complex symptoms that manifest as FACS.

Many adults with FACS will be placed in assessment and treatment units, residential care, and are abused and neglected. This is what I and many of us fear for our children's futures. I have met someone with Valproate Syndrome whose mother was severely disabled, was prescribed valproate, and was raped by a carer.

Those seen as independent enough to live in the community become victims of poor-quality housing, a hostile welfare policy, Universal Credit, Personal Independence Payment, inequality in the workplace, social exclusion as community facilities close, inadequate health and social care provision due to the fragmentation and endless restructures and changing providers in our NHS and healthcare services.

If you would like further information, I would be happy to provide it, but in confidence as these are obviously intensely personal stories that I do not feel this is an appropriate platform to discuss in further detail.

Do you have any - would you like me to expand on anything? Or should I continue now?

Julia Cumberlege: Shall we just hear, first of all, from you?

Emma Friedman: May I just have one...

Julia Cumberlege: Oh, right. Do...

Emma Friedman: Sorry, I'm going to break up after each point to give you the opportunity to ask any questions. Or whether you'd like to wait until the end? So, I will hand over to Carol...

Julia Cumberlege: Alright.

Emma Friedman: ...if that's okay, when I'm done. I'm okay on time, aren't I?

Female

Yeah.

Emma Friedman:

Postcode lottery. There is some excellent healthcare education and advocacy provision, but it is not consistent. There are doctors who laugh at mothers who question whether their child's complex symptoms could be related to valproate exposure. Doctors who tut when a woman planning a pregnancy says I read something on the internet. Parents who have to plead with the Local Authority for a statement or educational health and care plan. Parents who have to go to tribunal because the EAC plan is not reflective of the child's needs.

This is a growing problem because there is a statutory obligation for Local Authority to provide what is stated in these documents. They cannot provide what they are already required to provide and so are reluctant to assess someone else as also needing these services. The cuts to Local Authority budgets have devastated services essential for the wellbeing of people with FACS, Valproate Syndrome, and their families.

There is education provision that it not safe. There is respite being delivered by inexperienced carers so the families would rather not have the respite than knowingly put their child at risk. When our children become hospital in-patients for routine or emergency treatment, there are no staff available who understand learning disabilities, autism, behavioural disorders. So, the family cannot leave the bedside.

Most doctors did not receive the 2016 Valproate Toolkit due to CCGs not disseminating the information provided to them by the MHRA. Short-staffing limits the amount of time clinicians can spend reading drug safety updates and NICE guidance. The increased use of locums means information does not reach everyone. Staff who express safeguarding concerns about the provision offered do not have adequate whistleblower protections.

Some questions. Why have big charities for people with epilepsy, mental health illness, learning disability, autism, baby-loss, neonatal death, and rare diseases refused to promote the issues surrounding valproate and other pharmaceutical teratogens? Some charity information that is still available in neurology waiting rooms today is misleading and was out of date when it was printed.

I'd like to just raise these [REDACTED] from 2013 that give advice to women on parenting and pregnancy. I can let you have a copy of these, but they are misleading. They are reassuring and in 2013 it was established that there was a 40 per cent risk with valproate. It's not a case

of sodium valproate appears to have greater risks than other AEDs. It was firmly established two years prior to these being printed. So, we feel very upset and let down by that.

Why have politicians and successive governments not recognised the economic impact of adverse drug reactions and done something about it? Why are there DHSS files from the 1980s about the safety of drugs we use today sealed in the National Archives for 100 years? Why is the Yellow Card not promoted?

This week is Yellow Card Awareness Week, Med Safety Week. Global medicine regulators are joining together to promote the importance of reporting adverse drug reactions and raising awareness of medicines in pregnancy and paediatric medicines. So, there are hard copy forms, the information is available online, and there is also an app.

Why do we still not have clinical trial transparency? Why are trials relating to the safety of drugs we use today still not published? Why is the pharmaceutical and medical industry not held to account in the UK courts? I can give you the examples that include but are not exclusive: thalidomide, sodium valproate, Seroxat, benzodiazepine. Why doesn't the pharmaceutical industry contribute to a fund for those with adverse reactions?

How is it that a highly respected neurologist, who stated in a legal document in 2009 that they were unaware of neurodevelopmental effects of valproate, is invited by government, regulators, professional bodies, charities, and the NHS to give expert evidence, when it was firmly established by 2006 that valproate causes neurodevelopmental birth defects?

Why have we, as a campaign group, and others - parents and other campaign groups - why have we been subjected to accusations that us raising awareness and trying to give women an informed choice will lead to an increase in sudden unexpected death in epilepsy patients?

Everything we consume has risks. So, why aren't we doing more to establish what the risks are for all drugs and chemicals used in food and agriculture as well?

I'm nearly done.

We pride ourselves in living in a democracy and being a civilised society. There is nothing civilised in the policies that affect people with disability

and their carers in the UK. We are keen to change that and restore British values.

Julia Cumberlege: Emma, thank you so much for that. Very compelling, as you always are.

Emma Friedman: May I give a couple of the points that we would like to see happen now?

Julia Cumberlege: Right, so you want to speak again?

Emma Friedman: Yes.

Julia Cumberlege: Okay.

Emma Friedman: Okay, so what we feel that we need now are regional centres for FACS and valproate syndrome where informed clinical care can be accessed. They can act as places where clinical expertise in this area can develop and where support services and special education can be commissioned.

We'd like clinical trial transparency. All trials published. A requirement for all drugs that are prescribed in pregnancy to be assessed for teratogenicity prior to license. All drugs not proven to be safe in pregnancy to have a symbol of a pregnant woman in a red triangle on the outside of the box, as they now do in France with all epilepsy medications. All drugs that have been proven to cause harm to the foetus to have the pregnant woman in a circle with a stripe through.

We'd like all women who take a drug in pregnancy to agree to observational research on pregnancy outcomes and child development. Right, let's whizz through some of these. The Yellow Card to be promoted in all healthcare and educational settings. A precautionary approach maintained post-Brexit in all free trade agreements. A change in culture among healthcare professionals. Adequate whistle-blower protections. A change to product liability law. Access to justice. A review of the Consumer Protection Act 1987 and the limitation period.

[We'd like] all new experimental drugs to only be used on patients who agree to observational research. Reading and acting upon drug safety updates to be an essential part of CQC inspections. The UK to become a gold standard of medicine regulation globally.

As a country, our physiology, our cultural attitudes vary immensely due to our ethnically diverse population, our access to free healthcare, and the quality of our scientific institutions. So, if there was greater interoperability between the CPRD and the Yellow Card, then the prevalence of symptoms and the prevalence of prescriptions issued to those people who have been exposed to medications would identify

trends for further investigation by the MHRA. That could, itself, become a valuable, self-financing tool for the MHRA post-Brexit.

If the pharmaceutical industry gets a product here in the UK, based on those suggestions, then it would be seen as a quality product and it would be a passport to the global market. But we really need to see the pharmaceutical industry contribute to an adverse drug reaction fund, paying for lifetime costs of services required by people showing the symptoms on the patient information leaflet, and a lifetime loss of earnings payment.

First, do no harm. Many thanks.

Julia Cumberlege: Thank you. Thank you so much for that. Can I just say, we will be interviewing the pharmaceutical industry, the manufacturers, the MHRA, the professional bodies and so on. So, this is just the first part of these oral hearings, which is about patients. But you've given us the most amazing list of all the things that clearly need to be done.

Just looking at that list, what are your top three priorities?

Emma Friedman: We need adequate services for our children now. Our services are being cut. My son here didn't pass his six-week trial of a further education course into ICT and there isn't another suitable course in our area. So, the education provision is not there. The healthcare provision is not necessarily there. The therapies that are required when they are in school, therapies like speech and language therapy, or whether it's occupational therapy, physiotherapy, these services are patchy. The providers are inconsistent. People who live on the borders of CCGs and hospital Trusts, it's very, very inconsistent.

So, we need ring-fenced funding now to secure those Local Authority services and the NHS services that we desperately need and rely on to give us as carers and families, and our children, whether they are children or adults, dignity in their life.

Alright, so number one, ring-fenced funding right now.

Julia Cumberlege: Okay. I think...

Emma Friedman: Number...

Julia Cumberlege: ...that's perhaps enough to be going in with. But absolutely I can...

Emma Friedman: A judge-led public enquiry.

Carol Short: She's got a long Christmas list as well.

Julia Cumberlege: I can absolutely understand that. Cyril, anything you'd like to ask?

Cyril Chantler: Just one thing, that I think you've told me about before, I'm sorry. You said the files that are sealed for 100 years, can you just explain that again?

Emma Friedman: Yes. There are files held at the National Archive from the DHSS, Department of Health and Social Security, when medicine regulation used to be a department of them. So, the Committee of Safety of Medicines, Committee of Safety of Drugs. When I went to the National Archive and was searching for the agendas and minutes that - current problems in pharmacovigilance, the name has changed over time but they were quarterly meetings that took place to discuss the drugs that were coming out, any correspondence, any papers.

I could see that there were those from certain times that I could access. Then there was this bunch that are sealed for 100 years. I know that that period during the '80s was when there was a lot of research that was coming out about valproate. A 1987 paper about neurodevelopmental delay and odd behaviour being noted in rats exposed. So, knowing what the conversations were at these meetings, I know that these meetings that are sealed for 100 years, the minutes of them, the agendas, the supporting correspondence, they will contain information about those drugs in the '80s that - it will include something about valproate.

If it doesn't, well that is the major issue because it should have been being discussed at that time, when this vast body of information was being noted.

Sorry, does that - I've gone on a bit there.

Cyril Chantler: Yes, it does. It gives us something to work on, thank you.

Emma Friedman: Yeah, I do have the file reference numbers in here for you if you require them.

Julia Cumberlege: Okay. I'm going to ask...

Cyril Chantler: Yes.

Julia Cumberlege: ...Simon, if you've got any questions.

Simon Whale: Emma, can I just ask you one question about the Toolkit?

Emma Friedman: Yes.

Simon Whale: So, the Toolkit as it stands today, would - is there anything that you'd wish to do to improve the contents of the Toolkit?

Emma Friedman: The contents in the Toolkit are absolutely perfect. What's not worked is Sanofi have been very, very late in actually dispatching this leaflet to the pharmacies. The MHRA had to chase them up. So, these should be in all pharmacies now. All GPs should have them. All neurologists should have them. They should be given to all women of childbearing potential with a valproate prescription.

Simon Whale: But that's not now being done?

Emma Friedman: It's getting there, alright? We are noticing - we do have - there was a [REDACTED] programme [REDACTED] on 31 October where a young woman on valproate was having some more seizures. She had got a little baby. She was concerned and the doctors said oh, well we could increase your dose of valproate. But he didn't give her this leaflet, this booklet. He didn't get her to sign an acknowledgement of risk. He didn't check that she was taking adequate contraception.

So, the fact that we have spent, as patient groups, Royal Colleges, the MHRA, NICE - we spent ages putting these together, getting it agreed with the pharmaceutical industry as well. This doctor on a prime-time show is evidencing what looks like clinical negligence. He should have the information and be giving it to her, and he did not.

So, yeah. They're our concerns. That it's not consistent, but very, very happy - something that has to be sorted out is the dissemination of information from the CCGs to GPs. I think the pharmacist bodies have been very good and very, very supportive. But dear doctor letters, the drug safety updates, these are not getting to the frontline staff.

Simon Whale: Thank you.

Julia Cumberlege: Emma, I'm afraid we're going to have to bring this to a close...

Emma Friedman: Yes.

Julia Cumberlege: ...because we've got another group coming in a minute. But I just want to say thank you so much for all you're doing for all the women who have suffered from this. I think the way that you communicate all this, the work that you put into it, your knowledge, all the research you've done on everything, and I really do want to thank you for that.

If you've got other things you want to tell us, as a consequence of today or anyhow - anything that comes to mind, we are still very much open to

hearing from people. So, emails, letters, phone calls, whatever you want to - however you want to communicate, please feel free to do that because this is all ongoing.

But can I thank you so much for - and for hosting us on occasions where we also learned a lot. But today was very powerful. Thank you very much. So, I'm afraid we're going to have to say goodbye to you right now, and you're going to have to take your wonderful, wonderful poster with you as well.

[Laughter]

Julia Cumberlege: So, thank you. You're a great communicator. Thank you very much.

Emma Friedman: Thank you so much to everybody.

Simon Whale: Thank you.

Emma Friedman: It's been a pleasure to take...

Cyril Chantler: Thanks for coming.

Emma Friedman: Been a pleasure for all of us to be involved. Thank you.

END OF TRANSCRIPT

Session 2: Young people affected by valproate

START OF TRANSCRIPT

Julia Cumberlege: Just to set the tone, we're not like a Parliamentary Select Committee, which is very robust and lots of to-ing and fro-ing. This is much more like a conversation, because we actually want to hear from you, want to learn from you. None of us have got any sort of connections previously with Primodos or sodium valproate or surgical mesh, which are the three areas we're looking at. Of course this afternoon it's about sodium valproate. I think, have you any questions on that?

Branwen Mann: No.

Julia Cumberlege: Is that all alright?

Josephine Coyle: Yeah.

Julia Cumberlege: Okay. I don't know how you'd like to start. Branwen, would you like to start or would Josie start?

Branwen Mann: Well I'll start first and then I'll introduce her and she'll tell her story, and we'll see how it goes.

Julia Cumberlege: I should welcome your mother too.

Branwen Mann: Yeah.

Julia Cumberlege: Who we've met in the past, who is support I think this afternoon.

Branwen Mann: Firstly, I'd like to say thank you for seeing us today. To be honest, it feels like someone's going to pull a lever and just send us flying out of the room in a minute.

As you know, my name is Branwen Mann. I'm an individual with fetal valproate syndrome. I'm here today to speak for those who have been exposed to sodium valproate in the womb.

Before I speak about my statement, I'd first like to acknowledge those that did not live. There is a group of children that did not survive. There are many late miscarriages and neonatal deaths and stillbirths and early deaths related to sodium valproate. This is because the baby did not survive and did not develop as it should. I have a sister Tralissa and a brother Cavan, buried in Bristol. My mum also had a late miscarriage.

There are a lot of mums that have undergone this experience. One mother had to carry her dead baby in her womb for one week knowing it had died. The hospital said that she had to wait for it to come away naturally, and if the baby had not in a few days that she'd have to go back and have her baby removed. She waited a week, which is traumatising as she was dealing with her son's very challenging behaviour at a time when her husband was working all the time. She did this alone without support from anyone.

When a baby dies early not everyone wishes to talk about it. It gets swept under the rug as if it had never happened. These babies are a part of the story of fetal valproate syndrome. I am acknowledging all of the babies that did not make their first year.

I'm now going to talk about some of the challenges that we commonly face with the medical side. I have heard so many different families that they are having to fight for diagnoses, not just for fetal valproate syndrome, but of other health problems that have or have not been associated with it.

At the last sodium valproate APPG, doctor [inaudible] concerns regarding giving a diagnosis of fetal valproate syndrome, saying that many doctors were either not competent or confident to diagnose it. Accessing any diagnosis is challenging. I believe that this is partly because some of the conditions that are diagnosed are rare, doctors are not keen to spend the money necessary to ensure the right care is accessed and many would not make the leap.

Those that know me know that I've been having problems with blanking out and migraines all my life. My neurologist tested me and ruled out epilepsy. I wanted an MRI done. I asked her three times and she said no. On the fourth time I felt so frustrated that I literally stood up and stamped my foot demanding it. A week after the MRI I found myself with an emergency appointment. They had found a large and still growing pituitary cyst, a pineal lesion a low-lying [unclear] and Chiari malformation. I have been told that I am at high risk of blindness, stroke and even death at any time.

Many other valproate children have the same - have experienced similar stories. One girl shared that she was told at 11 that her astigmatism was a neurological problem. It was not until she was 19 that she was sent to see a neuro-ophthalmologist. At 23 she was told that there was nothing more that they could do, except test her every two years to see if she had started going blind.

Many mothers shared that doctors would not listen to the patient or the carer. Their experience would be dismissed and their child would not receive the care that they needed because of this. These mothers do not trust their doctors anymore.

My sister has bilateral cholesteatoma, her lifespan has been shortened and she has had an operation every two years. This is because there is no guidance regarding dysmorphic features and clear care. Her audiologist was syringing her ears when they needed to be microsuctioned. Inappropriate care is dangerous and we need to have the right care for our needs.

My GP told me that everything has to be done locally unless a local doctor sends you out of area. That means if you live away from a city, you'll find it more difficult to see a doctor appropriate for the needs of someone with fetal valproate syndrome.

I think that fetal valproate syndrome should be treated as a rare and complex disability as it is. There are clear guidelines in place for rare disease and specialised care. The patient is empowered and properly helped. They can access a team of specialists in different disciplines that they have needs within, all working under one umbrella.

I know that the full harm done by sodium valproate is barely understood or even recognised by anyone other than the family that live it. The effects have been so intense that many of us struggle to lead a normal life. Many of us - every day we struggle with multiple life-limiting complex and rare health problems. All of this just gets worse. We are deteriorating, symptoms change, develop and new ones come in. NICE have no guidance in place for teratogens. How are our doctors supposed to know how to care for us?

Now I'm going to talk about educational. When I was at private school I had to be pulled out of class in the middle of the day to do exercises with my teaching assistant. She had to be trained in physiotherapy to ensure that she could do my exercises properly and safely. I hated it. I'd say I was [unclear].

Then I hit secondary school. I was so happy I had a fresh start. I made friends. I was doing well in school for a few years. Due to hospital appointments I would either miss half a day at school or the entire day. This severely impacted my education. I wasn't receiving as much support as I did during primary school. I walked away with such bad grades.

During college I was absent due to operations and hospital appointments. If it weren't for the support of my teachers, I wouldn't have walked away passing Level 3 Award in Supporting Individuals with Learning Disabilities.

I know that a number of mothers who have just turned away from school, and have decided to home educate, because they're experience is that schools do not have the right things in place for their child. They have become so frustrated, as they see their child decline because of the lack of necessary resources for their child.

Learning has not changed and it never will. There is no one there for the young people who can talk to. At school we are unacknowledged disabled carers without the recognition in place that could get us the help we need. That includes counselling.

It is not easy to get a child into the right school. First needs of the child have to be identified and agreed upon. The right school has to be identified. Then you have to find the evidence to prove it is the right place. My mum dug her heels in and got my sister into a school for those with both autism and deafness, giving my sister tools to communicate in the future. Each and every one of us deserves the right school that fits our needs.

Caring- so many people with fetal valproate syndrome are often carers to our mums. Our mums take - well some take sodium valproate still and some don't anymore. Our mums took sodium valproate because they are not well: epilepsy, mental health, migraines and pain; our mums have special needs too.

In the fetal valproate syndrome family we have to support each other. Many of these families are single parent families. In many families all are disabled. Are we unacknowledged for our role as carers? The roles - responsibilities we have may seem so small but they're essential, ensuring that medication is taken, that enough sleep is had, helping to manage appointments as they grow older, caring for them if they've had a seizure.

I recently tried to get myself acknowledged as a carer. I was told that I could not be disabled and a carer. That does not fit with the script of a fetal valproate syndrome individual. Did you know that a young carer or young adult carer receives respite either in hospital - holidays and trips, peer supports, help at school and most importantly counselling? We see nothing of this.

There have been children excluded from school due to perceived bad behaviour. In one story a child was suffering from extreme stress caring

for a mother and brother. He has never recovered, lost in the system. I think he's a clever person, but he has now slipped through the net. Will he ever meet his potential? There are children whose lives are literally destroyed because of sodium valproate. Because we are full-time carers this severely impacts on our mental health. So many individuals with FVS have severe anxiety and/or depression.

Now, I will move onto toxicity. I was born to a mother who was given 5000 milligrams of sodium valproate when she was pregnant with me and my sister. I have listened to what her - listened to what her mum, her sisters and brothers say, and I understand. They mourn the person that she was before sodium valproate, even today.

Mum started receiving sodium valproate at 15 after they had tried everything else. Her doctor did not want her on sodium valproate. He did not know what to do as she was still having seizures. It was because she continued to have seizures that her medicine would be upped 500 milligrams at a time. It was during her pregnancy with my sister, Ronnie, when she had a major seizure in hospital and she was put up to 5000 milligrams.

I have watched my mum's health get worse and worse over the years. The adverse drug reactions caused by medicines caused oxidative stress that have caused so many chronic health problems for her, as it has for so many other mums.

My mum was given 5000 milligrams by irresponsible prescribers, professionals that are probably still prescribing today. Professionals that will never answer to what they have done to her and others. This is apathy at its worse. This is a group of women that had harm done to them. We do not know how many others there are. They have never had this openly acknowledged.

I have watched mum deteriorate over the years. But it was not until recently that I properly understood, because mum was overdosed again. She fought for three years to be acknowledged as having high lactate levels. She now has been diagnosed with hyperlactatemia.

Mum knows two ladies that were given 4500 milligrams during pregnancy that were also diagnosed with elevated lactate. Elevated lactate is not tested on people who take long-term medication. I have seen the effects of it. It should be.

My Nan told me about a patient consultation in 1979. She and my granddad sat opposite a long table of doctors, they were asked all sorts of

questions about how sodium valproate has helped my mum. My grandparents told the story of personality change, behavioural change and the development of additional needs. The doctors openly fought in front of them. There were some who did not like sodium valproate and others who were advocates for it.

Two weeks before he died, I met - a senior Peer of the Realm. He told me that there is a lot more - there was a lot more too about sodium valproate, the harm it can do, a lot more than you know. I believe him.

Mum was recently told that we would never receive appropriate healthcare. The intake was above and beyond medical understanding today. It would take very - it would take a very interested doctor to take the leap that was necessary to care for them individually and collectively. Some doctors have been amazed at just how healthy they all are considering the amount of sodium valproate taken.

Will these women ever be acknowledged for the harm done to them and their children? This group stands apart from others, because this type of overprescribing should never have happened. Is the scandal of the overdosed mums ever going to be acknowledged?

Now I'm going to talk about the potential effects upon the grandchildren. I talk to and meet young adults, the fetal valproate syndrome children who've had children. I've met young adults who have fetal valproate syndrome who've had children themselves. I have yet to meet one that does not have a child that is not in some way disabled. I'm a young adult. I have a long-term partner and I am capable of caring for a child. One day I would love to have kids, but the thing is I would like to know if my child would be affected by fetal valproate. I would like to know if my child is going to need long-term care. Until the subject has been researched, none of us will ever know for sure.

Now I will move onto adopted and fostered children with fetal valproate syndrome. Parents that adopt or foster are a minority but they are still there. If you are lucky, these children will come with a diagnosis of fetal valproate syndrome, although it is more likely that they will not be recognised as having fetal valproate syndrome. They lack the natural process of information and experience that comes with giving birth to a child with special needs.

In families of adopted children there is a massive emphasis on confidentiality and protecting the child's adopted family's identity due to complex history and safety of the child and their family. When there are

special needs - when there is a special needs child with fetal valproate syndrome this creates many unexpected complex medical challenges, as there is no contact with the birth parents. Their needs are unlikely to be identified for what they are.

It is one that needs to be recognised. Fetal valproate syndrome children come with many complex and diverse needs regarding behavioural and practical issues, as well as these issues that have the additional challenges posed by having special needs. There needs to be strategies and useful advice, not only to help adoptive family but professionals working with children with fetal valproate syndrome.

I'm now going to move onto Josie again, just to finish off her statement.

Josephine Coyle: Has enough been done? No. Has there been enough information? No. Has there been any support? No. Has anyone took responsibility for this? No. Have people been turning a blind eye? Yes and it needs to end now. This cannot be allowed to continue to happen to other families. Not only has Bridget suffered, we her family have too, we've been living this with Bridget for the last 20 years and counting, and who's been there for us.

We are not the only ones that have been affected by sodium valproate. There are many, many more families out there and many that have already lost their babies at an early age. It is time we stopped and the truth was revealed, and justice for the families that have had to go through this when it should have been prevented.

Back to Branwen.

Branwen Mann: As some of you may know I've actually been gathering the statements from young people with fetal valproate syndrome. It's all anonymous, I'm not going to give any names or anything, but these are just a few.

I can't understand what people are talking about. I don't understand time or money. I need help to cope with what others call the ordinary stuff. I don't have any friends. I need a support worker all the time. It's frustrating sometimes.

I get clicking joints, hypermobility in my knees which click the most. No one's diagnosed me with anything, but I know this is not right. But I know others also get this and some have a diagnosis. Why can't I?

I'm deaf in my right ear. I wear a hearing aid. I'm scared I will lose hearing in my left ear. How will I know what people are saying? It is frightening not understanding what is happening around you all the time.

I've also gathered statements from the mothers and - well the parents as well who are having children as well. 'My daughter has only just got an education healthcare plan. She struggles with communication which is key in job roles. I worry about how she's will support herself when I'm no longer around. Her future is very unclear. Her difficulties and emotional outbursts leave us uncertain'.

'My son has no sense of danger. He will get into the wrong crowds, he is so aggressive. My son needs full-time care long-term. If I'm not here who will give it? What if something happens to my mum? She understands me. No one else knows what I need.'

'I had to leave my job because I've got arthritis now. I'm 23 and doctors tell me that I'm not well enough to work. I've had to wait nine months for my splints. My muscles have become tighter. The physiotherapy has eased things, but I now may need an operation as it's taken so long to be seen by orthotics.

'I am concerned about my child's future. I am becoming more disabled and my child is still in primary school. With my child's complex needs, how do I know that my child will receive the best support when in this area? There is a postcode lottery, as it is the type of support that you can see is not good in my area. I have been told that if I want to feel that my child is safe that I need to start now to pick my way through the services available for us locally and nationally. But it is difficult when there are no clear pathways in my area'.

'I've identified my child's needs. But I now have to try and match those up with an appropriate school, after-school and holiday clubs and the services provided by the council, charities and other non-profit organisations. I hear others talk about the future for their kids, and I am so worried about his life and services receiving less funding. I'm finding it more difficult getting him the type of help that he needs today without thinking of him as an adult.'

'We deserve the right to support our communication needs. We deserve to get training in life skills. We deserve to have opportunities to socialise regularly. We deserve a diagnosis whatever it may be from specialists in that field wherever they may be. We need medical equipment when we need it. Our families and carers will need financing to support training in the areas such as lip speaking and living with hypermobility spectrum disorder.

We need people that we can go to for help in anything. We need access to good quality healthcare. We need to know that we are secure even when our mums have gone. We deserve financial security and a home for life. Most of all we deserve answers’.

I'm now going to move onto - oh no this is - well I think I know what it is. I'll read it. This includes research - oh no sorry I'm getting confused. Right, as a person with fetal valproate syndrome there are things that I want to know. Will my children be disabled? What is different about my mum that means that I have fetal valproate syndrome? What will happen as I grow older? My health will get worse. How much worse will it get? Can we stop it from happening to others?

Everyone said never again after thalidomide. Yet here we are today. There has been too much harm done and much of it is behind closed doors. It is important that we ensure a tragedy like this never ever happens again and do it. I do not think - I do not believe that the IMMDS Review will give the answer that will need to do it. It is time now for pharmaceutical companies to put their houses in order. Ethically and morally it should come back to where it all began. Future generations need to be safer, and more affordable medicine needs to ensure the wellbeing of the [unclear].

Thank you for listening.

Julia Cumberlege: Right well, thank you. That was a tour de force, amazing. Thank you so much and also Josephine, thank you very much indeed. What comes across to me is your exceptional mother. I think she's amazing, and how you're managing with Bridget and coping with that.

Branwen, you obviously meet quite a lot of young people who are subject to sodium valproate. As you say they have complex needs and some are different from others and some are single parents that are coping with this situation and so on.

Just thinking about all that you've said, are there any priorities? Are there any things, if only we could recommend this, it would make such a difference? Is there anything singularly that you feel would really make a huge difference to your life and those of other young people?

Branwen Mann: This is going to sound like a huge thing, it's unlikely anyone could ever do it. But what would make a huge impact in my life, and possibly others, is actually going to a hospital and having loads of tests done. Having a doctor sit in front of you saying, right so this is what's wrong. You're going to live for this long and actually, your kids they might be disabled, you

know what they will be disabled. There you go, this is the sort of help we can do for you.

To be honest I just need to know that when my mum's not around will I be okay. Will my sister be okay? There's nothing that scares me more than thinking of my sister being out there alone without me or my mum. Because as I've mentioned, I'm in a long-term relationship with my partner, what if I do move in with him and move away from family. Yeah.

Julia Cumberlege: Right, well thank you that's really helpful. Cyril, is there anything that you'd like to ask?

Cyril Chantler: No I don't think so. But we've met before and I've met your mother too, and we've tried to answer the question about the effect on the next generation, and [Rachel Banner], who got expert advice. But I take your point, it's not the same as you actually meeting such a person, and I think that is necessary.

Julia Cumberlege: Right, okay. Simon, anything you'd like to ask?

Simon Whale: Yeah, I'd like to add my thanks to both of you, really powerful words that you both spoke and really helpful from our point of view to hear what you have to say. I suppose there's one area which I know we've talked about before, and others have talked about, which is the benefits system and the struggle that people have. I know your family Josie has had really serious difficulties with that.

Josephine Coyle: Yeah.

Simon Whale: Is there a little bit more that you could tell us about that from your own personal experience or from what you've heard about others? Is there anything that you think we should be saying or doing to try and help improve the situation in terms of access to benefits.

Branwen Mann: Yeah, actually we're kind of stuck in a sticky situation with benefits right now actually to be honest. Mum, as you know, the epilepsy is quite bad. She's almost been dropped out of PIP, the process of PIP. We've been going through the process for, how many years now, two, three.

Bridget: Yeah.

Branwen Mann: It's never ending.

Bridget: Yes, she lost my paperwork.

Branwen Mann: Yeah, and so we're now having to go through the whole thing again. They're now saying that I should be working, but I just - I physically can't because of how bad my health is. I'm scared that one day we're going to lose our benefits and we'll probably be on the street. It's unlikely that will happen, but what if. You just don't know with that stuff, you just don't know these days you really don't.

Bridget: In Karen's family it's exceptionally concerning.

Josephine Coyle: Yeah.

Bridget: Because her area, I've contacted people in her area phoned around, support isn't there, there's no one they can go to. Regarding losing their home, I phoned up a number of different organisations, and they said oh we don't provide support in this area.

I went to the local disability thing for counselling. They said, oh we don't give help with that go to Citizens Advice Bureau, no, go to the Law Centre. I went to the Law Centre and they sent us to Citizens Advice Bureau who Karen had already seen.

It's just I'll go - I was - in our area it's completely different, we would automatically get support if there were issues with benefits. In Karen's area I don't understand it...

Josephine Coyle: There isn't anything there.

Bridget: ...they just fall through the - and people lose their homes, they lose - it's disgusting that there is - that this post code lottery exists. These are families that are disabled through no fault of their own. This is something we created, therefore there is a moral obligation to put that right.

Julia Cumberlege: Yeah, we absolutely understand that. Yes, we get that. Valerie, is there anything you'd like to ask?

Valerie Brasse: Yes, a couple of things I'd like to pick up on if I may. First, I was very struck when you said that 'we are carers, we do care for our mums yet we can't be considered carers because we're disabled, we have disabilities'. The benefits that you might have got as a carer, as a young carer, are not being recognised. I found that truly shocking actually, because the reality is we know that you do care for your mums. I'm just wondering if you could tell us a little bit more about how that plays out. It's something I hadn't really thought about before to be honest.

Branwen Mann: Well quite a while ago, actually I think I was about 18 years old I just started to look into this properly. I got in touch with someone who works

with young carers in [Hearts] or something like that. I can't remember what it's called. She actually sat down in front of me and she said there is nothing in place for disabled young carers, there's absolutely nothing.

Yes, there is something in place for disabled adult carers, because obviously that is very common - certain things. But the thing is I actually sat - I simply told her my situation. I told her what we go through as a family. I even told her that we actually care for each other and I told her about all these other stories that I've heard. She just sat there and just looked at me and said well I don't know what to do then. She physically didn't know what to do.

No one told me - I didn't even know I was a carer until I was about 18. I've seen my mum have loads of seizures, and I've had social workers sit in front of me and just go yeah, okay. They didn't say anything about us caring for her. They just saw me and my sister as disabled kids. There's just nothing in place. It's just shocking. I just want - we deserve to have something in place. You have disabled young carers you really do.

Valerie Brasse: Sure. I think it's something we do definitely need to follow through. The other question I just wanted to ask really was we know that you are connected to quite a few young people, quite a lot in many ways. But actually one of the issues for us is thinking about the services that need to be put in place, and how then do we identify all those that haven't appeared, who haven't come forward? How do we begin to connect to other families with children who are suffering from fetal valproate syndrome but are not connected to any local group or any campaign group? How do we do that Branwen?

Branwen Mann: Actually that was actually something I was going to look to do myself.

Valerie Brasse: Good.

Branwen Mann: I was actually going to start blogging and create my own group for those who are affected by fetal valproate syndrome. I'd like to do things like going around - I picture myself going around the world and telling my story and telling everyone's stories and stuff. Yeah.

Bridget: Branwen, tell them about the two girls whose mothers took sodium valproate that were in your class.

Branwen Mann: Oh my God, yes. Well, I've become very good friends with them. It wasn't until mum just sat and spoke with them that it was found that they might actually have fetal valproate syndrome. They won't believe it. But the thing is we think it's highly possible because of the stories, how they

relate to the ones that I've heard. We do hear a lot of stories like the ones of my friends. But like I said, I'm going to create a support group for just the kids with FVS, so we have a voice as well as - do you know what I'm trying to say?

Valerie Brasse: I do.

Branwen Mann: If you're all nodding you understand.

Valerie Brasse: I do. Thank you, Branwen.

Julia Cumberlege: Have you any questions you'd like to ask us?

Branwen Mann: No.

Julia Cumberlege: No. Can I just stress we are a review. We're not executives so we can't actually say 'you will do this that and the other NHS' et cetera. We can only recommend, and then we get the forces that really can make it happen involved and so that we do get results. We've already done that with surgical mesh.

But I do want to thank you so much for coming. Thank you very much, and for your testimonies. Perhaps you would give us those, because it would be really nice to have those. I'd just like to say, Branwen, I did say you've got an exceptional mother. I think your mother has an exceptional daughter. Thank you so much for coming today. Thank you very much. Thank you.

Branwen Mann: Thank you.

Josephine Coyle: Thank you.

Branwen Mann: Thank you very much.

END OF TRANSCRIPT

Session 3: Organisation for Anti-Convulsant Syndrome (OACS) and OACS Ireland

START OF TRANSCRIPT

Julia Cumberlege: So, just to set the tone for this afternoon. It's not like a Parliamentary Select Committee which is very robust and lots of questions and answers and all that. It's much more about a conversation. It's much more about us learning what you want to tell us this afternoon. Thank you for bringing some support with you as well. Thank you for coming. So, I don't know if you want to introduce yourselves for perhaps Sonia, who might not have met you before. So, Jo are you sort of in charge?

Jo Cozens: Yeah sure. In charge [laughs].

Julia Cumberlege: Or Susan, I'm not sure.

Jo Cozens: My name's Jo Cozens. I'm from Wales. I've got a son that's affected by the drug and I'm the Chairperson of the organisation for anti-convulsant syndrome. So not only valproate, we cover all the epilepsy medications and we're primarily a support group. My colleague...

Susan Cole: Susan Cole. I'm a trustee of OACS, Organisation for Anti- Convulsant Syndrome as well.

Julia Cumberlege: Thank you.

Carol Lapidge: I'm Carol. I'm - sorry, sorry about that.

[Over speaking]

Julia Cumberlege: Book ends, yeah Carol and Karen.

Carol Lapidge: I'm Carol. I work with Jo and Susan as well and I'm support on the Facebook page and wherever else I can get my hands on basically, on my phone.

Jo Cozens: And a trustee.

Carol Lapidge: Oh, and I'm a trustee, but most importantly, I'm a mum and that always comes first.

Julia Cumberlege: Thanks very much.

Karen Keely: I'm Karen Keely. I'm from Ireland and I'm Chairperson of Organisation for Anti-Convulsant Syndrome Ireland and a stakeholder in the FACSA Ireland.

I do the research and collect papers and support, and everything basically based around Ireland and I'm a trustee also in the UK.

Julia Cumberlege: Okay thank you very much indeed. I'd be really grateful if you could speak up a little bit because there's a bit of an echo in the room. So, who'd like to start?

Jo Cozens: Yes.

Julia Cumberlege: Yes, go for it.

Jo Cozens: So, as I've just explained, OACS is a support charity for families harmed and impacted by teratogenic effects of epilepsy medications. As a charity we're actually celebrating our twentieth anniversary next year. Previous to that, it was another organisation called INFACSA that was run by a lady called Linda Hamilton and that was running about four to five years previous to us. So, you can imagine - it's not a new subject and it's always been there.

As far as one of your questions regarding the robustness, the speed, appropriateness of those processes, actions followed by the relevant pharmaceutical applicants and holders of licences and manufacture, OACS Charity's view on this is that the warning signs of valproate were there from the start. So, I want to take us back a little bit in history on that. So, following the thalidomide tragedy of 1957 to 1961, in '63 the government asked Sir Derrek Dunlop to set up a committee to investigate the control and introduction of new medicines in the United Kingdom. In '63, the Committee of Safety of Drugs came about, and it was established as CSD.

As a result of the subsequent report to the Department of Health which reinforced the need for special trained doctors, pharmaceutical industry, academic departments of medicine, Dunlop became the first Chairman of the Committee in 1970. The CSD was replaced then by the Committee of Safety in Medicines, the CSM was one of the advisory committees established by the *Medicines Act* in 1968.

Fresh off the back of the CSM being set up, in France more and more reports of problems with valproate were being reported. Valproate was first marketed for the treatment of epilepsy as Depakene in France in 1967, only five years after the discovery of its anti-convulsant activity in rodents and was commercialised subsequently in more than 100 countries.

From the Antiepileptic Drug Development April 1977 document on page 20 and 21, it states that no trials were run, yet the drug was licensed in

1973 and how that came about [REDACTED] the original company that set up valproate. So, the history of licensing of valproate in England dates back to 1971. At that time, he was [REDACTED] and as such he made monthly trips to London. The President of the corporation asked him during this visit to see if he could perhaps begin to see if valproate might be introduced into England.

Labaz at the time didn't think that they would get the drug past the stringency of test requirements of the Drug Committee. [REDACTED] made an appointment with the Secretary of the Committee to see what procedures were required. Labaz had very little English documents [REDACTED] wanted to see whether the product may get approval.

A couple of weeks later, the news from London was positive. As a result, [REDACTED] began the translation of the French file and began putting it into a form required by the British. The British and French applications were different, but the data was exactly the same. Following on several meetings with the committee, in October '71 presented the committee with a document of around 300 pages, each of which was the extract of the French version put into English but rearranged to meet the DHSS requirements at the time.

As a result of this formal submission, the DHSS come back - a series of questions which [REDACTED] answered. At no time did the DHSS require any additional toxicology, pharmacology or clinical trials. The DHSS asked for only two things, a complete chemical process and also an entire publication that Labaz had published since the product had been obtained for authorisation in France. So, all of the documents that led up to their licensing.

The DHSS satisfied that the file was complete, they were prepared to rule on its merits and on 25 July 1972, exactly nine months after the submission, the only question that the DHSS has to resolve was, this should - should this product be authorised on the British market as such or should it be made to go through clinical trials to be held in England. At this point, no trials had been carried out. This was not a usual - not a usual procedure for authorisation of non-British products. Instead the UK allowed valproate in hospitals on an only limited basis. This was only the second time in British history that a drug was allowed in England without extensive trials.

Two years later, complete authorisation was granted. So, in less than 25 months, for less than \$25,000 at that time, this product was authorised for initial sales in a country which was reputed to have the most stringent

regulations in the world except for the United States. Since then valproate has been established itself worldwide as a major epileptic drug against several types of epileptic seizures.

The government document, released in 1974 which concluded not to put the warnings into the patient information leaflets to prevent fruitless anxiety in women. Under product licensing laws, there is a 10 year period in which you are able to prove that the drug is ineffective or has contra-indications.

In 1975, *Guy's Hospital gazette* stated and on page 10, the comment was, sodium valproate, a new anti convulsive review of the symposium of sodium valproate in Nottingham University, 23 to 24 September '75 organised on behalf of Reckitt-Labaz. The drug has been released with the warning that it has been shown to be teratogenic in animals. Very few women in this country have been taking this drug during pregnancy. The data on the offspring is inadequate. Many more women on the continent have presumably had pregnancies while taking the drug but unfortunately statistical data on the instance of fetal abnormalities were not available.

With the memory of thalidomide, few clinicians would be happy to allow their female patients to take sodium valproate at the time of pregnancy risk or during pregnancy until this point has been clarified.

Then, again, in 1981, prior to the 10 year product liability, the Drug and Therapeutic bulletin volume 19, number 24, 10 November '81. The concentration of valproate in the - can't pronounce that, can you help me?

Carol Lapidge: Which word?

Jo Cozens: The ...

Multiple speakers: Cerebral spinal fluid.

Jo Cozens: Yeah, cerebral spinal fluid, breast milk and free in plasma is about 10 per cent of the total plasma concentration. Valproate crosses the plasma easily and the plasma concentration in new born and other mothers are similar.

So, Reckitt and Labaz data sheet from 1981, women of child-bearing age, sodium valproate, like certain other anti- convulsant has been shown to be teratogenic in animals. In women of child-bearing age, the benefits of these compounds should be weighed against the possible hazards suggested by these findings.

Then, the new Committee of Safety of Medicines' report then from 9 January 1983. At the end of the 10-year product licensing, the Committee of Safety of Medicines current problems contents sodium valproate and congenital abnormalities raised in a paper. Two thousand, two hundred and eighty-five children were exposed to valproate in uterus. Symptoms included cleft palate, skeletal abnormalities, congenital heart disease, CNS, abnormalities of the gastrointestinal tract, facial and ear abnormalities, mental retardation - that's not my word, that's the word that is in this report - and genital urinal abnormalities and fetal hypoxia. Recent reports have mentioned apparent association with neural tube defects in women using valproate like other anti convulsives. It's known to be teratogenic in animals.

Everything that I have mentioned so far has raised a red flag, especially as I mentioned the actions put into place following the thalidomide scandal. The fact that the licence of valproate didn't follow the correct procedure, as a mum, as a Chairperson representing 20,000 plus families, that have been impacted, I feel personally and I think we all feel that this is quite criminal, how this actually happened and how it began.

September 1987, the Drug and Chemist extract teratogenic effects of many anti-convulsants presents a serious dilemma in treating and in female epileptics. There is a small but definite risk about two in three times normal of local malformations. Recent evidence suggests that valproate has a higher teratogenic potential than most and is absolutely contra indicated.

In 2013, we established that prescribing of Epilim and its side- effects to the unborn child, a summary of product characteristics for Epilim which was published in 1997 states, from an entry from Sanofi Winthrop, the manufacturers of Epilim at the time, give the following advice to prescribers. This extract is actually from a letter, my personal letter to me from the Welsh Government. In women of child-bearing age, Epilim should be used only in severe cases or in those resistant to other treatment. The SPC goes on to advise, women of child-bearing age should be informed of the risk and the benefits of continuing anti epileptic treatment throughout the pregnancy. This demonstrates that there was an awareness of safety concerns at that time and in 1997 by the drug company.

It is clear from the evidence that we have found that the robustness in looking back is not evident. Information has been withheld from patients since before the drug was licensed in the UK. Because of this, we were not

able to carry out an informed decision which they are legally entitled to and their human rights were taken away. That's how we feel.

It is also evident through our members that health professionals have not linked any children's problems and symptoms to the medication taken during pregnancy. It is also clear that the documentation that we have found that from the licensing of the drug in France in 1967, and previous to that, that time, it shouldn't have happened because after that it was launched in the UK and there was growing knowledge of the teratogenic effects of sodium valproate. With hindsight, it is obvious that the regulators should have done something back then. What they're doing now is great, but did they have the knowledge at that time, which they did. What is the price to a disabled child?

It will be very difficult to reach consensus on the characteristics of fetal valproate syndrome because they are so wide and as the children grow older, as they become adults - they will now be in their late 40s, the earlier children and there is no possibility of knowing how the syndrome will develop especially as each individual is affected differently, with different degrees of development. We have a good idea of the childhood difficulties but how they continue to develop as adults is unknown.

How will the syndrome affect them as they get older? Will their medical conditions worsen? What effect will this have on their abilities? You will not have the answers to these questions until you find the lost children - the lost children of sodium valproate. With regards to their lifetime needs, again, there's no knowing, there's no hard, there's no fast rule of what every child needs. You cannot prepare for this. The children born in the '70s must be found, all of them, and their needs can change dramatically in such a short space of time.

It's quite frightening because myself, all of us in this room, we're all paying for this drug. The cost to the taxpayers, now the London School of Economics and National Autistic Society have done some research on this. So, the research has found that 27 billion a year goes towards supporting individuals with autism. The lifetime cost of someone with autistic spectrum disorder and intellectual disability is estimated to be approximately 1.23 million per person. For someone with ASD without the intellectual disability, this is approximately 800,000.

OACS following a membership survey has found that most of our children affected have some form of autistic spectrum disorder and most of our children also have the various developmental and intellectual delays as well, which means that the cost of one single drug, sodium valproate - and

we're only talking about this one drug today - is going to be 20 billion plus and that, I feel, is quite an underestimate because there are a lot of children out there with quite complex needs.

So, the questions that we would like also to be raised. The review team to review all documentation given and relevant papers mentioned in the documents we can provide you today as well, of everything that I've talked about. Once you've reviewed these documents, we would like questions to be put forward to the relevant stakeholders, so the MHRA, Sanofi, healthcare professionals, epilepsy leads, pharmaceutical, the government.

We would like to know if the information was shared through the British National Formulary, to the GPs at the time, and clear clarification on why the Bodies felt that women did not have the mental capacity to make an informed decision. Throughout all of this, we've all as individuals had to explain ourselves to everybody. We've had to explain that, yes, we are intelligent enough to make decisions and I think historically the way epileptics have been treated was partly because why we are here today as well.

So, we want to know why we didn't have that capacity to make an informed choice when I know I can. We would like to know all the information that the drug company holds on valproate that has not already been shared with the regulators. Regulators tell drug companies what they need to provide, what documentation needs to be provided. Have they got any other documentation that the regulators have not asked for that we would like to share that's connected with this. Sanofi are legally bound to provide information requested by the regulators and as per the current French proceedings, a Judge has actually ruled that Sanofi had a moral duty to disclose all relevant information regarding contra indications. Is there further information as per the French court case that we should have been made aware of right here today?

Following the failed court case in 2010, many of the documents that [REDACTED] received at that time were actually redacted for 100 years. Could this be used as evidence in which I would say probably implies a further high-level cover-up because why else would a document be closed down for 100 years?

OACS would like the review team to immediately go back to the government and request a high-level judge to open the redacted papers with the remit to see whether there are relevant information within those papers that should be included as part of the review. It was recently

revealed that the government has historically advised that Legal Aid Board withdraw funding from other cases. OACS would like to know if this was the case in the legal battle in 2010 and Susan is going to go into a little bit more detail regarding that a little bit later on.

Can the review team ask Theresa May why she hasn't put an inquiry into her manifesto considering the seriousness of the issue, when the Labour Party have actually done that. It is clear from the evidence we are providing today that a public inquiry is necessary to open up these redacted documents if you cannot do this and the requirements to make these recommendations. OACS Charity feel that without these documents being opened, the review team do not have all the tools they require.

To Sanofi, do you have information of independent or in-house research in your archives that for one reason or another hasn't been passed on to the regulators? Again, regarding the teratogenicity of valproate, and OACS would like the review team to be able to see and review the Sanofi archives if they don't want to share them with us as a charity and an organisation.

OACS would like the review team to look at the Universities, College facilities - faculties, as they did a lot of historical research into valproate in the early days. We would like the review team to look at Parliament and the House of Lord libraries as well because a lot of conversations between MPs happened and there may be further detail on what happened, the decisions that were made back then regarding valproate.

Due to the high incidences of deaths and miscarriages relating to sodium valproate in France, the French Charity [Apasec] has done research on this and it showed that out of 5982 victims, there have been [1480] miscarriages and 140 deaths, we feel that it is vital that this is also looked into in the UK. It's something that we haven't done but France has had more numbers their end because it's been so prevalent in the media, that more people have actually come forward.

There are many symptoms of fetal valproate disorders and for every child that has ever been born of a mum that has taken valproate, should go through a checker in a multidisciplinary centre where they can be assessed and diagnosed with the new fetal valproate spectrum disorder and any other contra-indications.

Social welfare should be looked at, entitlement to any benefits, education, and also counselling offered. This should happen until adulthood. Our children, once diagnosed, will require yearly check-ups or

more check-ups depending on their situation. The logic behind this is based on our membership feedback. Not all of the symptoms show straight away. So, for instance, my son hasn't shown all the symptoms since birth and as he's getting older, more and more things seem to be popping out of the woodwork. Bad ears; he's now got to go for ear tests every year and have his ears cleaned out because of a cholesteatoma, which we were very fortunate to catch before it ate into his brain. He's had his middle ear bone removed which shouldn't happen to any of our children.

What we would like recommended to the government is to act right now and we would like an MOT for all our children right now because we feel that that is something that can be done and something that should be done. So, we would like that you recommend that the government right now organise full MOTs for all our children. We can't wait for the government to read the review. I don't know how long it's going to take, but if somebody is missed that could be one death and that's the reality of it, because some of our children have got heart problems that we don't know about. Some children it could be worse. There could be problems with their brain.

Any new child born to valproate should have a passport so that when they see their healthcare professional, their teacher or anybody related to that child, they shouldn't have to go and explain every new term in school, hi my name is Jo Cozens, this is my son, and this is the care that he needs throughout his life in school. That's what all of us do every single doctor's appointment and every time our children go up in school years.

All families should be compensated and given an option of whether they wish to have a trust fund set up, like the thalidomide trust or the ability to put the compensation into a trust fund of their choice. I think obviously that that is something that is quite important, and you'll probably hear that throughout the proceedings from most groups.

We would like counselling available. As a mother, I still feel guilty in the pit of my stomach that I took medication that has harmed my son. But as a person that wants to function and live day to day, I lock that key away and I don't visit it. I know that I probably should get some counselling and I know it's not good for my epilepsy but there are a lot of people out there that are going to find out about this and there needs to be counselling readily available for them.

Another thing that we're hearing day in day in day out and it's on the tele is PIP. Unfortunately, you can't - there's no cure for ASD. There's no cure

for FAS so what we would like is access to speedy PIP claims, avoiding the red tape for children affected. There's no common sense and god knows how much it must be costing the UK government to do this.

Finally, the government can with the help of all the stakeholders do a public - can they do a public service announcement? There's one way to get through to everybody and that is a public - the good old public service announcement on the television, have you taken this medication? Don't stop taking it, but please report in to whoever. Put in the newspapers, on radio, we really need to find the lost children. If we get into a position where hopefully, if there is a compensation fund set up then these people are entitled to it.

That's what I have to say personally myself, if you've got any questions.

Julia Cumberlege: Well thank you so much. Incredibly well researched...

Jo Cozens: Thank you.

Julia Cumberlege: ...and the history is very important...

Jo Cozens: Yes.

Julia Cumberlege: ... as are some of the issues you've raised I've certainly - well I've taken notes, we all have taken notes and we'll be exploring those. Can I just ask you one question? I think your phrase is very relevant about lost children. So, you have no idea how many children there are in the population?

Jo Cozens: The estimate is 20,000 plus. Rebecca Bromley, I know that - has probably put something forward to yourselves. That's where the original calculations have come from, but we think that that is - as the research has gone on, unfortunately, there's a lot more people affected intellectually that are probably missed off that calculation. We've been very reserved with that calculation because I didn't want to - as an organisation, we don't want to overexaggerate it. But was it a 15 year or the 10 year period? Rebecca Bromley came up with that.

Susan Cole: Yeah that was a limited period, I think yeah 12 years or something.

Julia Cumberlege: Now I don't know, Susan, are you going to go next, or I think Carol is going to go next?

Susan Cole: Yeah. I didn't write a speech as it were, but I've - I heard the word that this was going to be a conversational event rather than writing a speech so I've got lots of different aspects that I can talk about. But particularly we're a patient group and we're a support organisation and we do - I'm

here to represent them and not particularly my story but - so we've done quite a lot of surveys and things so I can talk through those. Also, really, we had - we were very lucky. We got a firm of solicitors to make a submission on our behalf who - they've spent hundreds of thousands of pounds of their time pro bono for us. Many many of the details are in that submission and I would like everybody to refer to that, bear with me if I don't have the facts to hand.

So, our submission examines the clinical history of sodium valproate in the UK from its production in 1881 of the herb valerian to its medical use in 1962 and licensing in the UK in 1973. It covers the regulatory history of sodium valproate. It covers regularity interventions by MHRA, NICE and EMA. It covers a failure of the regulatory and manufacturer to safeguard the patient, the responsibility of the medical profession, failure of the justice system. Of course, they've gone into that in great detail because a firm of solicitors will do that.

They've looked at prospects for legal actions. That's all in there and I hope that we can - you can all look at that. I'm sure you have or will do. We were very much part of the process of writing the submission. We were very much involved in it and we didn't just hand it over to them. We made sure that we knew what was being written in there and that's definitely our words.

The side that - the submission was submitted, completed - our submissions put in in April. So, we've had quite a period in the summer where we haven't really sort of got any sort of further with it, which is quite good but so just bear that in mind, we haven't done an awful lot of stuff in between but we have done some patient surveys on various aspects of the issues.

Right, my - I could go a little bit into my personal story and that is - right where shall I start? This is a story of - it's not just something that's happened. It's just not something that's just appeared. This has been going on for a long time. My daughter was born in 2000 which is nearly 20 years ago. This is the one that was affected. With the history of the advice I've been given, this has been going on since 1983, compiling all of that in a short space of time and presenting it to you is very, very difficult and I hope you can really scrutinise that. I think we all welcome this Review. It's been a huge weight off our mind to know that somebody's listening. So, I think we're all very supportive about the Review.

So, going back to - the story - I'm talking about the questions that we've been asking that people have generally been asking and myself. I wrote an

article in 2006 for a magazine. In that article it was part of a [REDACTED] campaign about mothers and epilepsy and the headings of that article - the sub-titles were pre-pregnancy planning, maternal instinct, long-term research, informed choice. These are subjects that are again in this Review again, again, again.

These subjects could have been broached many many many years ago. My article was edited and the sentence that they edited out was, just a small snippet of research which was that the - one study showed that verbal IQ of less than 70 was in eight per cent of carbamazepine exposed children and 22 per cent in valproate exposed children.

But there are many, many, many, many examples of these snippets of scientific research that have come up and we want this Review to find out what on earth went on with those bits of research that were quite clearly pointing to a terrible situation. As Jo said in - when we did take our court case, I was part of that litigation and we did have a situation where that enquiry should have continued but it was stopped because we lost legal aid. Not only to find that but we weren't given any papers. We couldn't find out what had happened. Papers were redacted. We went to the national archives. Things were - things were hidden. We're quite angry about them.

Now, I'm half German. I'm not English and there's a word in German that we don't have in English and that word is a verb, is schweigen and that means to stay silent, to say nothing. Now it's a very significant word in Germany that obviously - to stay silent about something, to not say anything. There is not a translation of that word in English but that is what has happened I think in all of the areas that are covered in this Review.

It's not just about the MHRA, the regulators, I don't believe. I don't think it is entirely about that. They are very culpable we believe, and we know that Carl Heneghan is going to be probably very much talking to you about the problems with the regulators and I won't go into that in great detail. As Jo said, the other issue that we've really had holding us back is the fact that this is a, unlike primodos, possibly similar to primodos, but certainly unlike mesh as campaigners, it's very very difficult to complain about something that affects your child. I don't want my child thinking that she's a problem. So, we don't make a fuss. We have to keep that very close and that's difficult.

So, for instance, things like media, we can't get the media involvement because we can't have our children on tele basically. Most people don't want that.

So, I can talk you through all the different things that I've tried over the past but the - risk, yeah - all right okay. Sorry about this.

Julia Cumberlege: Susan don't worry, you can always come back to us. This isn't a final thing and I'm conscious that we've only got quarter of an hour left and so I'd quite like to hear other people but if there's anything else just that you would like to tell us.

Susan Cole: Yeah, I mean I'd like to just go through the surveys. As I said we're a patient group and we have got a number of things that we went through with patients. One of the most important things was from the - when we asked our people who - what their neurologist told them at the time, they all told them what was on the patient information leaflet at the time. There was no - I think there was one case where a neurologist had told a patient and given them statistics and proper statistics that they could deal with. We believe this is completely outrageous and that should never have - that should - neurologists must make more of an effort to ensure that patients are given the right information and full consent is not about saying 'oh yes okay I agree with you'. Full consent is about having proper information.

The other survey that stood out with our patients was that when asked where they got their information from, who was most helpful to you in advising you, the one that came out on top was internet research. They had far more information from that. Also, who was most helpful to them. So that was knowledgeable, knowledge, and who was most helpful to them was the support groups, the Facebook groups, people like OACS and FACSaware and INFACT.

So not only did they get a terrible - we got a terrible lack of information and support from people, there are other issues. We tried following - politicians - many many many patients have written to MPs over the years and the MPs have not replied. We've got one case where the person was shown the door. Politicians constantly towed the party lines so when you speak to an MP, particularly local politicians, they obviously phone their head office and say what shall we say here. That comes back. There's no independence in a political system to actually ensure that checks and balances are made.

Likewise, with the science research, it seems to be a top down industry. There's not enough epidemiology, there's not enough coming from the paediatricians to find out what's happening. In our submission, we do want, and I understand that there will be some specialist centres for children with fetal valproate syndrome.

Julia Cumberlege: So, if there's material you'd like us to see, do send it. The survey sounds really interesting and I think that would be really helpful to us.

Susan Cole: Will do yeah.

Karen Keely: A document from the - sorry my name's Karen Keely from Ireland. This is referenced to Ireland. A document from the ICI dated 6 April 1973 states, 'there is some evidence of a higher than average incidence of contra genetical abnormalities in infants born to epileptic mothers. The precise factors in influencing these are unknown but the possibility that anti-convulsant therapy may be involved and the very slight risk of abnormal fetus must be outweighed against the risk of withholding treatment during pregnancy'.

Whilst it's not a case of concern, government documents released in 1974 concluded they did not put warnings out into the patient information leaflets to prevent - information - because they didn't want - to prevent fruitless anxiety in women. Under product licence laws, there is a 10 year period in which you are able to prove that the drug is ineffective. In 1975, Guy's Hospital gazette stated page 10, commented, sodium valproate, a new anti-convulsive review of the ...

Susan Cole: Symposium.

Karen Keely ... symposium of sodium valproate, Epilim, in Nottingham University, 23 to 24 September '75 organised on behalf of Reckitt-Labaz. The drug has been released with the warning that it has been shown to be teratogenic in animals. Very few women in this country have been taking the drug during pregnancy. The data on their offspring are inadequate. Many more women on the continent have presumably had pregnancies while taking the drug but unfortunately...

Susan Cole: Statistical.

Karen Keely: The Epilim has affected my speech. I have adverse effects to the Epilim as well. Sorry.

Julia Cumberlege: If it's easier for you Karen, we can take the material that you've brought today, and we'll have that in the office. So, we can read it ourselves.

Karen Keely: Yeah but I would like to read a little bit of this if that's okay.

Julia Cumberlege: Yes, indeed yes.

Karen Keely: The OACS Ireland Report.

Julia Cumberlege: Yes okay.

Karen Keely: Okay. Concerns relating to anti epilepsy drugs AEDs and fetal anti-convulsant syndrome FACS have been growing steadily in recent years in many countries including the UK and Ireland. OACS Ireland and the FACS from Ireland are a number of group of organisations which includes Epilepsy Ireland have been working to highlight the issue of sodium valproate in women since 2013. Our work has been centred around three main teams, working with relevant authorities including health services executive. Department of Health, the Health Regularity Authority and Pharmaceuticals Society of Ireland to reduce risks for current and future generations of children being born with [cerebral] - being born with severe physical and development disabilities associated with FACS.

To [unclear] seeking adequate support for those affected already - those already affected by FACS, campaigning for independent investigation and an enquiry on the historical use of valproate including issues of accountability and redress. OACS Ireland has close working ties with the UK OACS Charity and in our submission, we have chosen not to repeat many of the well-established facts and backgrounds relating to the issue. Instead we are focusing on current and historical Irish position below to highlight the facts is an international tragedy and not just limited to the UK.

We understand that Ireland is outside the jurisdiction of the Independent Medicines and Medical Devices Safety Review, but we fully agree with the OACS UK submission to the Review and support the calls for action highlighting therein. Since 1999, OACS UK has supported UK families to provide support and raise awareness for children affected by fetal anti-convulsant syndromes.

FACS, OACS Ireland is a branch of the OACS UK. It has a similar remit and provides support and representations for families in the Republic of Ireland and Northern Ireland. We want to ensure that people living with FACS along with their families will experience better recognition, improved public health services and support. OACS Ireland is a voluntary group made up of mothers and fathers of children who have been affected. We are currently in the process of becoming a registered charity in Ireland with the Charities Regulatory Authority. Many families in our organisation have received invaluable support from OACS UK over the years including myself. We are...

Susan Cole: Indebted.

Karen Keely: ... indebted to them, to the volunteers for this as well as ongoing encouragement in developing OACS Ireland. In addition to our work, in Ireland, OACS Ireland is a stakeholder in the MHRA Valproate Stakeholder Network, the VSN, a relationship which has helped inform progress and practice in Ireland in recent years. The FACS Forum Ireland is an umbrella group of organisations that have come together to advocate for better services and support for families and children affected by fetal anti-convulsant syndrome, FACS, and raise awareness of FACS to ensure appropriate risks reduction measures are implemented in Ireland. Members of the Forum include the Disability Federation of Ireland, DFI, Epilepsy Ireland, EI, Genetic and Rare Disease Organisation, GRDO, Medical Research Charities Group, the MRCG, Organisation for Anti Convulsant Syndromes Ireland, OACS Ireland and Migraine Association of Ireland, MAI and [unclear].

Valproate in Ireland - sodium valproate Epilim is a drug licensed in Ireland for the treatment for epilepsy and bipolar disorder and other conditions. Developed in 1960s, it has been authorised in Ireland since 1975. For many people sodium valproate can be a very effective drug, in many cases, the only effective drug. However, the teratogenic effects of valproate have been accepted since the mid-1990s while the effects on the development were highlighted for over a decade prior to the publication of the NEAD studies from 2008.

Despite these risks, many parents involved with OACS Ireland...

Do you mind if I take a drink?

Julia Cumberlege: It's all right. Would you just like to perhaps give us your papers so that we can then study them perhaps...

Karen Keely: Yeah.

Julia Cumberlege: ... but thank you very much. It's really important for us to see what's happening in other countries...

Karen Keely: Yeah because we have counselling [unclear].

Julia Cumberlege: ...and to have the Irish perspective is really useful to us. So, thank you very much for that.

Karen Keely: Yeah and I also gave in the 1977 workshop in anti-epileptic [unclear].

Julia Cumberlege: That's wonderful. So, if we could have that as well. If you can spare it...

Karen Keely: And the second part of this as well.

Julie Cumberlege: ...but we can return it to you, photocopy it ourselves and return it to you so that you've got it. So, I'm going to draw this to a conclusion, and thank you so much. I'm so conscious that you are people who are dealing with epilepsy which is a difficult condition anyhow, and then you are wonderful mothers dealing with these very difficult children but special children in some respects. So, thank you so much and please continue to keep in touch with us. We really want to keep learning and we're still travelling the country, going to other meetings and certainly we're accessible, you know how to get hold of us I hope and with our website and everything else. So, thank you so much.

Cyril Chantler: We will meet again.

Multiple speakers: Yes.

Karen Keely: Can I just say one thing?

Julia Cumberlege: Yes certainly.

Karen Keely: I have three boys affected.

Julia Cumberlege: [Unclear].

Karen Keely: I have three children affected.

Julia Cumberlege: You've got three children.

Karen Keely: Affected, 31, 23 and 19.

Julia Cumberlege: Right, well thank you so much for coming and I know you've come some distances today.

Multiple speakers: Thank you.

Carol Lapidge: Thank you for listening.

END OF TRANSCRIPT

21st November 2018

Session 1: Mashed up by Mesh

START OF TRANSCRIPT

- Yvette Greenway: ...I'll just introduce my partner Michael Mansfield who himself - you submitted some evidence - online.
- Michael Mansfield: Yes, on an email form, very short.
- Yvette Greenway: Yeah.
- Michael Mansfield: But whether you've got it actually.
- Julia Cumberlege: Right.
- Yvette Greenway: Because I think it's...
- Julia Cumberlege: Yvette, you'll have to speak up a bit because I'm a bit deaf.
- Yvette Greenway: Oh right, okay, sorry. Well, I was just introducing Michael. He has submitted some evidence himself as to how it impacts me but impacts him as well...
- Julia Cumberlege: Yes, that's right.
- Yvette Greenway: ...because obviously it's not just an immediate impact on patients. It's far-reaching...
- Julia Cumberlege: Yeah.
- Michael Mansfield: Mm-hm.
- Yvette Greenway: ...for people that have to look after you, that have to live...
- Michael Mansfield: Hm.
- Yvette Greenway: ...with what is happening. That can be very, very difficult and very trying and tiring for people.
- Michael Mansfield: Hm.
- Yvette Greenway: So Michael is my support mechanism [laughs], he keeps me sane. Okay so, my name is Yvette Greenway, and I lead a patient support group called Mashed Up By Mesh, it's only a small group, and I only founded it earlier this year purely because of my own experiences with mesh. I'm also joint

CEO of a mental health charity called SOS, Silence of Suicide, which has provided some data for us which I will refer to later. I also campaign on issues apart from vaginal mesh. I'd like to thank the Baroness and the rest of the review team for giving the patient groups a voice in these reviews. We hope that those representing medical professions will follow our example by offering honest and accurate evidence.

I'd like to acknowledge the determined campaign done by so many individuals and groups over so many years. Many of these ladies are firm friends, and it's through their persistence and their voices that I believe we're here today with this review taking place. Many work quietly and effectively behind the scenes, despite their own serious ill health in order to provide an information highway from which all mesh-injured patients can benefit. I'd like also to remember those who've died because of mesh complications and those that are struggling at home today, unable to do very much at all.

For mesh-injured women today is a day we'd never have envisaged. Not in our worst nightmares could we have imagined we'd be fighting for justice and accountability, laying bare the most personal and private highways of our minds and our bodies.

Purely through being implanted with a permanent medical device made from a material known to be unstable and liable to changes whilst inside the body - and which is subject to little or no clinical testing. Which would change our bodies and the way we live for ever, and not in the positive manner we were all told prior to surgery. We seemingly have no potential for stability or improvement to be achieved.

Figures compiled for *Panorama* by NHS Digital and the NHS Wales show the NHS has implanted more than 130,000 mesh devices in the last decade alone. In that same period, there have been 6000 procedures to remove, or partially remove the implants. It's acknowledged the real figure could be much higher. These figures only relate to NHS in England and Wales, do not include women who have paid to have the device removed privately or those who had a small amount of mesh removed.

We must all believe that through the review process robust recommendations including a complete ban on vaginal mesh, regardless of why it was implanted, are achieved. As patients, we allow the medical profession access to our bodies, our thoughts and our lifestyles. All manner of information to better assist them in reaching decisions about the best course of treatment for us. We, the patients deserve the same, we should be aware of clinicians' allegiances or involvements whether

they be financial or other. So we too can reach informed decisions about who is best to treat us, and how they should treat us.

I'm just going to briefly read some information about myself and my own experience of mesh. I'd just like to confirm I have no commercial, financial, legal connection or interest in the pharmaceutical and medical devices industry sector or any other body or organisation of interest to the review. Now I'm just going to go on to some of the points that have been raised by people that I deal with in the patient group Mashed Up By Mesh. I did keep it brief, and I have got quite a bit of evidence which I'm going to try and read out to you from some of these people, but there is quite a lot of it so I will have to - what time did I start? Was that about five past?

Julia Cumberlege: Started about five past...

[Over speaking]

Yvette Greenway: Right okay, thank you. Okay, so Mashed Up By Mesh is a patient group that supports mesh-affected individuals and was set up earlier this year by myself. The document that I sent to the Review team contains summarised and anonymised information from mesh-injured women, which we want to form part of our submission. Alongside the mental health surveys from SOS Silence of Suicide and I'll come to the mental health aspects soon.

So I've summarised briefly. Frequent comments from mesh-injured patients include the extent of the physical damages caused by their mesh implants. For example, vaginal and lower abdominal pain, bleeding, back pain, leg pain, chronic infections, exhaustion and nausea. Those basically seem to be repeated throughout the mesh community. The impact that the physical issues have on their family life, their social life and their work life because there are people that cannot go to work any more because their injuries do not allow them to do so.

A lot of people are relying on children and/or partners, if they have them, to help support them with tasks that they would normally and traditionally do but simply need assistance with that. Or they need the task done for them because they can't do it at all. Something I've already mentioned - the indifference that mesh patients are subjected to by GPs and consultants, many of whom do not even consider the patient's Mesh history, and if they do, they feel it's not responsible for their current problems.

One thing we're hearing a lot, especially in women of a certain age is that they are told that their symptoms are probably due to their menopause. That is being repeated over and over again. Now it's such a - implies a distinctive apathy within the profession that they could think that. In my case when I was told that, I had gone through the menopause when I had my hysterectomy in 2009. I'd never had any bleeding since I'd gone through the menopause, and then all of a sudden it started last year with the pain. But I was told that menopause can be a funny thing, and things can happen at any time. Quite frankly, I'm not a doctor, I hold my hands up, but I don't believe it.

There are huge concerns over what other physical issues could be caused by mesh and its compounds going forward. It's known that polypropylene resin contains an ingredient which can help trigger cancer. So there is lots out there, I think we're all aware it's quite easy to look it up on the internet, online. But there are concerns because whilst women are where they are now in relation to the physical damage, there is also a huge concern, well what other things are waiting just around the corner? Can this be responsible for things that we actually don't know about yet, maybe some people do but are we going to get to hear about it?

When will we get to hear about it? Maybe when it's too late, we'll be told about it. So we are trying to prevent that situation, so we're very keen to know if there has been research done and if any other - if there is a likelihood no matter how small that polypropylene resin could be responsible going forward for other illnesses that may develop within our bodies.

The lack of qualified and competent surgeons who can carry out full removals. There seems to be about a handful - literally a handful of surgeons who profess to having the capabilities and the experience to remove mesh. I don't think anyone can be fully experienced as of yet because the problem only seems to be gathering pace now that people are demanding that they have removals now. However, does there not need to be some kind of funding for training of these consultants, to ensure they know exactly what they are doing?

Actually to manage patient expectation? Because I've been told for example, it would be impossible to remove the whole of mine completely because of the hooks on the side, yeah? So I've been told it would be impossible, but some patients are being told it's possible to have a full removal, only to be told upon consultation, no sorry actually it's not. So I think there needs to be patient expectation management. We need a list of surgeons that have done mesh removal, full mesh removal.

We need that information displayed publicly so patients can go okay, how many operations - removals - has that person done? How recently have they done it, what's their background et cetera, et cetera? Then again it passes control back to the patients making an informed choice, which is something that has been lacking - completely lacking.

Okay. There's little and completely insufficient understanding and support of the psychological harm endured by mesh-affected patients. Again, I'll go through that in more detail shortly. There are thoughts of suicide and self-harm, there are instances of self-harm and suicide attempts. There is a complete lack of confidence by mesh-injured women in the medical profession. Women are concerned about any attempt at removal surgery, it is not always possible to completely remove the mesh. Therefore the question they're asking is, are they meant to live the whole of their lives in pain and despair?

That's a really good point actually, because even if someone manages to get whole mesh removed, what does that mean in terms of pain for the rest of our lives? If it can't be removed knowing that this mesh creates a reaction anyway which is ongoing within the body, what does that mean for us? That we just have to what? We live with it forever? Forever? That's a long time. I've been told, and again I haven't substantiated this, so I'm just telling you what I've been told. A lady apparently lost her womb after enduring severe bleeding following mesh implant surgery.

There is a feeling that mesh-affected patients have been used as guinea pigs in the absence - because there isn't necessarily any need for thorough trialling. That the medical devices can so easily slip onto the market and with the lack of information transparency. That there was no mandatory recording of interest held by members of the medical profession with product manufacturers and suppliers. Sadness that some lives have been irrevocably changed for the worse. Disbelief that mesh has continued to be used for so long despite problems reported by patients and these problems and reports apparently being ignored.

Anger and sadness at the loss of life due to mesh complications and worry about finances, especially as some people have had to give up work. Also, people have been trying to claim PIP - Personal Independence Payment - which I think we are fully entitled to, to varying degrees, granted. But if anyone knows about the process, it is an absolute nightmare. Basically it is designed not to give you anything, that's how it is designed. That additional stress for women that have got physical and psychological problems anyway, and then they are told no they can't get this benefit,

which they are fully entitled to - that is the least that they are entitled to. So, I do think that need to be looked at.

I think, Julia, I've actually mentioned somewhere that I think PIP should be granted to mesh-injured patients where it is confirmed in writing by clinicians. I think there should be automatic granting of PIP. Okay.

Julia Cumberlege: So, do we want Michael to come in now?

Yvette Greenway: Yes, would you like to say a few words, Mike, before I...

Julia Cumberlege: Because we haven't got very long.

Michael Mansfield: No, I'll be very brief because I'm sure you've heard this before. I just want to pick out what I think are for me anyway - coming relatively new to this whole dilemma, and catastrophe, really. First point is, and Yvette's made a lot of very good points, I don't [unclear] just the main one. The true lack of research in the first place...

Julia Cumberlege: Yes.

Michael Mansfield: ...before this was implanted. That is - then entails, it seems to me, a complete lack of monitoring having put it in...

Julia Cumberlege: Yes.

Michael Mansfield: ...to see how it develops with [unclear]. Thirdly, which Yvette just mentioned from her group, and I've been to every attendance of the medical authorities, the third thing is there is no clear information or advice as to what to do.

Do you have a bit of it removed? Well, the surgeon who was about to do it - he fixed an operation. I was there when he fixed it, in the end, said that he was only capable of doing a partial removal. In any event, there were no guarantees it would make any difference. Now you move to a full removal it's the same problem, there is no one who is able to say even if you have it all removed that this will solve the problem. Because there will be, I think after that knock-on effects in other parts of the abdomen, which might involve an infection. Having removed something that's grown into the tissue, something else has got to fill its space. Plus, it doesn't solve bladder problems and all the other things that you've heard about.

So this is a nightmare situation, a dystopia in which people are completely trapped. You don't know where to go, and that adds to all the other symptoms of - fatigue is one of those where it's impossible to measure it but on a daily basis you're just totally exhausted most of the time. On top

of worrying about what is going to happen. So those would be my main points just to follow on. I have to say I was utterly appalled because present at the [inaudible] consultation, there was an air of nonchalance by this consultant, arrogance. The thing that's concerned me most in the whole of this and why I got more than anxious and have come to everything is the, never mind the fatigue, incessant bleeding.

Now for me, any internal bleeding is a symptom and a sign of something that is seriously wrong because the body doesn't automatically do that. Therefore once you've got bleeding on a daily basis and it's not - sometimes it's a little and sometimes it's a lot. Every day the body is losing blood, that's got to be an extremely serious situation. But this consultant, and there I was witnessing exactly what Yvette has described, is actually treating her as a - well, you know women they have these periods in their lives when - and he compared it almost to some sort of menstrual discharge. I couldn't believe it. This was his assessment. Actually don't worry about it, and he was ready for the next patient.

I have to say, well, you probably know what I do. If I treated someone like that, I would feel I was not discharging my obligations, I wasn't in a caring profession.

Cyril Chantler: Did you point it out? Sorry to interrupt.

Michael Mansfield: No - well we - and I'll be honest no we didn't. I think we were both shocked, both got outside and went in the car, and we looked at each other and thought - have we just - what is this?

Yvette Greenway: I did go back to my GP, and I said I have no idea why you sent me to see this man.

Cyril Chantler: Yeah.

Yvette Greenway: I told her exactly what had happened and she was shocked and she said well he was recommended. I said well I don't know who he was recommended by and I don't really care, I said I'm telling you now that I will not be going back there. I have no desire - and I told her exactly what had happened.

Cyril Chantler: Yeah.

Yvette Greenway: But it was it was an absolute shock - it was [unclear] talking like this. Actually he deserved - on behalf of all women that are Mesh injured - he deserved to be stood in front of them all and let them all speak to him.

Michael Mansfield: I think it's a very good point you make because I'm used to asking questions all the time. But actually I suddenly experienced what a lot of people tell me which is, you're in the presence of an expert. He is supposed to be one of the leading authorities in the United Kingdom in this area.

Yvette Greenway: Yeah.

Michael Mansfield: You have to reflect, and so you're mildly humble about it all and think well maybe he knows more than we do? Maybe there's something we're missing here. The full impact of the way he's treated you doesn't really impact itself at the time until actually moments later. Then you think, we've just been through what everybody talks about.

So the complaint came later but as - I now fully understand how women experience, this is really dismissive is what it is, it's a dismissive attitude.

Julia Cumberlege: Can I just say we've heard similar stories across the country I'm afraid. We are going to be interviewing surgeons of course and surgeons who actually have taken out Mesh which we think is very important.

Michael Mansfield: Yes.

Julia Cumberlege: But I suspect, and we don't know we have to hear from them, but we've had some informal conversations, and I suspect they will say every case is different.

Michael Mansfield: Yeah.

Julia Cumberlege: Every woman is different, every body is different. So to actually come out with a directive, this is what you should do. It does depend on the person, on the individual patient. So I suspect that is - but you need to know the risks and I think your issues on consent are just - again we've heard a lot about that and I have to say it is shattering. I mean it is just awful that these things happen without proper informed knowledge that is given, you know.

Yvette Greenway: Precisely.

Julia Cumberlege: Can I just ask you one question, Yvette?

Yvette Greenway: Hm.

Julia Cumberlege: You're obviously a great campaigner, I think it's in your DNA when I see what you've done for suicides and things like that. Can I just ask you, you started your organisation...

Yvette Greenway: Mm-hm.

Julia Cumberlege: ...quite early - well this year?

Yvette Greenway: Yes.

Julia Cumberlege: In March I think, something like...

Yvette Greenway: Yes, it was. I can't remember exactly what month but earlier this year.

Julia Cumberlege: Yes.

Yvette Greenway: Yeah, yep.

Julia Cumberlege: Can I ask you what stimulated that? Because there are many other organisations, as you well know, that are dealing with Mesh.

Yvette Greenway: Yes.

Julia Cumberlege: I wondered why you felt it was important to...

Yvette Greenway: Yep.

Julia Cumberlege: ...introduce another one?

Yvette Greenway: Sure, okay. Well I don't think there can ever be too many. Number one that simple answer. I do work very closely now with Candia McCullough who I believe is giving evidence next on the Mesh UK Charity and a lot of the people she knows.

Julia Cumberlege: I very much agree with you. I think you can have lots of different organisations.

Yvette Greenway: Yep

Julia Cumberlege: They all bring something a bit different which is...

[Over speaking]

Yvette Greenway: Well this is it, yeah and I think we all try and look for different threads of information that we can post that hopefully will help people. So that's the idea, it's sort of creating an information base or as many information bases as possible. Every group does its own bit - every group brings something to the table. Some groups suit some people and other groups suit others so that's...

Julia Cumberlege: We're going to have to close in a minute I'm afraid, because we've got another group coming in.

Yvette Greenway: Okay, yes Candia [unclear].

Julia Cumberlege: I'm just going to ask my colleagues...

Yvette Greenway: Okay.

Julia Cumberlege: ...if they would like to put a question to you?

Yvette Greenway: Okay.

[Over speaking]

Julia Cumberlege: Anything they want to explore or is there anything further you want to say?

Yvette Greenway: Okay the mental health we have had more replies Julia so what I'll have to do is send you that through...

Julia Cumberlege: Oh, thank you.

Yvette Greenway: ...on email if I may, and I'll copy you in Val on it. Crikey okay yeah, and I just wanted - could I just express my support for a lady that I am going to refer to as [REDACTED] I believe some of you may well be aware of her case. She is a seriously mesh-injured lady and she is [REDACTED] She won her case for damages from an NHS Trust [inaudible]. They then decided to question her testimony is probably the best way to put it.

Michael Mansfield: Yeah.

Yvette Greenway: So they decided to film her covertly.

They have decided that from filming her covertly, they believe that she has possibly exaggerated her symptoms. Now I spent most of last night with this lady who was actually [REDACTED] and [REDACTED] she has gone [REDACTED], and she has got a new legal team in place that are helping her. She had been dealt with very harshly. So I think it's important we think about her today because she's been treated disgustingly. My concern here is the NHS Trust in my opinion, and I've seen all the paperwork all the documents as have other legal friends. Okay, there appears to be no valid reason for this and it has no substance.

She's being put through the mill, put through the grinder made to feel like a nobody, like a liar, which she is not [REDACTED] Just because an NHS Trust thinks that - well what do they think actually? Is this how they're going to treat all of us if we pursue claims for damages against them? Is this what they're going to do? Detract from the real issue here which is their negligence of the time, their use of products that should never have gone

anywhere near the human body. So to detract from that they start focusing on the patients and trying to sort of dismiss and belittle them and sort of diminish the integrity of that person.

This is what concerns me, I kind of wonder if this is sort of going to set a precedent here, so that is a real concern going forward. Yeah, I mean there is just so much to say, there was so much evidence here but...

Michael Mansfield: Questions.

Yvette Greenway: Yeah, I do have - sorry, sorry...

Michael Mansfield: Sorry she's written out some really good questions.

Yvette Greenway: I'll be very quick.

Michael Mansfield: Perhaps the easiest thing is to send them to you.

Yvette Greenway: Yeah. Yeah it is.

[Over speaking]

Michael Mansfield: Leave it actually. Leave the document, it's the one with the [photograph].

Yvette Greenway: Yeah, yeah. Yeah, okay.

Michael Mansfield: Just leave it.

Yvette Greenway: Okay so I'll be really quick. Okay, so were the long- and short-term effects of plastic mesh components implanted into the human body ever measured by pharmaceutical companies, regulatory authorities, clinicians et cetera, anybody? If not was there a requirement for this to have been done? If there wasn't a requirement, why wasn't there a requirement? If it has been done, what were the manufacturer's findings and did they share these findings with the medical profession, with clinicians? Because there are some reports that manufacturers such as, but not limited to Johnson & Johnson, may have made medical profession aware of certain findings, but there are equally other reports medical profession saying that they weren't aware of any problems.

So I'd like to know which way around it is. I did write to the MHRA, and Julia you've already had this as evidence some months ago and they refused. They said that we're were exempt under the *Freedom of Information Act* from responding to certain questions when I asked about clinical trials and the evidence that - the conclusions that those answers presented. So I think we should know how many consultants, NHS and private have any form of interest of association whatsoever with

manufacturers of Mesh products. Is it known if there were more, or less or no real difference in the number of patients referred for Mesh implants through the NHS as opposed to private referrals?

Something that has cropped up quite a bit and I think is an important point. How many meshes have been inserted at the same time as hysterectomies have been carried out? Because I'm aware of a couple of patients who said to me that they had very, very mild incontinence systems and actually have no understanding as to why they needed mesh in the first place. I mean is there a bonus upon a consultant reaching so many implants they get a golden handshake or something? I don't know, but this is how it's appearing.

I've mentioned about PIP, Julia, to you. Were any studies conducted into mesh device failure once it was implanted? What were these and what were the outcomes? If these studies took place, by whom were they conducted, by whom were they requested and with whom were the results shared? Also, who has monitored women with mesh implants? I think we all know the answer to this, that there basically hasn't really been anything done. But has any monitoring been done of women that have had Mesh implants across the board, I don't just mean NHS? That would be quite interesting.

If data was available, what percentage of consultants have been advising women to have mesh implants and not discussing other options that may have been available to them? For example, pessaries using their own human tissue, and basically that ties in for what reason did the medical profession choose to start recommending the use of mesh over any other methods or options that may be available? What evidential data did they use prior to deciding to use the mesh as opposed to anything else? I'll be really quick, I'm racing. Did any regulatory body, NHS consultant, GP ever ask how mesh will be removed if this was necessary and indeed how easy would this be to achieve and was it possible?

Did anyone ever study the impact upon mesh patients should device issues occur, i.e. inflammation, erosion, bleeding, pain. What steps have been taken since the vaginal prolapse mesh ban by NICE in 2017 and subsequent temporary ban earlier this year to ensure surgeons are being trained to remove this implant? Given that removing mesh is like trying to get chewing gum out of hair, and women are being told it isn't always possible to remove, what will happen to us, are we meant to live like this forever? Are studies being conducted now that can help to working towards alleviating some of our problems?

Will our problems we face now increase and worsen as time goes on, the mesh remains in our bodies, and of course, we age.

Julia Cumberlege: Yvette, I'm sorry I haven't been able to take in...

Yvette Greenway: We've got to stop?

Julia Cumberlege: ...all these questions.

Yvette Greenway: Okay.

[Over speaking]

Julia Cumberlege: Can I suggest that you send them to us...

Yvette Greenway: Yes, sure.

Julia Cumberlege: ...because they are very important?

Yvette Greenway: Yes, sure. Of course I will.

Julia Cumberlege: They are going to help us when we interview the regulators...

Yvette Greenway: Yep.

Julia Cumberlege: ...and various other people.

Michael Mansfield: We could leave this document now, so you've got it.

Simon Whale: Do that, that would be fine.,

: Please do but I think...

Julia Cumberlege: Yeah, we've got...

[Over speaking]

Simon Whale: ...we've got these questions, most of the questions you've just asked you've got in your [unclear] submission which is very helpful.

Yvette Greenway: Other things that I'll type up in a summary form for you.

Julia Cumberlege: Please give us that.

[Over speaking].

Michael Mansfield: Is there going to be a transcript of what she said? How is that going to work?

Simon Whale: Yes, there is going to be a transcript.

[Over speaking]

Valerie Brasse: Ultimately - so no - yeah, there will be a transcript ultimately. What our plans are, as I say, video record all of these sessions. The video recordings will go up on the website - in due course and before the report is published there will transcripts. Our intention is to make those available.

Michael Mansfield: Okay, thank you.

Valerie Brasse: With suitable reductions and redactions obviously where we may have to...

Michael Mansfield: Yes.

[Laughter]

Valerie Brasse: But then you will understand that.

Julia Cumberlege: Can I thank you both so much for coming. It's really helpful. I'm just so, so sorry of all that you've been going through and are going through. You're quite right with your questions, it's what has happened, what is happening now, and what can we do in the future to prevent further...

Yvette Greenway: Yeah.

Julia Cumberlege: ...terrible things like this happening.

END OF TRANSCRIPT

Session 2: Mesh UK Charitable Trust

START OF TRANSCRIPT

Julia Cumberlege: So, we very much welcome you here and perhaps you'd like to make a statement to start with or - and we'd like to welcome your observers as well.

Joanne Davies: So shall I just say what I've...

Julia Cumberlege: Yes, say what you want to say.

Joanne Davies: Yeah. There are a few points that I've been asked to raise on behalf of patients. One of them is, when pelvic mesh is inserted, it's usually intended to reinforce tissue in many specialities including urological, gastrointestinal and gynaecological. Once mesh has adhered to organs, blood vessels and nerves et cetera, a new speciality has been created. This new speciality is trauma. In the opinion of one of our professional members who owned her own clinic before she was disabled herself by mesh, surgeons such as those trained in warzone frontline pelvic shrapnel injuries should be employed for mesh trauma injuries. Gynaecologists are not trained for this [REDACTED] qualifications and experience can be supplied upon request.

So, the next issue is about claims, financial claims. Many patients are signed up by solicitors and often dropped due to time constraints laid down in law. Many are time-barred from any future compensation claims. All mesh-injured patients need the limitation in period interrupted, giving an equivocal reservation of rights to enable them to claim at any point in the future.

The next point is about care packages. Care packages are needed right now for mesh-injured patients. That includes adequate financial assistance and ample fuel payments, especially before the winter sets in. The cold is coming and they feel it terribly.

The next issue is mesh removal waiting times and partial removals. I really don't understand why patients are having to wait so long to get mesh removed while they're going back and forward to hospitals for appointments and different types of treatment. I'll give you an example, with something like if I got a saucepan stuck on my head and went to the hospital, they wouldn't take half off this week and the rest off in six months. They would take the whole thing off and I really don't understand why these patients are being turned away from hospitals and nothing is being done to help them.

Partial removals as well. I don't understand why a patient has to go in and have part of it removed and then go back and get the rest of it later. It just seems like it's adding more risk and more injury to the patient.

The next issue I'd like to mention is MHRA engagement. There doesn't appear to be any with the general public. Most people don't even know who the MHRA is. In America, most people know who the FDA is, but here they don't. I've talked about the MHRA for years because I've been in industry for the past 18 years and when I talk to people, they say who are they and I don't find that the MHRA is engaging as they should with the general public.

The next issue is, I think there should be a mainstream media announcement for everybody who may have been affected by mesh because at the moment, people who use the internet are being made aware of mesh, or they're being made aware of mesh by people talking to each other, but there are also other people, older people who live in care homes and their carers are wondering what they can do with them, how they can treat them. They have no clue and these older people don't even know that they've got mesh inside them or you know, what's happened to them. People really don't know how to care for these people and there are people just still wondering 'how did I get into this mess.'

The next issue I'd like to raise is post mesh removal. I think that many patients are being told that they're having a full mesh removal, but later on they discover they still have issues and they go for a scan and they find out that they haven't had a full removal of the mesh. I think that it's important that these patients are offered scans post mesh removal to reassure them that all the mesh has in fact been removed as far as possible because as we already know, if you look at mesh under a microscope, there are very fine hairs coming off them.

These are the sort of - I can't - filaments and once it's put inside the body, these break off and they travel everywhere so it's not actually possible to do a full removal, but it's possible to do a full removal in the area where the mesh was found. So an independent scan I think should be recommended for these patients.

I would also like to suggest that a material analysis is done on every piece of mesh that is removed from patients. Because at the moment, most manufacturers don't know what materials they're using and that I find highly shocking. I really do. I have often asked manufacturers to verify what materials they are using and they can't. I've rung their suppliers, they don't know. I've rung the suppliers in China, they don't know either

and they've even said to me, I'm the first person who has ever asked this question and they didn't know why I was even asking the question.

Cyril Chantler: Can I interrupt you, do you mind?

Joanne Davies: Yes of course.

Cyril Chantler: Because I know you know about these things, but I thought that they now only use monofilament macropore mesh. So, do they not know that's what they're using and that it's made of polypropylene?

Joanne Davies: I have worked with a mesh - not a mesh manufacturer - implant manufacturers where they have told me the material is this, but they can't prove it. So I have rung the supplier and they've said, why am I asking that question. So I'm saying that if the manufacturer is saying they're using these filaments, can they prove it, can they verify that's exactly what it is.

Sonia Macleod: So what you're saying is that what's in the design dossier, do they actually match the...

Joanne Davies: Exactly, yeah.

Sonia Macleod: ...confirm against the design dossier.

Joanne Davies: Yeah. Any responsible manufacturer will bring a material in and even if they've ordered let's say stainless steel 305, how do they know that's stainless steel 305? We need to know so they will take a sample off, they will get it tested and they all have the traceability as well. So when the auditor comes in and they say what material is this? Oh, stainless steel 305. How do you know? There is my evidence. Yeah? It's very important as well for the environment because manufacturers are - should be responsible for their materials until disposal as well. If they don't know what materials they're dealing with, how can they be responsible for that?

The material analysis post removal will also help determine what problems the patient may have in the future. It may help with many patients who have had that type of mesh, if we can prove that those people had that exact batch of mesh and then you might also find that you have a set of patients who once they have let's say Prolene mesh, they have Prolene but all of a sudden, you have a different type of material. So you're going to have a different type of symptoms, different types of treatments that these patients need.

The next issue I'd like to raise is paperwork. I believe that patients should get a set of paperwork, not only after they come out of hospital but before they go in. So everything is agreed before they go in. So like if you took your car for an MOT, you agree the work that's going to be done and you get a receipt for what's going to be done and when you come out, you get a receipt for exactly what has been done and you can put the two together and that's your record. You get one for a car and you should get one for your own body work as well.

The next issue I'd like to raise is adverse event reporting. I don't believe there's anything wrong with the adverse event reporting system. Surgeons do report, doctors do report, users report, and it all seems to work and when there's a problem with a device, it's put right by the manufacturers. It is the way the system works. Surgeons aren't reporting that mesh is faulty because they don't believe it is. They should be able to rely on the CE mark device as being safe and effective and they send their patient away and according to them, they think that the mesh has been fine.

So the adverse event reporting is applied when a surgeon perhaps has a catheter in the brain during surgery and that catheter splinters. Then the surgeon will use the adverse event reporting system. Yeah? Or if someone in a hospital puts somebody in a wheelchair and the wheelchair broke, they use the adverse event reporting system.

Now for a surgeon to report surgical mesh as faulty, it would have to break during surgery. So maybe he took it out of the packet, it wasn't sterile, or the plastic had split already. That surgeon would use the adverse event reporting system, so there is no gap there. These devices aren't supposed to fail.

The next issue I'd like to raise - I think this is the final issue - is about manufacturers, surgeons, systems, quality and trade. In general in the UK, in the manufacturing industry manufacturers are not happy. In fact they are quite angry with the UK's MHRA and their designates. Surgeons should be able to rely on safe and effective devices every single time and they should be able to know that if they come across a faulty device, it will be put right and it will never happen again. That's what our quality management systems are for.

The last issue I'd like to raise is quality and trade. Trade depends on quality. Thank you for listening.

Julia Cumberlege: Thanks very much indeed. It was very useful. Candia, is there anything you would like to add or say now?

Candia McCullough: We actually met with the MHRA and we were well received. We had a three-hour meeting, didn't we? I had this question about how the charity can work with people. Because I think that you know, we need to all communicate and - it's quite frankly, it's all been fractured, nobody's talking between anybody and it surprised me but like I said, we were well received.

One thing I asked which I thought was very pertinent, considering my own personal situation - the MHRA, are they considering the cost and the impact to the government, for example for allowing these medical devices? They said you need to talk to DOH, Department of Health. I thought oh my god, another meeting, seriously you know, it's just too much, you know but to just encapsulate a part of it - and I tried to do it on my statement. Literally I ran out of time and I had to submit it and we had an extension. It was still - I just couldn't write enough, it's too traumatic.

Following my surgery, I had seven years where I found myself on benefits, okay. I had carers. I had carers of I think it was 21.75 hours a week, a godsend. I couldn't be a mum without those carers but it forced me and my husband to separate so that's how come I ended up in a scrap heap if you like. Because that's how it was, that's exactly how it was. So, when I add my benefits to my care package and then one stint in hospital for four weeks at Lymington Rehab - because I couldn't string a sentence together. I couldn't do it. I had dysarthria severely, I couldn't understand things, couldn't read things, couldn't remember things. I was just a wreck.

I understand that that one stay was £80,000 and if you look at the care package I had and the benefits that I had in that period, you're talking about a quarter of a million. So now I'm going to have to tell a little bit more about my case.

So I had a hysterectomy. I was told 'I am only going to take your womb, I'm going to leave you with your ovaries and that's all I'm going to do'. He lied. He did four additional surgeries - excuse me, I'm too upset sorry - four additional surgeries, gave me four mesh kits and he's lied every step of the way along the line. We are owed something back but I'm going to quantify the cost to the government. That's what I want to try and keep my focus on.

So now quantify this - I've kept every single appointment letter of the time because I didn't know what was wrong with me. I knew these letters

were important to me and I knew they'd tell a story one day and they would help me work it out, what happened. There is - I think I've had 362 hospital appointments. This excludes blood tests and GP appointments in the last 10 years. Hospital visits. I don't know how much they cost - £100 a pop? I don't - £150 a pop? Medications - I've had 75 different types of medications for pain, infections, everything for the last 10 years. Remember, I didn't know I had mesh. I didn't know anything about it so I am empirical data. I have all my evidence. I've kept everything. I've done my findings. I've found - and I offer them to the review team to use my case as an exhibit to what is happening in mesh.

I don't have a choice. I have to expose my story, but I'd rather it be used in the correct way that lessons do get learned. Because I did find myself as empirical data and that means empirical evidence. When you've got a pure test subject that had been treated to extra mesh - extra surgeries she didn't know about or she never consented to and she has this much harm and it's cost government this much money on one section of my care excluding my appointments, out of that I've had 65 MRIs, scans and nobody told me once about the mesh. Nobody told me that the scars on the front of my pubic bone suggest that I've had bladder surgery. I mean seriously, the scars were there. They're ancient scars now, but they tell a terrible tale.

My story gets worse. I wish it didn't. I wish it didn't happen to me but anyway, I went around the world. I don't know if you've all read my statement. I went to Finland to get the truth [REDACTED] to my implanting surgeon, I asked him what did you do to me? You need to tell me what you did. I was calm, I was polite and I recorded my appointments for the last three and a half years because something was not right. Something was really not right.

He told me he didn't do anything to me. I know he's scared but I gave him the opportunity. I flew there with a translator in the event that he forgets his English even though [REDACTED]. Still proceeded to tell me this. I then went to the US. I flew to two mesh removal surgeons and in each one of those times, I've let them treat me how they treat other patients. I've recorded - I put myself in a terrible situation in a way. I've let them examine me. I've let them trim bits. I've had so many biopsies, I've lost count. It's ridiculous. The whole thing is ridiculous but it does show exactly what is going on for patients.

I've never been rude. I'm not rude. I needed the help. Patients - this is how it is for patients. Even if you're treated badly by a surgeon or doctor, you swallow every pill, you do everything they tell you to do because if

you don't, you will never get the help and what do you want when something's wrong? You want the help. You have to do as you're told. So I've done it all.

So out of all of this, it's cost me £40,000 in the last year or thereabouts travelling around here, there and everywhere, undergoing surgeries, and they don't want to admit to the fact that this mesh is a problem, that it's something more darker than that. You've got problems on your own territory here in this country and for that I must speak out and I will never be able to stop. Because what happened here is - I mean it's terrible. I'm really sorry. I know she's well respected as a surgeon.

I went for mesh removal in 2015 [REDACTED]. When I woke up, I woke up to [REDACTED] who was trained by [REDACTED] at that time and he told me I had no mesh. None at all. I have four pieces and he was telling me that I had nothing wrong. I'm sorry, they lie. Surgeons lie for whatever reason, I don't care, but when you lie to a patient that relies on that information because they're trying to get themselves back on their feet, get back on their work, get on with their life, it is criminal. It's criminal in moral terms, legal terms, every term you can put - humanitarian. Every level of wrong.

Why lie to protect [REDACTED] did a surgery on me that he shouldn't have done? Why not help me? Why leave me so that it tears through my skin or it tries to perforate through my stomach or it tears my toilet tissue as I walk or I videoed it coming through my rectum. I have disclosed everything to you that I can think of. I've shown you pictures of my vagina where it's all trauma-d. I've showed you distortions in my vagina where it's changed form. I think I've sent you the video where it's actually torn through my rectum. I have nothing to lose, but to share with you everything.

I urge you if you haven't seen it, it's still on the line. I haven't pulled it down, I haven't put restrictions or anything like that. I want you to read that statement again and again and again because I'm offering it to you as evidence, empirical data to prove that if arguably for one second in your mind you felt that - oh well it's her own silly fault, she went for that operation, she had the chance to do research or something like that - I didn't. At the time I looked at the NHS research to see what the hysterectomy will do, there was nothing on there about any mesh at all. So in no way did I know that they would do additional surgery, bladder surgery, colorectal surgery.

Doesn't it sound crazy to you? That someone like me can actually work it out for - I mean that must be crossing your mind, how did she work it out

for herself? How does she - she's got no medical knowledge. She was like literally bedbound, dying and vulnerable. Stretch it out there for [REDACTED] She was dying. This is me. I know it's me. I'm talking like it's the third person but to me it represents everyone because even if you consented to this bladder surgery, I'm going to tell you empirically and emphatically is probably the better word, nobody would consent to this. Nobody. Who would consent to - and I did bring some things with me because I just think these are some of the things that you can't make this up. Nobody can exaggerate this. Nobody at all.

Plastic bits coming out of your vagina. Why would you have plastic bits coming out of your vagina? They're sharp, they're shard-like, they feel like really gritty. One of them in particular, the bladder one - this is how it makes me feel when I'm sitting here. I feel like I'm sat with that inside of my vaginal area around my bladder cutting through my urethra. Yeah? Who'd want that in their body? Watch. I'll pass it round if you like but you can see like on one of them, they just split and they're very sharp. They're the ones that you know, when you get your parcel tape and they are sharp. That's how it feels like, just sat there just on the inside of the pelvic area.

I couldn't manufacture this. Those 342 appointments or 362 appointments didn't happen because there's nothing wrong. I feel like it's impossible to explain - but I can explain this. Here's some Stanley blades, yeah? When - after my surgery [REDACTED] she said there was nothing wrong, I went and I got my surgical notes about a year later afterwards and it showed that I had four mesh kits being implanted. When I was being examined, they put a hand into the vaginal area and I guess they're shifting the colon out of the way and they're feeling the part of my spine. As they were doing it, it felt like kch, kch, kch against my spine. That sharp. Yeah?

I don't know what they were doing. I honestly do not think that any of these guys realise how bad this stuff is. I genuinely think that they probably got a cure but they don't. There is no way anyone would consent to that, would they? Or that. Or the fact that you lose your sex life or the fact that you can't be a mum anymore or that you're going to need carers. Who would consent to that? Death is a risk of this surgery. [REDACTED] I know that you know I'm sure there's a few people that have died. She had one mesh. I have four. She's the same age as me but I've never been able to be a mum.

Recently we lost [REDACTED] and I had an amazing bond with him because I got told I didn't have mesh. I took him in [REDACTED] terrible thing but as a

woman, you want to look after your family as long as you can, you know? I couldn't do it - I was on my knees. I got told I hadn't got mesh. I thought I could take him in. I thought I could look after him but I couldn't. I couldn't because you know when he [REDACTED] I couldn't bend down and help him. Our family broke so many times over but as empirical evidence, use my case, use it to do everything. I have nothing to hide.

There's more evidence, there's more recordings. I've been recording these guys in hospital for the last three and a half years and the last - the first recording that we ever did - and bear in mind, I just want to get my health back, I want to get my life back. The whole time, the whole 10 years that's what I've been doing - going round the world, everything and that's what you would do, that's what you'd all do and quite rightly so. I'm losing it. Sorry. I've lost my thread.

It's too much. I've lost my - what was I saying, sorry?

Joanne Davies: Going round the world.

Candia McCullough: Yeah. Yeah I feel like I'm going round the world [laughs]. What was I going to say?

[Inaudible discussion].

Candia McCullough: Oh yeah. Anyway so he went into a home. To find out that I've got all these mesh kits and I could have been helped but imagine it was [REDACTED] hailed a hero. She's not a hero. There's laws in this country that have been broken. There's a Nuremberg Code, duty of candour that's been in effect and it happened - duty of candour actually took place in June 2015. I feel under [REDACTED] the October. That law was in force. It was already in force. I don't understand - I don't know how somebody of that stature, hailed a hero, can lie to patients, tell them they've got nothing in them and for it to tear through their skin. I've actually sent you the video recording of my last ever appointment with her which was April 2018. I still am her patient on record. I am still her patient.

She doesn't want to see me again. She's quite happy to still tell me to this day that yeah, no and on there, you will notice that I asked her for a mesh removal appointment referral and you will see her hanging her head in shame. She knows. I'd like you to ask her about my case. I have no qualms. I've faced her. I've given her the opportunity like my mesh implanting surgeon, like the mesh remove - these people should be in trust but who was protecting patients?

I understand kickbacks are paid for, blah, blah, blah but I'm going to tell you something else as well. I also know that since my surgery, although she may have helped me get back on my feet - I'll give her that. I will give her that. She did help me get back on my feet. I nearly died but what I don't understand is how I had a whole new myriad of symptoms and I've actually got new lumps like attached to my ribs and it can be felt in the groin as well and picked up on MRIs because that's how I found out for sure was last October, which again I've sent the MRIs to you on - with my statement that show I have mesh in me, but they're not meshes that are different or anything like that. They can be seen.

Out of those 62 MRIs, now I've got most of them because obviously I've been round the world to try and get the help. So obviously I've got, you know - and I can see that it's easy to be seen. Scans and MRIs are to me not rocket science. Not at all. You can quite clearly see them. It's down to the trained eye and we've been told a load of lies about the scans and MRIs.

What I'd like to propose is that we have at the charity scanning equipment so that people can come and see for themselves. It might be something that they might be able to do themselves or we might be able to get a radiographer in time, but I would like to offer that service through the charity and fundraise for that because I want people to now feel safe and that they've got somebody on their side, not for profit. We could do it for donations or something for the charity so the charity just does respite breaks. Those respite breaks are essential. They are not much but they're about family.

So going back to family a little bit. I didn't go to the park with my children for two years because I didn't know what was wrong. I couldn't walk properly. I couldn't see properly because it does, it affects everything. There will be a whole list of symptoms I wish to provide in time through all my diaries because I was asked to keep a diary following implants and then I got told off for doing it so I had to stop it but I've still got that diary and I want to put across to you that you will end up with neurological issues, respiratory issues, autoimmune problems from day one because that's what happened to me. I was very sick and then also equally very disabled.

So picture this if you will. You're all women, for [unclear] this exercise and they're going to do a simple - so they're going to tell you that they're going to do a little mesh to hold your bladder neck up or something. Maybe they'll do a prolapse fix. They'll just say put the mesh, the mesh at

the top of your vagina. They will not tell you that they're going to anchor it to your spine and this wretched stuff is going to go through your bowel.

So I've got a piece of mesh. I don't know if you've ever seen mesh yourselves. I'm sure you possibly have. This one is actually hernia mesh so obviously it's slightly different but the essence is the same. Nobody wants to give me any vaginal mesh. I don't know why not but anyway, this one is brand new and on the edges, it's serrated and it's very sharp. One side is particularly rough. The other side is not so rough. Nothing says which way up, but see the thing is, to have that inside of us, it scratches at our bones, yeah?

You can feel it on your bones like I can feel it across my spine here. I shouldn't be able to feel that. We shouldn't - this is just - this is madness, absolute madness, how this can happen, but if you put that across - say for example we're going to stick it from the top of your vaginal fold across to your spine now, look at those sharp edges that can go across any sort of [unclear] your bowel. Now I remember one of my doctors screaming at me saying, the bowel doesn't feel anything. Oh it does.

Can I share with you something very harrowing? I don't think I can hold it for – can you play it please Ian?

Male : Sure.

Candia McCullough: Where was - there was two. So this is about - this one can cover a few stories. Okay first one is, lignocaine infusion. So when you have lignocaine infusion - because I've had 75 different types of medicines, I've tried everything, nothing works. Nothing works. Nothing is a cure, they only help you get you through or anything like that. It just makes you more sicker, okay, but in particular this lignocaine infusion which I've been having since 2010, there was some help. There was some help but it doesn't solve everything.

The other one was a speculum insertion. So it's very routine stuff for women, you know. They put the speculum in, they crank you open - I'm sure you've read my statement - and as it did that, it turned me into minced meat. That's the only way to describe - and these are surgeons. These surgeons ran out on me. Left me chomping on gas and air. They couldn't handle it and I'm going to give you some idea. We'll just play it. This is - you might not want to hear this. Is that in the right place here?

Male: Yeah, just hit play.

Candia McCullough: At the top of the...

Male: [Unclear]

Candia McCullough: Okay. Shut your eyes, please.

[Recording played (indiscernible sounds on recording)]

Candia McCullough: I'm on gas in here at this point. I've had all my medicines.

Male: This is [unclear].

Candia McCullough: This is [unclear].

This lady didn't know she had mesh. This is reality. I have to [unclear]. At this point, I felt possessed. My back's there. These screams are coming.

[Recording ends]

Candia McCullough: I promise you, I wanted to die. I wanted to die. I didn't want to live through that - not again, too much, but [cries] - too much because so much pain, but apparently, the bowel doesn't feel. You see what was happening is I felt my muscles relax right down. The muscles relaxed right down and something was skewering me from inside. Now I can't fabricate that. I can't - because I didn't know - the date of that - I can't see because of the crying...

Male: 15 September.

Candia McCullough: 15 September. I got told in October I didn't have any mesh. So it's very real. All of this is so, so, so real. The only way to describe pain to you is to let people witness it. Hear it. My legs were up. I was trying to - I was trying to breathe through it. I was literally trying to work with everyone. I was having lignocaine infusions. [Inaudible] through your veins to help you deal with the pain.

So the only way to make people actually really understand mesh pain was to actually play that to you. It's too much. Shouldn't be happening. Should not be happening at all. I will never be able to endorse this type of surgery for anyone. Not for cancers, not for anything because if that's the cure, then there's something very wrong. Very, very wrong indeed and I really hope that the right thing obviously gets done because if you've got empirical evidence of something, you can explore it a little bit more.

The other thing I was going to say is this is supposed to be well thought of as a cure. You're supposed to inject it into your vagina and the principle behind that is, it helps the skin cover over the mesh that's been exposed. Did you know that? That's disgusting. That's disgusting because the

infections and everything? These ladies aren't lying. They were never lying. They were never malingering. They're not scrap heap but their - literally lives have been turned upside down for what? It's not a cure. It's not a cure. It's toxic. Makes you very, very sick because that's what happened to me. I felt very, very sick. I felt very, very poisoned and I couldn't walk properly.

So for the first eight years [REDACTED] I never reported that my left leg wouldn't go flat to the bed because I didn't know what was wrong with me, yeah? She also released my left leg. So first time ever, she released my left leg. That means that she took something from my pelvic area to release that left leg because I didn't even report it to her. I've given you all the transcripts from the appointments so you'll know verbatim what was said, who said what, by who and all the rest of it.

She did save my life. I'm back on my feet, but I'm very disturbed by everything I've seen, witness - I knew instinctively that I can't help anybody, not really, but I can try. I can try by sharing my experiences and teaching people. I am going to propose something in a way that is going to help everybody move forward. I want to do some training with people to help people deal with this. Because only I really truly understand how bad this is and that's what I can do. I can teach people from what I've learnt. I can help them. I can provide a scan equipment. Obviously I know fundraising and all of that and that's quite challenging.

We've also saved 26 people from suicide this year. We've only launched this year. So since Good Friday when we launched, we've saved 26 people because we understand what's really going on for people. We're already making that difference but we're new. We're new but we're very effective. I can't explain why but I think you know, [REDACTED] with us, there's something that's special about [REDACTED] a lot of people, okay? There is this thing about the bond between mesh injured people is so strong, so very strong. Because despite everything, we're all drawing together in terror, trauma, horrible nurse - it's so hard to know who to trust. It's really, really hard. Especially with your lady area. That's - you know, we're taught that's just for our husbands and then we have to trust people time and time again.

So what happens for me now? Is there any justice? I haven't seen any actually. I'm going to be honest with you. I want people to take on my case. I want people to use this as an example. I want people to be dragged over the coals for what they've done. Whether they've lied or something like that, absolutely. Absolutely. I'm owed and so is everyone else. Without a shadow of a doubt, everyone is truly owed for this.

Compensation will never, never, never, never give back or take away what's happened to me and my family.

My youngest daughter - she is 15 now - she's never known a fit and healthy mum. The other two had terrible troubles, even though they were at school because they saw me as a hero then - living in Paris, social, going to Galerie Lafayette, drinking champagne with my friends to not able to do any of those things anymore and needing them to then care for me. That's why I decided to do a charity to help families because that's what it means to me.

Yeah, I think they should be answered and I think people should be paid. I think - I don't think the government should be out of pocket for this. You know, a quarter of a million for one part of my - is what I worked out - I couldn't be bothered after that. It's just too much money. Who's going to take it on? Where do we go? Where's the book that says where we've got to go for this? You know. You ring up solicitors, you ring up solicitors. You know they're looking for something specific to get an angle on. I want that [REDACTED] pulled over here for this. He's [REDACTED] see why not. Make an example of him.

He lied to me. I've got him on record - we've got the transcripts. Something's got to happen because this is just so wrong at every level but the thing is, since I've done my group, I set up my group February it was, last year and this goes on and it's every level of wrong with this. Since doing this, I know now - like I said, we've saved 26 people. One of those ladies was willing to jump. She's actually on my website - jump off a bridge, had the - I don't know - the compunction if you will to join a Facebook group to see if there was something out there. She found ours, we saved her life. She was the first.

She was given additional surgery too. So she went for a breast op and came out with hernia op. The surgeons lied to her too. Then she found out and the battle continues. You see the thing is, if say for example we thought you've got a medical device in you, okay it's a problem, okay we'll take it out and your - I can't even think of what the word is sorry, hopscotch free or whatever it is, I can't think - scot-free, you're off scot-free. They'll take it out. You can't know. People are losing organs for this.

Julia Cumberlege: Candia, can I just say, I mean what you've been through is so ghastly. Just so ghastly and I think your courage to keep going is really awesome. I think it's amazing how you managed to do that and your presentation to us today I'm sure has left us all with really an awful lot to think about and

it was - certainly we shan't ever forget it and I do want to thank you for coming to tell us all about that.

I would also like to thank Joanne as well because I know you've done a lot of research on all of this and both your personal testimonies are really important to us and I want to thank you so much for coming and for your husband here, thank you as well for coming to support you two remarkable women.

So I'm afraid we've got to draw this to a close and you've had the most horrendous day. I think to come here and tell us as you have has been just amazing. So I want to thank you very much.

Attendees: Thank you.

Candia McCullough: Thank you very much.

END OF TRANSCRIPT

Session 3: Meshies United Group UK

START OF TRANSCRIPT

Teresa Hughes: What can I say apart from that the mesh has become a scandal, it's become a shambles. Ten years I've been at it now and I have spoke to you before. I have tried and tried and what I particularly want to go on about is the lack of help that hasn't been forthcoming and the lies we have been told and also, a lack of the care pathway we tried to get and the group that I created in 2008 which is Meshies United Group UK.

The lack of informed consent and actually, the flawed procedure. So, there's a wide lot of things I wish to talk about but we'll just stick to a few. So, in 2006 I had this operation. We have met before and I have told you so I won't go into all the detail about that. But it did go wrong somewhere along the line and it took from 2008 to 2013 before I got any answers. That was seven surgeons and one cancer specialist. I was lied and lied and lied to. Okay?

Within that, I formed this group and my husband wished I hadn't because it became part of my life that he wasn't part of.

David Hughes: Yes, he was, he was very much part of it because he liked to listen to it all the time.

Teresa Hughes: Well, in that way, yes.

Julia Cumberlege: So, you did a lot of counselling through the telephone [unclear].

Teresa Hughes: Yes. So, what I did on a smaller scale is what you are all doing now. I went around the country and I visited hospitals and I visited the sick and disabled and I was disabled myself. I was quite fortunate then to be able to do that with the help of David which drove him mad. The tales were sad. We cried a lot together because we couldn't get help. There was no help at all. We were told that it was all in the head, that we didn't have pain, we didn't have injuries. All these phone calls kept coming in, so a lot of them were from Scotland, I should say. I sent them up to Scotland to another group. That's how Scotland came on board and I stayed with England.

So, we kept taking these calls, not just me, there was two other ladies with me. One was called [REDACTED] and one was called [REDACTED]. We helped - I can't put the number on what we did help. We sat and we just listened to these people for hours. I had to cut them off after an hour. I couldn't

take much more from some of them because they wanted to kill themselves. This went on for years.

Then [redacted] and I, we met with [redacted] at Department of Health and I said to [unclear] how I can't take any more of these people who want to die. You have got to do something about this. They just sent a letter saying the benefits outweighed the risk. That's all I got back. So did [redacted]. She wasn't interested. She wasn't interested whatsoever. I'd ask her did she want to have it done to her to see how she come out the other side. Because I was angry.

So, I wrote to Jeremy Hunt. I have given you freedom of information there and I asked to meet him. I got no reply. I did a petition, took it to Downing Street. That was 2012. I met with the MHRA on two occasions. David was with me all these times. We went to the European Commission in Brussels and these are all at a cost to me. I spent thousands of pounds. I didn't go around asking for money off anybody.

We went to the Royal College of Gynaecology, didn't we, David? We went to see Professor [redacted] well- renowned professor and various other organisations. As the years went by, must have been 2012, 2013, they all came back with the benefits outweighed the risks. That was all we used to get. Letters like that.

So basically, that was where we went with a mesh group, being a mesh group trying to get answers, trying to get help, trying to get a care pathway in place. That was one way the group formed.

If I go onto the informed consent, as far as we're concerned as women who have had these mesh procedures, we don't feel we were informed properly, given enough information. I don't know what they're given now at this present moment but I certainly wasn't told what it was made of and what could happen to me. That was also with a lot of women that I spoke with, they hadn't been told how they could end up, you know, weren't given that decision.

We were told maybe it was an 85 per cent success rate. So, if you were in the unlucky 15 per cent, there was no care pathway for you, God help you. You were left to die. You were left to rot. You were left with your injuries. You were left with nobody to go to because nobody would take you on. They would lie to you. They would tell you there was nothing wrong with you and that you were just a hysterical woman. I came up against all this.

I won't repeat myself in that way but it took its toll on me. It's took its toll on my marriage and it's took a toll on my husband and son. For me to be here today to talk about it, it's rather traumatic as well. I know you understand that.

We were never told they were permanent devices. We were never told it could tighten, shred into the tissue. We were never told we would lose any intimacy with your husband, how your vagina would be scarred. We weren't told about nerve damage. We weren't told you could end up self-catheterising and that it could migrate around the body. So, there was really no other alternative offered to us rather than mesh, transvaginal mesh for stress urinary incontinence.

Julia Cumberlege: Can I ask you then are there alternatives that you have discovered now that you feel should have been offered or could be offered now because science has moved on?

Teresa Hughes: Well, it's going back to the colposuspension. It's the old traditional method, that's mainly the one that hasn't been taught now to these surgeons. So, basically what's happened is maybe that should have been on offer but if there isn't enough surgeons to do that operation, it can't be offered because this has become the quick fix because of the money. Pharmaceutical companies. Although cost is £415, I think for a kit, as to the colposuspension, you can end up with five to seven days in hospital having to recuperate. So, that is - maybe that should have been offered. Exercises. There wasn't a great deal on offer to be honest and I don't see a great deal now on offer.

Julia Cumberlege: Have your members who contact you, women who were suffering, have some of them had the colposcopy?

Teresa Hughes: Yes, they have.

Julia Cumberlege: Has that made a difference to them?

Teresa Hughes: To one or two, to two, no. It was - it didn't work on two of them.

Julia Cumberlege: They're suffering just the same as [unclear].

Teresa Hughes: Yeah, it didn't work. So, I don't know what the odds are on that not working. But at least you haven't got mesh in you, you see. That's the difference. This mesh which you know of now, it's just breaking up and it's causing all sorts of auto-immune problems for us. I just got fibromyalgia, costochondritis, dizzy spells, that's besides everything else. I don't know what's happened to my body really since this mesh was put in.

There's been that much. So, the difference between that operation and the mesh is the fact that the mesh migrates, breaks, goes brittle. It's not just immediately this happens.

I mean, one lady, she was 10 years down the line. She was singing its praises and then this day, it all went wrong. She said it was just, she said it was like a bad smell of fish and she couldn't get help from her GP. Actually, she ended up with [REDACTED] and he ended up cutting her labial folds off in the end because she was in that bad a way with the mesh and that was after 10 years. He had to reconstruct her underneath. That lady is still suffering and she helps a lot of people even with her suffering.

So, she then tried a colposuspension actually but it didn't work. So that's in the last three years.

Cyril Chantler: Can I ask, have you seen the new guidelines that have been issued for consultation?

Teresa Hughes: I have looked at them briefly.

Cyril Chantler: What did you think?

Teresa Hughes: I don't think much of them at all. They're not saying the operation should be banned. They just - there isn't really a lot there being changed as far as I'm concerned from 2013, was it, the last one?

Cyril Chantler: No, they've just come out.

Teresa Hughes: No, no, from the previous one. There isn't a lot in there apart from - what were they saying - women should only be seen by a trained surgeon. I'd like to know who's trained them.

Cyril Chantler: [Unclear] they do suggest some alternatives that should be considered before.

Teresa Hughes: Before the mesh. That's not a lot, is it? It's not helping with - I mean, they are only guidelines at the end of the day and they don't have any clout over the MHRA. The MHRA are the people who shouldn't have put this on the market, actually. They are the people who are held responsible as far as I'm concerned and they are the people that need looking into. Especially on the money side. I've said this all along. I came up against the MHRA and they sent four policemen to try and lock me up because I was protesting outside.

But they had to meet me in the end and I met them twice and I was on the NHS working group committee with them. I have to say they were

quite an aggressive people as far as this mesh is concerned. They weren't nice people at all.

As for the NHS working group on mesh, that wasn't fit for purpose either because people - I don't know whether they're aware that 18 months down the line, I was on this committee and I was sidelined 18 months down the line along with the other people who were patient representatives. We were only told they kept on two from the MHRA [REDACTED] and Neil someone, can't remember his name and a surgeon. The patients' representatives were removed and they gave themselves a new title which was very good of them. I thought to give themselves a new title and they brought all these people in and we didn't know who they were.

I spent a whole morning and a day 18 months later looking for a final report because I couldn't get hold of it. They wanted me to read it and give my thoughts to them the next day at half past nine in the morning. Well, I have to tell you, I'm not even awake at half past nine in the morning. So, to read a 63-page document that I couldn't get hold of was never going to happen. But this group they created called the Oversight Group, we were never included in what they were talking...

David Hughes: That's why it was an oversight.

Teresa Hughes: Pardon?

David Hughes: That's why it was an oversight.

Teresa Hughes: Yeah, it was an oversight, a big oversight actually and Professor Keith Willett has a lot to answer for. I'd like to ask him why he did this. But I was so angry at the time, I wouldn't take his call. So, four patient reps, they actually resigned within this 18 months that was left when this mesh Oversight Group was created. We never got any minutes from them. We had to keep asking, where are the minutes. It was just impossible. It was a fiasco. It was a disgrace and he needs investigating for that alone and the cost of what it was and what it achieved. Because it achieved absolutely nothing. They didn't listen, they kept talking about success, they weren't interested in whether we were injured, how we could get help. There was nothing there. How I kept my temper I don't know.

Julia Cumberlege: I know bureaucracies are very difficult to deal with. But I wonder, Simon, do you want to...

Simon Whale: Teresa, could I ask you, you talked about care pathway earlier. I think it would be really helpful from our point of view to hear a little bit more if

you've got thoughts about what a good care pathway would look like for people who are suffering at the moment.

Teresa Hughes: Well, you need contacts. We talk about putting us in touch with the trained surgeons. Well, the trained surgeons were the ones who put the mesh in so we need to gain trust of these people, who they are, why they're called trained surgeons. What have they done to be called trained surgeons? It's all in this loop saying people that are out there. Are you with me? I mean, I was lied to by [REDACTED], Are they part of this trained surgeons? I don't know because I could never go to them if that was the case. So, how do we get over that one? Communicating, sending people to be looked at, we need these women to be looked after with their injuries. Is that what we're talking about? Is this what you're after, the care pathway?

Simon Whale: Yeah. I mean...

Teresa Hughes: That's one way. We need surgeons.

Simon Whale: What about other types of support for women?

Teresa Hughes: Well, they definitely need counselling, definitely. Because I tell you what, I wanted to do myself in many a time and that's no kidding. You know, I've sat on the end of a phone with a woman, many women who wanted to die and they never knew, yeah, I want to die with you. This is how bad it is. So, there is counselling there to be had.

Other methods of what can be used or not used instead of this mesh?

Simon Whale: Would it help to have help and advice about how to get through the benefits system for people who need to claim benefits?

Teresa Hughes: Well, it would. I mean, it's a minefield out there. I've been there myself. You do need help but we have these injuries, they're invisible. I'm sure you've heard this before. They're not recognised. Who's going to recognise us as being injured, disabled, why are we like this? That's another area. Do you have any?

David Hughes: No, it's absolutely right in that sense. They do need help. We've been through the process of a PIP assessment and it was bloody horrendous. That's as much as I can say, it was bloody horrendous.

Julia Cumberlege: Did you get it in the end?

David Hughes: We still don't know. This is four months ago and we don't know what's happened, what the result is. After four months. That makes it worse

because you're waiting and waiting and waiting. We don't know. But the actual time spent having the assessment, I wouldn't wish anybody to go through because it's not there for your benefit. It's there to take anything - to not give you anything and that's what you feel when you go in there and you start talking to somebody. They don't want to listen to you. They don't want to know what's wrong with you. They just want to know what you can do or what they believe you can do because when we got the report back and I sat and read it, I didn't want to use the word lies but that's what was put down.

Teresa Hughes: Yeah, it would help if people were given some advice or...

David Hughes: Well, it would.

Teresa Hughes: ...somehow to - I don't really know how you can help, to be honest. I don't know. In that way. But if...

David Hughes: Well, if there was advice...

Teresa Hughes: The government or someone.

David Hughes: ...to help people get some sort of benefits if it was duly needed and was correct, yes, that would be good.

Julia Cumberlege: David, can I ask you what impact it's made on you?

David Hughes: Yeah. It's a funny one, really, this because I am a very positive person which is a good job but I get depressed. I get fed up. But I can't, can I? That's it in a nutshell, really. I've watched Teresa go through hell and I know even going forward that's not going to improve. It may go worse. But I've got to get up each day and start again. It's made a big difference to our life, as I'm sure you can understand. I could talk about it but it's not going to make any difference. The fact of the matter is it's not been easy and it's not been easy for a lot of people because I know people have separated from their partners through this and I can understand why.

Sometimes we live, breathe and eat it until it just gets on my damned nerves, to be honest. That the conversation will go around - sorry - to the same thing and I just want to turn off. One of the things when we had the PIP assessment and going back all over the past, I do not want to go over the past. I want to move forward. The best that we can do. But that's not at all easy to do. But I will, but that's me. That's not everybody unfortunately.

Julia Cumberlege: We have heard similar things from other partners and husbands actually. I know. Is there anything else you want to tell us?

Teresa Hughes: I'm lucky to be here today, to be honest. I had two heart attacks.

Julia Cumberlege: Just the fact that you've come today means a lot to us. Thank you so much. We thank you and David for coming. Is there something else you wanted to say?

Teresa Hughes: No, I was just saying when I had my heart attacks a few months ago, the choice there was for living or dying and giving me stents or stents and mesh. But I was told.

Julia Cumberlege: I'm so sorry what you've been through, both of you. I mean, it's been horrendous. Absolutely understand that. But I think the support that you're giving to other women is really very remarkable and very, very helpful to them. The fact you're here today is important to us.

Cyril Chantler: You have done a lot, I mean, a huge amount. We wouldn't be here without the efforts of you and people like you.

Teresa Hughes: I'd like to see this mesh banned, basically. It shouldn't even be out there, it should never have got this far.

Julia Cumberlege: We're going to be looking at what's happened in the past and what should have been done and hasn't been done and who should have done it. We're also looking at present people who are going through such suffering with mesh and what we can try and do to help them. As you were saying, David, we want to look forward to make sure that this sort of thing doesn't happen again. [Unclear] all the things we can think of to try and prevent this sort of tragedy from happening. But I do want to thank you so much for coming.

David Hughes: I think we both appreciate the difficulty that you've got.

Julia Cumberlege: [Unclear]

Teresa Hughes: No, you have because I've been sort of in your place on a smaller scale and David's been there as well and we know what it's like to sit and listen to harrowing tales, unfortunately. So, I just hope -what about compensation anyhow, I just thought of that one. I want compensation. How can we [unclear] that one?

David Hughes: You've got compensation, you've got me. That's the only compensation you're going to get.

Teresa Hughes: I want compensation from the government, I've just realised. Why can't I have it?

Julia Cumberlege: Thinking about the sort of redress that we can help with. Compensation is quite a difficult word and we obviously have to think about that in some depth. Because we of course can't access anything. I mean, in terms of we're not executive. We can only recommend and then it's really for other people to pick up our recommendations. But you will recognise that we have the pause where we said this should stop happening until the five different areas that we knew were doing harm should be mitigated that should stop.

So, we have taken action already to try and improve things. We do know the numbers of people who were having mesh inserted has gone down dramatically and I don't say it's all for us because of us. It could have been very well for all you and your groups, different patient groups for bringing this to the attention. But that's good that we're seeing a tremendous reduction in the numbers. So that's important.

Cyril Chantler: We are working on many of the suggestions that you've made to us both when we met before and in writing.

END OF TRANSCRIPT

Session 4: Welsh Mesh Support Group

START OF TRANSCRIPT

Julia Cumberlege: I want to say that to set the tone we're not like a health select committee which is a very robust affair and you know there's a lot of questions and answers and that. We're seeing this much more as a conversation, so it's really up to you to tell us what you want us to hear.

Jemima Williams: Okay.

Julia Cumberlege: We're here to learn and to take on board what you're telling us. We know who you are because we've got name plates here. So I imagine Jemima you're going to speak first.

Jemima Williams: If that's okay, yes, I will.

Julia Cumberlege: Thank you for being [unclear] which was very generous...

[Over speaking]

Julia Cumberlege: Thank you for that.

Jemima Williams: No, no, not all, we - at last we're having our voices heard. We've been campaigning for a very long time and I feel that we all really deeply appreciate this, all of us. So I want to read things to you because I've got a really dreadful memory and quite often I get quite muddled up. So I'd rather - what I will do, I won't read out my whole statement because Den and I wrote our statements separately and so overshadowed and I don't want us to repeat everything.

Dennis's presentation has got a lot of what happened to me purely because it leads to knowledge of what is happening right across the country. So if I may I'm going to stand up and read a little of what I've written.

Julia Cumberlege: Yes, and can I say if you feel you've had enough of something we can always take your testimonies.

Jemima Williams: Yes.

[Over speaking]

Jemima Williams: I've got some separate ones. Mine I've highlighted and scribbled on but I've got some separate ones that will be legible hopefully and you may. So, yes, so firstly I would like to thank you Baroness Cumberlege and Sir Cyril Chantler and the rest of the team for coming down to Wales. I'd like to say that we were all deeply upset that there was no official support at that meeting either from the Welsh Cabinet Health Secretary Vaughan Gething, or from the Women's Health Implementation Group, WHIG, despite your and our invitation to them to attend.

We are shocked and deeply disappointed that a meeting so important regarding the future safety of patients in Wales, especially considering the serious nature of our injuries, has been ignored by the very people that should be protecting us. Your call for evidence should have actually been made mandatory because more patients then would have come forward for the whole spectrum of the things that you are...

We believe that that was a serious waste of government money that it wasn't made mandatory and a waste of time, your time and effort, and taxpayers' money because it should have been made mandatory. So in Wales we need - well all across the UK, we need to see urgent action for treating mesh-injured patients, cross border funding for people living in Wales and in rural parts of the UK, where they're unable to get to the places of clinical expertise, which actually not one of us in Wales has seen come to fruition as yet.

Although as a direct result of our work with the Welsh Government, with the help of Scottish mesh survivors and with the help of global mesh survivors, we've actually - the Welsh Government has paid attention to us and Vaughan Gething has set aside £1 million. He's set up the Women's Health Implementation Group in order to carry forward the recommendations that Welsh mesh survivors and global mesh survivors have made to them.

We need access to surgeons that are experienced to deal with our own particular problems wherever they may be in the UK. We urgently need expertly trained surgeons with access to updated equipment such as translabial and ultrasound scans. Hernia and rectopexy patients must have access to treatment urgently as well as pelvic mesh-injured women. There is horrific suffering with no other option for patients than surgical mesh if they have a problem.

[Redacted] has a prolapsed rectum and a hernia and his only option in Wales has been for him to have hernia mesh and a STARR repair, which causes horror to our family because of what I've been through and what I'm going through even after 16 years. We are very pleased to see the NICE guidelines have urged that these translabial scans, et cetera, should be made available. I hope they'll be made available on the NHS immediately.

Many mesh survivors' own personal experience is that they are far more successful in visualising the mesh which is not actually MRI opaque. We also need expertly trained radiographers with the skills to be able to read them. At present in Wales due to a freedom of information that I sent off we've been told that there is only one 2D scanner available for these translabial scans and only one expert that can read them.

As you've all heard, there are many people suffering in the UK today. We need urgent financial help. Many have had to give up their jobs, many relationships are broken. Some mesh survivors are very, very young and have young families and they've been left in wheelchairs and some can't afford these wheelchairs and there's no access to funding and they're now unable to earn money for themselves in order to buy them.

Benefit assessors are forever patient shaming. We've had this experience, I went myself. This has really got to stop and somebody needs to stand up and help us in this because our injuries are so taboo and it's very difficult. My assessor was meant to have been a male. Luckily he was away that day and so I was assessed by a female and she was absolutely

horrible. Anyway, what I'd like to say next I think is most important for all mesh survivors.

What about the children? Mesh survivors are extremely worried about the effect that our serious health problems are having on our children even the young adult children. We do not believe that there's been enough attention paid to this. We have heard that families have been broken apart and some very young children have been taken into care. The emotional and mental strain on the whole family is appalling and there is often a complete lack of understanding by health professionals and there's no support.

We feel that the children and partners need support through expert counselling. Here are a few quotes from some of the children of mesh survivors. A 20 year old student daughter whom everyone thought was coping very well despite her mother being told to prepare her children for her death. 'Every time I think of my graduation day I cry. I am worried that you will not be around. I need you mum. How will I know and learn what to do when I have a baby of my own?'

A nine year old son – 'I hate my mother. Why can't she just be brave? I don't want her to come to my school with a walking stick.' A 20 year old son suffering with severe depression, locked in his room for the last two years submitted a very eloquent letter to the review team. At the end he says, 'I doubt whether my mother will be around to meet my children,' and his reminder of the earliest Hippocratic Oath, first do no harm, and his appeal to the review team to do the right thing.

Mesh survivors, patient advocates - you hear heart-breaking testimonials from Welsh sisters and brothers and of their families all too often. Better understanding of the effect on families is needed and counselling must be made available to all of those affected. We want answers but more importantly we want urgent action to be taken in order to help patients now. Bear with me for just one moment.

Mesh survivors would like to ask the question, why hasn't the use of hernia mesh and rectopexy mesh been investigated by the UK Government? The Scottish Cabinet Health Secretary, the present one, has recently announced plans to do so. What about the rest of the UK? Please all of you remember our children's words, first do no harm.

This is a global medical health disaster. Most mesh survivors want to see a complete ban on the use of surgical mesh implants. We feel that any research, any new research should be carried out on willing patients who

have already undergone a surgical mesh implant operation with lifelong follow up. Expert treatment should be urgently made available to us all. As you know, from reading the recent random FDA reports that we sent in as part of Welsh Mesh Survivor experience, people are coming forward to report these adverse events, up to 18 years after the implant surgery has taken place.

I am still awaiting adverse events reports from the MHRA. My freedom of information request has hitherto been ignored. In our view, the MHRA are not fit for purpose. In the recent NICE guidelines, the new recent - they say that they will - well consider the division of mesh slings for women with voiding dysfunction. It still leaves the mesh in situ which will grate and cut and slice. The same must be said for a partial removal. I've experienced all of these things.

We all know that a failed mesh implant can lead to hardened broken pieces of mesh being embedded, grating and cutting and slicing into pelvic organs, into the vagina, the rectum, and erosion occurs. It may become embedded in spinal tissue which is what has happened to me. Allow me if you will to give you an analogy. Say you had a major car accident with a milk cart and ended up with a broken milk bottle left deep inside you.

When one centimetre migrated and was poking through your vaginal wall your surgeon says to you, don't worry - or into your rectum, this - men and women, hernia mesh, don't worry, we'll trim off that part and we'll give you some cream, some oestrogen cream, and we'll make a plaster over that with your natural tissue and you'll be fine. But the milk bottle is still inside you. It's still cutting you, it's still grating, it's causing such extreme pain that people attempt suicide, some people attempt suicide. I almost jumped off a cliff in 2005.

It was only the thought of my children and it was only hearing children behind me playing in the field that brought me back to think, oh my God, what will my children do and what will my husband do? We've got seven children between us. My youngest was aged four when I had my implant. I can't say anymore, I'm sorry. No one is thinking about this sensibly, logically, or compassionately.

It's not about a little bit of pain. Please go onto YouTube. There is a discussion between CMO Sally Davies and Jeremy Hunt and they talk about pelvic mesh. This will be the last I'll say now because I've really - I'm at the end of. So CMO Sally Davies and former Cabinet Health Secretary Jeremy Hunt they talk about us as though we are cattle - 'these women'. Some have pain but some women can benefit. Complication

rates are 15 per cent to 20 per cent and I'm thinking one in 15 women that have mesh implants, one in 15, have to have mesh removal. That's the NHS's own figures.

So then Sally Davies goes on to say, if you have a good surgeon, I mean a good surgeon - we all thought we had a good surgeon. She then goes onto say, and if you have the right patient. We were all told that we were the right patient to have this operation. Then they talk about consent. Mesh survivors are not just talking about pain, we are talking about pain that leads some people to commit suicide.

Some have a high risk of sepsis. I've been told this. I've been offered a colostomy. I don't want a colostomy. I want to be able to live my life. Then they go on to talk about consent. Mesh survivors are not interested in being consented to these operations, in future patients being consented. Mesh survivors mostly all of them want to see a ban on this. We don't want future patients to have to go through what we have gone through and consent is all about protecting the surgeon. It's not about protecting the patient.

Because even if you are consented it doesn't mean you're not going to feel pain after. It doesn't mean that you're not going to have complications after. But what it does mean, is as has been found out in Scotland recently, possibly yesterday, if you've been consented my darlings, you cannot sue. That's all I've got to say. Thank you for listening.

Julia Cumberlege: Jemima that's very powerful [unclear].

Jemima Williams: Thank you for listening.

Julia Cumberlege: I don't know if your husband wants to [unclear]

Dr Dennis Williams: Yes, by all means. I mean if you're quite happy for me - I've got various things that I want to talk about and I'm sorry if there's any crossover because there certainly will be in some of it. I'm here to support my wife really and the Welsh Mesh Supporters Group but I'm also a GP, well at least I'm a recently retired GP. Therefore I think I'm in a unique position in that I'm the partner of somebody who has suffered with a mesh for 16 years, and I've actually dealt with patients myself who presented to me when I was ignorant of mesh and subsequently when I knew more about it.

If you don't mind I will read what I've got here but I won't read it as verbatim. I know that over the last few months you've heard

innumerable horror stories about patients who have had mesh inserted and the complications that it can cause, and our story isn't any different. Jemima has given birth to four beautiful boys and had several miscarriages so it's not surprising that she developed some stress urinary incontinence after that.

She managed it very well to start off but when she actually had incontinence during intercourse she became very upset understandably and wanted to go and see someone to get it sorted out. Being in the medical profession I actually knew many of the local gynaecologists because I trained in Cardiff as well. So I recommended a consultant that I knew very well and had a lot of respect for. In order to not push ourselves through the NHS we decided to go privately so we saw him privately for a consultation.

Almost within half of hour of us being with him he suggested that he'd put this wonderful stuff call mesh in which would solve all the problems. He didn't suggest urodynamics, he didn't suggest referral to a physiotherapist for pelvic floor exercises, none of this. He just said, look, I'll do this, you'll be a new woman, it will change your life. It certainly did change her life. It just has gone on from there. About three weeks after the operation Jemima was in excruciating pain so we went back to see him and some of the mesh had perforated through into the vagina, at the vaginal vault.

This was - he said, oh, no problem, I'll sort that out, very unusual, never seen this before, you're unique, we'll sort it. So he basically trimmed the bit of mesh off, stitched it back up and said, go away you'll be fine now there'll be nothing else going on. About two months later Jemima was admitted as an emergency to the district general hospital and ended up with a laparotomy where they removed a lot of the vaginal mesh that they could find. We were actually told by the two senior consultants that were involved in her care that they'd completely removed the mesh.

So we went home, Jemima was okay for a few weeks, plus a couple of months even. By okay I mean she was recovering from major surgery. Then she started complaining of exactly the same symptoms that she'd had previously but we'd been told that the mesh had been removed and in my naivety I said, 'well look it's not there anymore, they've said it's out'. But because her symptoms got progressively worse we ended up going back to the hospital seeing the same consultants that we saw before.

After a lot of pressure and a lot of the fact that she was really toxic and unwell and they knew they had to do something she ended up in theatre

again and surprise, surprise they removed more mesh. But again told us, now this mesh has been totally removed and that's not just to my wife but this is medical colleagues telling me knowing I was a doctor that they had removed all this stuff from my wife. Jemima has still got mesh inside her. So we were lied to by professionals who I trusted. I actually disbelieved my wife and believed them and it caused a tremendous amount of problems.

We actually nearly split up because of it. It's actually left - I have to say, as Jemima has already said, our youngest son was four year old, he's never actually seen Jemima the way I knew her. Before he was born she was a very bubbly, active, physical lady, walked miles. If she said I'm going to take the baby out in the pram literally she would walk four or five miles with a baby in the pram, see she was so active. Now she's on a stick, she can't move. We can't drive for more than an hour before she's got to get out of the car.

Jemima Williams: Now I can't drive. Anyway...

Dr Dennis Williams: No, [unclear] now darling, thank you. So despite my insistence that her symptoms were due to - not due to mesh I was proved wrong and she was proved right. In truth it was Jemima who taught me about mesh, she was the one who researched it, she was the one who got onto the worldwide web and found all these men and women in other countries around the world who were suffering similar problems, even though she'd been told on several occasions that she was unique.

Once I became aware of mesh myself and started taking some interest in it, not as much my wife did, because she's suffering the symptoms every day. But I suddenly realised this was a major issue and so I went to my colleagues. It just so happened that Jemima was registered with my group practice but not - never seen by me but seen by my female colleague. Because she'd been so ill she was seen quite frequently and they thought she was a hypochondriac.

When all this thing about mesh came through I thought I'll try and enlighten their minds. We actually had an academic practice meeting and I sat down and I said, 'right, I'm going to give you a talk about mesh and tell you how much I know now.' It was like on deaf ears, they just didn't want to know, it was nothing to do with them. They felt that this was a gynaecological problem and that as GPs all they could do was refer the patients on.

If I could get onto that, if I put my GP hat on for a moment, we all know how busy GPs are, we know they're under great pressure because of workloads, they're under financial restraints, all the other things that go on. I've worked in it for 40 years so I know. One of my favourite quotes is the difference between a consultant and a general practitioner, as I'm sure you've heard many times. But a consultant knows more and more about less and less until he knows everything about nothing, and a GP is one who knows less and less about more and more until he knows nothing about everything.

I only say that just to give an idea of how diverse the GPs knowledge has to be. If you go into an average GP waiting room I suspect there are very few patients with the same diagnosis at the end of the day. So your morning surgery can have 20 patients that will be different, different diagnosis, different disease entities. So [unclear] the GPs are not gynaecologists, they're not surgeons in the main, there are very few gynaecologists and surgeons who have gone into general practice.

They will have had some training in obs and gynae whilst they were students and some will have done the DRCOG as I did. But their main knowledge base is gleaned from general practice, from experience within general practice of dealing with these ladies who come into see us. The GPs are the first port of call for the majority of patients and I come from my own experience if somebody - if a lady came to me with stress urine incontinence or pelvic organ prolapse what would I do as a GP.

I'd do a brief examination, I'd make sure that she didn't have a urinary tract infection, all the simple things that you can do easily in practice but then I would recommend that she be referred to a gynaecologist for specialist advice and possible treatment. When that occurred the GP will send a letter off to the consultant and we wouldn't hear - see the patient for months because the waiting lists on the NHS as you know are very long in some areas, particularly in parts of Wales.

Eventually we'd get a letter from the gynaecologist saying, yes, I agree with your diagnosis, this lady has this, I intend to operate and we'll be writing again in due course when the operation has taken place. Therefore we wouldn't see that patient again for several months unless their symptoms have deteriorated. But eventually we'd get another letter which would say, the operation has been done, patient has been discharged back to your care essentially.

Not one mention of how - what - that they've put mesh in. Not one mention about any immediate post-operative side effects. These letters

certainly in my experience until recently were very brief and they would just literally tell you the minimum. GPs certainly were never informed that mesh had been inserted. So the GP is ignorant of this fact. So if somebody - if a lady then came back with early mesh rejection or in the first six to eight weeks post-op the GP would do the normal thing.

He'd check if they were pyrexia, checks whether they've got a UTI, possibly do a vaginal swab if they think they've got a foul discharge, all these things, and only send them back to the consultant - and then perhaps treat them possibly with analgesia and antibiotics if they thought it was appropriate. But they would only send them back to the gynaecologist if they think there was something wrong with the patient due to the operation itself.

That didn't take place that often because if you treat them you mask things for a while, and because the GP didn't know there was mesh that had been inserted mesh didn't even come into their minds. They didn't know anything about surgical techniques, they didn't know about the materials that were put in. I could guarantee you if you walked into any general practice in the UK and showed the GPs a piece of mesh very few of them would know immediately what it was. They have no idea. It's not because they don't want to know, it's because they've never - they don't work in that sphere.

So GPs as a rule are ignorant of what is going on with the gynaecologists in hospital. The worst part of it is when you send the patient back to the gynaecologist and say, look, there's something wrong with this patient they'll do - they often get sent back to the GP saying well everything is fine, nothing wrong, don't worry about it. So GPs don't know the early signs of mesh rejection, they don't know the long term signs of mesh rejection.

As Jemima said earlier, some patients 16 to 18 years post-operation are getting mesh rejection or the - you know yourself, if you've ever seen mesh that's been pulled it's like Bakelite. It gets - and it's brittle. So that therefore creates tremendous problems for the GP who is trying to deal with a patient. If you think about it if someone comes back to you 10 years after they've had a mesh insertion for a POP or SUJ, unless they're specifically talking about gynaecological issues then they're not going to think for one minute it was due to the initial operation.

They don't and they'll often come along with pain, unexplained abdominal pain, pain in their legs, lower back pain, dyspareunia, all these sorts of things. These patients then get sent anywhere but where they should be

sent. They go to orthopaedics, they go to general surgeons, they will go to physiotherapists but most - and they end up in the pain clinic. The majority of these people end up in the pain clinic. Then they get given painkillers, they get analgesics, they get other medications such as amitriptyline and stuff like that which makes them worse.

When we had a meeting in parliament a couple of years ago there was one gentleman there who spoke about his wife who had actually become toxic because of the medication she was given for her mesh problems, which created - in fact she was really extremely unwell because she had a terrible reaction to the medication.

Jemima Williams: A lot of people become zombified by it.

Dr Dennis Williams: So again what I'm trying to get to with all of this is that there isn't an excuse for a lack of knowledge but in the GPs - from my GP view they're not informed of what is going on. I've listed several things here that may be relevant. My colleagues in general practice need to be much better informed of the side effects of mesh and a programme should be established as soon as possible to educate them.

GPs need to be aware of the fact that some mesh operations result in a side effect rate of 15 per cent to 20 per cent and that was quoted by Sally Davies herself and that at least one in 15 women will need their mesh removed quite early on. So these are the things that I've plucked out of the air to try and enlighten my colleagues a bit more. GPs - the names of all patients who have mesh inserted during surgery should be entered on a registry. Well that's been said by half a dozen, the BMJ, and other journals.

It's now in the new NICE guidelines that this has to happen. Fine, that's good but GPs are not - should have that available to them as well. If they ask for that information they should have it. In all honesty it might actually be relevant since we're now sending paperless information to GPs, you can just as easily send that information across with the discharge letter and the patient, so they've got that information available to them.

GPs should have open access to the surgeon that's done the operation. There is nothing worse than you phone up about a patient that you're concerned about and you get put through a registrar who has never seen the patient, and the consultant is unavailable. That is not on. We spoke about this in Cardiff. In my day when I first came in - and I know it's in Sir Cyril's day - we had very great sort of camaraderie between the GPs and the consultants, the local consultants.

You knew them all and they knew you, you were on first name terms but it made life so much easier for the patients. Because you wouldn't break confidential information but what you could do is say, well Mrs Jones how is she doing, that's all you needed to do? Then you could say, well I'm going to send her back to you, is that okay, when can you see her because I think it's quite urgent. That's the sort of thing that used to happen and patients had much better care that way.

I've suggested that GPs should possibly have access to urodynamics and physiotherapists for pelvic floor exercises especially if waiting lists are long. Because this can be done through general practice as long as they have the access to do it, and that saves waiting for outpatients and all the other things that have to be done. Whether that financially is viable I don't know. GPs should be encouraged to discuss the consent information leaflets for proposed mesh surgery with their patients.

In order to do this effectively GPs must be aware about the short- and long-term complications associated with the use of mesh and how difficult many of those complications are to treat. They must also be aware that mesh is meant to be a permanent implant. Lots of GPs aren't, they're really not. If anything goes wrong with a patient whilst they're in hospital the GP should be informed immediately, not by a letter which is going to come weeks later.

Because again this is after the horse has gone isn't it? You need to - if you've going to have a cohesive treatment and support for these patients you've got to know what's going on. If we're going to rectify this tragedy that is mesh, then all health professionals have to admit that it is a major problem and we must work together to get a positive result out of it. We have to. Unfortunately I feel that it will be some time before this happens. I think many surgeons and gynaecologists do not support the suspension of mesh and they certainly don't support a ban on it.

They appear to consider the side effect rate of up to 20 per cent to be acceptable as far as the use of mesh is concerned. Unfortunately even the new NICE guidelines suggest that the continued use of mesh is acceptable if non-surgical treatments are attempted first. I'll come on if I may to go on to the new guidelines afterwards.

My own view is that it is not acceptable to risk a patient's life by inserting mesh for non-life-threatening illnesses such as POP and SUI. It seems illogical to me when we know that we've got this. Another analogy - if a car manufacturer were to place a component in a car that they knew was going to fail in five per cent of cases, not the 20 per cent that we're talking

about with mesh, and then it would likely cause serious injury or death to the passenger, what would happen?

There'd be a public outcry, enormous sanctions and fines would be laid on the manufacturer. But that's exactly what we're doing with mesh. Every time we insert mesh we are actually taking a risk with the patients' lives. You know from the information that you have been given that that is actually true. The figures, the MHRA and NICE and all of them have got their statistics are useless because it's never been recorded properly and that's the biggest issue that we've got.

You've the figures that they've given for side effects are all guesswork but they're not really because - I remember we sat in the Scottish Parliament and the MHRA came to speak to the Scottish Parliament. He said, we have only two cases, this was the gentleman from the MHRA, he said, we have only cases reported with the side effects against mesh. Behind them were 40 women sitting who all had mesh injury and he was laughed out of parliament, not only by the women but actually by the parliament.

Jemima Williams: By parliament themselves.

Dr Dennis Williams: So what my wife said about the MHRA not being fit for purpose is probably true in many ways...

Jemima Williams: It is true.

Dr Dennis Williams: ...unless they start sorting things out. My wife has touched on the fact about the financial aspects that the mesh sufferers are going through. Mesh has a lot of implications. In our own family, as I've said, [REDACTED] didn't know how bad he was and how passionate he was about what had happened [REDACTED] until we actually asked him to write it down, and if you read his submission you will be touched. Lots of patients...

Julia Cumberlege: We're getting a bit short of time.

Jemima Williams: Yes.

Dr Dennis Williams: Oh I do apologise. Can I just therefore...

[Over speaking]

Jemima Williams: ...we'll leave...

Julia Cumberlege: ...it would be helpful if you could leave that with us.

Dr Dennis Williams: I will leave this with you. Can I just add this one quick thing on the new guidelines because this has really concerned me greatly? The new

proposed guidelines - I like the fact that this can be specialist assessment and treatment centres. The - I do apologise, I've lost my track here.

Julia Cumberlege: Don't worry about it.

Dr Dennis Williams: What I was going to say, just one last point is the mesh guidelines- the new guidelines that are coming out from NICE are not fit for purpose. I think they give a green light to surgeons to keep putting mesh in. If you actually look at the surgical procedures that they recommend for SUI and POP once the people have gone through the non-surgical treatments when you get to the end there are three options for SUI and one of them is the insertion of a mesh sling.

If you look at the POP ones, if you [unclear] there are three and there's one mesh in that and there's one mesh if you decide to remove the uterus. They sling all these operations together if they are comparable, they're all a good option. But what NICE has done there is at the end it says, if the surgeon - if the patient chooses a surgical procedure that a surgeon that she has seen can't perform then she can ask to be referred to another surgeon.

How many patients if they've gone through the whole process of the non-surgical treatment and everything else for their SUI are then going to say well I'm going to have another surgeon because you can't do what I want to do. Patients aren't that well-informed and the mesh is continued to be put in and is going to continue to cause problems.

Cyril Chantler: Can I just ask you something about those NICE guidelines because there's something which I didn't quite understand. There didn't seem to be anything I could find saying that we must be careful not to say put it through the [unclear]. You shouldn't put it in if you can't get it out.

Jemima Williams: Exactly.

Cyril Chantler: Did you...

Jemima Williams: No, I haven't seen that.

[Over speaking]

Dr Dennis Williams: Yes, I think - I mean they have said there are certain procedures that they no longer recommend haven't they...

Jemima Williams: Yes.

Julia Cumberlege: Yes.

Dr Dennis Williams: ...and that's one of them?

Jemima Williams: [Procene] mesh they...

Dr Dennis Williams: The other thing is that it's - patients are not going to - that's what it's got in here too. If you look at that paper it's about 45 pages long.

Jemima Williams: It is.

Dr Dennis Williams: The last 13 or 14 pages are entirely on mesh complications and how the surgeon should treat them. There's not one on natural tissue.

Cyril Chantler: Are you going to respond to the consultation?

Dr Dennis Williams: Well they said it's too late now because the date was yesterday that we could respond.

Jemima Williams: The nineteenth.

Dr Dennis Williams: The nineteenth.

Jemima Williams: I did put some - because Jane Hutt, my AM, wrote to me and asked some questions and so I wrote to her after we'd read through it and we'd discussed a few things. But as stakeholders I didn't think that we could actually write to express our concerns or indeed our recommendations. So we put that forward to the Welsh Government in the email to my AM. But can I just say to finish that surgeons really, really need to take more care.

They need - I have to stand up sorry, they need to write down legibly because reading through some of my notes you cannot understand what has happened. The notes need to be more comprehensive in what they have done, either to put the mesh in or to remove it, because never once was I told that my iliac artery had been perforated and stapled, and that my colon was accidentally stapled and my urethra to the pelvic wall and the nerve had become trapped, never once.

They sent me for a colonoscopy whilst that had happened, whilst I was all stapled up like this. They cannot remove those staples from my iliac artery. Nobody ever told me anything around that. I was told that I had some bleeding and I had to have quite a transfusion. If I can just read this out briefly, it's very quick. I had a text from one of - well Sir Cyril actually met her in Cardiff and spoke to her and he came and spoke to her afterwards but she had to have surgery last week.

This is what I'm saying, we need more care. She says, it was scary times going down into theatre, scary times though as just as I was about to have my anaesthetic he said to me, 'so you're having done what you had done last year then.' She had undergone an operation before to have mesh removal and they couldn't find the mesh and so it had to be abandoned because she was bleeding. I said, 'no, I had mesh removed from my bladder last year but they couldn't find the rest' and he was confused.

At this time, someone came into the room from the theatre all gowned up and said to me, 'so you're having bladder and bowel repair then today'. Again I said, 'no, as I had told Mr So and So I only wanted my bowel done' as I would put up with how my bladder was and I didn't want it touched. I panicked at this stage and the anaesthetist said, 'I'm not going any further until this gets sorted'. Then someone went into the theatre to check with Mr So and So who then confirmed it was just bowel.

You can imagine by this time I was scared to death as just about to be sent to sleep, the lack of communication is appalling and should not have been an issue. Good job I had my wits about me on that day. It's appalling, that's absolutely appalling and more care has to be taken and that's all I've got to say.

Dr Dennis Williams: Thank you very much.

Jemima Williams: Thank you very much for hearing us.

Dr Dennis Williams: Sorry to go over time.

Jemima Williams: On and on and over time.

Julia Cumberlege: Can I just say one thing? You started off Jemima talking about urgent action is needed.

Jemima Williams: Yes.

Julia Cumberlege: Well you will appreciate in England - and unfortunately we only cover England - we have taken some action which was the pause but this - and so...

[Over speaking]

Jemima Williams: We do really, really appreciate that.

Julia Cumberlege: Yes, so we're not here just as a bureaucratic organisation, we have actually taken action and we're thinking about further action that we need to take so I thought...

Jemima Williams: Yes, that's wonderful.

Julia Cumberlege: But I mean I know that won't help you but...

Dr Dennis Williams: Well we think that the Welsh Government have to follow suit.

Jemima Williams: I just want future patients not to have to go through what we have been through and I want the patients that have been damaged by this to be treated and to be treated with compassion.

Julia Cumberlege: Yes. Well thank you so much.

Dr Dennis Williams: Thank you, shall I leave this with you?

Jemima Williams: I'll leave this. Could you - Dennis could you please...

Dr Dennis Williams: Yes.

Jemima Williams: Thank you.

[Over speaking]

Dr Dennis Williams: Thank you very much indeed.

Jemima Williams: Thank you very much.

END OF TRANSCRIPT

Session 5: Scottish Mesh Survivors

START OF TRANSCRIPT

Julia Cumberlege: Well the next session that we have is the Scottish Mesh Survivors group and unfortunately because of the distances and the difficulty in getting here they're unable to come today but they have left a testimony that we're going to ask Valerie Brasse, who is our secretary, to read that.

Valerie Brasse: Dear Baroness Cumberlege and the Review Team. Thank you for inviting us to provide a written statement on behalf of Scottish Mesh Survivors. Scottish Mesh Survivors represents the thousands of women in Scotland who've been implanted with mesh. The hundreds who've already suffered life-changing injuries and the others who've not yet realised polypropylene resin are the cause of their health problems. We have been campaigning on this issue for six years, lodging a highly successful petition at the Scottish Parliament and securing the first government suspension in the world on mesh implants in June 2014.

We have given evidence to not only the Scottish and UK governments but also Australia and New Zealand where we supported mesh-injured women there to bring about change. While nothing we can do now can alleviate the life-changing injuries suffered by so many women, we are determined no others will suffer as we all have by ensuring all patients and surgeons in future are made aware that mesh is an avoidable risk. It is a lifetime risk. We are calling on all health providers across the United Kingdom to develop uniformity through care pathways and properly informed consent to ensure all patients are given the realistic information they need to make the choices that can change their lives, free from the influence of surgeons.

The Scottish developed patient information leaflet for synthetic vaginal mesh tape procedures for the surgical treatment of SUI in women is now used across the UK. We believe this will give patients a greater understanding of the non-surgical and surgical options available to them. This is something which should be made available in GP surgeries as well as all treating hospitals. Many of us were not even offered physiotherapy prior to surgery despite the fact that it can alleviate symptoms in the majority of cases. Physiotherapy must be the first line of treatment before any surgery is offered. We would also call for the introduction of pelvic floor exercises to be routinely offered to all pregnant women and female high school pupils and greater importance given to prevention.

Our focus is also ensuring that the thousands of mesh-injured women across the country are given the medical help, treatment and support to allow them to live their lives as best they can after the catastrophic outcomes they have suffered. Unlike other parts of the United Kingdom surgeons here in Scotland had favoured the transobturator mesh tapes, associated with the highest risks of chronic pain and nerve damage. We have seen devastating injuries as a result with many of our members suffering crippling side-effects with many now in wheelchairs or dependent on walking aids.

At the present time we believe there is no surgeon in Scotland who can fully remove mesh implants and we face a daily battle trying to get funding for the recognised UK expert mesh removal surgeon and clinic which is based in London. We believe the UK and Scottish governments must as a priority invest in and develop training for specialist mesh removal surgeons, calling on expertise from abroad if necessary. We call for the development of specialist centres offering such service to be accessible to all mesh injured patients regardless of where they live. We call on the government to ensure that these surgeons are not those

who've had any financial links with mesh manufactures or those who have flouted mesh suspensions to continue implanting women, as happened in 750 cases here in Scotland. Those surgeons do not have the confidence of patients and should not be offered as our only option as currently happens. Mesh-injured women should not be subject to the risk of further injury by 'have a go' surgeons.

We believe the United Kingdom and Scottish governments must as a priority invest in and develop training and re-training for gynaecologists and neurologists for non-mesh surgical treatments such as colposuspension and autologous fascial sling. There is urgent need for the proper provision and use of translabial ultrasound scanners across the United Kingdom as this is the only method available to clearly identify mesh inside our bodies. It is a minimally invasive procedure and cheaper than an MRI scan. Currently no surgeon in Scotland is offering this service. It is unacceptable that women here are forced to find funds to attend NHS or private clinics in England or elsewhere for what should be a routine part of monitoring.

As so many mesh-injured women go on to suffer autoimmune illnesses such fibromyalgia, lupus, arthritis as well as constant infections we call for an annual health check to be made to each of us. Research has shown that chronic inflammation can lead to cancer, which is why we believe each of us should be carefully monitored. We call for mandatory reporting of all mesh-related adverse events throughout the United Kingdom for surgeons in line with what has already been agreed in Scotland. We call for a mandatory database, independent from industry, to be established and used across the United Kingdom as the only effective way of monitoring mesh and for this to be considered as a pilot for all future medical implant procedures.

We are calling for the government to scrap the current medical watchdog, the Medicines Healthcare Regulatory Agency as 'not fit for purpose'. It has presided over the metal-on-metal hip scandal, the PIP breast implant scandal, the heart valve scandal, the mesh scandal and many more with little regard to the effect on the quality of life of injured patients. While such an agency is in any way 'paid for by industry', we do not believe it can administer an effective watchdog system. We believe the whole current process is fatally flawed and must be discarded. Unless it is we believe the mesh scandal and others will continue.

This excerpt from the MHRA Committee on Safety of Devices 19 July 2012 is all the evidence needed to explain why radical change is urgently required. They stated, 'if a device is causing havoc but functioning

normally it can only be removed from the market if the device itself is not performing properly or is unsafe'. This shows our current regulator has known of mesh problems for years and chose to do nothing. If they cannot do the job they were given and properly protect patients, who can. Mesh manufacturer Boston Scientific was allowed to investigate itself when it was at the centre of allegations, that it used 'counterfeit polypropylene resin from China'.

The MHRA response caused further concern when they said even if there was counterfeit material there was no evidence of safety issues. Again, they relied on the manufacturer's own assurances rather than an independent investigation. Despite all the pay-outs in the United States and the moratorium on mesh across the United Kingdom, the MHRA continues to state that the 'benefits outweighs the risks', even when non-industry funded world accredited research shows the very opposites 'the risks outweigh the benefits'. When up to one in five can suffer life-changing injuries from a procedure is that not enough to stop and carry out an independent investigation? If you are the MHRA sadly it's not. It is criminal that a Dutch television company were able to get quite far along the regulatory licensing route to register the mesh bag usually used to carry oranges as a mesh implant. That is how shockingly lax our current system is.

We fully support innovation but the current system for implants is fatally flawed and puts patients at dreadful risk. In a catastrophic failure of duty only a tiny fraction of surgeons ever reported adverse incidents to the MHRA. This allowed mesh manufacturers to continue marketing implants some of which had not even been tested on humans with impunity and vigour, making billions of pounds as a result. Mesh implants were seen as a 'cheaper, faster fix' which required less experienced surgeons and saved in quotes, the NHS £200 per procedure. But nobody counted the human cost of that ill-advised £200 saving. In fact the NHS and ultimately the tax payers will face the cost of billions of pounds of treatment and lost jobs as well as the impact on so many families while manufacturers currently face no sanction in the United Kingdom despite the devastation they have caused.

We call on government to follow in the footsteps of the US State Attorney Generals of Washington, Mississippi, Kentucky and California who are taking legal action against manufacturers accused of in quotes, misrepresenting the serious risks of mesh, close quotes. Other states are awaiting the results and the first trial begins in April in Washington. With mesh manufacturers in the United States having already paid out over

three billion to victims, we believe they should be footing the bill for all treatment women here are having to access as well as compensation for the ruined lives they have left in their wake.

We call on the government to take all possible criminal and civil legal action available to pursue mesh manufacturers and to establish a compensation fund to support victims and their families. Too many women have already died or are dying because their symptoms were dismissed or ignored. ██████ went numerous times to her doctor with pain and chronic inflammation type illnesses but instead of being sent for the scan which might have saved her life she was sent to a psychiatrist after being told her pain was in 'all in her head'. ██████ finally got the scan three years too late to be told she only had weeks to live as she developed cancer. ██████ dying wish and legacy is that all mesh-injured women receive the health checks and monitoring she was denied.

But her case is not isolated. We believe there have been many deaths linked to mesh but they've not been highlighted as such with the exception of Eileen Baxter, 75 from Loanhead who became the first in the United Kingdom to have mesh mentioned on her death certificate. Prior to her death in August she spent years in agony suffering recurrent infection and pain only to be dismissed and assured that it wasn't her mesh that was the problem. It is of huge concern to us that despite the evidence of catastrophic injury and deaths, the Scottish Government is still intent on offering mesh, albeit in exceptional circumstances. Why continue to take those risks when there are alternative methods which have none of the devastating side-effects of mesh.

The mesh suspension you have recommended in the UK must remain for the following reasons. First, the risks from mesh cannot be mitigated. Clinicians and Clinical Societies have continuously failed to reassure us how they will mitigate the risk. Better training of surgeons doesn't work as the risk is with the mesh device regardless of surgical skill. Two, the risks from mesh cannot be predicted. Clinicians are unable to identify which patients are high risk of developing chronic pain and disability and which are not. It is Russian roulette. Three, the risks from mesh are lifetime. There are reports where after several years of the good outcome surgeons talk about, women can start developing serious injuries later in life.

Four, not all the risks of mesh are known. There are more reports of autoimmune diseases and cancer but the clinicians continue to deny them. Five, the risks from mesh are irreversible. No woman goes back to her normal, even if the mesh device is completely removed. Clinicians

continue to tell us the improvement rate after mesh removal is 50 per cent. This is not good enough. Six, the risks from mesh are entirely avoidable. The present alternative continence procedures, colposuspension and autologous fascial sling are not associated with the irreversible adverse events of mesh. This makes mesh procedures entirely avoidable. If no mesh is used women cannot develop mesh-related injuries.

After six years of campaigning for the safety of women in Scotland, the United Kingdom and beyond we can assure you that no lessons have been learned from the mesh crisis. Therefore your action to suspend the procedures last July was absolutely essential and must continue until the risks and the above six points can be mitigated. Despite campaigns to raise awareness across the United Kingdom, many GPs still remain oblivious to the many side-effects of mesh. As they are the front line for women seeking help we believe there needs to be an urgent and comprehensive training programme rolled out to ensure that they recognise the effects on their patients and what is available to treat them.

We call on the UK Government to continue the UK mesh counselling hotline indefinitely, not just until April when it's due to close. So many mesh-injured women have had to give up jobs. They have lost marriages and homes as a result of being injured. But we still have to fight tooth and nail to claim benefits or even a blue badge to allow us to park with ease. We call on the government to categorise mesh injuries as a recognised disability so injured patients can access the services and support they desperately need. Not all disabilities are visible.

Scotland's First Minister Nicola Sturgeon has given mesh-injured patients her unreserved apology. We call on the UK Prime Minister to follow suit with a meaningful apology. We agree with and support all mesh-injured groups and women across the United Kingdom and beyond because we all want the same thing. Recognition for what has happened to us, the help and treatment we need to get on with our shattered lives and the changes that will ensure this kind of catastrophe can never happen again. Even our own Scottish safety review on mesh was a 'whitewash', which has since been discredited in great part due to the number of so-called independent experts who failed to declare their interests.

We have been let down by the clinicians who were supposed to look after us as patients and by the government officials who were supposed to look after us as safety campaigners. Our trust is now in the independence of your Review as you did believe patients. As Scotland's former Health Secretary Alex Neil who ensured Scotland became the first in the world to

suspend the use of mesh said 'these injured women were all I needed to see to know something was very badly wrong with this procedure'. It is not enough to say sorry or that lessons will be learned. Those were the same words that were said after Thalidomide or the blood [prodex] scandal.

The human cost is far too high for this scandal to pass without meaningful challenge. To quote another mesh victim, 'I feel as though I am an unsuspecting, unwilling participant in a cruel experiment that has gone wrong'. This is how many of us feel. What has happened to us cannot be allowed to happen ever again. We would like to thank Baroness Cumberlege for taking the steps she has already taken and applaud her and her team for putting patients at the heart of this long overdue review. We have been heartened by her stance and determination to hear our voice which has been our campaign slogan from the beginning. Yours sincerely Elaine Holmes and Olive McIlroy.

Julia Cumberlege: Well, can I thank very much Elaine Holmes and Olive McIlroy, and on behalf of the Scottish Mesh Survivors that was a very powerful testimony and we are very, very grateful to have received it and will take note. Can I thank you, Valerie Brasse, for reading it so clearly and so well. It's been a very interesting session. Thank you.

END OF TRANSCRIPT

26th November 2018

Session 1: Association for Children Damaged by Hormone Pregnancy Tests (ACDHPT)

START OF TRANSCRIPT

Marie Lyon: My name is Marie Lyon. I am Chair of the Association for Children Damaged by Hormone Pregnancy Tests and I've agreed today to give oral evidence on why we feel that there is a link between hormone pregnancy tests and adverse effects.

Daniel Mason is here. Daniel is a patient representative for our members. I will be telling you today about his experience living with the effects of hormone pregnancy test.

Julia Cumberlege: If I could just say very briefly that we've had informal meetings and a lot with patient groups, and thank you for arranging those meetings which have been very informative and helpful to us. We're now in the next stage which is the oral hearings and this is your chance to put on the record your views, statements you want. We'd like to hear also from Daniel this morning.

Just to say that we do see this as much more as a conversation rather than just a - well, like a Select Committee, which is very robust. We're not into that. Just to say that we've only got just under three-quarters of an hour, so it's up to you to keep to time. I hope that's all right.

I think this is another member of your team who has just come in. Nicky, I wonder once you've taken off your coat and sat down whether you'd just quickly like to introduce yourself because I think you're here as a patient representative. Is that right?

Nicky Gubbins: Yes.

Julia Cumberlege: Right, okay. Well, I think we know that. Thanks very much. So, Marie, it's over to you to however you'd like to do this, whether you'd like us to hear from Daniel or from Nicky first or whether you'd like to make a statement first? What would you like to do?

Marie Lyon: My original intention was to make the statement first. But if it would help for you to listen to the patient representatives first...

Julia Cumberlege: Please, yes.

Marie Lyon: ...I really don't mind. I've spoken to Daniel and I'm sure Nicky would feel the same, they're willing to basically give their evidence whenever you feel it's appropriate. So, I will leave the decision to you.

Julia Cumberlege: Right, okay. Up to you. Why don't you start with your statement?

Marie Lyon: In that case, yes, if you don't mind, I will. Obviously, I've already introduced Daniel and Nicky, so you understand that they will actually be telling you their experiences.

Our association was established in '78 when we first became aware of evidence linking an association between hormone pregnancy tests, congenital malformations, miscarriages and stillbirths. Exactly 40 years later, we're still fighting to prove the association between HPTs and adverse effects, and by that I mean the scientific association. Throughout the 40 years, the burden of proof has been placed on us. We are asked to provide the science to prove a causal association between HPTs and adverse effects. We feel this demand is both unethical and unrealistic and it appears that even today, science negates the need to acknowledge medical ethics and moral responsibility.

The phrase used repeatedly is it's all in the past and it's not relevant today, and yet the components contained in Primodos are in medicines today with no definitive proof of their safety. Is it all in the past and not relevant for parents in their seventies who are still full-time carers for their children now in their forties and fifties? Is it all in the past for mothers, including me, who live with the constant guilt that we didn't question our trusted family doctor. Were our doctors even aware that the tablets they gave us were 40 times the strength of a lower contraceptive pill?

What about the children damaged by HPTs? Well, you can decide if it's all in the past and not relevant today after you've listened to Daniel and Nicky share their experience of living every single day with these life-changing effects.

Is the Primodos campaign relevant today? Yes, it is. By failing to acknowledge and take action on the warnings of adverse effects with HPTs, the regulatory process was allowed to continue unchallenged when it was clearly not fit for purpose. Neither Schering nor the regulator took action to protect the consumer by withdrawing the drug until further testing had been carried out. Instead, the Chief Medical Officer of the Committee on Safety of Medicines contacted Schering and, I quote, in an unofficial way I want to warn them about his study which had revealed

one in five babies would be born with birth defects, which is an overall 20 per cent risk. If you take Primodos in relation to normal abnormalities, it's 10 times more than the normal abnormalities.

Dr Inman said he wanted to give Schering time to remove the drug from the market to avoid medicolegal problems by taking action now. This was six months before the first government health warning was released to the medical community. In fact, documents show that Schering assessed their own inactivity as potentially illegal by stating medicolegally we would get into difficulties both as a company and as individuals.

Today, we have victims of sodium valproate and surgical mesh who would have been spared their agonising injuries if these failings had been acknowledged and a robust, independent regulatory process implemented, a process where regulators would place the health of the consumer first by acknowledging, investigating and more importantly acting promptly on adverse reaction reports. Appropriate safety measures must prioritise consumer safety and not protection of the pharmaceutical industry.

Sadly, the current failures indicated by surgical mesh and sodium valproate prove the regulatory process is still not fit for purpose today. The Hippocratic oath, which is still relevant today, is the earliest documented expression of medical ethics and includes the requirement to prescribe only beneficial treatments and refrain from causing harm. Primodos was not a beneficial treatment. It was a test. There was no therapeutic benefit when used as a pregnancy test, only associated risk and eventual harm. It is indisputable that the requirements at the heart of the ethical code in the Hippocratic oath were completely disregarded.

It is important to reference the Hippocratic oath to highlight the ethical and moral failures by the regulator and Schering, failures which have never been acknowledged or investigated. Instead, the focus remains firmly on proving the science.

A further requirement of the review is to assess the historic evidence relating to the science and what was known in its lifetime and whether there appears to be flaws in the gathering of that scientific evidence or questions over its independence or interpretation. Documents we have show that there were flaws in the gathering of historical scientific evidence and doubt about its independence and interpretation. The most recent example is the expert working group review published in 2017. The group concluded there was no causal association, yet when measured

against the WHO World Health Organisation Uppsala paper on assessment of causality, evidence of a possible causality is clear.

Measures contained in the assessment model are - is a positive association in animal studies which show malformations and embryo lethality present. The expert working group reports state that a combination of norethisterone and ethinylestradiol showed consistent embryo lethality in different animal species. Evidence of malformations in Schering's animal studies were also in the report.

A second measure from Uppsala is a reasonable time relationship to drug intake. The report also states the likely window for HPT use covers most of the critical period of foetal development, therefore the first criteria for possible drug-related effects was considered met. Both of these statements are from the 2017 group report, yet the group failed to acknowledge this evidence as proof of a causal association. Additional evidence of abnormalities and embryo lethality is contained in many animal experiments conducted by Schering in the 1960s and '70s. These experiments show malformations and dying off of the majority of fetuses at doses close to the human equivalent.

Once again, science is to be the focus of a review into failures by the regulator, not why many warnings were suppressed by the regulator, not why it took five years after removing the indication of pregnancy before the first government health warning was issued in 1975.

A further warning issued in 1977 states further results have now been published and the association is confirmed. Norway did take these warnings seriously and banned Primodos in 1970 immediately followed by other European countries. The UK regulator did nothing. Instead, in February 1970, with, and I quote, the approbation of the government Chief Medical Officer, Dr Inman, Bayer Schering discreetly withdrew the indication for use as a pregnancy test but crucially, did not inform anyone in the medical profession that the indication had been withdrawn. The review also asked whether the processes pursued when safety concerns were raised have been sufficient and satisfactory. I think it is apparent they were not. Measures to protect the consumer including warning leaflets or withdrawal of the drug were not pursued.

Also asked is whether problems could have been recognised by the relevant bodies. Documents found in both Kew archives and Landesarchiv Berlin prove that the problems were recognised, disregarded and suppressed. The Committee on Safety of Drugs was established in June 1963, and in 1964 incorporated the metabolic reactions research unit.

These government agencies were established after the thalidomide tragedy, specifically to ensure this could never happen again. One of the terms of reference for the research unit was to assemble and assess reports about adverse effects on drugs with the main objective to study mode of action on certain hormones. The hormones weren't specified.

The first safety warning that we discovered and I know that there were more, but this was the first one we discovered about certain hormones was raised by Dr Edwards in 1958, quickly followed by many documented warnings from scientists and members of the medical profession culminating in the first scientific review published in the scientific journal *Nature* in 1967. The regulators once again did nothing except document their awareness of these warnings. They took no action to alert either the medical profession or the public until 17 years after the first - sorry, after the first concerns were received and eight years after the first study was published.

Dr Inman stated we have no excuse for the eight year delay. I feel there was also no excuse for the 17 years of inaction after the first warning in 1958. There were 3540 adverse effects reported on the yellow card system relating to ethinylestradiol and norethisterone, which are components of Primodos. The MHRA acknowledged that the yellow card system is associated with an unknown level of under-reporting. It's said to be about 10 per cent of all reports that actually get sent through, which Dr Inman also acknowledged and also stated the system was unfit to detect a teratogenic effect. The review asked if the same bodies could and should have acted on concerns sooner and, if they did not, the reasons why. The same bodies should and could have acted on concerns immediately the first warnings about its safety as a pregnancy test received by the regulator.

The reason why no action was taken is simple and contemptible. The regulator wanted to protect Schering's oral contraceptive pill which had the same components as Primodos. The failure to act on these concerns also ensured protection of Schering's total group sales of two billion Deutschmarks.

In 1966, there were three deaths and 51 adverse reaction reports on oral contraceptives in one month. In '67 documents reveal there was a raised pregnancy wastage after using sex hormones of 16. The expected wastage as quoted was seven and a half, more than double.

In '67 Dr Inman stated there is a definite relationship between oral contraceptives and deaths. '67, the annual report on adverse reaction

committee discussed the first study to show a definite risk between thromboembolism and OCs. The committee also established the risk increased by 10 times when using oral contraceptives. They further comment, studies from the medical research council also confirm this causal relationship.

An extract from *Medical News* dated October '67 contained details of a Mexican survey which found a much greater incidence of congenital defects in babies of women who had continued taking oral contraceptives when pregnant. The regulator's response to these warnings was 'we have not altered our view that there is no justification for the withdrawal of oral contraceptives provided they are prescribed by doctors with the knowledge there is some risk.' Yet, documents prove this risk was not disclosed to doctors until 1970. Exactly 50 years after the 1967 warnings, the current regulator concluded in the expert working group report published in 2017 women should be reassured if they inadvertently become pregnant while taking these hormones for contraception.

The documents containing the information on oral contraceptives were discovered in Kew archives, together with minutes from the Committee on Safety of Drugs which stated a change to a lower dose could reduce the total deaths by 50 per cent.

The regulator felt the reports on congenital abnormalities and abortions linked to a pregnancy test with the same components as the oral contraceptive would cause panic amongst women who would stop taking the pill. It was feared that this would have a major effect on the world population, a fear shared by the World Health Organisation, which is documented in the files. This factor is referenced in Dr Inman's memoirs as part of the reason he decided not to withdraw Primodos from the market.

The review's terms of reference will consider and take account of the historical context including requirements of any regulatory or licencing regimes for medical devices and medicines in force at the appropriate time. These regulations and licencing regimes were in place at the appropriate time in the *1968 Medicines Act*, Section 28 Part II, which states, action could be taken if the drug could no longer be regarded as a product which can safely be administered for the purpose indicated on the licence or can no longer be regarded as efficacious for that purpose.

The Act also provided legislation for suspension of the drug with immediate effect if there were concerns about its safety. The Act was enforced in December '68 when the Sub-committee on Toxicity rejected

an application from Schering for a drug containing estradiol and norethindrone acetate, quote, since the possible benefits are considered to be significantly outweighed by known toxic hazards.

The review asked about obtaining patient consent. Patient consent cannot be obtained if the patient is not fully informed of the risks and benefits associated with a drug which is usually contained in a patient information leaflet. There were no patient information leaflets. For the 25,000 packets of Primodos dispensed from the drawer in the GPs surgery, or even when obtained on prescription from the chemist, the only information was how to take the tablets.

The review asked whether problems could have been recognised by the manufacturer sooner and more effectively. Schering had recognised and acknowledged the problems for many years, but effectively suppressed them with the help of our regulators and the German Health Agency, the BGA.

Files in Landesarchiv Berlin contained almost 7000 pages of evidence relating to the problems and concerns relate to Schering both by independent leading scientists and senior employees of the company. Documents which include a request to Schering from an influential member of the BGA, the German Health Authority, to provide studies, again this is a quote, which do not show a statistically significant correlation between sex hormones in early pregnancy and deformities. He also said 'I want to reassure you we're advocates for Schering'. The review asks where the science is not broadly acknowledged or accepted whether the available historic and scientific evidence can reasonably preclude a possible association between HPTs and teratogenic effects, or needs to be revisited.

The available and historic scientific evidence cannot preclude the possible association. Proof of this is contained in an in-depth review of the science which proves an association between Primodos and congenital malformations, not from the expert working group who concluded after almost two years there was no causal association, but did not rule out a possible association, not from the government's study by Dr Poulter who concluded if there was an association, it was only a weak one. Not even from the Commission on Human Medicines who concluded there was no causal association, despite all epidemiological studies analysed by the group, showing statistical significance in supporting an association between hormones and birth defects.

The independent review of the science does prove the association. It was based on a review of all scientific evidence by Professor Carl Heneghan, a clinical epidemiologist and a leading expert in evidence-based medicine. I contacted Professor Heneghan after publication of the expert working group report which I did not accept and I did not - either the conclusions or the recommendation, and I asked Professor Heneghan if he would review the evidence we have already provided to the expert working group.

His response was quite clear. If he agreed to review the scientific evidence, he would publish his results whether they were good or bad for the association members. I accepted.

The systematic review and meta-analysis completed by Professor Heneghan is a comprehensive assessment of historic and scientific evidence which concluded the use of an oral hormone pregnancy test in pregnancy is associated with increased risk of congenital malformations. The values for elevated risk in Professor Heneghan's analysis range from 40 per cent for all malformations to 647 for the VACTERL syndrome.

I forwarded a copy of that report to each member of the expert working group but I've yet to receive a response. We also have crucial new scientific evidence from Professor Neil Vargesson whose study using the components of Primodos on Zebrafish revealed life-changing malformations similar to those suffered by our members. Zebrafish studies are widely acknowledged as the gateway for indications of harm to humans. Today, the results of Professor Vargesson's study would preclude the drug's acceptance of use as an oral hormone pregnancy test.

Taking into account the evidence related to HPTs and adverse effects and the availability of non-invasive pregnancy tests, it seems inconceivable that no information or advice on these alternative tests was offered or even discussed; inconceivable until you take into consideration the financial reward for Bayer Schering and - sorry - the incentivisation to the GPs.

Since the early 1960s, scientific evidence has been available for many independent studies, documents, correspondents and scientific publication. This evidence was suppressed and, in some instances, destroyed. Dr Inman, after Dr Inman had destroyed details of his study, he asked Schering to subpoena him so he could discredit the results in a court of law. As a government employee, he was enabled to give evidence on behalf of Schering without being subpoenaed and was desperate to distance himself from the findings of his study. This was particularly

important when a bulletin from the World Health Organisation referenced the study by Dr Inman and concluded, quote, further evidence of an association between the use of HPTs and subsequent birth of a malformed child has been published.

The review asks whether further action is now required, whether any forms of redress, and whether there is a moral, social or ethical responsibility to consider a system of compensation. There is a moral, social and ethical responsibility by both the government regulators and Bayer Schering to provide redress to our members. Funds should also be made available to continue the research initiated by Professor Vargesson into the safety of norethisterone acetate and ethinylestradiol. The funds are essential for further research to protect future generations of women and our children.

The children affected by hormone pregnancy tests should have funds provided which fully acknowledge the dreadful impacts HPTs have had on their lives, provision for disability related additional health costs and independent living. Our members already face an uncertain future with many cases of deteriorating health.

There should be financial acknowledgement for parents of the years of guilt they still suffer watching their children cope with life-changing disabilities, also parents whose children had their lives cut tragically short from the effects of these drugs. Funds should also be allocated to women who suffered abortion and loss of their newborn babies from the adverse effects of HPTs and women who could not take the risk of another pregnancy after the birth of a deformed child. This is particularly cruel when they were categorically assured the deformity was not due to a HPT.

The responsibility for the provision of the funds should be met by both the UK government and Bayer Schering. It should also be the responsibility of our government to pressure Bayer Schering to meet the cost of these funds. I also hope that the German government take responsibility for their collusion in keeping Duogynon, which is Primodos, on the market and act compassionately to compensate the German victims.

An apology would be meaningless without an admittance of guilt both by the Government Health Agencies and Bayer Schering, who continue even today to deny an association with congenital abnormalities and hormone pregnancy tests.

I would like to conclude by thanking the many members of the scientific community for their invaluable support, with special mention of Neil Vargesson, Carl Heneghan, Jesse Olszynko-Gryn, John Abraham and Tim Lewins. Heartfelt thanks also to our wonderful, indomitable members who motivate me by their unfaltering support and consistent encouragement; to Yasmin Qureshi chair of the APPG and the many MPs who have supported the members of the association and their constituents; to members of the review team who treated our members with compassion and empathy during the patient representative meetings held this year. Last, but certainly not least, my husband Mike, without whose unwavering support I would not have been able to continue with this campaign. Thank you.

Julia Cumberlege: Marie, thank you so much.

Marie Lyon: It was a lot.

Julia Cumberlege: That was very clear, very concise and well put, so thank you very much. We haven't got very long, but can I just ask you, and it's helpful you're setting out the history of all this and, of course, it's gone on for a very long time as you've pointed out to us today and in your written submissions and I'd like to thank you for those.

But it's always moving forward and I just wondered, this year, we've had further information that's come through the EMA, and I wondered if you had any views on that. This is about the Brown...

Marie Lyon: Research.

Julia Cumberlege: ...Paper, yeah. Any thoughts on that?

Marie Lyon: The review for the EMA was actually initiated I think by the MHRA. I didn't have any particular surprise at the results as I didn't have any particular results at the results of the MHRA Zebrafish review. What I did find strange was that - I was in that first review and I listened to the evidence. What was evident when they actually gave the conclusions was that they had not actually acknowledged some of the positive, a lot of the positive remarks made by scientists in that room. They had not acknowledged that it was actually an indication of harm to humans and that filtered through then to the EMA report.

Again, as I said in my initial submission, you won't find any Medical Health Regulatory Agency finding any association whatsoever, 1) because they won't acknowledge the evidence and 2) because they don't actually look for it.

Julia Cumberlege: Thank you very much. Any questions you'd like to ask? Simon, anything you'd like to ask?

Simon Whale: Well Marie, first of all thank you very much and to Daniel and Nicky as well for such eloquent testimony. There is so much to go over, as Julia says. This is a story that's been complicated and lengthy and you've lived through it to such an enormous extent. I suppose the - I mean, you've touched on this already, but what are your top priorities for what should happen next? If you had to say to us there's one thing above all else that we should focus on, is there something of that nature and what is it?

Marie Lyon: Absolutely. The first thing that I would hope is that the science is finally recognised. That's imperative for us, for the mums, because that then will assuage some of the guilt that we took the tablet. That is essential. There has to be recognition at long last that there were huge amounts of scientific evidence available. So, the fact that now we have the additional evidence from two very reputable scientists I would like to hope that once and for all, find that yes, there is a possible association and, again, it's how that's looked at. With some associations, they don't want to look for that. When you look at the Uppsala recommendations, it does actually meet.

The second thing would be that in some way or other Bayer Schering are contacted, that it should be a government-based contact, because there is equal responsibility both from our regulators and from the executives of Bayer Schering. That then I would hope would get a response in relation to how can we solve this? How can we actually make sure people like Daniel, people like Nicky, or other members, actually receive the redress which they need, number one to actually enable them to continue with independent living, and number two, to acknowledge the suffering of many of the mums that they've actually again, in the Sixties and Seventies, they're actually still looking after children of 40-50 years of age who are incontinent, blind, can't speak. That's a huge burden. That burden will actually end up being passed on to siblings. So, it's never ending and it will never end until the science is acknowledged. That's the most important thing.

I think it's wrong that we have to look for the science to be acknowledged first, but that seems to be the way that the government want it to be.

Julia Cumberlege: Everything flows from that.

Sonia Macleod: When you say the science will be acknowledged, what are you meaning by that?

Marie Lyon: That there will be once the meta-analysis was completed by Carl Heneghan and he found independently, and I must stress that, that there was an association, and that was - it was as simple as that. In fact, he says there is an association between congenital abnormalities and HPTs. Once that's acknowledged, I really don't see how it can then go back to there isn't a known association.

Initially, we were asked to look for a possible association. That's already there in the expert working group report, and if you look at all those studies, the forest plot graphs, every single one found a significant association. So, my feeling is - and this was there back then, that was there in the early days. But again, my frustration is it's all the science first, which I appreciate if there was no evidence. With the evidence we have, I actually think it's about time that was acknowledged.

Julia Cumberlege: Anything else? Well, thank you so much and thank you very much all of you for coming today and also your observers. Very, very grateful.

Marie Lyon: We know you're short of time.

Julia Cumberlege: If you've got further questions you want to ask us, please do. We want to keep in touch with all the patient groups, and we may come back to you if there's clarification that we need.

END OF TRANSCRIPT

Session 2: Jason Farrell

START OF TRANSCRIPT

Julia Cumberlege: So, if we could start perhaps by you saying who you are and then I think you've got a statement that you're going to be making...

Jason Farrell: I've got stuff to go through, yes.

Julia Cumberlege: Yeah, well exactly.

Jason Farrell: Exactly.

Julia Cumberlege: So, your stuff, we would welcome hearing. If we start and if you could say...

Jason Farrell: You can just stop me - shall I just go and you just stop me when you want?

Julia Cumberlege: Yes, just before we do that, can I ask you are you being sponsored by anybody? I presume that no.

Jason Farrell: No.

Julia Cumberlege: No. So, you're an independent journalist...

Jason Farrell: Yes.

Julia Cumberlege: ...who actually when you do work and it gets on television or whatever, you then get paid for the work you've done.

Jason Farrell: I get paid a salary and whatever work I do throughout the year doesn't affect my salary.

Julia Cumberlege: That's from *Sky News* or something?

Jason Farrell: Yes.

Julia Cumberlege: All right, thanks very much. Just to make that clear.

Jason Farrell: Okay, so I am Jason Farrell. I am a correspondent for *Sky News*. I'm currently Home Editor but I've also been a Political Editor. At the time I started looking at Primodos I was actually Investigations Correspondent, looking into a number of different issues around whatever we really chose to look at. I was contacted by [REDACTED] in 2011 who is an alleged Primodos sufferer who said he had lots of documents in his loft that he'd discovered from his mother that he wanted me to look at. That is where I would really like to start with my submissions, because that's where it started for

me, going to meet this man in [REDACTED] who had all these documents that interested me almost immediately in what they said. I won't reference every single thing because I'm sure you know a lot about a lot of them.

So, obviously I saw the study from Isabel Gal and the concerns that she raised in 1967. I saw the report by Dennis Cooke, the statistician, who also raised concerns about the correlation between the use of Primodos and the number of abnormalities across the UK, and I saw references to the report by Norman Dean from the Royal College of GPs. All these things spiked my interest that the various correspondence that he had between the drugs company, the representatives in the UK and Berlin expressing concern.

I really wanted to start by talking about that, because I'm not a medical expert. I am, as you say, just a journalist who looks into documents and sees what he sees and tries to extrapolate information from those documents. So, whilst I don't think that I'll ever be able to sit here and prove a causal association between Primodos and birth defects, I think what I can prove, and I think what is evidenced in this, is that there was enough alarm, enough concern, that it was raised with the regulators and the manufacturer that they should have done something. I feel that the main question of the day is whether these victims were let down by the lack of action based on the knowledge they had and based on the necessity of the drug. Whilst they've also looked at sodium valproate and I understand that there is a different level of need in that drug, I think this is a big question on Primodos and it's a slightly different question.

I also think that - I will refer to this in a bit, but the review team that set out to make their review - the expert working group which published in 2017 stated very clearly that they wanted to look to the future. I think that was a mistake. I think if you're going to look at this, I think you've got to look at what went wrong in the past. I'd make the comparison to Hillsborough. If you were to say let's look at Hillsborough and see how we can improve stadiums, it would be pointless, because we've already done it.

But if you say let's look at Hillsborough and see who made the mistakes, that's the right way to look at it and I hope that's what this inquiry will do.

I want to start by talking about the letter that Dr Pitchford wrote in 1968, Alan Pitchford and Patrick [unclear] Medical Directors of Schering in the UK wrote to Dr Friebel in Berlin and they had seen the statistician's report from Dennis Cooke, which I've got here. I'm sure you've got all of this, but if you haven't got any of it, he talked about the strong correlation

between the Primodos usage and malformations in general society off the back of what we'd already seen from Isabel Gal.

He wrote to them and he said, we must reach a decision regarding our own product Primodos and it's possible relation to foetal abnormalities. As manufacturers, it's our moral duty to do all possible to ensure the safety of the preparations that we market. Where suspicion of this kind has been aroused by an investigator whose integrity and ability cannot lightly be challenged, the onus of proof must lie with us. It is for us to establish that the drug is safe to use.

I think that's probably the most sensible thing that's ever been said about this, and the response that he got from Friebel was that they had done - he said that they were doing their own research - they'd done their own research in Berlin that actually contradicted what Dennis Cooke had said about the number of abnormalities related to - the German figures suggested that actually there was no correlation. But the figures that he was referring to only recorded deaths from abnormalities. As we know with Primodos quite a lot of abnormalities don't actually necessarily lead to death. So, already, I feel that Friebel from Germany was being dishonest to Pitchford in the UK.

His second line of defence was that studies were in progress with rats and mice. I haven't seen that but I've seen that recorded in *The Sunday Times*, but they also say this was untrue and the UK would later discover that what was being tested was contraceptive pills Anavar and Gynavar. Pitchford then turned to the regulator, the Committee on Safety of Medicines who again proved a poor ally by saying that they were unhappy about the use of pregnancy tests but insufficient information for any definite action - sorry, there was insufficient information for any definite action to be taken.

Now that was Dr Inman who wrote that. Obviously, I think that becomes more relevant down the line that it was Dr Inman who decided not to take action from the UK authorities that could have helped support Pitchford's case to get Primodos removed from the market.

Then obviously in January 1969, the Royal College of GPs privately circulated their survey amongst the drug companies and we know that Norman Dean called for the drug to be removed, although the President of the College, Dr Kuenssberg wrote to the drugs companies saying that he hoped that they would not be worried by Mr Dean's, Dr Dean's personal opinion, and it seems that they were not.

As far as I know, that study remains unpublished. We talked about that. I know you wrote back to me about it. What I do have is, I think you probably have, which is this letter that he wrote to Pitchford, the Dean wrote to Pitchford saying - it gives an overview of the figures and saying these figures are not conclusive of themselves. But if these data are independent of Dr Gal's, it is alarming that they show trends in the same direction, and in this letter he calls for the drug to be removed.

Yes, 'in view of these findings, tentative though they are, it would be my own view that since there is, in any event, no sound medical reason in my opinion for such hormone preparations, Primodos should be withdrawn from use, Dr Dean'.

So, just in case you didn't have them, I've got that. I've also got *The Sunday Times* article which illustrates some of these points that I'm making about the letters that have been written.

So, Dr Inman wrote back again about this data from Norman Dean that the data you have so far is quite unhelpful in coming to a decision. *The Sunday Times* journalist who wrote this article in '78 I think sums it up quite well. He says the ineffectiveness of the committee had a simple cause. 'Before it was willing to pass judgement on a drug, it demanded the highest standards of scientific proof which was credible but ignored the common sense approach that the possible risks of a drug have to be balanced against its value and the fact was that since the early 1960s, hormone tests had been unnecessary because the simpler urine tests were available'.

Schering knew this and Dr Pitchford wrote to Friebel again in 1969, 'there is very little justification for use of Primodos when more rapid diagnosis can be made by means of the slide tube test. It is extremely disturbing that results of statistics in human studies and animal studies all point clearly to the possibility that Primodos may interfere with pregnancy'.

According to *The Sunday Times* in this article, Schering issued a booklet in 1969 to doctors saying 'an existing pregnancy is unaffected by Primodos'. So, it's not just that they sort of tried to see what would happen next. They were trying to reassure doctors that this was okay. The same year, Roussel dropped its indications for pregnancy.

Pitchford wrote a letter in August 1969, 'a long-term study', he said, 'in humans is nearing completion. A computer analysis should be available shortly and interim analysis reveals statistically significant abnormalities in patients receiving hormone pregnancy tests. By this time the Swedes

banned it in 1970, the Finns in '71. In the UK, sales continued to rise until 1972 and of course Primodos was the market leader. They knew from their own research that they'd done in 1968 that threequarters of the use of Primodos was for early diagnosis of pregnancy'.

Now, I'll come to it later about the labelling and the indication change in 1970, but there was clearly no attempt to warn doctors and no requirement to do so by the regulators. Even in 1974, subsidiaries were instructed to tell doctors 'Schering expert panel was of the opinion that despite the exceptionally widespread use of prescription there have been specifically been no adverse effects occurring until now upon the embryo, on the foetus or the existing pregnancy'. That ignores the scientific evidence.

Compare it to the FDA, who summarised in January 1975, sex hormones should not be used in pregnancy for any purpose. Such use of hormones may seriously damage the foetus, including heart, limb reduction defects.

So, it wasn't until I think even in April when they had their prelim findings from Greenberg and Inman, it wasn't until after *The Sunday Times* had actually highlighted the consequences in May and the inconsistencies, that the committee actually released a warning to doctors which was clearly inadequate because it was continued to be used until 1977 when they had to release the warning again.

Again, if you haven't got those warnings, I have them. I'm sure you have them. But it's quite unequivocal in 1977 that they say that the association has been confirmed.

I just wanted to run through all of that to remind ourselves how much panic there was in the UK about this particular drug. I know that we've submitted an interview that we're probably going to broadcast this week of an employee who was actually told by scientists, she says - and again, this is a woman who has no axe to bear with the company, she's worked there and had a good career, she said. She really likes working for the company, but she says, she was told by the scientists not to use the drug, the receptionist in the company itself, because it might lead to deformity with her baby. Why were they telling that to one of their own employees and not saying it to the public? I think that's pretty damning.

With regard to Norman Dean's study, I also want to submit to you the Royal College of GP's advice that they were taking around the trial compared to - because it strikes me that they decided not to release Norman Dean's study ahead of the trial in 1982. They say, it was of the

opinion it would be unwise to the Royal College to appear to be taking side in litigation of this nature and if they were going to hand over all their information to the plaintiffs, merely on the basis of one short letter, they might appear to be doing just this. It would be advisable for them to wait until there was a court order compelling them to disclose the information.

So, they clearly had the information and they chose not to release Norman Dean's report. We actually got a private letter from Norman Dean that he wrote in 1973 where he said he had a bad conscience 'although really not on my own behalf about this whole business', which I can again give you that.

I just want to go on about what they say in the Royal College of GPs about Dean's report because it's someone else who has assessed it and this person says, sorry, I'll get their name in a minute because it comes up in the writing. It says, 'the conclusion that Primodos definitely does not cause malformations is a slightly different matter and he would not be prepared to say that. The true position appears to be the question is one of the greatest possible controversy and uncertainty and the medical world cannot really give a definitive answer either way, although it indicates towards a view that malformations are not caused by taking the drug'. [Inaudible] went on to say that his own personal evaluation is that he thought there was a distinct possibility that the use of hormone pregnancy tests might cause abortion. But this was a more controversial matter than the question of malformations and when written, he had written a short paper suggesting this. It's possible that he will ask searching general questions about the coincidence of hormonal pregnancy tests and the damaging nature to the foetus, and he would therefore be forced into mentioning its possible the connection between these drugs and abortion. Why is the Royal College of GPs worried about doing that?

Some of the cases, they say on their records, would probably provide better evidence for the plaintiffs in the main action than they already have. Why are they worried about releasing that? They've given it to the drugs company. They've already taken sides. They didn't just give it to the company; they were paid to provide it to the drugs company. This letter here, that decision was influenced by the previous receipt of money from Schering from information supplied to them about HPT.

I don't need you to read the whole letter because I don't want to take that out of context, but it's clear from this that they were paid to provide that information and yet they weren't prepared to provide it to the plaintiff. This is the Royal College of GPs.

Cyril Chantler: Sorry, they were paid...

Jason Farrell: They were paid to do the report.

Cyril Chantler: Yes, by Schering.

Jason Farrell: By Schering according to this.

Cyril Chantler: Thank you.

Jason Farrell: Yes, so I've got that. So, the letters I refer to and stuff from [inaudible] and stuff from *The Sunday Times*, much of it is in here if you need it, the letters to Friebel if you decide to make any use of that. You've obviously already seen stuff from Berlin but I think this is really the most shocking thing. I know we've - we're not sure now what this 5:1 - the question now of 5:1 risk.

Cyril Chantler: You mean absolute as opposed to relative risk?

Jason Farrell: Yeah, my understanding on the 5:1 risk is that it's a 5:1 risk. The relative refers to when it's almost a 5:1 risk. That's what I was told. When you asked me and I checked up...

Cyril Chantler: I see.

Jason Farrell: I spoke to Tobias and unfortunately he's not here today.

Cyril Chantler: I know. We were going to ask him.

Jason Farrell: But that was his interpretation. That was his interpretation of it. We always referred to 5:1 actually. We never said 20 per cent in the piece.

Cyril Chantler: Yes.

Jason Farrell: So, if the risk is two per cent and it's a 5:1 increase, then obviously, the risk is only 10 per cent. So, my understanding of that is not 100 per cent clear, but we've always interpreted it as a 5:1 risk means you've got a 5:1 risk.

I'll make reference to another document that seems to make the same assumption in a minute. But the fact that over five years, he says he'd been monitoring pregnant women, and showed that those who underwent hormone tests had a risk or relative risk of 5:1 giving birth with child malformations. He wrote this in January 1975. So, as we said, months before they decided to do anything about it.

Then he says the research is not completely finalised but one might expect publication of these findings within the next six months. Then in order to avoid any unnecessary tension, one decided to go for the unofficial route and pass the findings to the manufacturer at this stage so that they can take measures to avoid medicolegal problems. I mean, that is just not the way that the regulator should be behaving.

If you add it to what we've seen in the way the regulator didn't respond in 1969, one can perhaps see the motivation behind the way in which Inman acts. It's not necessarily just thinking of the company. I think he may well be motivated by his own mistakes.

My worry about that is this is a guy whose name is on the report that ultimately led to the stuff being taken off the market. If he's motivated to warn the company, to warn them about medicolegal challenges and, as we learn later, to destroy the documents, has he given us the full picture of just how bad things were? It is significant that Dr Detering writes in 1978 that he destroyed or obscured all materials in which the investigations have been based which would make it impossible to trace the individual cases which form the basis of the investigation. I understand that Dr Inman is saying that he had done that to prevent individual claims being based on his materials. What right did he have to do that? I don't think he had any right to do that.

In 1975, Pitchford is still bashing away at the sales department. As far as he's concerned, they should immediately change the text on the data card for Primodos to include pregnancy as a contra-indication to send this amended data cards ASAP to GPs, gynaecologist and obstetricians. This would be sufficient from a medicolegal point of view but he was of the opinion that things should not be left at that. 'Even if we do not have the committee's findings, there are mounting suspicions against hormonal pregnancy tests, so we should seriously be withdrawing the product, the matter is urgent.'

He writes a letter in '75, in March '75, to Dr [Eash] because the sales department has made a decision not to do this. He says he is still of the same opinion expressed in 1969 when he wrote to Dr Friebel regarding Primodos oral, and he attached a copy of that letter.

So, he says, he's the one who is responsible for the safety of the product before the UK authorities and must say, for the record, that he is not at all in agreement with the sales department's decision. The sales department, by the way, have said that listing pregnancies as a contra-indication in the UK would be tantamount to concession which might be construed as a

precedence by authorities in other countries. They decide that they're not going to change the indication until they're forced to. So, they clearly aren't that interested in this new information.

Sonia Macleod: Jason, what date was that?

Jason Farrell: Yeah, third of the third 1975.

Sonia Macleod: Okay, thank you.

Jason Farrell: March. It's in the Berlin Archives in file 13198. This is all a compilation of events put together by Detering.

I bring you on to points that were later made to the manufacturer by their lawyer. Again, I know I've raised these but I thought I may as well put some of them on record here. Because it's not just their own scientists in the UK and various experts wooing on this but their lawyers do point out they've made mistakes.

Mr Clothier pointed out that after thalidomide there was a duty for the manufacturers in the pharmaceutical field to retest their products in order to determine beyond doubt that they were harmless. He went on to talk about the letter that Pitchford wrote to Dr [Bye] requesting that...

Cyril Chantler: Sorry, Mr Clothier is our...

Jason Farrell: Clothier is...

Julia Cumberlege: QC.

Cyril Chantler: He's the QC.

Jason Farrell: He's a QC.

Cyril Chantler: Geoffrey Clothier.

Jason Farrell: So, this is Pharmaceutical School's pharmaceutical division notes on a meeting held on 21 December 1977 at Temple in London with Mr Clothier and various representatives from Schering.

He requests - Mr Clothier went on to ask - talk about the letter Pitchford had sent to Bayer suggesting that this would be dynamite in the hands of the claimant. Another memo from Dr Pitchford and Friebe in '69 was raised by Mr Clothier. This memo was a summary of events that stated that Schering should abandon the product for use in pregnancy testing. Mr Clothier wished to know what had been done in response to this.

There's a question about whether they should have undergone a study at the cost of £9000 which would have been fully justified now he says.

He said, and I think this is important, and I keep coming back to this idea that they've changed the instructions in 1970. He said, changing the wording of the instructions in March 1970, 'this wording was not explicit enough and should have shown a contra-indication. This point is, of course, vitally important in the Williams case, which is obviously the case that was being put forward in 1978 - sorry, 1972. Dr Detering agreed with Mr Clothier on this, the wording did not inhibit - the wording did not inhibit doctors from using Primodos in pregnant women. So, they agreed on it.

All the instructions state that there would not be a result. All the instructions state is that there would not be a result in someone who is pregnant. The wording would not have implied to the Williams' doctors that the Primodos drug was dangerous in pregnant women.

So, I don't know what they changed. I don't know exactly how they - it's clearly stated that they did change it in the report that came out last year. Mr Clothier summarised at this juncture the benefits risks ratio changed very significantly and there really should have been something done at that time to indicate some degree of concern. He went on to state that continued studies would have been useful to Schering, a study which shows that the drug could not have caused the malformations.

Cyril Chantler: Sorry, what date is this? I'm getting confused.

Jason Farrell: It's the same thing, so 1977, 21 December.

Cyril Chantler: Thank you.

Jason Farrell: Mr Clothier raised the fact that he had nothing on file for the years 1970 to 1973. Crucial years when they were told they were looking into all this. They've got nothing on file.

Mr Clothier felt that if this case was tried to the end by a judge, the chances are the company would be found in neglect of its duty. Mr Clothier said that it seemed to be - this is where I come onto the 5:1 chance, so he says - this is kind of weird, but Mr Clothier stated that there would seem to be a 5:1 chance that if there is a malformation in the child, the mother took Primodos while pregnant. It is the fault of the drug. It's a slightly weirdly presented sentence but I interpret it that he's saying that if there is a 5:1 chance the mother who took Primodos has a deformed child, then it must be the drug's fault. The drug must be at fault. But you

can read that and interpret it how you like. But it's interesting to me that he says 5:1 chance rather than 5:1 relative risk. But then he is a lawyer and he may have just pronounced it wrong.

But what really interests me about this, is that this is 1977 and the public haven't been told about a 5:1 chance, or a 5:1 relative risk. Never.

Sonia Macleod: Yes, they had. In Isabel Gal's '67 paper, the relative risk was 5:1.

Jason Farrell: She said that?

Sonia Macleod: She didn't pronounce it as such but if you...

Jason Farrell: If you look at the figures.

Sonia Macleod: ...analyse the statistics in her figures it's around 5:1.

Jason Farrell: Actually, that matches - I see what you're saying.

Sonia Macleod: Yep, yep.

Jason Farrell: So, the Gal figures would potentially match the Inman figures.

Sonia Macleod: Potentially yes.

Jason Farrell: If it was a relative risk of 5:1.

Sonia Macleod: I think. I would need to go back over the Gal paper, but my reading of that originally is yes.

Jason Farrell: Right, okay. I don't think that was - if that was the case, then you could say that public were aware of the Gal paper from 1967. But I don't think this has been explicitly made clear to the public that there was a 5:1 risk or if it has, obviously we know that over the course of those...

Cyril Chantler: I'm sorry, saying the public are aware it's not - it's saying it's in the public domain, not that the public were aware.

Sonia Macleod: Yes.

Jason Farrell: Yes.

Cyril Chantler: We need to be clear about that, is that right?

Jason Farrell: Whether what was in the public domain? Well...

Cyril Chantler: The relative risk.

Jason Farrell: ...as with the Gal report - if he's referring to Gal's report, I don't know if he is. I don't think he's necessarily collated the...

Cyril Chantler: Can I just for a moment assume that what we're talking about here is a relative risk as opposed to an absolute risk...

Jason Farrell: Okay, let's assume that.

Cyril Chantler: ...of 5:1 and that that was in the public domain in 1967.

Jason Farrell: Yep.

Cyril Chantler: Now, that's not the same as saying the public were aware...

Sonia Macleod: No.

Jason Farrell: Yes.

Cyril Chantler: ...because what's in the public domain...

Jason Farrell: Obviously if they were aware, they wouldn't have been taking the drug.

Cyril Chantler: ...the public aren't necessarily aware of what's in the public domain, correct?

Jason Farrell: Well, the most important thing isn't it is where doctors were at...

Cyril Chantler: Yeah, okay.

Jason Farrell: ...and people subscribing to that. Because they're the only people who can really advise the public.

Anyway, Clothier says they need an epidemiologist on their side, they need to get this looked into. I'm not going to go through the whole of this stuff but again...

Julia Cumberlege: Sorry Jason, can I just ask then, following on from what Cyril was asking, were the doctors aware? We say it's in the public domain.

Jason Farrell: No, they were aware in 1975 that the...

Julia Cumberlege: The public don't necessarily know. The doctors were aware.

Jason Farrell: The doctors, as far as I can tell, there is no evidence that the doctors were aware until 1975...

Julia Cumberlege: Right.

Jason Farrell: ...when the letter went out. I don't know if you've seen it. I'd be very interested to know if you've seen anything to the contrary on that. But the first thing I can see from the UK authorities is the letter that I just waved at you a while back, sent in 1975 warning them.

Sonia Macleod: But in 1970, when the indication was removed, doctors were notified via MIMS.

Jason Farrell: They were notified?

Sonia Macleod: Yes.

Jason Farrell: Okay. What I don't get then is...

Sonia Macleod: It wasn't drawn to their attention but the Proplist was sent to all prescribers in GPs and hospitals and that showed that the only indications on these that were left were for the treatment of secondary amenorrhea. The indication for pregnancy test [inaudible].

Jason Farrell: So, why then in 1974 - and I'm just curious - did Schering write...

Sonia Macleod: I can't answer that is the answer. I don't know. It is odd. Because they did.

Jason Farrell: Yeah, so you've seen this letter that they wrote saying we need to change the indication.

Sonia Macleod: Yeah, but the indication was changed in 1970 by the McGregor Committee and that's what I [unclear]...

Jason Farrell: Had there - so, yeah, I don't understand why they would have done that. Because that's what I was coming to. I don't understand this. But it makes sense. It makes sense on one level that if they really had stopped the indication and the doctors knew about it, why did the sales go up from 183,000 to 223,000 in 1970 and in 1971 go up to 233,000? If they'd made it all clear to doctors that this is not - look, I - this says to me that they didn't change it. But if they did and sent out a message, then I hadn't been aware of that.

Sonia Macleod: I think there's a difference between changing the indication and certainly sending out a 'dear doctor' letter that is very much evident.

Jason Farrell: Yes.

Sonia Macleod: Whereas the Proplist and MIMS you had to look for the information. It wasn't overtly presented.

Jason Farrell: Yes.

Sonia Macleod: So, that may explain the difference in the numbers.

Jason Farrell: Yes. Well, you guys have to decide whether you think that's good enough.

Sonia Macleod: Thanks.

Jason Farrell: But I don't think it is. I actually think it makes it all the more horrifying actually that they quietly did it. Because then that just goes to show, doesn't it, that they knew and as I said to you, they also know that the majority of the use of their drug was used by pregnant women.

So, either a horrific lack of communication for which the users of Primodos can bear no responsibility and the drug company and the regulators can, or it was deliberately surreptitious. I can't possibly answer that. But what I can say...

Valerie Brasse: Jason, can I just ask have you come across any other example by Bayer Schering where an indication has been removed and they followed it through with very clear publicity?

Jason Farrell: No.

Valerie Brasse: Anything else? So, we haven't got any comparables?

Jason Farrell: Oh I see, no, no. I mean, I'm not here to talk about any other drugs...

Valerie Brasse: No.

Jason Farrell: ...but I did do a report on valproate, sodium, where...

Valeria Brasse: It was just that comparable, whether they behaved similarly.

Jason Farrell: ...where they'd seen the science and decided that patients shouldn't know. I'm sure you've seen that. If you look at the names on the list you'll see Dr Inman on there. I think there's a sort of 'we know better' approach. I don't know.

Yeah, I find the valproate thing very interesting and quite a complicated dilemma. They were worried people were going to die if they stopped taking the drug. It's not the case here. They didn't have that moral dilemma. The moral dilemma that they had, the decision they chose has left us where we are with mothers with epilepsy having to deal with children with terrible disabilities. That's the decision they made. Maybe they can justify it. You can't justify this. Whether they quietly changed some aspects of the way in which the drug was - I just don't see how they can say they weren't promoting it as a pregnancy test or that they had

properly followed all the procedures to allow this drug and for doctors to know and for patients to know that it shouldn't be used.

I also feel that whilst this drug was on the market and being used in that way, they should have been looking at doing the proper tests which is clear that they didn't do. It feels to me like it's all very well for Dr Inman to be doing a quiet study on humans for five years to see whether this drug actually did cause malformations and after five years decided that it did, well humans aren't guinea pigs, they're not lab rats. The fact that he did this study for five years is in itself damning enough that he just decided okay, we'll just go off and quietly do this and five years down the line we're going to say actually, do you know what, there is a problem.

That's what Tuchmann-Duplessis tells the company in February 1978. They ask him, did we as a company carry out all the studies that we were supposed to and Professor Tuchmann's opinion we should have done much more. Expressed the view that after discovering a certain dose was embryo lethal in rabbits and rats we should have certainly carried out teratological studies in primates in 1968. He stated that the state of the art at the time 'was such that any ethical company using a drug with pregnancy as one indication should have known that primate studies should have been carried out. He declared that the lack of primate studies was, in his opinion, a very important and fragile point for Schering.

He stated in overall terms his general impression of the situation was quite pessimistic. Four quotations will suffice to express his opinion. This is in a letter from Dr Wiseman in 1978 on 17 February, to Dr - sorry, this is from Dr Detering to Dr Wiseman. The four quotations are, the only point where you can argue is over the question of causality. If you can throw doubt on causality, perhaps your culpability will be decreased. There is no doubt you will be considered guilty because you haven't done enough, you must face reality; the eventual outcome will only be a gentleman's agreement. This is the leading expert at the time that they've called in to assess what they're doing.

I've also - obviously, I've already submitted some evidence about the fact that they were aware that this was being used by some women for abortions. I'm not going to go into that because you've already seen submissions but that also to me suggests even if there's a chance that this pregnancy test can cause some to have an abortion they don't want feels to me like they should have taken it off the market.

I feel that the regulator's response was summed up in this letter that Dr Inman wrote about Dr Gal which I think maybe you've heard mentioned

before where he says that Dr Gal fears that by not drawing attention to the hazards that a large number of abnormal babies may have been during - may have been born during the eight years that have elapsed since she first raised the issue. He says, 'we're defenceless in the matter of the eight-year delay'. He knows they've made a mistake. He says it here. 'The regulator knows he's made a mistake. Shouldn't have waited eight years to take it off the market'.

What I don't understand really is why they didn't. I think a lot of us struggle with this because I don't think that people who develop drugs are sinister monsters and I'm not a conspiracy theorist.

So, the first point I was going to make about this I've already made about it being forward-looking. I think they got that wrong. I'm very confused about what happened which they talk about the way in which it was - the labelling was changed. There is always confusion about why it was withdrawn from the market, did they withdraw it, were they told to withdraw it? Did they withdraw it for commercial reasons? Their lawyer advised them to suggest that we say something along the lines that sales in the UK do not justify selling the product, i.e. it's not commercially viable. So, they weren't actually willing to ever say - he says the decision still to be made on the wording used for the discontinuance of Primodos, he felt a low profile was necessary. [Wallace] believed that if a company stated the product was being withdrawn because of a fall in turnover figures, it would be said that we'd have other products that would experience a greater fall in turnover, so why did we not discontinue? So, they had a big discussion about what excuse they were going to give to withdraw it.

I've already given you a very full attack document on this. I think I've made my feelings quite clear about it. I'll just reiterate a couple of points. I don't feel - I don't understand why they came to the conclusions they did on the animal studies when they've got lines in there about studies, talking about the increase in malformations in the study should be considered drug related. If that's the case, then it's drug related, but apparently it's not. It's a shame that you haven't got Tobias here because he's done a full assessment of the animal studies. I don't think I should try and replicate or even do a poor example of that.

On the epidemiological stuff, again I just looked through it and thought it doesn't make sense. The conclusion doesn't make sense. They have this line in here, for example, 'the study to be considered the most robust, [Hynan] in 1977, showed us a statistically significant two-fold increase of cardiovascular anomalies. But then it knocks it down saying that the

exposure was questioned by the publications of Wilson and Wiseman in 1984.

Well, Wiseman worked for Schering, and Wiseman's study was knocked down by Hook. I haven't got the date for his study. I actually pulled it out, but it got rained on. But I've got another. It's online. The Hook study is online. You've seen it, so you know it. He essentially said the relative risk actually rose if you apply the way in which Wiseman did the study unbiasedly and this would result in increased measure of the effect.

As you know, we've argued that to say that the studies have flaws and therefore the risks might have been lower, equally those flawed studies might not have calculated the true extent of this. I don't think that's really been assessed by this group. It just doesn't feel to me like it's been assessed properly.

The other thing that concerned me, again they make this reference in the Greenberg one, which again observed a statistically significant risk and is considered to be amongst the better-quality studies of the time. But then they say the comparator group were not women who also sought a pregnancy test. So what? I did ask them why does that matter? In the press conference. They didn't seem to be able to give me an explanation. But there it's mentioned several times in this report that women who didn't seek a pregnancy test might be a reasonable comparator group.

I'm sure when you hear from Jesse this afternoon who is giving evidence, there is no reason for making that assumption. Unless there's a scientific reason which they haven't given in this report for making that assumption, I don't see why they do. I don't see why the report they produced in October had this forest graph in it but it wasn't in the eventual report. This forest graph which plots the assessment of the epidemiological studies for all congenital abnormalities shows that eight of them showed a veer towards an association and only two veered against.

Quite frankly, if we look at the ones they did include - if you look at the ones they included, they all seemed to show an association. On Friday, I interviewed Carl Heneghan I don't know if he's going to give evidence to you guys.

Julia Cumberlege: Yes, he is.

Jason Farrell: Well, he said to me that it looks like they did do the pooled data metadata analysis but they didn't include it. He's done the metadata analysis, he's pooled it and he's found that there is an association. So, he's looked at

the same stuff and he's a pretty reputable guy with no axe to grind, totally independently, looked at this and said it's wrong. It's wrong, they've done it wrong. I challenge them to look at his stuff and see if he's got it wrong because I don't think he has.

He said to me, you know, you start just by doing vision check and looking down the line and seeing if you can just make a general assessment of how it looks, which is what we did very unscientifically. But he has very scientifically shown that VACTERL and limb reductions and I think particularly heart problems, there is an association, which is the opposite of this conclusion.

I worry that when Alison Gebbie was giving evidence to MPs about why they'd changed the document and, as we found out, they took out the line saying that it was not possible to reach a definitive conclusion, I worry that she said that they were told to strengthen it up. Who told them to do that? I really worry about that because of all the rest of it that's gone before it. That's the last thing you want to do when you've got so much doubt from history, is to just create more doubt. I just don't think that it's acceptable anymore for the victims to be the ones left having to prove anything. I don't think they deserve that. I don't think they have to prove anything.

I think if the drugs company wants to come here and say here's the test that showed why we kept it on the market, then fine. But they've never done that. I therefore think that this, along with what we're now seeing from Carl and what we're seeing from Neil shows there's more than prima facie evidence there was a problem, that the real evidence that we've got in hard writing here from those letters from Dr Pitchford, from what we've seen from the stuff in Berlin, real evidence is that they didn't act on the warnings that they know they had.

I will also give you, if you haven't got it, the World Health Organisation document that was produced in 1975, '77 sorry, which I've just highlighted all the different reports around the world that were making the same conclusions. I don't know if you've seen the reports from India that were done in the Eighties, came to the same conclusions. It's all there. It's all just - there's nothing - there's not that definitive piece of evidence. But when you put together as Pitchford said, the statistics, the animal studies, the human studies, you put it all together, I don't know how you can come to any other conclusion.

Then I think the other thing which I just wanted to say that obviously we will give to you is the thing that we raised in our documentary about the

relationship between Primodos and Gestest and you see the court case that happened in America and there was a pay-out and obviously you've seen the interview that we have done with the mother in Florida who talks about how that came about.

The last thing that I found as I was going through my notes was something that Isabel Gal put together for Jack Ashley, actually, it was a report, where she - I won't actually - I don't think I'll even go through and repeat all the things that she said. I've just highlighted in here what I think as the points I'm trying to make, which she says that basically the regulators failed to act for eight years.

She sets out the various reports that they were aware of and quite compelling arguments as to the points in which - I thought it was interesting that she said right back at the start when she produced her report in 1967, that it had produced prima facie evidence that abnormalities may be drug induced. They told her that in 1967 on 22 June. I just don't understand why, if she'd already done that and she proved that prima facie evidence, why they didn't act more rapidly.

So, I just think perhaps she should have the last word on all of that, seeing as she started it. That's really, along with all the things I've already submitted, all I have to say.

Julia Cumberlege: Yes. Jason thank you so much. I must say that is hugely impressive. Some of us have had views about journalism. I used to be on the Press Council but that, I must say, is just formidable. Thank you very much. Simon Whale would just like to ask a question.

Simon Whale: I'm just conscious of time Jason, but I'd just endorse what Baroness Cumberlege has said, that's been very, very helpful and impressive. One thing I wasn't sure about was whether there was anything you wanted to say about the collapse of the litigation here in the UK in 1983 and the circumstances surrounding that. I'm not sure how closely you've looked at that or whether you've got anything you want to share with us about that?

Jason Farrell: Well, I've only got - I've done interviews with people who were involved in that, and obviously there was suspicion around the way in which certain people who were deemed to be experts who were going to stand and represent the plaintiffs then fell away. They clearly felt that they had a strong case and they were discouraged eventually by their lawyer from going further because the experts that Schering put up against them were deemed to be too heavy in number and expertise for them to take on.

Look, I don't have any firm evidence around how that happened or whether people were offered various things to not give evidence. I would say that one of the key expert witnesses for Bayer was Briggs who I referred to there. If you want to understand more about Briggs it might be worth you talking to Brian Deer who - or I've got an interview with him that I can submit to you which we didn't run in the piece. Basically, he ran an article which showed that Briggs had made up medical evidence and he wasn't as reliable as perhaps people thought he was in 1982.

It's not my journalism, so I wouldn't want to talk about it really. But I have got an interview with Brian Deer or Brian Deer is still alive and well and still a journalist and could talk to you about Dr Briggs. But I feel from the way in which the company was advised by their lawyers ahead of that litigation, it looked pretty likely that they were going to lose. I think that possibly the plaintiffs at the time were poorly advised.

Obviously the case was left open by the judge as well, because it wasn't a definitive decision. Val Williams actually sent me an email. I've never really spoken much [REDACTED] because she's a bit of a side figure from the rest of the group. She'd probably be a really interesting person to talk to. I don't know if you've spoken to her but she was [REDACTED] and she did actually say to me in an email I think on Friday that she could - there's no reason why she couldn't reopen her legal challenge and that that might be a way forward. Partly because I've worked with a lot of different groups, campaign groups, and I'm hugely impressed that this one has survived for so long. But in all campaign groups, there are factions and people break off - that is probably actually less so in this group than most that I've come across. I mean, I could go back through my - I didn't expect you to ask me that question, so I can go back through my notes and see if there's anything specific about the way in which that case collapsed.

But I think another interesting thing, I know you had - oh, I've forgotten his name who came in here, I just saw him leaving, chap with shortened arms. [REDACTED] So, [REDACTED] some interesting letters as well about this because he wasn't aware of the case at all, but then he had a letter from his lawyer saying, oh steer clear of trying to take legal action because there are 30 witnesses lined up to give evidence on behalf of the company, and he wasn't even part of the group.

So, there was definitely the sense that the company had loads of witnesses. I think if you look through the documents in Berlin there is a lot of work around trying to persuade Tuchmann to become one of their expert witnesses. If you consider what he said about the way in which they had behaved, it's quite extraordinary that I think by the end of it, he

does agree to become a witness on their behalf. I don't understand why he did that if his view was that they were guilty.

But obviously we all know it's extremely difficult to take - to get damages in a medical case and it very rarely every happens.

Julia Cumberlege: Jason, can I suggest if there are things that you want to add or whatever, please feel free to do so and perhaps you'll accept that there may be things we want to come back...

Jason Farrell: Yeah, sure.

Julia Cumberlege: ...and question you about things. So, thank you so much for coming today and thank you for the work that you've been doing.

END OF TRANSCRIPT

Session 3: Dr Jesse Olszynko-Gryn

START OF TRANSCRIPT

Julia Cumberlege: Perhaps we could start. If you would like to formally say who you are, then I think you're going to give us a statement are you? Are you going to tell us a bit about what you're doing?

Jesse Olszynko-Gryn: I could.

Julia Cumberlege: Why you're interested...

Jesse Olszynko-Gryn: Sure.

Julia Cumberlege: ... in this subject that would be very helpful. So perhaps if we could start and you could perhaps do that?

Jesse Olszynko-Gryn: I'm Jesse Olszynko-Gryn I'm a Wellcome Trust Research Fellow at the University of Cambridge, in the department of History and Philosophy of Science, where I also did my PhD. The PhD was requested as evidence by the MHRA, investigation into Primodos, which is - because of one of the chapters in it, that it investigates the history of hormone pregnancy tests. That's the point at which I became more involved in the MHRA review and the campaign, and decided that - yes?

Julia Cumberlege: Sorry, can I ask you to speak up a little bit?

Jesse Olszynko-Gryn: Oh sorry, yeah.

Julia Cumberlege: Because I...

Jesse Olszynko-Gryn: A lot of ventilation...

Julia Cumberlege: I know, it's a bit difficult...

Jesse Olszynko-Gryn: Okay.

Julia Cumberlege: But I should also have asked you whether you have any declared interests in terms of sponsorship or anything like that? Or any connection with Primodos?

Jesse Olszynko-Gryn: No. I mean, all the research is funded by the Wellcome Trust. But they're pretty hands off. The PhD I completed in 2014 is a history of pregnancy testing in the UK. That focuses mainly on urine pregnancy tests from the early 1900s until the present day. That's the book that I'm currently writing. That's how I found out about Primodos and

other hormone pregnancy tests, when I was doing archival research, including at the Schering Archivs in Berlin, and at the National Archives at Kew. So about 10 years ago.

Really until more recently I didn't really know what to do with that information. When I talked to other historians about hormone pregnancy tests, usually they didn't believe me or thought it was sort of a really strange story, (a) because until - I think especially Sky News reporting and the MHR investigation, nobody had heard of these - or very people outside of the - those immediately involved had heard of these tests. It just seemed to most people today, a really unlikely product - so using one of these hormone pills for pregnancy testing.

So, I kind of sat on the research for a while until I saw, I think, a news report showing some of the campaigners at the same archives I'd visited, looking at the same documents. Then I really didn't know what to do as a historian because I'm used to just going and looking at archives that nobody else cares about and then just taking my time writing articles and books, without this pressure of that kind of interested review or inquiry.

In the last two years, I prioritised, so Primodos moved up in terms of the - my - on my - it moved up my to do list and I got - and then I managed to convince some other historians that I knew already in Sweden and Norway and Finland and now West Germany and hopefully Spain and Italy and the Netherlands and Belgium, to also do the same kind of work I was doing, which was to reconstruct the history of the marketing and the regulatory processes around hormone pregnancy tests in those countries, which weren't particularly coordinated in the 1970s. That's an ongoing project.

In terms of, just to wrap up where I'm going next. I was recently hired as a Chancellor's Fellow at the University of Strathclyde to start work in January at their Centre for the Social History of Health and - Social History of Health and Healthcare. I'm starting this new position in January and then I'll be in a position to apply for more funding from the Wellcome or other sources to continue this work with my European colleagues. Because (a) it's - I mean it's timely - obviously it's of interest now to people like yourselves, but also from a historical intellectual perspective, it's an extremely fascinating story that deserves to be investigated more deeply than it has been so far.

Has all sorts of consequences, I think, for the historical understanding of Thalidomide, of Diethylstilbestrol teratology and generally the science and public culture of birth defects and the media and how the public and scientific awareness of the relationship between drugs and pregnancy risk and congenital malformation has been understood in the 1960s, '70s and '80s.

I think that (sort of invest) doing this kind of work - this historical work that I'm doing with my colleagues - I think will potentially be complicate and transform our understanding of this area, which I think to date, puts a lot of emphasis on - it begins and ends with Thalidomide as if that was the whole sort of 1960s - Thalidomide happened and we all learnt our lessons and that was it, In fact the - probably the more - the truer but much more complicated story is - would involve really reckoning with the history of these kinds of products and other kinds of drugs as well. Sorry if I rambled on a bit. I hadn't prepared this statement. Maybe I should have.

Julia Cumberlege: Well you know with Primodos, that there's really been a very long history about all this, and what has happened in the past. I just wondered if you actually knew if there were any options for pregnancy testing between 1950 and 1980, and whether there were costs associated with that and the sort of time taken?

Jesse Olszynko-Gryn: Yeah, so the - I mean one of the - I don't know if you've seen the article that I co-authored, that came out a few weeks ago in *Biomedical...*

Sonia MacLeod: What was the title?

Jesse Olszynko-Gryn: The title was, *A Historical Case for Regulatory Failure*.

Sonia MacLeod: Yes, yep.

Jesse Olszynko-Gryn: Okay, good. So that's - I tried to get that out in time for it to be taken into consideration by this review, it's published...

Sonia MacLeod: You submitted it as evidence, we've got it.

Jesse Olszynko-Gryn: Yeah, okay. I wasn't sure if I'd submitted it in time or not. It's published in *Reproductive Biomedicine & Society* online. In that article I tried to put all the relevant information I had at the time in terms of alternatives that were available, and cost factors and that sort of thing. That's I guess in terms of what history can and can't bring to the table, I think work that other people are doing on

laboratory animals or epidemiological work that's reanalysing data is something that I'm not qualified to do myself, or comment on expertly.

On the other hand, in terms of providing a context, especially regarding alternatives that were available at the time, I can definitely do that confidently because my whole - I mean I've been working on this for 10 years now, so I probably - so if that's what you want, then I'm the right person to answer that question. There were definitely alternatives available at the time, and that's one of the reasons why the case is so interesting, you know, the case of Primodos is so interesting and so, in some ways, infuriating.

Because not only were completely harmless and fairly cheap and reliable and practical alternatives widely available in this and other countries, but the fact that they were available was widely acknowledged at the time, privately and publicly, including by experts that were directly involved in the regulatory decision-making processes around Primodos and in terms of the marketing. Schering at the time also knew about Pregnosticon, the first urine immunological test for pregnancy, that came out in 1962 - so the first test kit - and perceived it as a direct commercial threat to Primodos.

Before that, in the '50s pregnancy tests were more cumbersome. They involved injecting, as you know, toads with urine and then seeing whether or not they laid eggs or emitted sperm. Although highly reliable, those tests were expensive and required access to a laboratory. GPs had to send urine specimens to the lab and get samples - get a lab report back and see the patient again to deliver the results. So, sending patients home with a couple of tablets was more convenient, especially for overworked, busy GPs and they were cheaper.

There's a more complicated story about the fact that tablets as medications were reimbursable on the NHS, whereas laboratory tests weren't. Throughout the '60s GPs were petitioning the Department of Health to try to make it so that they could be reimbursed for doing on the spot two-minute pregnancy tests, which were in circulation by the '60s. But because of the intricacies of Ministry of Health or Department of Health bureaucracy...

Sonia MacLeod:

What...

Cyril Chantler: I hadn't realised that. You say they were paid for the - using Primodos?

Jesse Olszynko-Gryn: No, yeah, they were able to get the - they were able to claim it back. My understanding, they were able to claim it back on the - is it the EC10 or the form

Simon Whale: FB10.

Sonia MacLeod: Was that not only if it was not...

Cyril Chantler: If it was prescribed.

Sonia MacLeod: ...indicated as a pregnancy test? Because my understanding...

Jesse Olszynko-Gryn: Yeah.

Sonia MacLeod: I may be wrong, is that if the form indicated that it was to be used as a diagnostic test, it wasn't reimbursable.

Jesse Olszynko-Gryn: I think, yeah.

Sonia MacLeod: But if it didn't indicate that, then it was reimbursable, does that sound correct?

Jesse Olszynko-Gryn: That sounds - I think that changed in the course of - I think initially...

Sonia MacLeod: When did it change?

Jesse Olszynko-Gryn: I don't know precisely. I think it's tricky to reconstruct. It might be possible to get a more precise timeline for that. Whether or not, how that operated in practice, in terms of whether doctors - I mean it's not clear to me how closely the actual practice mapped on to the regulatory regime or the reimbursing. And regardless, I think - I'm just checking my slides now for the cost - I think Primodos sort of around 1960 was 5 - is it shillings when you have a slash? Yeah, five shillings...

Cyril Chantler: Yeah, it is.

Jesse Olszynko-Gryn: ...on the NHS. You have to convert that to decimal, I guess. But - whereas a [unclear] ...

Cyril Chantler: 25p.

Jesse Olszynko-Gryn: Yeah. The [unclear] test was, at the same time, roughly - the Family Planning Association was doing them for 25 shillings so five times the cost.

Sonia MacLeod: It required sending off stuff...

Jesse Olszynko-Gryn: Yeah.

Sonia MacLeod: ...so yeah.

Jesse Olszynko-Gryn: There's more - and Marie Stopes and FPA by 1965 were charging £1 for a urine test. Private labs charged £2. Predictor, the first home test, that came out in 1971, cost £1.75. I don't think it's the only factor. A lot of the women who took Primodos say that they were given free samples and I think that was a fairly widespread practice, so I don't think that's in contention. I think it's one of many factors that made the hormone tests seem more appealing than the animal tests at the time.

Although, I think the really crucial thing that I tried to map out as robustly as possible in the article and one of the reasons I wrote the article is just that I - if you need that information, I can - you can - it should be in there. If you want further - if you want me to submit further clarifications in writing, I'd be happy to do that, if there's things that aren't clear in the article. Like this question about reimbursing, which I did...

Sonia MacLeod: It's one of the things I've struggled to get a very clear time line on...

Jesse Olszynko-Gryn: Yep.

Sonia MacLeod: ...I'm glad you're struggling with it too.

Jesse Olszynko-Gryn: I mean, I think I wrote - I sort of - I mean I fudged that a bit. I wrote initially it was reimbursable on the NHS because I think that did change at some point. I wasn't sure when, so I kind of wanted to leave that bit intentionally vague. For some of the other points, we have a clearer timeline for. I don't know if the - I mean it's an important detail, it might not be decisive for a lot of things. But, in terms of...

Valerie Brasse: Sorry, Can I just check...

Jesse Olszynko-Gryn: Yep.

Valerie Brasse: ..., this Pregnosticon, would you say was the first of its kind...

Jesse Olszynko-Gryn: Yeah.

Valerie Brasse: ...on the market? That was 1962.

Jesse Olszynko-Gryn: Yeah.

Valerie Brasse: That was obviously not available to women to just go to a chemist to do it...

Jesse Olszynko-Gryn: No.

Valerie Brasse: ...themselves. So, it had to be by a GP. The GP had to give them test kit?

Jesse Olszynko-Gryn: Okay, so the timeline for that is – yes. Well until 1965, when private commercial laboratories in London and other cities start to serve women directly as clients. They take out advertisements in classified ads, and even put ads in the underground and on bus stops, on buses, on the sides of buses, and the train stations. They're charging usually £2 for a test, which is quite a lot of money in those days, if you talk to people who remember doing these.

But they're doing a lot of business. From '65 - again there's a lot - if you're a middle-class woman in London, you might be more likely to go to one of these labs. If you're living in a village in South Wales you might not - probably wouldn't know about them and you would go to your GP. In 1969 the Pharmaceutical Society changes its line and allows pharmacists - so chemists - to do tests, sort of back room testing. So, in the '70s a lot of women will go to their pharmacy or GP or family planning clinic.

Julia Cumberlege: Can I ask you then, are you talking about the GPs who were giving...

Jesse Olszynko-Gryn: Yeah.

Julia Cumberlege: ...out these pills. Do we have any idea geographically whether there were clusters of GPs doing this?

Jesse Olszynko-Gryn: I mean, I wish...

Julia Cumberlege: Was it across the country as a whole?

Jesse Olszynko-Gryn: Yeah, it's across the - I mean I wish we had more detailed geographical data. It might be possible to reconstruct, and I haven't tried this yet with just the membership of the association. That would obviously - there's obviously a huge sampling bias, but at least it would give us some sense. I sense from interacting with them is

that, they do tend to cluster in South Wales, around Liverpool, Scotland. So maybe in more economically deprived, post industrial areas.

The data I have from published records is anecdotal, but there were - there was a GP, a busy practice in Bristol, that I mentioned in the article, that preferred Primodos just because it saved them a lot of time. They were dealing with 750 antenatal care patients and they just decided as a matter of course to send their patients home with pills instead of doing urine tests, which they called cumbersome. Then in the *Sunday Times*, when they did a survey in 1975, found 10 out of 12 doctors in South Wales were still using HPTs, which is also suggestive of a regional bias. But I don't...

Simon Whale: Sorry, are you linking it to the economic conditions of those particular places, or is that just a coincidental factor?

Jesse Olszynko-Gryn: No, I think, I mean it's speculative. I think it's suggestive of economic conditions and maybe more importantly, lack of access to laboratory services. So how near or far you are to a cooperative hospital laboratory. Laboratories by the late '60s early '70s are also complaining of being overworked. When they - pregnancy tests are the last thing they want to be doing. They think it's fairly trivial and low priority. So, if they can get out of it, they will.

They're not dealing with - so people working in laboratories aren't at the frontline. They aren't dealing with anxious women, face to face and don't really see the need, necessarily. I was talking to my German colleague the other day and she has evidence that I think in contrast to the UK, products like Primodos were being used more frequently in Germany and West Germany as an off-label abortion pill. Because abortion wasn't legalised in Germany until much later. In the UK, it's quite early, 1968, '67, '68. Although access to abortion was also fairly patchy. So just because abortion was legal in the UK didn't mean that it was easy to...

Cyril Chantler: Sorry, how did it become thought that a pregnancy test could cause an abortion?

Jesse Olszynko-Gryn: Well the way it works is by inducing menstrual like, withdrawal bleeding, which was from the beginning suspected as causing, in many cases, miscarriages, including...

Cyril Chantler: But it wasn't marketed for that purpose.

Jesse Olszynko-Gryn: No, it was never - right, but we're in this different - I think - again - I guess the really crucial thing maybe historical perspective can bring to the table is the fact that we're living in a different- we're in a different world. If I could transport you back...

Cyril Chantler: But you can because I qualified in 1963, so I do actually remember it. Social media didn't exist in that sense. So, there must have been a conversation going on amongst young people at that time - including people my age - that this test - if you want to have an abortion, you should go to have this test done.

Jesse Olszynko-Gryn: I think to qualify that, I think young, fairly affluent people, especially in London, students - I've talked to some people like that who do remember taking Primodos or Ammenore Forte because they thought they maybe pregnant and they didn't want to be pregnant. They were hoping it would...

Cyril Chantler: Yeah.

Jesse Olszynko-Gryn: ...induce menstruation and maybe that would be a miscarriage. But there was enough room, enough uncertainty.

Cyril Chantler: Do you know of ..is there any evidence that you'd be able to come across that they would take the Primodos as part of a campaign to induce an abortion? They might do something else as well as having Primodos? Do you see what I'm getting at?

Jesse Olszynko-Gryn: No, I think...

Cyril Chantler: You know, they might - say take double the dose or take something else, which might induce an abortion.

Jesse Olszynko-Gryn: Yeah, that you get that also with the birth control pill, in this - Yuzpe regimen, of where you take an overdose of contraceptive pills as an abortion pill through the - that practice is used in several countries up until the morning after pill was put on the market.

Sonia MacLeod: What time frame are we talking about for that?

Jesse Olszynko-Gryn: The - for the...

Sonia MacLeod: For using the oral contraceptive as an abortive agent. Are we talking 1960s to '70s or '70s to '80s?

Jesse Olszynko-Gryn: Yeah, I would have to double check. But again it depends on the country and how accessible these products are. National histories are

very different. It's hard to research when if it's an informal practice of taking an overdose that wouldn't have left a paper - or explicitly not left documentation. It's going to be hard to reconstruct. I want to just be really clear, there is some anecdotal evidence. I think practices like this were more widespread in countries where abortion to access was, in the '70s, was less available. In the United States there's more evidence and in West Germany, in the '70s, there's more evidence that these products were used in this way.

In Britain there's also lots of anecdotal and published evidence that doctors were prescribing these products on good faith as pregnancy tests and that women were taking them on good faith as pregnancy tests. Maybe the more typical encounter in the UK in the '70s, '60s and '70s was for a woman to go to a doctor and say, I think I might be pregnant. The doctor would say, well let's have a urine sample or, well okay, here are these tablets, come back and see me if you don't bleed. Then we'll - then sometimes - then we'll do a urine test. So, it was sometimes used as a screening test, as a preliminary test before ordering a more expensive urine test.

There was a lot of - there wasn't a - there was a range of medical opinion on whether these drugs were potentially harmful or even beneficial. So, because progesterones were also being used to prevent miscarriage in the '60s, there was a sense that depending on the timing and the dosage, they might even have a beneficial effect on an early pregnancy. So, I don't want - I really don't want my main intervention here to project - to kind of give the impression that these drugs were being used primarily as abortion pills in UK.

Sonia MacLeod:

Yep.

Cyril Chantler:

The reason to ask isn't that at all.

Jesse Olszynko-Gryn:

Okay.

Cyril Chantler:

It is so that we can interpret the evidence that exists, relating the use of Primodos to damage to the foetus...

Jesse Olszynko-Gryn:

Yeah.

Cyril Chantler:

...because was it likely the women was taking some other...

Jesse Olszynko-Gryn:

Well that...

Cyril Chantler:

...intervention at the same time?

Jesse Olszynko-Gryn: One thing that I think should be done in terms of, if that's one of the remits of my being able to be here, is I think it would be really helpful to systematically, and maybe you're already doing this, but - interview and collect case notes where they still exist from the association numbers. It's a couple of hundred people and it's a long time ago, their memories won't be perfect. Some of them have recovered their case notes, others haven't been able to. I don't think - the evidence is not going to be - the data set is not going to be one that you can do really robust statistical analysis with, but I think that will help in terms of getting any qualitative sense at least, in terms of how...

Sonia MacLeod: Do you think that they might be - do you think they would be representative of women taking it as a whole, or do you think they might not be?

Jesse Olszynko-Gryn: Obviously they're the ones who were pregnant and then had - you know gave birth to children with malformation, so they're not going to - weren't - who were negative results, who weren't pregnant or who miscarried, knowingly or unknowingly, or who gave birth to perfectly fine children. The other thing - one of the things that bugged me about the previous review and in terms of comparing the Primodos users to other kinds of women, and what other kinds of products they may or may not have been taking, it's an interesting question.

I talked to women, it was their first pregnancy. They were hoping to get pregnant. They were married. They went to the doctor, as women were increasingly starting to do in the '60s and '70s, when they thought they might be pregnant. You know, not to stop smoking or drinking, all that stuff comes later.

So we are in that sense - you remember - but a lot of this - it doesn't even really start with Thalidomide. It might start later, in the later '70s in terms of with the intense pressure that's now on women, even before they conceive to radically modify their lifestyle and stop taking all medications and stop smoking and drinking. We're in a different world, but there is - in the '60s there is starting to be more of an incentive. Not yet - even - I don't know when routine 13-week ultrasound starts, but that's later again, right?

Sonia MacLeod: Mm-hm.

Jesse Olszynko-Gryn: But I - I mean I talk to women - association numbers - who did - I believe them, I've no reason to doubt them. They were hoping to get pregnant, they went to the doctor and were just sent home with pills. Then of course, again the other thing that's changed is women, or people, maybe especially women, have a lot more faith in medicine in the '50s and '60s than they do now. Maybe they just didn't question the potential risk of taking pills that the doctor gave them - I think in a lot of cases, in pretty good faith.

It depends who you talk to. If it's a GP or a paediatrician or an obstetrician or teratologist or geneticist, there were a lot of - there's a really heterogeneous ensemble of experts that are looking at this, at the time, from very different perspectives and had very different ideas about what's safe and what's not safe, depending on their expertise and what kinds of cases they're coming up against.

I talked to a pharmacist too, he was available for - if you need more of this kind of evidence. It's hard to get these kind of data points. I mean aside from doing it, I don't know how you would - I mean you did put out a call for evidence, so I don't know how many GPs or pharmacists from the 1960s responded. It's hard, as a historian, for me to get at...

Sonia MacLeod: Not a huge number.

Jesse Olszynko-Gryn: ...you know.

Sonia MacLeod: Especially...

Jesse Olszynko-Gryn: They were crucial because this is - you get - the experts leave a paper trail, they're in the archive, you know what the experts...

Sonia MacLeod: Say.

Jesse Olszynko-Gryn: ...say to each other because they wrote letters and it's well documented in terms of whether they were concerned about miscarriage or birth defects, or not. It's harder to know what rank and file GPs and pharmacists thought. The one pharmacist I did manage to talk to said, he was a bit - he was surprised when he got prescriptions for Primodos, because he'd heard about the risks in the news. But he prescribed it anyway. Or he figured - he assumed that any drug that was potentially risky would have been taken off the market after Thalidomide, so he prescribed it anyway, despite his own personal misgivings. I feel like - was there a question that I...

Cyril Chantler: No, that's fine.

Sonia Macleod: No.

Cyril Chantler: You've given me the answer.

Jesse Olszynko-Gryn: Okay.

Cyril Chantler: Not the answer I sought, but you've answered the question, thank you.

Julia Cumberlege: Can I say, I think we could continue this conversation for some time, but we've got other people coming today, so we need to be conscious that they're waiting. So, we need to get them into the room. Can I thank you so much for coming? Perhaps I'm - well I'm pretty sure that there are other questions that we might want to ask you. If we could do that through...

Jesse Olszynko-Gryn: Yeah.

Julia Cumberlege: ...other means...

Jesse Olszynko-Gryn: Okay.

Julia Cumberlege: ...that would be really helpful. You may want to ask us some questions.

Jesse Olszynko-Gryn: Can I make one final point? I just remembered what and it will be very brief - sorry for rambling. The one thing that hasn't been clear that is unclear and hard to reconstruct is - so you have - we know about the women who went to the doctors, took Primodos because they thought they were pregnant. Maybe they were more or less anxious than other women who didn't - weren't prescribed Primodos. So, at the time one of the estimates from 1971 is maybe 1 in 200,000 women in the UK were given Primodos as a pregnancy test, I believe.

At the same time, just in terms of the scale, an estimated 1 million women were given urine pregnancy tests. So about 10 times as many, just in terms of very rough numbers. It's not like the choice was between an anxious woman going to the doctor and getting Primodos, or a woman who's not anxious and just doesn't go to the doctor at all. Ten times as many women would have gone to the doctor because they thought they were pregnant and just been sent - given a harmless urine test. So that was, increasingly the norm in the

'60s and '70s and already much more prevalent than the urine - the hormone test. That's - I just wanted to...

Valerie Brasse: That's actually very helpful because I was going to ask at what point did it stop and one outweigh the other, in the timeline? So, you would say early '60s? Mid '60s?

Jesse Olszynko-Gryn: I think urine tests were always - I don't think Primodos ever really matched urine tests.

Valerie Brasse: Okay, so they were always minority?

Jesse Olszynko-Gryn: Yeah. Then - yeah in terms of being used diagnostically. I think in the article I have an argument about the fact that labs were, in the '50s, struggling to - the demand was increasing, and the lab's supply was kind of plateauing. I think then, that's when companies like Schering saw that they could capture a small part of the growing market that labs were failing to meet.

Once the cheaper, once the 1962 test came out and allowed for decentralisation of testing, so they didn't have to be concentrated in these large centralised labs but could be done in every GP surgery or pharmacy back room, then you really get an explosion in the number of tests being done. But even before then, it's probably hundreds of thousands, if not a million. Okay, thank you. Please do feel free to contact me. I'd be more than happy to dig - especially at the question - others that you ask, to try and get a more precise chronology....

Sonia MacLeod: I will have a look through what we've got...

Jesse Olszynko-Gryn: It's an important thing to do. But it would really help to have the...

Sonia MacLeod: Yeah.

Jesse Olszynko-Gryn: ...yeah.

Cyril Chantler: Let us know the change of your email address if you go to Strathclyde.

Julia Cumberlege: Yes.

Jesse Olszynko-Gryn: Yeah, okay. Will do. Thank you.

Julia Cumberlege: Thank you so much for coming. It's been really, really helpful.

Jesse Olszynko-Gryn: Thanks a lot.

Julia Cumberlege: As I say, I'm sure it will continue...

Jesse Olszynko-Gryn: Okay.

Julia Cumberlege: [Unclear] discussion. Thank you very much.

END OF TRANSCRIPT

Session 4: INFACT and Fetal Anti-Convulsant Syndrome Association (FACSA)

START OF TRANSCRIPT

Julia Cumberlege: So really if I could just say the purpose of this event, this meeting this afternoon is for the first time for you to put formally on record what you want us to hear and what you want to say. We have had informal meetings but this is now a much more formal occasion. However, I want to say that it's not like a parliamentary select committee which is very robust - this is much more like a conversation and we really want to hear from you. Of course we've had these informal meetings and now we're into oral hearings and these oral hearings are actually being recorded and they will go on the website so everybody, patient groups, know what other patient groups have been saying and so on.

So I would like to thank you very much for all the work that you've been doing in the past and to suggest that first of all if you could just say who you are? We know who you are [laughs] but it's good for our recording so people realise what this particular session is about. So I understand Janet you're going to start, is that right?

Janet Williams: We've had a bit of a swap Emma's actually going to start the reading today if that's okay?

Julia Cumberlege: Emma is going to start?

Emma Murphy: Yeah, is that okay?

Julia Cumberlege: Well I think if you could just introduce yourselves?

Emma Murphy: Okay.

- Julia Cumberlege: I don't mind how you do that but you're very free to say it and of course Warren, perhaps you could introduce yourself as well. So it's over to you how you want to play it, it's your session.
- Emma Murphy: Okay, I'm Emma Murphy I am Mum to five infected children by valproate and I'm from the Independent Fetal Anti-Convulsant Trust.
- Janet Williams: I'm Janet Williams I've got two adult boys affected. Again a CEO of the Independent Fetal Anti-Convulsant Trust and FACSA.
- Warren Matthews: Hi I'm Warren Matthews I'm a father of three beautiful daughters 17, 12 and eight and I'm going to be giving evidence of a father's perspective.
- Julia Cumberlege: Right and could I ask you speak up a little bit because this room is a bit like a...
- Emma Murphy: Okay.
- Julia Cumberlege: Right.
- Emma Murphy: Firstly, I would like to take you back to the thalidomide disaster of the '60s, remembering the reason why the Medicines Act of 1968 was first put into practice. Due to its horrific damages thalidomide will always be remembered as the world's worst medical disaster, receiving compensation most deserved in 1973. The same year sodium valproate received its full licence after a 12-month period in epilepsy clinics within the UK. However the lessons which should have been learned from thalidomide clearly hadn't, with evidence shown in INFACT's core bundle already presented to the review team.

Though archived documents we know that the drug company requiring a licence for sodium valproate reported their findings to the committee for the safety of medicines in 1972-3 that the drug has shown to be teratogenic but with no further clinical trials required. The drug was issued its full licence in 1973 with a statement in the CSM minutes of meetings from 18 July 1973 which read, the sub-committee believed however that the character of the evidence was strong enough for an assurance to be given to the main committee on the account but accepted the point regarding anxiety.

Nevertheless, they thought it would be best if prescribers were all made aware of the nature of the evidence and recommended that a statement similar to that proposed by ICI could be included in all the relevant data sheets but not on packaging inserts so that there will be no danger of the patients themselves seeing it. We know this paternalistic way in which it

was dealt with was accepted in the '60s and '70s however, there was no attempt to change this approach in the years following. With no actual warnings from the drug company on their patient information leaflets until the introduction of litigation in the year 2000.

The problem with the patient information leaflet is that most pharmacists use the white chemist box due to there being 100 tablets in the Sanofi box and so the majority of women never received a pill with their valproate. Due to the CSM instructing doctors not to tell their patients of the dangers of valproate in pregnancy, this has continued through the years with no new instructions from the CSM or the MHRA for them to do otherwise until the mandatory regulations were introduced in April this year.

However, new information for the product licence for Epilim noted information given by the Committee for the Safety of Medicines and stated from the main committee March 1974. On the evidence before them, the committee advised variation of the product licence to delete the requirement regarding monitoring condition that the indication for use reads as follows; for use in generalised focal or other epilepsy in women of childbearing age, it should only be used in severe cases or those resistant to other treatment. It is important to know that this information given in 1974 is that which was given as new warnings in the valproate toolkit released in 2016.

It is yet again vitally important to know that should this information have been used by doctors when first given to the committee in 1974 it would have saved hundreds of lives and thousands of children experiencing catastrophic damages. Due to the failure of legal action against doctors in 2003 and government's awareness of the instruction of the CSM in 1973 and the following failure of legal action against Sanofi in 2010, again with government's awareness that the drug company had informed the CSM of the teratogenic effects in 1973 INFACT were set up to run a parliamentary campaign for justice.

We began in 2012 with MP meetings which brought awareness of Valproate Syndrome into view, albeit at the time INFACT were not aware of the archive documents. In 2013 we had media attention through BBC Inside Out London and Panorama which brought the damages caused by valproate to the forefront and with our first meeting with the MHRA taking place soon after in August that year, 2013. Our discussions with the MHRA continued and resulted in a review on the warnings by the European Medicines Commission which began 12 months later in 2014.

In January 2015 INFACT discovered the archive documents stating that governing bodies were aware of the teratogenic dangers and had been since 1973. Due to our involvement with the MHRA and support from MPs our then chair of the APPG for AEDs in pregnancy, Teresa Pearce MP, raised the issue in a Prime Minister's question on 24 June 2015 and was soon followed by a meeting with the Health Minister Jeremy Hunt and Minister for Life Sciences, George Freeman with the meeting attended by the MHRA and Department of Health. The MHRA claimed that doctors had been told to use their own discretion when discussing valproate with women.

However, when we produced the archive documents stating otherwise, the tone of the meeting changed with a promise from the Minister, George Freeman, to ensure changes took place with a statement that this would not continue on my watch. At that meeting it was discussed with Minister George Freeman that there were 28,000 women of childbearing age prescribed valproate and figures from the Office of National Statistics showed that around 0.08 per cent of those prescribed valproate becoming pregnant. This means around 336 were exposed in one calendar year and that 40 per cent of those were actually affected. Meaning around 134 children are affected every year.

Bearing in mind the drug has been on the market for 45 years this means there may be as many as 6000 to 7000 affected. With the EMA review at its end in 2016 the new valproate toolkit was introduced, intending to encourage doctors to warn women of the dangers of valproate in pregnancy. INFACT had continuously stressed at the time that it was felt that doctors would fail to do so without it becoming a mandatory action, something which the MHRA and pharmacovigilance director Doctor June Raine was adamant would never happen.

The new toolkit was watched closely by INFACT only to find that doctors were failing to inform women of the new warnings and pharmacists failing to give out the new patient information leaflet in the white chemist boxes. Following an INFACT survey, media attention and a backbench business debate in October 2017, the MHRA along with Lord O'Shaughnessy set a meeting with our APPG Chair Norman Lamb and informed us that the new warnings were to become mandatory to ensure women received the advice required if they were to continue taking the drug during their childbearing years.

Janet Williams:

Since this came into action in April 2018 we continued to experience problems with it and still pharmacists failing to give the warnings to put the new stickers on the white boxes and to give the pharmacy cards to

the female patients. INFACT, following another survey, met with the MHRA to discuss this who have now passed on the matter to the enforcement agency and who are working with us at present. As you're also aware, in May this year INFACT were asked by the Health Minister to respond to the Department of Health's remit and for us to explain why we felt the government had to take action.

The remit read, to build an evidence case for exceptional treatment by outlining the specific needs of both children and adults affected by sodium valproate and their subsequent care needs and how they are different to those who suffer from mental and physical disabilities but are not affected by valproate. The case should also include evidence and information on the clinical regulatory and commercial benefits and any evidence of negligence or clinical malpractice, taking into account the existing evidence and standards at that time. In order for INFACT to respond in full to the Ministers' remit we put together a 300-page document as core evidence and required legal representation to do so.

We therefore approached [REDACTED] and a report was put forward by [REDACTED] chambers, which supported INFACT's evidence. Six months on and INFACT still have not received a response to that remit from the Health Minister and the Department of Health. INFACT have an ongoing national database where women can complete a form with their details if they have used valproate in pregnancy and have an infected child, whether diagnosed or not. At present we have around 2000 on the database who have been affected physically and/or mentally by valproate, the majority of which have neural developmental disorders and are on the autistic spectrum with poor speech, memory and understanding.

A large number of these children are now over the age of 20 and they continue to require a huge amount of support from their parents. The excessive stress these valproate sufferers experience to understand the outside world and the circumstances of their actions in many cases has caused mental problems such as anxiety and depression and seizures. This in turn puts an enormous amount of pressure and stress onto the parents, especially the fathers, with them having to give up work to take care of the children and their wife due to her epilepsy and a vast amount of seizures brought on through the stress.

We have dad Warren with us today who will give it from the father's perspective. Due to the family's situation with both parents unable to work we are aware that neither of them will receive a pension when they're reaching a time and age and then so are likely to require support

from the state for the rest of their lives too. As parents we continue to watch our children suffer no matter what age with the majority of suffering from birth with a major malformation in neural developmental problems and carrying this burden with them throughout education. Many families have had to continuously fight for diagnosis for medical and health support and treatments.

Many endure countless hospital appointments which can be changed at the drop of a hat by the authorities when their autistic child is set and prepared for it. The majority requires endless GP appointments due to recurrent infections and for support from social services. Many of those affected by valproate find it hard to cope at home, struggling with noise, especially that from all the siblings, sound, smells due to hypersensitivity and the older affected people unable to learn a life skill and live alone without ongoing support. So I've come to the conclusion.

Through new research, a paper released only this week we are now aware that the amount of valproate taken by mum during pregnancy does not conclude if her child will be affected or not. Instead the findings show that any amount of valproate in pregnancy will affect the child, causing brain injury. This new paper written by Doctor Bromley and others states, individuals with Fetal Valproate Syndrome who present with characteristics, facial presentation should be considered at high risk with difficulties regardless of the dose of valproate exposure or the presence of a major malformation.

Due to this our latest work with Doctor Bromley and Professor Jill Clayton-Smith we await the new diagnostic criteria for valproate exposed children which encompasses autism and we classified Fetal Valproate Spectrum Disorder. Over the years there have been so many children who have suffered as a result of systematic failure. This is the opportunity to put things right and to help those harmed by valproate ensuring near normal life. This will not be achievable through clinics, diagnosis or medical intervention alone but by allowing them and their families, supporting them the life-long financial help they require.

For the majority of families living on council estates where they endure violence and bullying and those living in private lets where their parents are at constant alert that their tenancy agreement could be ended at any time, they remain most vulnerable and feel life is unsafe for their children. The time has come where we have to stop these families from suffering at the cost of government's hidden truths about valproate and the drug company continuously making hundreds of millions every year on the back of it. It's time to change cultures and behaviours towards those

disabled by this drug and to ensure they have the opportunity to live a life where they are able to own their own home and are not discriminated against through the system simply because the government refused to tell their parents the drug will be poisonous for them while in the womb.

In 2016 the Minister for Life Sciences George Freeman in the letter stated, if it happens that there are lessons from the Department's historic handling of this, I will of course be happy to consider a statement of regret if appropriate. So during your summing up we ask you to consider the above. The many children affected. Those especially who are now in their 20s, 30s and 40s and the amount of pain and suffering they and their families have endured as a result of devastating effects of this medication. Let's also remember the many families who have experienced loss a result of valproate in pregnancy.

The death of a child is unbearable as for any family so it is important you consider them too. When making your recommendations we ask you to consider a guaranteed future for children affected ensuring diagnosis for their education purposes. The present geneticists train the new generation to ensure diagnosis and the constant knowledge of Fetal Valproate Syndrome. For future planning to make it easier to replicate guidelines to forge a pathway for other AEDs in pregnancy. That a respectable care plan is offered to those affected, to support them through their lifetime, allowing them a mortgage and sustainable life.

The families experiencing bereavement due to valproate exposure receive a posthumous payment and that the benefits system recognises Fetal Valproate Syndrome for benefits such as Employment Support and PIP, awarding them funding for life in these circumstances and that the funding to allow the forming of a diagnostic clinic is ring-fenced so as to stop any future government from withdrawal.

Julia Cumberlege: Thank you very, very much indeed, that was very clear. Can I just ask you - you clearly have gone through all this very often with enormous thoroughness and you've done the remit, you've told us what you want and, thinking all about that, what do you think is really the most important thing that you feel that we should be recommending? Out of all this that you've been through, that you've seen, that you now have experienced, and in the past, but is there anything in particular that really shines through if only the Review would really concentrate on this area? Or is it just too complex for that?

Janet Williams: No, I mean for us in particular the main area is to make sure that not just the children affected, but the families are ensured that they can afford to

live how they need to live. We know that bringing up a disabled child costs more, we know that a lot of these children when they reach adult age are unable to work. The majority of them will be on benefits for the rest of their life as will the parents who've been unable to work and do not have a pension behind them. So for them to make sure there's financial stability has got to be first and foremost I think.

Julia Cumberlege: Well that's very helpful yes. Thank you for that. You talk about trying to change the culture within society really towards these children and presumably to the adults and families as well. How on earth are we going to even think about that? How are we going to do that? I mean it's a huge task isn't it?

Janet Williams: Well for us, I mean that's something that's already working on at present with the work we've been doing with the MHRA, changing the way that doctors think as far as warning women about the medication when they're prescribing it, about the way that pharmacists dispense the medication, to making sure there's warnings on the boxes, but I also think it's important for it to be recognised within schools like Downs Syndrome would, like autism itself would, and I think that's the sort of structure that we need to be going through now to make sure that the health system and the education system do recognise this condition.

Julia Cumberlege: Finally, a question from me and then I'll pass it to my colleagues. Numbers are a real problem in this area...

Janet Williams: I understand that, yeah.

Julia Cumberlege: Have you got any clarity now on the numbers that you think we should be addressing?

Janet Williams: Well, it's like I've stated it here, I mean we did discuss this previous with the MHRA as well and we know the figures that we worked out with the MHRA with, it was George Freeman wasn't it back in 2015 and they've stated that there was round about 135 or something that was affected every year, going off the percentages. So obviously it's going to fluctuate because of the amount of and the way that they've sort of been prescribed over the years, but we reckon there's around about maybe 5000, 6000, top 7000 children that will have had a diagnosis and will be affected.

Sonia Macleod: Is that children who are diagnosed at the moment?

Janet Williams: No that's just affected, that's the whole, yeah.

Emma Murphy: That's the whole.

Simon Whale: That would include people who haven't yet been diagnosed?

Janet Williams: Of course, yeah.

Emma Murphy: Yeah.

Julia Cumberlege: Right [unclear].

Cyril Chantler: You mentioned Emma the figure of 40 per cent are children from mothers taking valproate. That's direct effects. There are two things that I don't understand. One is how can you be sure there aren't smaller effects because we know it affects general IQ that you wouldn't know about in addition to that, and secondly there's the effects on the other children in the family and the parents of the tension and the stress that Lauren so well described, so the French scheme say they received 323 for what they call direct victims in utero exposed children but they also recognised 764 indirect victims, parents and siblings who I take to be children in the family and the effect on the parents. Do you have any observations on that?

Janet Williams: Well, all the research that's been done over the years and no doubt that will be discussed when the medical professionals come in. The 40 per cent comes from research that was done and was started by Doctor Bromley in 2013 and she stated that there was 40 per cent of these children that had been exposed to valproate had actually got neural developmental disorders which included autism. So that's where the 40 per cent comes from.

Cyril Chantler: Yes. I'm arguing that it may be more, that's the point.

Janet Williams: Well I can only state what the medical profession has told us. We actually know that if a woman gives birth to a first child and that child is affected then there's a higher percentage chance that her second child is also going to be affected too. So when it comes to affecting other siblings unless that woman has changed her medication in any way in-between, it's quite possible that if the first one's affected then the second one will be also.

Cyril Chantler: Okay, thank you.

Julia Cumberlege: Can I then ask you, clearly women who are epileptic and take this drug because they feel it's suddenly helping them in their epilepsy and that's absolutely understandable and then they're pregnant and then they have a child and the child is disabled. Then you've just said that also there's a

likelihood the second child would be disabled so is there no sort of research done on the first child to ensure that this could have been the cause?

Janet Williams: Well, we know there has been a lot of research over the years on this and of course if Professor Jill Clayton-Smith is here later on, no doubt she'll be able to explain to this to you about all the research. We know for a fact that valproate does cause this particular syndrome and these problems to varying degrees, so I mean obviously there has been a huge amount of research done on this and we know that the drug company itself back in '72, '73 there was a clinical trial on epilepsy for 12 months before it had its full licence and they actually stated that the drug was found to be teratogenic anyway, so we've known this from a very, very early age. Very, very early on.

Julia Cumberlege: So it was the case that this drug was still in the women's blood system or whatever...

Janet Williams: Yes.

Julia Cumberlege: ...and so it wasn't necessarily that she took more pills, it was there anyhow are you saying that? Or are you saying you need more pills in order to - I'm thinking of the second and the third and the fourth.

Janet Williams: Yeah I mean to be honest in my situation for example, I was on 1200 milligrams with both boys, yet we've got women that come to us where the drug doses has changed but the children have still got the same problems so it seems to be - and again I can't quote this medically but it seems to be from our perspective that it also depends on the mum's metabolism and how quick that drug gets into her system as to how badly it affects that child.

Sonia Macleod: How are old are the children when they're usually diagnosed? What's your average sort of diagnosis?

Janet Williams: Well again that's something that varies. We have children that've been diagnosed at birth because of their facial features, then we've got children that have gone on to be six, seven maybe eight and shown the autistic spectrum disorders and received the diagnosis at that point.

Sonia Macleod: So you wouldn't necessarily know between your first child and your second child [before]...

Janet Williams: In some cases probably not no.

Sonia Macleod: ...if your first child had been affected. I mean sometimes you would but sometimes you [unclear].

Warren Matthews: I think as well for a new parent with a new child, they don't know anything and obviously children progress at different speeds. I know for ours they all walked different times, spoke at different times so the same between the first and second; it's a hard thing to try and gauge because you're new parents, it's a new experience isn't it.

Simon Whale: Can I just ask about current prescribing practices so until - do correct me if I'm wrong but my understanding is there's an intention now to change pack sizes so we don't have this issue between the original pack and the white box and the labelling and so on. What's your thinking on that? So when that gets implemented let's not say if, let's say when it gets implemented because that's what we're all expecting, does that reduce or completely remove the risks that you're most concerned about or is further action needed?

Janet Williams: Well, we hope that that will really bring the numbers down because at the moment it seems to be the biggest problem is with the white chemist box. So we're hoping with the smaller purple Epilim boxes, obviously that will then take that into the equation so yeah, hoping that will help tremendously.

Simon Whale: So that should...

Janet Williams: Hopefully yeah.

Simon Whale: ...stop the risk of future exposure provided people act on the patient information.

Janet Williams: Well you can't guarantee that. Obviously if people take that information and act on that information then hopefully yes.

Simon Whale: Yeah. Provided they act.

Janet Williams: Yeah.

Valerie Brasse: I was going to ask you the question. You've been actively campaigning for such a long time and you've learnt invaluable lessons about what happened with valproate. There is the next generation of drugs that are coming out called Keppra, I don't know how you pronounce the full name. But if you were to say now, well what should they be doing that maybe they're not doing as a result of the lessons you've learned so this doesn't happen again?

Emma Murphy: We have brought this up with the MHRA because I now have a child affected by Keppra, devastatingly. We have brought this up because it is an issue and they have said that they are at present not going to act on it until Epilim has been resolved and I find that an insult. I find it an insult to the women and I find it an insult to the children who, we know all epilepsy medicines are harming children and I think it is a disgrace for the MHRA to not be learning now as we are here working on Epilim, it's a disgrace that they're not working on the other medications.

Janet Williams: We know that the other medications do have warnings in the patient's information leaflets. Nine times out of 10 those leaflets are that big that a lot of people don't pay much attention to them unfortunately. So for doctors to be giving women of other medications an informed choice like they would with other things that are prescribed. You know, you usually pick a medication up from the pharmacist and the pharmacist will ask you, so why they can't do that with the other medications? When we started this campaign all we wanted was women to receive an informed choice. We didn't necessarily ask for the pregnancy prevention [path] and for it to be [banned] as such so for women on other AEDs just to receive that informed choice and to be told that that would be a possibility, really would be a good place to start.

Emma Murphy: It's currently not happening. We have women contact us every single day, the newer ladies being switched from Epilim to now Keppra are coming and they're just not being told of the dangers and that's what we mean when we speak of there needs to be a culture change. Behaviours need to change because these medicines, they're teratogenic and they're harming babies. We can move forward and another 10 years have a Keppra epidemic of this. We've got to learn from this and stop this, and hopefully the work that we have done it will make it easier to implement changes with the other medicines. Also we've campaigned for six years, it's taken six years to get these warnings in.

Valerie Brasse: Do we have the same white box problem with Keppra?

Emma Murphy: With all of them.

Valerie Brasse: So having you've got to the point where you're getting smaller pack sizes now with valproate, we're still left with Keppra coming in white boxes without a patient information leaflet?

Emma Murphy: Yes.

Janet Williams: Well all the medications they all differ as to how many is in the actual box so for there to be say 28 in a box then you've got the month covered even if everyone just takes the one a day.

Simon Whale: Have you discussed with, in your discussions with MHRA have you talked about the sort of pan-AED approach as opposed to just an Epilim approach to pack sizes?

Janet Williams: That has been mentioned.

Emma Murphy: Yes.

Simon Whale: What's their position?

Janet Williams: But again they said they want to deal with valproate first before they move on but I think we need to be stepping up a little bit with other AEDs before that even happens. We need to be looking at making sure women get the patient information leaflets, get the warnings, get the prompt if you like. Just to give them that informed choice that it is a possibility. You can't always guarantee that that's going to happen. We do have one or two ladies that have come to us whose child hasn't been affected which is brilliant. So obviously it is quite possible that that could be the case with the other medications but I think an informed choice of some description needs to be there.

Simon Whale: But as you said it's not just the patient information leaflet is it because you're right, not everyone reads that and that's not...

Janet Williams: Well this is it.

Emma Murphy: There needs to be a culture change within healthcare professionals because women are asking the questions, they are purposely making appointments to ask these questions and doctors just - they just state that these medicines are okay, they control your epilepsy.

Janet Williams: In one meeting in particular with the MHRA there was a person there from NHS Digital and he actually turned round to us and said that the doctors in some circumstances are not giving these warnings verbally because the warning comes up on the screen and he called it prompt fatigue. So the warning will come up and I haven't got time for that, hit the button and it'll go away. So the warning's not going across because of this prompt fatigue and that's the culture that needs to stop within the NHS because these women no matter what medication they're on need that informed choice and need to be pre-warned.

Simon Whale: Pharmacists should be doing the same.

Janet Williams: Of course they should, yeah.

Julia Cumberlege: Can I ask about epilepsy? So on the whole we hear a lot about Epilim and Sodium valproate. Are there other medications that are equally effective to prevent seizures to help women who are epileptic?

Janet Williams: Everybody's different. So just because it suits one person doesn't mean to say it's going to suit another. Epilim didn't work for me but it worked brilliantly for Emma and I would imagine it's going to be the same with other medications. Personally I've tried about eight different medications along the way, different combinations and the medication I'm on now is the best I've ever been and it's taken me all that time to find it. So obviously there's going to be other drugs out there that will be suitable.

Julia Cumberlege: Do we know if those other medications have the same impact on pregnant women?

Emma Murphy: We do know they are teratogenic, not to the degree that Epilim is.

Julia Cumberlege: I see.

Emma Murphy: That's the huge worry.

Julia Cumberlege: Yeah, great. Well other things - I don't know if anybody wants any other questions?

Valerie Brasse: Just one more from me actually. It's just about the - not the numbers so much because we're now talking about that we think the best estimates are of families affected but how are we going to reach - if the issue is about getting the support and care packages people need, how are we going to find those who have yet to surface? The pragmatic way of doing it.

Emma Murphy: This has been an issue and when we first started this campaign, maybe it was me being naïve, but we asked for a public health conference to be held, that the Minister Jeremy Hunt at the time would hold a press conference and alert ladies to this because it needed to be in the public domain and since then we have struggled with media to get it out in the public domain. I think for this there needs to be a public press conference.

Janet Williams: There needs to be something out there if we need to bring these ladies forward for them to be aware. If we're looking at reaching the women that need the help for the children, there definitely needs to be some sort of - awareness campaign isn't the right - I don't know the right terminology for it but there definitely needs to be something. We've done media, newspapers and TV but that's, it just doesn't reach people.

Emma Murphy: It just doesn't reach. We thought when we'd done Panorama we thought we would bring these ladies, it just didn't.

Janet Williams: It didn't happen.

Emma Murphy: It's so disappointing that we can't reach these ladies. They need help.

Janet Williams: A lot of the time I think the sad thing about it is some of the women tend to be - don't want to accept the fact that the problems that their child has, has been caused through them taking the drugs. We've all gone through the guilt trip and believe me it's not nice. So some ladies don't really want to accept that this has been caused by the drugs.

Simon Whale: Can I just ask about, just on this point of how do we find everyone else who hasn't yet been identified or had the diagnosis or joined groups like yours. We were trying to work out whether it's feasible to seek the help of GPs in this because the GP's medical record of all their entire list should give them the opportunity to say, well I know how many women I've got on my list, I know how many women who are diagnosed epileptic I've got on my list, I know how many women who are diagnosed epileptic and taking valproate or have taken valproate are on my list...

Janet Williams: Yeah.

Simon Whale: Isn't that part of the way forward in terms of finding the people who haven't yet surfaced?

Janet Williams: Possibly.

Emma Murphy: Yeah.

Warren Matthews: Maybe an audit? Some kind of audit.

Janet Williams: Well it's like everything else with the prompt fatigue. The GPs are really dealing with a lot at the moment, a lot of other issues as well and to put that onus onto them as well as everything else, I don't know how we go about doing that. I mean obviously yeah, they probably would be the best people to reach these ladies, definitely.

Emma Murphy: But if we're struggling now with the warnings it's going to be hard to find these ladies.

Sonia Macleod: Plus I guess you are going back up to 40 years...

Emma Murphy: 40 yeah, exactly.

Janet Williams: Of course.

Sonia Macleod: You are going sometimes to paper records, it's not going to be a straightforward...

Julia Cumberlege: Right. Are there any questions you'd like to ask us? We want to keep in contact with you, this isn't just a one off. So as we've said to other patient groups please come back to us if you want further information.

Janet Williams: Well, we haven't really got any questions, we've got a copy of the oral submission here for you if you want take that with you?

Julia Cumberlege: Thank you. That will be very helpful.

Janet Williams: We've got some ideas as to maybe how things could be done. We've got information in here as to how these figures have been reached and where they've come from, so it may give an idea as to the follow up to what we've said.

Julia Cumberlege: Thank you very much. All right, well thank you so much and thank you for all you do. When you're out of this room [laughs].

Emma Murphy: No thank you as well.

Janet Williams: Thank you very much.

Julia Cumberlege: Supporting other woman and their children and thank you Warren for coming and telling us about your [unclear].

Warren Matthews: Thank you.

Emma Murphy: Thank you.

END OF TRANSCRIPT

Session 5: Dr Rebecca Bromley, Professor Jill Clayton-Smith and Professor Peter Turnpenny

START OF TRANSCRIPT

Julia Cumberlege: We've got this tremendous expertise here in the room this afternoon this sort of trinity of expertise. I'm not quite sure how you really would like to play it, it's your session but if you could start just by introducing yourselves so it's on camera so that when we come to put it all together, the evidence that we have we know who we've been talking to. So would you like to start?

Jill Clayton-Smith: Okay, would you like me to tell you a little bit about how I became involved in this or just names?

Julia Cumberlege: No if we could just have your names to start with could we?

Jill Clayton-Smith: So I'm Jill Clayton-Smith. I'm a clinical geneticist and I work at Manchester University Hospitals Foundation Trust. I've been a clinical geneticist for over 30 years now.

Julia Cumberlege: Thank you very much. Yes...

Rebecca Bromley: I'm Rebecca Bromley, I'm a neuropsychologist, so I'm interested in how brains develop and function and I work up in Manchester half-time at the University and half-time at Royal Manchester Children's Hospital.

Julia Cumberlege: Right, thanks very much.

Peter Turnpenny: I'm Peter Turnpenny, I'm a clinical geneticist working in Exeter where I've been for 25 years.

Julia Cumberlege: Thank you very much indeed. Now you want to say about yourselves did you?

Jill Clayton-Smith: So I first became interested in this whole topic of the effects of anti-epileptic drug exposure in babies in the early 1990s and that came about because I'd seen in my just routine clinical practice just by chance, a series of children who'd come into my clinic for diagnosis. So my interest is in rare multiple malformation patterns and intellectual disability syndromes. I'd seen a few patients over a relatively short period whose mums had all taken anti-epileptic drugs during pregnancy and whom we'd investigated

really quite significantly and hadn't found any other explanation for their symptoms.

So one of the thoughts was that this might be due to anti-epileptic drugs and doing a little bit of reading at that time, basically the only information in the literature were anecdotal case reports mostly, well there were case reports and they were saying the same thing that I was thinking and that the signs and symptoms of the children I was seeing were similar to the ones that had been reported. So I thought there must be something in this and actually at that time in 1995 we had a little paper published called Fetal Valproate Syndrome about exposure to sodium valproate in pregnancy. But quite rightly a lot of other people when we drew attention to this said, well anecdotal reports are not a very good level of evidence and you're seeing a biased subset of children, which we were because there were presenting with problems to our clinic, so you need to really find some evidence that suggests there really is a problem with anti-epileptic drug exposure.

So at that stage I got in contact with a few other colleagues, my colleagues from Manchester and Liverpool, and we set out to apply for some funding to setup a study so that we could follow children exposed to anti-epileptic drugs in pregnancy right from pregnancy, not just wait and just see the children who'd been exposed and were presenting with problems. So then followed quite a few years of, we managed to get funding actually from the National Lottery to do that and we made lots of applications to other bodies for funding but actually when you're wanting to follow up children long-term a lot of funding bodies aren't interested in that, they want to fund a study where after two years or three years you'll have quick results and you'll have a paper, they don't want to wait more than six years to fund a study.

So we encountered quite a bit of difficulty in getting study funding but we did setup a prospective study and with a lot of goodwill as well from everyone we followed up a cohort of children to the age of six. Several other studies around the world had started to do the same thing and so we got to the point where there was enough significant evidence to say that there were problems seen in the children of mothers who'd taken anti-epileptic drugs during pregnancy. Then my own interest I guess has moved on to what's the description of these sorts of problems, what are the sorts of problems that children encounter and what's the natural history of these problems? I've actually...

Julia Cumberlege: I'm sorry can I stop you just for a second.

Jill Clayton-Smith: Yeah.

Julia Cumberlege: So you did the research, it was published and what year was that?

Jill Clayton-Smith: So was it 2003, the three-year-old?

Rebecca Bromley: No so it was a little bit later, we collaborated with some US colleagues so there's two strands to the cohort. So the first publication was on malformations that came out lead by Kimford Meador in 2006 with the three-year-old IQ and in 2009 also led by Kimford Meador. There was then a published paper led by myself on our UK only data in 2010 and then we published our six-year data in 2015 and Gus Baker was the lead on that paper.

Julia Cumberlege: Sorry and the 2015 publication was?

Rebecca Bromley: Led by Gus Baker and it was on the IQ of the children at six years of age.

Jill Clayton-Smith: So the difference between our UK study and the American study which we'd joined with is that we also followed up a control cohort of children so we could compare the outcomes with matched control children and that gave us a little bit more power to our study. So my work after that has been involved with the natural history of this condition and I've been able to over time follow up children from childhood and into adulthood, we've seen some adults now well into their twenties and seen the change in signs and symptoms in these children and then just more recently I've been involved in leading a European group which has drawn up some guidance on management of children exposed to sodium valproate in pregnancy to try and have some expert consensus even though there's no randomised control trial evidence about the best way to care for these children. So that's the point that I'm at now.

Julia Cumberlege: Right thanks very much. Do you want to take that on further...

Rebecca Bromley: Yeah so just to add just very slightly, so I actually get involved in this working on the study that Jill mentions and that formulated my PhD and then we've gone on following that cohort to establish a number of other cohorts including one we have at the moment which is funded by NIHR, National Institute for Health Research, where the question is less about valproate it is about the other widely used anticonvulsant medicines at the moment and that's what we've currently got going on.

Peter Turnpenny: So I became involved with this field in the mid to late 1990s and I do recall one of our national dysmorphology meetings where Jill actually together with her colleague Di Dyer had a set piece presentation on this condition

Fetal Valproate Syndrome and there was a lot of unanswered questions, quite a number of pictures of patients couldn't recognise them and I had to say at the end of that session I didn't feel I would have very much expertise at being able to do that.

But it wasn't very long after that that I met a patient, a mother and her child in one of my clinics and the child had been exposed to valproate and I think carbamazepine if I remember correctly and this was a very persistent mother and I saw her on two or three occasions and I realised that there was a significant issue here and that I had to make a choice between either walking away from being involved or getting a little bit more involved. So I decided to do the latter and that led to a study of which I undertook with my formal trainer in Aberdeen Doctor John Dean. We gathered together a group of patients through the patient support groups mainly and assessed them and wrote that paper up in the year 2000 and then we combined with that work with our colleagues from the ophthalmology department where I work and they assess these children's eyes and that separate paper came out about the visual effects of this problem.

We all recognised that this was a cross-section study it wasn't a prospective study. It was always going to be subject to ascertainment bias but nevertheless I think by then those of us who were seeing patients were all convinced that there was a major issue here and that these patients didn't all have the same set of features for no good reason and what was in common for all of them was that they had been exposed to this drug. So a number of other papers came along as a result of that I contributed to doctor John Dean's work in the north east of Scotland which was very thorough in the population that they looked at and I think that was a very good contribution.

At that point Jill's study, Manchester and Liverpool was also getting underway and beginning to produce very interesting and helpful data, crucial data I would say. In the mid noughties I also got sucked into the legal case that was being built that eventually was shelved in 2010. I wrote a lot of reports for that which brought me into contact with a lot more patients and families and gave me a much wider, broader clinical experience of the whole area and partly as a result of that I also received referrals from outside my region to assess.

So I think over the years I've developed quite a reasonable clinical experience of this and have contributed as well to Jill's current work with the consensus group working with the support groups as well. I think one of the things I'm now recognising is that whereas this particular issue was

quite in front of people in front of our specialty for a period of time, I'm beginning to realise that I think the expertise level that is there amongst our colleagues has dropped away and I think that's something which has to, well it's a shame but I mean it's perhaps one of those things, and some efforts need to go into re-educating our colleagues as to how to recognise this condition.

So I think one of my main thrusts has been really the diagnosis and how to achieve that. I think it's not easy to diagnose and you can come up with criteria on paper and if you know that the child has been exposed to the drug then that's one thing but then you have to obviously assess the child and come to a judgement as to whether or not the child has been affected and that is far from easy because often the features are subtle. So we have a framework for that but I still think it requires considerable expertise to actually see patients in the clinic and form an authoritative judgement about a diagnosis.

Julia Cumberlege: Right well thank you very much indeed. Now is there anything else you want to say to us before we put some questions to you? No? It just sets the scene for us.

Rebecca Bromley: Sure.

Jill Clayton-Smith: Yes.

Julia Cumberlege: So thinking about the past history, thinking about what you've been so diligent in trying to achieve and particularly your studies and things do you have any views about the way the regulators have actually taken on this particular issue? Because clearly you've found a lot of things that you feel are very pertinent to parents and to the children. Do you think action should have been taken earlier to actually ensure that people were made more aware of this particular problem?

Rebecca Bromley: Do you want me to start? I did have a little think so I apologise in our written submission we maybe didn't cover this in as much detail as we could everything else but the document got so big and wild it's only when we look back over it we realise that maybe we hadn't addressed this so well. I did take a bit of a look at this last week in preparation for this discussion and I think the overriding issue here is wider than just regulation. Generally data took a long time to cumulate and that was really because we have a very passive post-market surveillant system. So it's based on spontaneous reporting, so alert clinicians writing something up like Peter started off, or flagging it through the yellow card system or the American equivalent or other countries.

Or we have researchers who pick and choose based on their interest what they want to look at and then obviously what funding's available also drives that. So we don't have a very well, and this is still the case today, we didn't have for valproate and we don't to date, we don't have a streamlined system, co-ordinated system whereby newly licenced medicines are routinely checked at the human level and whether that be immediately for malformations and other physical problems that are immediately obviously at birth or whether that's in terms of follow up, it doesn't happen we have a very ad-hoc system. So data is slow to accumulate.

When you look back at what was known with valproate versus how information sheets changed, I think the wording from what I read last week, there was some risk information there but I think it's how it was worded that was maybe slightly misleading or caused confusion. So for example until 1999 a lot of the data compendium sheets talked about risks with valproate and other anti-epileptic drugs and untreated epilepsy. So actually if you're a doctor reading that and having to tell that to your patients there's a lot there that doesn't differentiate valproate and certainly by 1985 there's a very clear differentiation in terms of Spina bifida for valproate versus the other anticonvulsants and verses the control population.

I think certainly by 1990, 1991 other malformations there were then kind of limb defects, heart defects again the data was there to show that they were much more prominent in the valproate exposed group than other anti-epileptic drugs and yet the data sheets didn't change, it still talked about this encompassing risk across all these three groups. I don't know if you agree with?

Jill Clayton-Smith: I would think that that's a major contributor that they lumped all anti-epileptic drugs together into something called Fetal Anticonvulsant Syndrome instead of separating them out and once we did our study and separated out the different groups following up children who'd only been exposed to one particular drug as opposed to different combinations, it became clear that there were differences between those groups.

Cyril Chantler: The phenytoin was recognised much earlier, wasn't it?

Rebecca Bromley: It was but it's level of teratogenicity isn't at the level of valproate.

Cyril Chantler: Thank you.

Peter Turnpenny: I think that it's also true to say that neurologists as a group felt their duty of care quite understandably was to treating their patients' epilepsy,

pseudo-disorders and achieving effective control which is entirely understandable and right and so in valproate proved to be an excellent drug for that and as a group they were all more or less doing the same thing, they were all agreeing with each other that this usually, that this was a good drug and in many, many cases there wasn't actually a very effective alternative. Also they were not prepared to look at the data as it was and come to the conclusion that this was necessarily a dangerous drug for quite some time. So I think in terms of how that would stand up if it ever came to court, all the neurologists were basically doing the same thing and so they could always back each other up.

Rebecca Bromley: And in particular, you read the editorials from the time [in Cape], so the neurologists who were often asked to write editorials covering data that maybe Peter put out or Jill or somebody else and there was this kind of fall back, well will other drugs also carry the same risk but actually if you delved into the data and Jill's has separated it out by drug, the risk of valproate was far superior than what it was with phenytoin particularly once you get into the higher dosages with valproate. But I think again it comes back to research really didn't evolve quickly enough, it wasn't coordinated whether that be by the regulator or the company or someone who should have had oversight, we were left in a situation where our [unclear] and methodologies sometimes are poor as well and so you can see why neurologists had questions.

Jill Clayton-Smith: So we had quite a few really conflicts of interest in the system so as Peter says, the neurologists were wanting to treat the epilepsy in the best way that they could and were sometimes, I'd be into meetings where they'd been quite hostile about the suggestion, I've had the comment you will get a good drug banned thrown at me in the middle of a meeting. You can see why they want to treat the epilepsy as best as they can and they're worried about this situation of sudden unexpected death in epilepsy. Then there was also an issue of not wanting to worry mothers I think that came into it.

So when people were looking at the wording on the information, people were concerned for I think for the reasons for them were valid ones, that they didn't want to put anything on the information sheets that would cause anxiety or concerned mothers. If you were to speak to mothers now most of them will say they would have preferred to have known even if they'd been anxious about it and that's the one thing I think that upsets a lot of people that they might have continued on whatever medication but they wanted to make their own informed choice. Then of course there were the interests of the drug companies making the anti-epileptic drugs

and so I think there were many conflicts here all coming together and we didn't have one system that superseded all of those and took them away.

- Valerie Brasse: So are we still in the same position when thinking about the next generation of anti-epileptic drugs?
- Jill Clayton-Smith: I suspect we probably are yeah.
- Rebecca Bromley: Yeah.
- Julia Cumberlege: So is the one system then, you say you're looking for one system. What would that system look like?
- Rebecca Bromley: I think in the US now Christina Chambers who is at the California Teratology Information Service they've just proposed a system to the American regulators whereby you use the combination of routinely collected healthcare data so data mining across different child prescription records, mums' health records, infant records but along with the detailed direct observational studies that get you the real detail, the ability to control for confounders, the clinician-led blinded assessments and I think that's something that when we met with the European Medicines Agency earlier on this year that it looks like that group was proposing to the European medicines agency and hopefully that's something that they will take forward.
- Cyril Chantler: Have you written that down?
- Rebecca Bromley: There is a paper coming out but it's being led by the European Medicines Agency.
- Cyril Chantler: So when can we see it?
- Rebecca Bromley: We haven't seen the draft since our meeting unfortunately.
- Peter Turnpenny: At a time that I was thinking about possibly trying to do a study in the South West similar to perhaps what Jill and colleagues have done, I made some enquiries as to how I could find these women who'd been prescribed this medication and come through the antenatal clinics and so forth, and I quickly faced a barrier that this was going to be almost impossible and it was just such a huge task to try and overcome that hurdle and I was a single handed consultant for quite some time, I just didn't have the wherewithal to try and challenge that to be honest, so I think there is no system that you can go to in antenatal clinics or on data collection in a public health sense and find these patients.

Jill Clayton-Smith: I think I'm right in saying that there isn't a code either in the International Classification of Diseases or any of the other ontologies that we use that would enable you to go to databases and pick out the cases to follow. Then the other issue is surveillance because we're looking, I mean the commonest effects are developmental effects, surveillance is expensive. Developmental assessments are really expensive to do if you use a good quality developmental assessment and part of what Becky is doing at the moment is working out how best to do developmental surveillance and whether you always need these very expensive detailed face-to-face surveillances or whether you can work from things like parental reports.

That's one of the barriers I think and that's what we found with our studies because every time we worked out a budget for a study that we wanted to do, the budget was massive because we had to put in all this psychologist time and so that I think has been a major barrier.

Julia Cumberlege: You have my sympathy on that I quite understand. Can I just ask you and then I'm going to pass to my colleagues. In the evidence that you very kindly gave us and I think it's fantastic to have three of you working together as one, it's really helpful but you mentioned that you're currently producing a consensus guideline document regarding Fetal Valproate Syndrome Disorder which they expect to publish next year we're told, so you're going to publish next year.

Jill Clayton-Smith: Yeah.

Julia Cumberlege: Obviously you can't tell us what's in that because you're going to publish it next year but can you just say to me the sort of purpose of this and why you're doing it and what you expect the result to be?

Jill Clayton-Smith: So this was one of the initiatives of one of the European Reference Networks which have been setup which actually we're just about to be forced out of. We have some networks of expert centres throughout the EU where one of the aims of the networks is to share expertise between different centres, work out best methods of diagnosis and care and for those diseases which are curable, work on cures. So one of the initiatives we had was to look at how we might better care for individuals who've got Fetal Valproate Syndrome or Fetal Valproate Spectrum Disorder as we prefer to call it now.

So what we did is in these very rare diseases you can't find much in the way of randomised control trials which tell you whether one way of management is better than another so what you have to do is get all the evidence you can from the literature so do a deep literature search, look

through all the information there is there, get together all of your experts and get their expert views and draw together a list of recommendations which you can then grade for how certain you are that they're correct and then make a list of recommendations for care plans based on the best evidence that you can. So we went through this process, we gathered individuals, when you're doing a consensus document like that also you need patient involvement...

Julia Cumberlege: Absolutely.

Jill Clayton-Smith: So we had patient involvement because it's no good having a care plan that's not feasible for patients. So we've been through the process of the literature review, drawing up guidelines, doing a commentary in the document which talks about our evidence for the guidelines, drawing up some revised diagnostic criteria and then presenting that in an overall document which we're going to publish. Then also one of the things actually that the patients suggested were that lots of patients and GPs don't like reading very, very long documents so we've also done some supplementary sheets that are quick read summaries for the groups of people like teachers, GPs, paediatricians and patients.

So we're just in the final stages of doing that and putting that together and hopefully we'll be submitting that for publication soon, probably targeted at one of the paediatric journals because that's where most of the people doing the care will be.

Julia Cumberlege: So this isn't about prevention, this is about care?

Jill Clayton-Smith: It's about care. There is a little section on prevention but it's really only echoing the recent guidelines, yes.

Julia Cumberlege: So the patient groups have been absolutely centre to all that...

Jill Clayton-Smith: Absolutely yeah, they've been just as much a part of that group as any of the other experts.

Julia Cumberlege: We have learnt a huge amount from the patients.

Jill Clayton-Smith: Yeah they're amazing. I did a presentation in Brussels last week with Janet Williams we did a presentation between us and she was just amazing it was very powerful.

Julia Cumberlege: Thanks, so.

Cyril Chantler: Can I go into numbers please because I'm really confused. I've been told there are 20,000 women who've taken valproate in pregnancy. I've been

told today they think there are 6,000 affected people, children and in this country affected by it. The French say that there's 30 to 40 per cent of between 41,000 and 76,000 children exposed between the start of the marketing of their valproate in '67 and 2016.

We know about the IQ effect and the French also talk about the people who are quite reasonably asking for support: 323 direct victims in utero exposed children and 764 indirect victims, parents and siblings, and certainly we've met lots of families where the effects of valproate aren't just confined to the child who's affected but affects everybody else in the family and in any case how do you know that a child who's not seriously got all the features of Valproate Spectrum Disorder doesn't actually have suffered some loss of IQ for example?. So have I explained my confusion and can you help me?

Peter Turnpenny: I think the figure that you started with there, 20,000 exposed children...

Cyril Chantler: Women who've taken it.

Peter Turnpenny: Women who've taken it over 40 years something like that, more than 40 years. That's too low.

Jill Clayton-Smith: That's an underestimate.

Rebecca Bromley: On a telephone conference with MHRA last week they said currently there's about 23,000 women still taking valproate in the country annually at the moment.

Cyril Chantler: Okay that will cover...

Rebecca Bromley: Yes 14 to 45 yes.

Peter Turnpenny: Childbearing age.

Cyril Chantler: So that's okay right.

Rebecca Bromley: So it's much bigger over the years.

Jill Clayton-Smith: It used to be many, many more.

Peter Turnpenny: Some time ago I produced a back of the envelope calculation and it's very difficult to anything better than that I think. Based on the numbers of women that we know take anti-epileptic drugs, so that is a statistic that's reasonably hard, you can find that data. Then over the years valproate has been a very frequently prescribed drug, not quite so much now thankfully so you can reach a proportion of those women who are epileptic, with epilepsy who are on a drug, will be taking valproate and from that figure

you can roughly work out over nearly 40 years how many women there are who took valproate during pregnancy because you've also got data on how many babies were born during that period.

Then you can reach a, based on a figure of well what's the frequency of problems, and so at least 10 per cent malformations but possibly 20 or 30 per cent and possibly even more neuro developmental problems we then can reach a figure on the number of individuals exposed to the drug who you think will manifest some problem. But it will be a spectrum so that there will be easily...

Cyril Chantler: What is that figure please?

Peter Turnpenny: Well that's the figure that I came up when I did that calculation was 20,000.

Cyril Chantler: 20,000.

Peter Turnpenny: Yes, and I was encouraged to hear I think at Jill's meeting in March that somebody else had done a similar back of the envelope calculation...

Rebecca Bromley: Yes, it was myself, and Professor George Moore had done something similar

Peter Turnpenny: ...and come to a very similar figure so I was reassured that I wasn't off the wall on that figure.

Sonia Macleod: So that's 20,000 affected individuals.

Jill Clayton-Smith: Affected.

Rebecca Bromley: Affected. I worked it out on prescription data from 1994 I think until 2010 because that was the prescription data that came out from...

Sonia Macleod: Yes so it's now accumulative with...

Rebecca Bromley: Yes.

Cyril Chantler: Then you're working on the 30 to 40 per cent

Rebecca Bromley: 30 per cent.

Peter Turnpenny: Yes, I can't remember which figure I actually chose in the end but [unclear].

Cyril Chantler: But is that, I'm only after...

Rebecca Bromley: Yeah so it's taking the spectrum not just the malformation.

- Cyril Chantler: But now how do you respond to what I said well, we've got the recognised Fetal Valproate Spectrum Disorder by experts but what about these children who've been damaged, albeit less severely than that and what about the effects of every other child in a family which is necessarily under massive strain and stress which the French seem to have identified?.
- Jill Clayton-Smith: Yeah, so our 20,000 was encompassing those with neuro developmental effects alone, not all the physical [unclear] IQ.
- Rebecca Bromley: Not IQ. We didn't necessarily factor in the other things we don't need to know about because a child may scrape into the average range for example for IQ but may have marked social problems and that's something I certainly see frequently at lower dosages is that again maybe the social skills, the regulation of behaviour tends to take a hit quite early on at lower dosages and then you get a hit of cognition and then you see the structural malformations come in and that actually is what we predict for a teratogen, you get functional problems at lower dosages.
- Cyril Chantler: Sure but that's not included in your 20,000?
- Rebecca Bromley: We included IQ...
- Jill Clayton-Smith: IQ, the IQ lowering.
- Rebecca Bromley: ...but not other things no because we haven't researched them well enough to gain a figure to...
- Peter Turnpenny: I would take the view that the 20,000 covers the range. So that a proportion will be very easy to diagnose by nearly all of us and at the other end of the spectrum they'd be far more difficult to diagnose and their effects would be relatively minimal and actually teasing out whether they've got damage due to exposure to valproate or they come from dysfunctional families or some other problem. It might be very, very difficult.
- Jill Clayton-Smith: So one of our key roles as clinical geneticists is to exclude other causes because that's really important that we've made sure it's not another reason for the neuro developmental effects because there is no specific diagnostic test. There are people looking at diagnostic tests and there is definitely research going on, but at the moment we don't have a blood test we can do to say you've been affected by valproate in utero. So it's a diagnosis of exclusion, and we have to factor in that for every child who comes to our clinic where we make that diagnosis, we've also done a

detailed chromosome test, maybe a fragile X test and any other test we think are indicated to rule out other possible causes.

Cyril Chantler: Because we've met families who have ascribed other problems they've had to valproate, lack of mobility for a start. But we've also talked to your colleagues, geneticists who say well that's not actually part of it, but we've also heard about other muscular skeletal disorders that they think are part of their valproate. So in the document you're producing will you deal with that?

Jill Clayton-Smith: So in the document we've produced we have in our diagnostic criteria, drawn up criteria which are essential to have, criteria which are very suggestive so you would find these significantly more often than you would in the general population, and criteria which are supportive and we've divided them into those categories with a scoring system and part of the essential is that you have ruled out other conditions as well.

Cyril Chantler: My final question is, just to reassure everybody just my final question. We've also been told by families of their continued concern about a person with valproate passing it on to their own children and we've also been told very reliably that's not possible.

Peter Turnpenny: Certainly intuitively it's not possible. I think we always have to keep an open mind as to whether there's some mysterious epigenetic factor or something like that but the fact is at the moment that the research has not been done and it's waiting to be done.

Cyril Chantler: But as a geneticist you can't perceive of a way?

Peter Turnpenny: It doesn't fit our models.

Jill Clayton-Smith: There is no evidence at the moment but I think we covered that in our, there's one paper in the literature in an animal model which suggests an intergenerational effect not for the malformations but for the autism spectrum phenotype. But that is one animal model, it's not been replicated, it's not been done in humans so at the moment we would say that there isn't any evidence, however it still needs to be researched because you can alter your genetic makeup by environmental factors so that still needs to be researched but at the moment there is no evidence.

Cyril Chantler: Thank you that's very helpful thank you.

Julia Cumberlege: Right, Simon.

Simon Whale: Yes, a couple of questions if I may. There was one thing that you said presciently at the beginning which was intriguing, well several things you

said that were intriguing but there was one that stuck out which was, you said that the level of expertise among your colleagues has fallen away and I assume you mean recently or over the years. I just wonder if you could elaborate a bit on that and as to the reasons why?

Peter Turnpenny: Well some years ago I ran a study day to which some of our colleagues came and I think that the problem was flagged up at these national meetings that we all go to but I think after a few sessions you would assume that everybody's got enough knowledge there so it wasn't terribly exciting to bring a new case to show to these groups and many of our colleagues who were part of our community at that time are actually now retiring or retired. I think that the group of the next generation of clinical geneticists coming up behind hasn't benefited from those closed sessions and in-depth discussion sessions we had around this topic that we had at that time. So I think that needs to be revisited would be my view.

Jill Clayton-Smith: I think the training has changed. The way we train has changed, genetics has really grown as a subject so many geneticists used to be focussed on these rare malformation conditions and that was their bread and butter, now you do cardiac genetics, cancer genetics, neuro genetics and you only do a very, very small part of your training on the rare malformations and paediatric genetics. Some centres you do very little so I think it's a reflection of that.

Peter Turnpenny: A huge emphasis now on how to interpret DNA findings what we call the genomic era which has added a whole new level of training needs.

Simon Whale: Right. What are the implications of that for the diagnosis of FVSD in the future?

Peter Turnpenny: Well I think they're very considerable and not just this condition but others actually, others yes.

Jill Clayton-Smith: They're all rare diseases yeah.

Peter Turnpenny: There are efforts to try and make this whole process easier, there is computer programmes and expert resources but actually in response to, I wanted to comment on something you said Sir Cyril, there's actually substitute for seeing lots of patients and when somebody says hypomobility is not part of this I would challenge that because some children are hypotonic and have hypomobility and we can recognise a similar posture that some of the more severely affected children have and...

Cyril Chantler: So that's not genetic that's...

- Peter Turnpenny: That's clinical, that's because it's clinical.
- Jill Clayton-Smith: It's clinical yeah.
- Cyril Chantler: It's more a direct effect.
- Peter Turnpenny: Yes.
- Jill Clayton-Smith: So in other EU countries because we've, the French have done quite a lot of work on Fetal Valproate Syndrome, in other EU countries the way that they've addressed this rare disease expertise is that they have setup networks of expert centres in rare diseases. The French have a particularly well developed one where they have about eight centres in their country which are really experts in rare disorders and they train and develop expertise and have a lot of patient involvement too and that's how they have maintained their clinical standards I think because those centres work really well. But that's perhaps what we're lacking a little bit here is that we need some centres of expertise.
- Cyril Chantler: You support that because we've been thinking about that. Because we did that for end stage renal failure [unclear].
- Rebecca Bromley: To add to that as well neuropsychology would be the people that would assess brain function in this are incredibly rare. You tend to have your paediatric neuropsychology teams in only major neuro site centres so you're talking in major children's hospitals throughout the UK but they tend to be funded for specific things. So for example epilepsy, brain injury, metabolics, you have very few people who would be able to assess a child with Fetal Valproate Syndrome have experience to bring to that assessment to match the profile. Does this profile make sense or is this something else that's going on here? So to add to the difficulty and challenge around clinical geneticists I think we always need to think about the wider team as well that would be needed for diagnosis.
- Peter Turnpenny: Absolutely, definitely.
- Cyril Chantler: Could we extend the scope to deal with other possible effects of drugs in pregnancy?
- Rebecca Bromley: Absolutely.
- Jill Clayton-Smith: Yeah it's the same skillset really that you use yeah.
- Simon Whale: Could I change the subject and talk about registries because there's a lot of thinking around registries in relation to at least two of the three areas that we're looking at and I wanted to just ask you your thoughts on how

important it is to have a registry, whether there's one already in existence for valproate because I understand there is a UK epilepsy and pregnancy register which we've struggled to find out much about, so can you...

Rebecca Bromley: I'm on the committee it that's [unclear].

Simon Whale: Right so you might be the right person to ask [laughs] about that but how important do you think it is for there to be a registry and is that the basis on which we could start to build on?

Rebecca Bromley: I think registries are setup to answer different questions so the UK pregnancy and epilepsy register is women who were recruited while they're pregnant on any anti-convulsant or actually not on an anti-convulsant, actually have a controlled group as well. That was established by Jim Morrow in 1996 and has really contributed a huge amount of data to our understanding of the risk associated with valproate and some of the other anti-epileptic drugs.

We have similar registers again for women with epilepsy in North America, the Australian register has been very successful, then more recently we've had a collaborative European approach that now actually extends past Europe and includes data from India and Australia and that's called Eurap we did reference those in our submissions. So the registers there that are to generate data predominantly on malformation outcome for women they work very, very well. What we see is that the disease specific ones have worked a lot better than the pharmaceutical ones, so certainly a lot of the US based pharmaceutical companies over the last 10 years setup their own malformation register at the request of the FDA but actually they mythologically weren't brilliant to be honest and didn't really recruit many individuals and their comparisons to control samples were a little bit limited.

So I think the disease specific registers for generating risk data work very well, they aren't greatly funded they struggle which is a narrative obviously that you've already heard from us. Moving forward to what you would do valproate specific, I know the MHRA are currently looking into this. I was on a telephone conference with them earlier on last week, last Monday about that and they seem to have an idea about tracing valproate use, but also following it through to the longer-term outcomes of individuals exposed to valproate. Not 100 per clear how that they were going to do that but it's in the very early stages and it's certainly something that they've got planned.

Registers if they are nationwide can be challenging to get round to see everybody. That is a downside of them no doubt, but actually here in the UK because our geography is quite small we are actually quite uniquely placed in many ways to do the longer term follow up within registers and certainly we've done a couple of follow up studies now with the UK pregnancy and epilepsy register where myself or we've had Uni staff have gone out all over the country collecting this data and obviously in comparison to North America it's a lot easier for us to do that. So I do think that we're well placed. There isn't currently a register for Fetal Valproate Spectrum Disorder or Fetal Anti-Convulsant Syndromes is there, I think? We all hold our own little databases but there isn't a register per se .

Jill Clayton-Smith: The only register that I know of within Europe is that there are a group of fetal anti-convulsant patients within a register system called [Jeneda] which is run from Strasbourg where patients actually enter their own data into the register and they have a cohort of mostly French Fetal Valproate Syndrome patients.

Valerie Brasse: How comprehensive is the register here? The one that you're sitting on the committee on?

Rebecca Bromley: The UK Pregnancy and Epilepsy register - so it gets reports from the GP at three months as to the physical health of the child. It doesn't go any further than that due to funding reasons and then...

Peter Turnpenny: But it's only certain centres though isn't it?

Rebecca Bromley: Yes so it's not every, the majority of women opt in or as Peter said certain centres will say to women there's this register running you might like to take part, and then more and more I'm trying to then ascertain separate funding to out to answer a specific question so for example we answered one around valproate levetiracetam in 2016; we published that data and currently I've got a student project that we're working to setup at the moment on topiramate. But again I guess back to what I said at the beginning it's all very ad hoc, it's all dependent on what we've got time to do, where we can get the money, where we can access the populations. We would love to be able to follow every woman up who was enrolled on the register that would be our dream but currently...

Valerie Brasse: But you're talking about following them up once they're on the register.

Rebecca Bromley: Yes.

Valerie Brasse: My question is what proportion actually go on the register...

Rebecca Bromley: Oh sorry in the first place.

Valerie Brasse: It's triggered by the women and then the GP put in...

Rebecca Bromley: It's very variable. It's certainly dropped I don't know the numbers it's certainly the last sort of five, ten years we've seen as clinicians that become more busy and aren't entering women themselves, the numbers that are recruiting have dropped quite substantially.

Jill Clayton-Smith: It's the obstetricians also who were the main people entering patients onto the register and again I think it has dropped. We run registers for many rare diseases I guess, and the ones which work best are the ones where someone gets something out of the register so it's either a research register or it's an NIHR funded portfolio study or something which you get accrual figures for entering all your patients onto the register. So if it's all completely voluntary it's not so easy to maintain.

Julia Cumberlege: I understand that, yes. [Unclear], Sonia is there anything you want to ask?

Sonia Macleod: No.

Julia Cumberlege: I'm sure Sonia will come back to you in due course.

Sonia Macleod: I probably will.

[Laughter]

Julia Cumberlege: But anything else you finally want to tell us because we're just up to the time limit now?.

Jill Clayton-Smith: I think one thing that I'm concerned of just with my contact with families over a long time is that this has all, Fetal Valproate Syndrome is being seen as a paediatric disorder but now we're seeing the adults come back to clinic and they have got problems. Most of the adults, well virtually all the adults, they come back they're in their mid-20s going up to 30 they're still coming back with their parents, they're struggling with getting a driving licence with being able to live independently, with managing money. So practical skills, and so I think we still have a lot of work to do in actually finding out what the long-term implications are.

Cyril Chantler: You certainly see these [unclear] centres as being very much multidisciplinary covering the whole age spectrum but also other skills like social advisor and care pathway navigators...

Jill Clayton-Smith: Yes.

Peter Turnpenny: I think it's also my observation is that some of these young people have been through further education even, with support very often, but actually leading independent lives in the normal sense is really a struggle for them. So at one level they appear to be doing okay but actually when you try and put them into society to function independently...

Cyril Chantler: The state benefits system doesn't work for them.

Jill Clayton-Smith: No.

Peter Turnpenny: No. They've fallen between the gap, absolutely yes.

Julia Cumberlege: Yes we've heard a lot about social isolation. We do know they haven't been able to lead normal lives, get married and all the rest of it.

Jill Clayton-Smith: So their parents haven't...

Julia Cumberlege: So anything else Professor Bromley?

Rebecca Bromley: I don't think so.

Julia Cumberlege: Doctor Bromley. I made you a Professor.

Rebecca Bromley: Yes thank you, thank you.

[Laughter]

Rebecca Bromley: I guess just one comment is that I think it's worth saying that this is not a situation that is, the lack of knowledge and the slow accumulation data is not specific to valproate and it's not specific to the anticonvulsants. To be honest we probably know now more about the anticonvulsants than we do about certain neuro-behavioural teratogenicity of most of the drugs. We have data from the US that when they looked at the time it took on average to determine teratogenic status it was 27 years, and that was based on malformations. If we were looking at the impact on the brain we could probably double that if I'm honest.

So we have a huge system failure really within medicines it's not just specific but unfortunately valproate has been the first major teratogen I think to hit this ad hoc system and really show its inadequacy unfortunately.

Julia Cumberlege: Thank you so much. Thank you very, very much. I think that the parents and the children and the young people and the 20 year olds and plus are very lucky to have you taking such an interest in this subject so thank you very much

Jill Clayton-Smith: Thank you.

Rebecca Bromley: Thank you.

END OF TRANSCRIPT

27th November 2018

Session 1: Sling the Mesh

START OF TRANSCRIPT

Julia Cumberlege: Would you like to start by saying who you are and what your organisation is? Are you going to make a statement first, or is Michelle coming in first?

Kath Sansom: I'm going to speak first and then Michelle is going to speak. Then hopefully there's the video that you're going to be able to play on your laptop. I think - I arranged that with Donna, I think.

[Over speaking]

Valerie Brasse: When did you send it?

Kath Sansom: Yesterday, I think, a YouTube link on an email. That must have been to Donna.

Valerie Brasse: If you check with Donna and we can perhaps play that afterwards while you're making a statement.

Kath Sansom: Yes. Are you happy for me to start?

[Over speaking]

Julia Cumberlege: Yes.

Kath Sansom: My name is Kath Sansom. I run Sling the Mesh campaign. This is my colleague, Michelle Moffatt who helped me write our formal submission to the review team. Mesh has been called the thalidomide scandal of the 21st century. It is the same story of patients suffering from a treatment that was supposed to help but instead has caused for some patients devastating harm, all because of a lack of quality evidence before it was mass-launched with all eyes instead on profit.

In Sling the Mesh, we now have more than 7100 members with shattered lives. Eight out of 10 of them suffer pain that affects their daily life. Seven out of 10 of them have lost their sex lives. More than half have ongoing urinary infections, and as a result of that 1 in 12 are becoming antibiotic-resistant. A third have had to give up work, and one in five have had to reduce their hours at work. One in seven women's marriages have broken down.

The devastation is huge, yet surgeon societies and regulators refuse to admit the scale of this and want to keep using mesh. I shall sum up why in 10 points. (1) For those affected by the thalidomide tragedy, their injuries were upsettingly obvious. For a woman injured by a mesh implant, her chronic pain, infection, reduced mobility, lost sex life and resulting depression and decimated quality of life is mostly invisible. It is easy to ignore or blame it on other health problems.

(2) Traditionally, women's pain is downplayed by patriarchal medical community who refuse to see how bad the mesh scandal is. Our survey found that 53 per cent of women knew that mesh was causing their problems within just six months of having it implanted, but by comparison just eight per cent of surgeons diagnosed their mesh complication.

(3) Mesh was aggressively marketed. TVT, for example, soared from just 214 implanted in its first year in the UK in 1997 to nearly 12,000 by a decade later in 2008. By comparison, the Burch colposuspension dropped from around 3800 a year to 300 in the same time period. If it hadn't been for the TVT, I believe that Burch would have become the gold standard via a laparoscopic approach. Some surgeons now don't know anything else other than mesh. Many have lost their traditional skills. No mesh equals no job.

(4) Nobody wants to admit mesh was approved with flimsy evidence. Too much research was flawed by problems like industry funding, small numbers of women in trials, short-term follow-up. They're mainly focused on the fix and not the new problems caused in its wake. Or studies, for example, like one last month that came out in *JAMA*, that report quoting a mesh removal risk at 3.3 per cent. Other stuff that has gone wrong is, in 1997 the TVT was destined to be a category C under SERNIP, yet it was pushed to category A despite concerns. Paperwork for this upgrade appears to have been lost when NICE took over from SERNIP in 2003.

(5) The MHRA failed women and did not properly regulate mesh. In 2012, its York report missed out loss of sex life risk which stands at 14.5 per cent. This kept the overall risk percentage rate low at one to three per cent. When I asked the MHRA press office why this had happened, they told me it was because loss of sex life, or dyspareunia, is not considered a general risk. In 2014, the MHRA issued a patient safety alert. They admitted they don't have enough resources to police device regulation.

(6) Approval of medical devices is so weak, nobody checks what they're made of, how they're designed or if clinical trials prove they're safe. Problems only come to light after huge media campaigns.

(7) Hospital coding is a mess. There isn't even a HES code for ventral rectopexy mesh never mind its removal. There is not a proper code for mesh eroding into organs or urethras. There is no code for partial snips of the mesh. A broad mesh complication code of PK96.2 was created in June of this year, but surgeons do not seem to have been told about it, and to be honest, it's too late.

(8) A study by Doug Tincello of Leicester showed that 8 out of 10 surgeons who were surveyed say they leave the old mesh behind if it fails and just put another one on top.

(9) There were no patient-recorded outcome measures. Nobody properly looked at the negative side effects of mesh as reported by patients.

(10) There is a black hole of missing data. Only a third of surgeons reported to the BSUG database. In 2012, BSUG adopted the internationally recognised five-digit mesh complication coding system by the ICS and IUGA. This should have given us rich data on mesh problems and the time-lag for them to cut in later, but no surgeons bothered to use those codes. In addition, the BSUG database shows that the TVTO has a risk of 2.3 per cent, and the TVT has a higher risk of 2.8 per cent. So, by their own admission, the TVT is more risky yet we are constantly being told it is the other way round.

The fact is, nobody actually knows the true scale of this disaster. Every woman with a good outcome following a mesh operation is only okay for now. In *Sling the Mesh*, many women are fine for months or years before mesh causes problems. One woman had mesh slice her urethra after 18 years.

So, what are the solutions? We say incontinence and prolapse can be fixed using tried and tested methods without mesh. Mesh adds an additional layer of risk. In our group, three-quarters of our members have had incontinence mesh at 74 per cent; 46 per cent of those have had a TVT and 26 per cent have had the obturator mesh. Incontinence can be eased or fixed for 80 per cent of women using physiotherapy. There are biofeedback gadgets or medication. If this doesn't work, there's native tissue slings, Burch colposuspension or Kelly's plication.

In our group, prolapse, 16 per cent of our members have an abdominal pelvic organ prolapse and 11 per cent have vaginal pelvic organ prolapse

mesh. So, there's actually more having the abdominal pelvic mesh. For pelvic organ prolapse, there is physio, rings and pessaries to try before going to surgery for suturing or for the right patient the Manchester repair. For bowel complications, it is accepted that a rectal prolapse outside the body needs surgery, but this can be done using resection rectopexy with no mesh, the Delorme's technique or suture rectopexy, all without mesh.

Around 50 per cent of the population have some kind of internal rectal prolapse, and surgery is not always needed. But again, suturing can be employed, or in cases of obstructed defecation it can be eased with diet and lifestyle changes. I need to point out, bio-mesh is not the future. It is not strong enough, and four per cent of our members are reporting debilitating pain and foreign body reaction. Composite mesh is not the answer either. This incorporates both polypropylene and bio-mesh. It is just double trouble.

What does Sling the Mesh want? We want a continued suspension until you can provide accurate long-term data on safety. If you do not uphold the suspension, then we want mesh to be pushed to the third and last-resort option only to be used when a non-mesh surgery has failed. We would like training programmes so surgeons relearn non-mesh operations before these skills are lost forever.

We desperately need accredited mesh removal training programmes so that there are more surgeons able to remove mesh. Finally, we desperately in the UK need a Sunshine Payment Act so any financial links to industry of a doctor or hospital can be checked to gauge if there is likely to be bias in any reports which they write.

Julia Cumberlege: Thank you very much. No doubt you will give us a copy of that, because I wasn't able to take down all your wonderful figures and facts and everything else. Michelle, would you like to tell us your story.

Michelle Moffatt: My name is Michelle Moffatt. I've been heavily involved with Kath writing the submission for the independent review. I want to follow on with three more major issues of concern. These are, (1) lack of informed consent; (2) risk of dyspareunia and loss of sex life being ignored; and (3) the need for a national registry and national recall.

Looking at lack of informed consent and patient autonomy, what are the problems? Even today, mesh-injured women are being misinformed by some consultants who tell them their complications have nothing to do with the mesh; it's been blown out of proportion by the media; and it's all

in their head. Only last week, a member of Sling the Mesh was told by her GP that a TV tape is not a mesh. Again last week consultants recommended to two members of Sling the Mesh that a mesh device should be inserted from April 2019 once it becomes available again on the NHS.

One of them is a 29-year-old mother who has not completed her family. She reported her surgeon spoke very highly of mesh, was not told of any risks and that the negative comments on mesh were media hype. We know that women who are still to have children should not receive mesh. The other woman already has a mesh inserted and is suffering mesh complications, yet the surgeon recommends placing another mesh on top of the original. These are examples of failures of informed consent.

The pelvic mesh scandal represents failure of all ethical principles. One of the most important is the issue of lack of informed consent. This is a substantial aspect of the pelvic mesh scandal in which 83 per cent of women respondents in a Sling the Mesh survey in 2017 stated they were not given informed consent before surgery despite the Montgomery ruling.

The GMC guidelines on informed consent published in 2008 are open to interpretation and we believe in bad need of revision. The draft NHS England specifications for management of SUI and POP and for the management of mesh complications, as well as similar guidelines drafted by NICE, are vague on informed consent. And they are vague on specific risks related to all pelvic mesh procedures, except to tell the patient that mesh is a permanent implant and difficult to remove.

The purpose of RCOG's draft management aid is to provide patient information to assist women to make informed choices about choosing surgery for SUI, yet the draft doesn't include the additional layer of risks caused by mesh such as chronic pain, mesh erosion into other organs and vagina or dyspareunia and loss of sex life. We question, why? These omissions in the guidance allow room for pro-mesh surgeons to downplay or ignore risks.

The estimates given in this draft guidance on risk on multiple mesh complications must be defined clearly with specific scientific references. These omissions have led us to believe that the current estimates in this guidance have been selected to downplay risk. Without this full information, a surgeon cannot give true fully informed consent. Leaving doctors to communicate risks without stating precisely what these are is likely to lead to history repeating itself.

The EC SCENIHR committee issued their opinion on the safety of surgical meshes used in uro-gynaecological surgery in December 2015, and I would like to read what it states. Many patients are still undergoing mesh surgery as a first option without having all the necessary information regarding the potential risks. Unless worldwide standardisation of guidelines and statistically accurate information identifying the potential risk in the use of these products is adopted, then true informed consent cannot and is not being obtained from the patient.

So, what are the solutions? In the absence of a continued suspension on mesh, there needs to be at the very least stricter controls including a review of the informed consent process for women being offered pelvic mesh. A much higher standard of informed consent is needed with all potential risks explained. For example, add a section with Q&As. Can mesh damage sex life? Can it damage nerves? What might happen if my mesh needs to be removed? Can any surgeon perform a mesh removal? What are the removal waiting times?

Patients should be given appropriate time to digest and research mesh benefits and risks. A standardised list of all risks of adverse events is needed such as haemorrhage, mesh erosion resulting in organ perforation, nerve damage leading to disability, infection, chronic pain, dyspareunia loss of sex life, and that these can occur any time after mesh insertion, often within 5 to 10 years. Currently these risks are not explained sufficiently in any of the guidance being drafted by NHS England, NICE and RCOG.

The same informed consent process applies to partial mesh removal. If NHS England can prove that simple localised excision, their term for partial removal, is an appropriate pathway for women presenting with chronic pain, then they must ensure robustly fully informed consent process is in place both verbally and in writing. NICE guidelines, the draft guidelines, state that there is a paucity of data on removals, so we don't know how they've been able to continue recommending the use of partial removals. We are absolutely against partial removals, as they do not address the multiple complications suffered by women. Partial removals prolong the suffering of women. They entail multiple surgeries and, therefore, raise the cost to the NHS.

Comprehensive standardised patient information leaflets are missing, and we need to have them made available urgently. NHS England and NICE draft guidelines need to carefully review the guidance currently provided on informed consent and finalise only after the outcome of this review. It should be made clear in this guidance which patients should not have

mesh: women planning to have more children, diabetics, women who already have a pelvic mesh device, and so on.

Statistically-accurate information of potential risks needs to be made available for full and true informed consent to be obtained from the patient. Currently this is not available. Mesh, therefore, needs to continue to be suspended, or at the very least only used in third-line last-resort treatment until accurate risk statistics are known, as mentioned before by Kath.

My second point is on dyspareunia and loss of sex life being ignored as a risk. What are the problems? The majority of women on Sling the Mesh were not told that dyspareunia was a mesh complication risk.

Dyspareunia is defined as painful sexual intercourse, and in this context is caused by mesh eroding into and through the vaginal wall. In the NHS England draft specification, dyspareunia is not mentioned. Instead the term sexual difficulty is used. In RCOG's draft management aid, the term sexual function deterioration is used. The medical term dyspareunia must be used.

Dyspareunia includes excruciating pain that means a woman loses her sex life. In a Sling the Mesh survey in 2017, 7 out of 10 respondents reported suffering from dyspareunia and loss of sex life. Women whose mesh has eroded or is eroding through the vaginal wall are in chronic pain and at risk of infection. Their partners can also become injured. This loss of sex life puts huge strains on marital and partner relationships including relationship and family breakdown.

In the Sling the Mesh survey already mentioned, 1 in 7 reported suffering marriage breakdown and 53 per cent had strains on their relationship as a result of dyspareunia. Dyspareunia leads to poor mental health including anxiety and depression, of which 60 per cent of respondents in our survey stated they had anxiety and depression. Dyspareunia alone affects women emotionally, physically and economically when relationships break down. This is one risk that has been totally downplayed, totally ignored by medical institutions, surgeons and in many of the scientific studies which, therefore, keeps the complication rates low. Dyspareunia has been absent from RCTs or monitoring databases including HES. This is a shocking omission.

If suspension of mesh is lifted, what are the solutions? Ensure the definition of dyspareunia and its implications for loss of sex life are clearly stated in a standardised list of mesh risks, and explained. NHS England draft service specifications and guidelines need to carefully review the

terminology that they currently use. Ensure dyspareunia as a complication is captured in a mesh registry, a national recall and all reporting mechanisms and RCTs. This will allow for the true figure of dyspareunia to be known. Currently this is not available.

My third and last issue is the need for a registry and a national recall. What are the problems? The number of mesh-injured women in the UK is unknown due to vast weaknesses in reporting and flawed research over the past 21 years. There is still uncertainty about the rate of complications in the long term due to lack of long-term data. There is a history of failures, particularly regulatory and adverse event reporting relating to the safety of pelvic mesh devices.

What are the solutions if the suspension of mesh is lifted? The establishment of an independent national pelvic mesh registry as a priority is needed to protect patients, improve outcomes, identify best practice and reduce costs. Legislation must be put in place to mandate what must be measured in all patients with pelvic mesh implants since voluntary entry of data has failed miserably and to ensure reporting requirements are adhered to and complete information is maintained.

National recall to be conducted as a priority of all women who have received pelvic mesh devices. Only through a recall can the true statistics be found on outcomes. Patient-reported outcome measures, PROMs. A questionnaire needs to be developed for pelvic mesh insertion, partial removal and full removal. Independent studies can then link PROMs data with the national mesh registry and national recall data. Correlations can then be found between PROM scores and various surgical factors, patient factors and material factors including implant brand.

To summarise, there is an urgent need for accurate statistics through a national registry and a national recall and PROMs to enable true informed consent that includes accurate statistics on mesh risks that have been missing to date, for example, erosion into vagina and other organs, chronic pain and dyspareunia. Ultimately, we want to continue suspension of mesh until long-term accurate data on risk and on safety is obtained.

Julia Cumberlege: Thank you so much. Both your presentations have been very forceful. Thank you for that. Can I first of all, Michelle, ask you a question and then I'd like to ask Kath also a question. I absolutely understand what you're saying about consent. We've heard it from a lot of different patients through the course of this review. When you go and visit a surgeon and you have a problem - you're suggesting that not always the full facts are

given to the woman - the woman and the surgeon are very often in a room together, consulting room or whatever. How can you ensure that the woman is given the full facts, figures, everything that's needed for proper consent? Are there tools that you think would be helpful both to the surgeon and also to the woman?

Michelle Moffatt: I think the only way is for the conversation to be recorded and that there is a copy for the patient and for the doctor. There is a lot of denial going on, and we can't trust all doctors with the truth. So, it has to be recorded. The process needs to be made - the controls need to be stricter. There needs to be a more prescriptive consent process with, as I mentioned before, the standardised list of complications and the explanation of those complications so that there is no - so the patient has the full information and is able to go away and digest that information before she decides which option is best for her.

Julia Cumberlege: Are you saying it should be recorded?

Michelle Moffatt: Yes.

Julia Cumberlege: Are you suggesting it should be a video recording? Or should it just be written? What is the recording?

Michelle Moffatt: I think both. That's an ideal situation. An audio recording is something that the patient can have as well as the doctor.

Julia Cumberlege: I think the audio is - I've seen it done - has been successful, because you can take it away and think about it. That's helpful. Do you think there should be some sort of a checklist for the surgeon covering these different areas? Do you want paper records?

Michelle Moffatt: I think there should be - yes. The consultant process should be a written process with a checklist of all the risks and the definition and the explanation. And that's also given to the patient, so it's completely transparent.

Julia Cumberlege: And signed by both?

Michelle Moffatt: Yes, absolutely.

Julia Cumberlege: Thank you. I've just been given a message that your video is ready to play. Before I ask you - would that be helpful if we played the video now?

Kath Sansom: Yes. Can I make a point on informed consent?

Julia Cumberlege: Yes.

Kath Sansom: I know we're going to be doing some work tomorrow with HQIP looking at apps and patient leaflets, standardised leaflets listing all the risks and listing what can go wrong. My concern - even with every check that you try and put in place in the hands of a pro-mesh surgeon, they are still going to downplay those risks to a woman. They might not describe the word dyspareunia properly. They might just say it's a - I didn't know what the word dyspareunia was until I did this campaign. Things might not be described properly. They might downplay it as short-term, don't worry, you'll get over it very quickly.

It is my concern that with every best will in the world - even with all these checks in place, I am not convinced that every single surgeon in the UK will give a woman a properly informed consent, because you cannot - recordings are maybe a way forward, but you can't be in every single consulting room in every single hospital in the country. It's a real concern to me.

Julia Cumberlege: But of course the numbers of these insertions has been going down.

Kath Sansom: Yeah, but that's only because of the campaign, the media campaign and women becoming aware of the complications. I really want mesh to be pushed to the third and final option. I know in the NICE draft it's still second option. I think it should be third and final option. That's the only way you're going to get a proper consent for women, because they will know then how risky it is for it to be a third and final option.

Cyril Chantler: You mention *JAMA*. I used to be on the editorial board of *JAMA* years ago. We formulated a notion then that the patient is the pilot and the doctor is the navigator. In other words, you need to do it together. It occurs to me that maybe these guidelines ought to be approved by patient group and a professional group working together. You talk about the RCOG guidelines. Shouldn't guidelines perhaps be approved...

Kath Sansom: Are we talking NICE draft guidelines here?

Cyril Chantler: No, whatever guidelines are for anything. Should patients and profession approve them together?

Kath Sansom: Yes, indeed. But often historically patients haven't been invited on to these things. So, although, for example, I'm a stakeholder for the NICE drafts, that's very different to being invited on to the committee and having an input, and that hasn't happened.

Julia Cumberlege: Thank you.

Simon Whale: I was going to make a similar point and I think you've answered that already. But in terms of the concern about conformity amongst surgeons, to what extent would it help - this assumes that pelvic mesh operations continue. This part of the conversation is based on that assumption, which may not be the case, but if it were to be the case, if you've got accredited centres for insertion, not just for removal, does that in your eyes reduce the risk of non-conformity or inconsistency in consent?

Kath Sansom: It would help reduce risk but it wouldn't eliminate it, because you're still going to get pro-mesh surgeons within accredited centres, in my opinion. But it does reduce the risk because it's then not carte blanche in every district hospital across the country.

Simon Whale: So, you'd support accredited centres for insertion not just removal.

Kath Sansom: Yeah, but I'm still really keen to get across the message that mesh needs to be the third and final last-chance saloon and not the second option, because that's what the situation has been for 21 years. It's been second option; it needs to be third and final option.

Julia Cumberlege: Shall we see this video?

[Video plays 29:55 to 34:00]

Julia Cumberlege: Thank you very much indeed. A very powerful video. Can I ask you, Kath, about your comments about the MHRA's response to the particular issue we're discussing, pelvic mesh? In your evidence to us, you say that it highlights the concerns particularly because it's close to industry and potential conflicts of interest. Could you talk a little more about conflicts of interest?

Kath Sansom: With the MHRA?

Julia Cumberlege: Yes.

Kath Sansom: It concerns us that people who work for the MHRA have been recruited from previously working inside industry. It concerns us that there is funding in part from industry for the organisation. It concerns us - the York report concerned us greatly from 2012 that the evidence was there for dyspareunia, for example, and they just decided not to include that risk, in my opinion to keep the risk figures low. It concerns me that they're not fit for the job that they've been set up to perform. It concerns me in 2012 they held a meeting on medical device safety - I didn't bring my notes in, but it wasn't really addressing the issue. It was saying they

couldn't pull things off the market unless they weren't performing properly.

I just don't think they have regulated or properly logged adverse events. They haven't publicised their yellow card system, for example. Another problem is that surgeons cannot log an adverse event from another surgeon's work. For example, I've had a mesh implanted at hospital A but I've gone to hospital B for my removal. Hospital B's surgeon cannot report my adverse event because it's the work of surgeon A, without getting his approval. That has helped keep adverse event reporting low. That's a big problem as well. Does that help?

Julia Cumberlege: We clearly need a regulator. Thinking about the MHRA, what are your suggestions for better regulation?

Kath Sansom: They need to be independent from industry. Have you got some suggestions, Michelle?

Michelle Moffatt: No. Of course, based on the grandfather product, the regulation is lax. The current regulation needs to be vastly tightened up so that you can't just have one agreed based on the evidence of the original product. It needs to be tightened up so that there are a lot more processes to go through. At the moment, there are no trials at all, are there, for the majority of products. We are the guinea pigs. We were the guinea pigs, the ones that had these - that has to stop. We're not against innovation but we would like to see some much stricter controls on these devices.

Kath Sansom: Every medical device that is launched on the market needs some kind of database. Every medical device that is now launched needs some kind of registry to track it, because there are so many new products coming on the market. Derek Alderson has said that this week, President of the Royal College of Surgeons. There are so many new products coming on the market, and the problems only come to light when you get patient campaigns like this one.

Julia Cumberlege: Are you also suggesting that the standard equivalence process should be altered?

Kath Sansom: Yes, that needs to be looked at.

Michelle Moffatt: Definitely.

Kath Sansom: You can't just approve a product because it's equivalent to something that was equivalent to something else that was equivalent to something else

that actually dates back to 1996 that isn't even on the market anymore. There needs to be a tightening up of approval processes.

Julia Cumberlege: Finally from me, can I ask, do you think there are circumstances in which you would really support mesh? You've talked about it as being the last resort. So, presumably you wouldn't want - you might want another pause in terms of its use when there's more research done. My concern is that we really are trying to get through this review at some speed, very thorough but some speed, because we're very conscious of the people who are suffering now. I'm just wondering...

Kath Sansom: I'm aware there's a vast body of women like me who were rushed for a mesh when mine would have fixed with physiotherapy. There are some women, for example, who do need to try the Burch colposuspension or the autologous sling route. If that fails and then they want a mesh, because they're desperate for fix and they're fully consented and they properly know all the risks, then as a third and final option. But only as third and final option, because for women with mild incontinence - and we have a vast amount of those in the page who didn't even really need surgery - that's the women you've got to stop being rushed through to surgery.

The figures - let me check it here so I'm giving you proper figures - it shows you that back in the year 2000 there were round about 3800 Burch being performed for incontinence. But when TVT was at its peak there were nearly 12,000. You haven't suddenly got a nation of more women wetting their pants. You've suddenly got a nation of women who are being encouraged into operations they probably didn't need in the first place. So, what I'm saying is...

Michelle Moffatt: Pelvic physio would have been all they needed. But that service is not automatically offered. That's the problem.

Kath Sansom: That service needs to be strengthened up for the physiotherapy option. If that doesn't work then you've got your non-mesh surgeries. Then if that doesn't work and the woman is consented, then mesh. That's what I'm saying about the third and final option.

Julia Cumberlege: Simon, I think you wanted to...

Simon Whale: No, Valerie.

Valerie Brasse: I do. Following up directly on that point, one of the things you said earlier was that there is clearly a group of women who should never be offered mesh. But I'm wondering - this is what slightly worried me about what

you were saying - the second and third option, mesh should be the third option. Is there potentially - maybe we just don't know; maybe the registry if we have one will deliver what we'd need to know - a group of women for whom actually it is better indicated for them? And the worry about going through the second and third process is, by giving an operation which potentially could leave them scarred would make it more difficult for the mesh they might subsequently have to work for them?

I don't know the answer to this, but as I say, it's something we need to think about, that as easily as you can say there are women for whom we should never offer mesh, maybe there are some who actually might benefit from it, if we can begin to find those women, and for whom giving them a second operation when the failed conservative treatment doesn't work, it's not working - maybe we need to think about that. I don't know the answer.

Kath Sansom: My concern here is, we're talking about finding the correct patient. In my opinion, there is no such thing as a correct patient simply because, as I'm sure you'll be hearing from the review, it is a Russian roulette risk. You can't line me up a group of women and say, you probably won't suffer because of X, Y and Z. You can't actually tell. Within the page, you wouldn't be able to line up women and know who's going to suffer and who is not. So, in my opinion there isn't a correctly selected patient. You'd be better to ask Suzy Elneil, because she will know better than me, but my opinion is there is not the correctly selected patient. You can't tell.

Valerie Brasse: Can I ask one more question? I know that when you've been talking about adverse event reporting, the yellow card, you have mentioned the MAUDE system that operates in the States. I wondered whether you could say particularly what it is it about that system that you think is really worth following.

Kath Sansom: The thing I like about MAUDE is that it's an open database, so any patient can go on and check it. For example, if I go on as a patient, I've been offered whatever it is - TVT - you type it in, and anyone who's had a problem with that TVT - or type in Gynaecare or that brand, you can look up what the problem is. MAUDE is open to scrutiny whereas the MHRA database or the yellow card isn't.

Valerie Brasse: So, just that, just the openness and transparency.

Kath Sansom: The transparency, yes.

- Sonia Macleod: One of the things we're looking at is not just the retrospective but going forward as well. Is there anything you could think of that would act as preventative measures before we start? I'm thinking more pelvic floor education, things like that. Is there anything positive we can do in that direction?
- Kath Sansom: Definitely. A better education programme among teenage girls in schools. Start that as part of the school education programme that it's okay to discuss pelvic floor. It's part of your body. It's part of your health. I'm particularly concerned because there is a rise in young girls doing long-distance running and high-impact training, so I do think there's more impact on young girls' pelvic floors. I think after babies there needs to be a six-week GP check-up.
- I think there is a programme - there's a group called Pelvic Roar. They would like that six-week check-up to be replaced by pelvic floor specialist with additional training in things like mental health, breastfeeding, so you've got whole care of the woman. At that very early stage, you'll be learning the importance of your pelvic floor, taking care of them. I think you're probably aware in France, you're offered a standard physiotherapy. We need to bring it right back to the basics of when a woman has first had a baby to look after your pelvic floor for life.
- Julia Cumberlege: Perhaps actually before she has the baby.
- Kath Sansom: Indeed, yes.
- Julia Cumberlege: Cyril, would you like to ask...
- Cyril Chantler: Kath, you said that TVT had more complications than TVTO. That slightly surprised me, because I have understood that the complications of the obturator fossa tape are considerably more difficult to cope with than the TVT.
- Kath Sansom: They are. It surprised me. This is in the BSUG report. It's called, The Stress Urinary Incontinence in the UK, 2008 to 2017. So, it's BSUG's own data that they've brought a report out either last month or the month before. You'll find it on page 19 and page 24, but that's their own figures. It actually shows that TVT has a higher risk than TVTO. It surprised me too, because we've all worked on the basis that the TVTO - which is the type you had - carries more risk going through the obturator. And Suzy will speak more: it's a more difficult mesh to remove. But you're, like, where are we in this?

Cyril Chantler: That is I think the point: it's more difficult to remove. In terms of putting it in, I understand it's less risky than the TVT.

Kath Sansom: The injuries to the obturator nerve are more risky, I would say. And in removing it also, going through that area is...

Cyril Chantler: That's the point. It's so difficult to take out.

Kath Sansom: So, it surprised me also to see those figures.

Cyril Chantler: The other thing about the new NICE guidelines - you presumably will be responding to those.

Kath Sansom: I have already. I read all 3000 pages. Lovely evening I spent doing that.

Cyril Chantler: Are we able to see your response, or is that confidential?

Kath Sansom: It will be published on - would you like me to email to you what I sent to them? Would that be helpful?

Cyril Chantler: It would be very helpful. The final thing is the national recall. Can you explain how that could take place? Would you be using HES data to identify the women? On the registries, the women aren't identified.

Michelle Moffatt: That's an issue because of the vast underreporting on the HES.

Kath Sansom: And you wouldn't pick up the private patients.

Cyril Chantler: I'm absolutely with you about a national database, but it doesn't exist at the moment. The registers that do exist are only partial, and they do not identify the women. The only way I can see of actually identifying - I don't even know that's possible - is using HES data, and we know what the problem is there. But I wonder if you've given any...

Kath Sansom: The only thought I'd had is from a surgeon who I know won't want to be named but said, the only way you're going to be able to do it is to write to every single women that's had a mesh operation.

Cyril Chantler: It's a question of how you find them.

Kath Sansom: Indeed. That's a real trawl, isn't it? So, we're stuck in this position whereby that's a trawl, it's very expensive, but that's in reality the only way you're going to find out the true figure of risk. Everyone is playing around with figures and no one really knows just...

Julia Cumberlege: And it would take a lot of time to achieve it.

Kath Sansom: Yes.

Simon Whale: And some women don't know they've had mesh inserts.

Kath Sansom: No, indeed. So, we're stuck in this awful position of 21 years without a database not really knowing the true risk but all of us knowing it's a lot higher than *JAMA* is telling us 3.3 per cent mesh removal, because it's not all about mesh removal risk anyway. We're stuck in a horrible position of not knowing figures.

Simon Whale: I'm sure we will carry on going after today, because there are plenty of other things we'd like to talk about, but can I go back to the full versus partial removal point, your concerns about partial removal. Have you from your members got any information or data about how many full removals actually end up as partial removals?

Kath Sansom: How many full...

Simon Whale: A woman goes to a surgeon for a full removal, but the surgeon is unable to complete the full removal. Do we have any - from your membership, is there any information about how many women have been through that process of having to do a second full removal operation?

Kath Sansom: Only anecdotal, but if you want that information it would be so easy to set up a poll. I can do that. The women respond very well. We usually get about 600 or 700 respond in a poll. But I haven't got that information. It's all anecdotal.

Simon Whale: I think it would be quite interesting.

Kath Sansom: Yeah. I think it should be done to be fair, because then at least you get an idea of where women are at. For NICE guidelines to suggest that partials are okay based on a paucity - that's their word - or very low evidence is not good enough to be able to set up a guideline on - let's just snip women's mesh - because we know from patient voice that's not good enough. I can set up a survey because at least we'll have some data.

Michelle Moffatt: Also if NHS England spoke directly with the mesh removal surgeons, the handful - we only have a handful in the country. They are full-time removing at the moment. They've got a backlog, and they're the ones that can tell them about the partial removals. I know one surgeon is against partial removals, because it's much more difficult for them to do the full removal later. A partial removal will not sort out the problem. The woman will present again, and the only option is to remove the whole thing. They're not going directly to those surgeons; we know that.

They're not contacting them as part of the engagement process, which is a bit alarming.

Julia Cumberlege: I have to say, you've been very comprehensive. Thank you very much. If there are other things you think we should be examining, thinking about - we've had your evidence that you wrote in and that was very helpful, and we've had the session today. If we have questions, perhaps we could come back to you as well. But can I thank you both very much indeed for coming.

Kath Sansom: Thank you.

Michelle Moffatt: Thank you.

END OF TRANSCRIPT

Session 2: Ms Suzie Elneil

START OF TRANSCRIPT

Julia Cumberlege: So, if you'd like to just start by saying who you are.

Sohier Elneil: So, my name is Sohier Elneil. I'm a urogynaecologist based at University College Hospital in London. I also work in the Department of Uro-neurology at the National Hospital for Neurology and Neurosurgery. So, I look after women who have got complex pelvic floor disorders, not just neurological but also non-neurological problems.

As far back as 2005, I became aware of the problems that women were suffering with as a consequence of not just mesh but the access to care for problems that they had following mesh insertion. The reason I brought in the two sectors is because a lot of the women were actually referred to me in the neurological hospital for pain management initially, rather than in the main women's health division.

So, that's the background that I come from. Over the last decade and a bit, we've been working increasingly with women who have had difficulties as a consequence of implants - various implants.

Julia Cumberlege: Before I ask a question on conflicts of interest, which I'd like to explore with you, can I just ask you how long you've been associated with mesh?

Sohier Elneil: So, I've worked with issues with mesh really from the time of my training. So, as a junior doctor, both at Cambridge and at University College London, it was part of our training to also be involved in learning how to put in mesh and it was part of our - basically, to be signed off as a urogynaecologist, you had to learn how to do the procedure. It was part of the requisite for your training.

When I became a consultant in 2004, the advice at the time was that mesh was a good option for women with stress incontinence, so many of us were advised to use it as a therapeutic option after patients had been through the usual pathway of care for stress urinary incontinence and prolapse. Subsequent to that, I still maintained my skills in other different types of surgery, so that it was possible to offer women the whole armamentarium of surgery rather than a specific single track.

Julia Cumberlege: So, you don't do obstetrics?

Sohier Elneil: I don't do any obstetrics, no.

Julia Cumberlege: No.

Sohier Elneil: Not since I've become a consultant.

Julia Cumberlege: Right. Okay, thank you very much. It has been raised - brought to our attention by other bodies that there is a bit of an issue with conflicts of interest. Conflicts of interest associated perhaps with the regulator, but also with surgeons. I just wondered if you'd like to tell us a bit about that, if you feel it exists, if you think that there are things we should address?

Sohier Elneil: Yes. I mean I think - certainly in the early parts of the 2000s and up to, probably, 2010, it wasn't unusual for many doctors to be supported by different pharmaceutical companies and implant device companies. To go to meetings, to support their research, to help them with meetings in their hospitals, and to support them with - basically progression in their clinical arena of work.

I'm perhaps one of the few who did not have any such intervention or any such relationship with the mesh - particular mesh companies. I will agree that I have worked closely with implant device companies like Medtronic, which - I've used - for the sacral neuromodulation and pacemaker device companies and, in the past, with Allergan, who does Botox in our patient group.

Those are the sort of predominant groups I have worked with, but not with the mesh companies. I think what I have learned in the last few years - it's been a learning exercise for many of us - is that many of my colleagues were involved quite closely with various mesh companies.

Julia Cumberlege: You said since 2010. What's happened since after 2010?

Sohier Elneil: In 2010 there was a sort of a very strong directive that doctors and physicians in the UK - and it came really from the pharmaceutical industry directly - that we should...

Julia Cumberlege: Sorry, it came from?

Sohier Elneil: From the pharmaceutical industry...

Julia Cumberlege: Oh, right.

Sohier Elneil: ...that we had to make it extremely clear for what purpose money was given, and that it should not impact on your judgement call to use specific medicines or to use specific devices or implants. So there was a very strong drive and many people tried really hard to adhere to that. There were also - if you looked at the converse, one of the problems was that in order for people to actually attend meetings and international forums and so on, it's a costly affair. For many people, it impacted hugely on their

ability to go to those meetings. But it was expected that you had to be upfront, be very transparent about what you were using, why you were using it, and so on.

So, that was a very strong directive and most hospitals made sure that clinicians working in the field were well aware of the rules.

Julia Cumberlege: So, talking about the meetings, which I can understand could be very useful for training purposes, if it's made very transparent who is putting on the meeting, who is funding it, and when the surgeons or whoever go to those meetings it's made plain, do you think that deals with the conflicts of interest?

Sohier Elneil: I think as long as you are upfront about it, it should have dealt with most of the conflict of interest. What has come to light more recently is other funding opportunities which were not so clear. But, for instance, all the societies request that you are upfront. You have to do a disclosure agreement. It has to be on the website under your name. Everybody needs to know in what capacity you acted with that particular company.

But there have been other things that I have become aware of recently where there were funds given for other reasons which were not perhaps so obvious to the rest of us. But that is also - that was taken on a personal level, so it wasn't something you could judge people on. People - that's how it happened in that facility or that institution.

Cyril Chantler: I don't understand, sorry.

Sohier Elneil: So, for instance, some people had research projects funded by certain groups or certain companies. So, you wouldn't necessarily be aware that that has been happening in the past. It's only now that people are aware that that's what's happening.

Julia Cumberlege: So, is there clarity now or is there...

Sohier Elneil: Yeah.

Julia Cumberlege: ...still a bit of an undercurrent?

Sohier Elneil: I think there is more clarity now, definitely. My impression is that most people are talking about what's happening.

Sonia Macleod: But if you have a research project that is funded, you publish it [unclear] have to declare.

Sohier Elneil: You do. You have to declare. It has to be on the publication.

Sonia Macleod: Yeah.

Sohier Elneil: The journals will ask you for that...

Sonia Macleod: Yes.

Sohier Elneil: ...otherwise they will not publish it.

Sonia Macleod: Yeah.

Julia Cumberlege: Right. Thank you very much. Can I just ask you - I mean, clearly, a lot of the work that you have been doing has been taking out mesh, doing the removals, either partial or whole. But are there issues where you think there are reasons where you really should insert mesh? Also, if you feel there are occasions when we should have mesh alternatives? If so, what are those?

The first part is are there times when mesh should be used?

Sohier Elneil: That's a very difficult question. I think there will always be patients who need mesh, but it really is the last resort, and other therapeutic options should have been offered and trialled first. If there is then a failure and there is nothing else that is possibly available, then yes, there is a role for mesh.

I think what happened to us in the field has been that mesh was always kind of a second or third - had a second or a third role in the patients' pathway of care. But it kind of moved up hugely and became almost the primary therapeutic option offered. I think that might have contributed a little bit to what's happened to us in this field.

I think it has got a role, but it has to be very, very clearly well-defined. In addition, I think the high vigilance state that we've got now should apply to that, so these patients must be followed up regularly for the rest of their life and not to be discharged and not seen in the community.

Julia Cumberlege: We're talking specifically about pelvic mesh, insertion into the pelvis?

Sohier Elneil: Yes.

Julia Cumberlege: Yes, okay.

Sohier Elneil: Yes.

Julia Cumberlege: Because there are other areas...

Sohier Elneil: Yes.

Julia Cumberlege: ...perhaps...

Sohier Elneil: Yes.

Julia Cumberlege: Hernias and things like that.

Sohier Elneil: Yeah.

Julia Cumberlege: Okay. Right. Yes, any questions?

Valerie Brasse: Can I just ask, who should be putting the mesh in? I mean we've got now - we've seen the sort of specialised commissioning framework.....

Sohier Elneil: Yeah.

Valerie Brasse: ...for dealing with complications. But it sort of rather leaves the putting in of the mesh much more local.

Sohier Elneil: Yes.

Valerie Brasse: Where do you stand on that?

Sohier Elneil: So, I mean I think - I mean one way of looking at it is you could say there should be the good mesh guide or the good mesh insertion guide. That would be in centres where you - patients have access to the therapy but really within a setting where it's not just generally used or passed through a rubber-stamping sort of system.

I think one of the problems that has occurred has been - for instance, the concept of multi-disciplinary team meetings to make decisions, but in many situations it's quite clear there's almost a rubber-stamping approach to that. So, depending on who is the most vocal in the group - and we are starting to see this, and this is why some of the work we are doing now with mesh removal needs us not to work like that. We need to be much more aware that just okaying something because the majority of the group think it is, without having the voice of dissent there, is not appropriate.

I think with mesh insertion there is a drive to sort of just say, well, it's appropriate, it's good, just use it. Anybody can use it. The training has not always been up to speed. Many people who were inserting mesh - certainly from my experience in removing it - often had - were not urogynaecologists or female urologists. They were in name, but not necessarily in training. There wasn't a distinct sign-off process. There wasn't a mentorship programme in place or a supportive programme in place for ongoing membership and preceptorship of support.

So, I think if - where we are now and where we'd like to be in the future, I think that would have to change. We'd have to have a much more sort of - almost like a hub and spoke approach, where you would have patients through a very sort of centralised group of assessment. But with - if you're going to work with peripheral units to work together so that you can say well, this is a - we think this patient should have X, we know this centre can provide X, and they can be seen in that centre.

There needs to be a bit more freedom of movement, but with a directed core of assessment and vigilance for that patient.

Valerie Brasse: So, can I just be clear, are you saying that the MDT approach per se is not the answer?

Sohier Elneil: Not always. I think it is in a lot of situations but it's not perfect. It's not perfect and it is very much dependent on who the members of the MDT are. It depends on the voice of the members because some people's voices are, let's say, more equal than others. Therefore, that has an impact on how the decision-making goes. That's something that, as physicians and clinicians, we've got to address. How we address it, I'm not sure, but it's something we need to think about.

Sonia Macleod: In the hub and spoke approach that you're suggesting, if you're suggesting sort of centralised hubs, how do you determine where they should be, who they should be? How do you accredit them? How would that work?

Sohier Elneil: So, most major units act as a focal point anyway for complex pelvic surgery. So, you could actually use them as your hubs already. They've already got the focal group of surgeons working in them. They've already got - usually - the training throughput and the trainee throughput and so on. But actually, creating a way that they could communicate with - either they could be the people who refer into them or the people around them, or geographically that work with them, so that everybody feels equal in the decision-making process, I think that's quite important.

I think there is a tendency - and before I came into this hearing I did inquire from my colleagues in district general hospitals around me to see what their thoughts would be, and many have said that they feel kind of outside the process of decision-making. Even the current situation with the mesh, they feel they didn't have a word or a say immediately. But they quite welcome - and it was their suggestion, actually, that they would feel much more secure if they had a central point they could work with, refer to, take decisions with, for their own patients as well as for the centres' patients group - the group in that particular centre.

It's a bit more complex, I think, than what we've got currently, but it may be a way forward.

Cyril Chantler: So, would it be mandatory that - say, you're a surgeon in the spoke, in the district general hospital...

Sohier Elneil: Yeah.

Cyril Chantler: ...that they would need to get clearance from the hub at UCLH because they're [unclear] to actually put mesh in any way into a patient? Is that what you're saying?

Sohier Elneil: I think - yeah, I think that's - I mean, when I spoke to two of my colleagues - in fact, two of them last night, they made that point, that it actually would validate the process if they knew that what they were doing fits in with the guidance. Because most of the hubs are working very hard with the situation we have currently to try and make it strong. The spokes, as it were, haven't got the same - they haven't got the support, fully. They can get it but it's going to be difficult if you're in a spoke.

So, actually buying into the hub and having that input actually makes their life much easier.

Cyril Chantler: So, you - a woman goes to see...

Sohier Elneil: A person.

Cyril Chantler: ...somebody in Essex and...

Sohier Elneil: Yes.

Cyril Chantler: ...she's got stress urinary incontinence, and they decide together that this is what they want to do...

Sohier Elneil: Yeah.

Cyril Chantler: ...they would then contact you.

Sohier Elneil: Yeah.

Cyril Chantler: Send you the history and the - and what they intend to do.

Sohier Elneil: Yeah.

Cyril Chantler: All this, of course, would be open because the...

Sohier Elneil: Yeah. Yeah.

Cyril Chantler: ...copies of letters to patients.

Sohier Elneil: Yeah.

Cyril Chantler: Then that would be cleared off. Yes, this is the appropriate thing.

Sohier Elneil: Yes. Appropriate, yeah.

Cyril Chantler: Then, of course, it would be registered on the...

Sohier Elneil: Yeah.

Cyril Chantler: ...new register.

Sohier Elneil: Yeah, in the new, non-partisan register, as I refer to it.

Cyril Chantler: Yes.

Sohier Elneil: I think that - so, it needs to - I mean, we've adopted a method for the last two years which has worked to some degree, although I don't think it's as fine as it should be. It involves using technology to Skype in and talk to each other once a week so that we can discuss complex cases together. We've found that even - although I'm based at UCLH so it's, in theory, a hub - I'm not suggesting it should be the hub, I'm just saying it is a possible hub - is that we found it as helpful to us, getting that perspective from the community, as vice versa.

So, our community colleagues in the DGHs will say, well, hang on, this patient lives in such a place, we think this may be more appropriate. So, we've had that dialogue and I think it's been helpful to us. It's not perfect, but it's certainly a different way of doing things.

Cyril Chantler: But that would be particularly for mesh.

Sohier Elneil: Yeah.

Cyril Chantler: The other interventions for stress urinary incontinence wouldn't require that process?

Sohier Elneil: They're not - no, they wouldn't. I think, because of the situation we have with mesh, it might be a very good way - we've done it for everything. We've done it for all prolapse and continence surgery, and that's been helpful to us. Chronic pain, et cetera. So, we've done it that way.

Julia Cumberlege: So, if a surgeon and the patient agreed that it should be colposuspension...

Sohier Elneil: Yes.

Julia Cumberlege: ...that would be part of this - seen altogether? Or...

Sohier Elneil: At the moment, we do that, yeah. Our unit does that. Even if you want to do a colposuspension, we pass it through all of us. Is that okay? Are we happy? Yes, we are. Fine. We'll go ahead with it. But I suspect in the future - because at the moment we haven't got the clinical skills for everyone to do a colposuspension, we are in a difficult situation. But if all things were equal, in theory, because it's a non-mesh procedure and it's not an implant, then yes, in theory, you could do it locally in your local group assessment.

But for the time being - I think for the next - certainly, the group I'm working with and who are working with me, we feel we should discuss them all together.

Julia Cumberlege: So, that wouldn't be a part of the registry?

Sohier Elneil: No. I think - to be honest, Baroness Cumberlege, I think what's happened with stress urinary incontinence over the last - it's not just what's happened with mesh now, but the mesh that even dates back to the eighties, and the fact that the follow-up data has been poor in urinary incontinence generally. I think it may be sensible that all urinary continence procedures should be on a database. That would be - I wouldn't see any difference - I would expect we should do that because it has a long-term consequence on the quality of life of women.

We don't know the efficacy long-term because we have not kept good data. We don't know what other possible complications can arise. Colposuspension has also had their own issues years ago, so it's not that it's the perfect alternative. So, I think until we're up to speed training-wise - everybody is equal, which will take years, maybe another generation - we should have everything done properly on a database.

Sonia Macleod: In terms of surgical skill, is there a sort of feel about a lack of surgical skill with the traditional non-mesh techniques...

Sohier Elneil: Yeah.

Sonia Macleod: ...and how widespread is that? If you just said you think it will take a generation...

Sohier Elneil: Yeah. I think it will because there is a group who have - my perspective, there is a group who have been in positions as consultants for, say, the last decade. Many of them have lost those skills. They did have them at

the very beginning, but they've lost them. They could probably relearn them. It will take time. But we've got a group in the middle, what I call the five-year consultant group, who have never learned them. They need to completely relearn. They're going to be the ones seeing out the next decade and a half. So, that's really another generational group.

Simon Whale: Could I just ask about your experience in terms of mesh removals, as one of the very few specialists in the country currently doing it? I suppose I'm interested in knowing, if a woman presents and is a - you've agreed to conduct a full removal, how often is it that you're unable to conduct a full removal and it becomes a sort of default partial?

Sohier Elneil: Partial, yeah. I think I would say - so, we tried, in the beginning, to scan everybody before and after. Now, we're doing it a little bit more often, difficult to say. I would say most patients with obturator meshes, which are the transobturator, I am sure most of those patients have got something left behind. A little piece. How much is dependent on the type of mesh, the approach, et cetera.

With regard to the retropubic mesh, they almost are always total removals because their angulation is under the urethra. So, we usually do it in two steps, for many reasons but one of them is that I think from a morbidity perspective it's better for patients. That's my personal view, but you remove the vaginal portion and let that recover. Then you bring them back three or six months later, by which time you also know if they've got recurrent stress incontinence. You then remove the abdominal or pelvic portion separately, but at the same time do either a colposuspension or autologous fascial sling to treat the incontinence.

So, we do it in two steps. Now, in those procedures, particularly if you do the dissection over the bone and into the vulval tissue, you will get it all.

Simon Whale: Right.

Sohier Elneil: The problems comes in technique and what people's perception is about what really needs to come out, rather than - so, for instance, if somebody says I have pain at a particular point, some clinicians will think well, we'll just remove the mesh from that particular point. Not necessarily all the others but we tend to do complete removal.

So, retropubic mesh is, I'd say, total in two stages. Transobturator meshes, we think about 30 per cent always have a little residual bit left behind. But we're currently trying to develop our scanning technology in-house so that we can actually scan during surgery, so we can actually modify and see whether there is any residual mesh at that point.

Simon Whale: Can I ask about - when you remove the mesh, are there any - in your experience, are you seeing inherent defects from the mesh that you're removing? Or are you witnessing poor insertion and the effects of that?

Sohier Elneil: A lot of poor insertion. Some mesh in the distal urethra, proximal urethra, not in the mid-urethra, folded, too tight, et cetera. You can actually see it taut across the urethra.

The mesh itself, as a characteristic - you can't honestly say it's the mesh that's done the problem, other than sometimes you will see abscess formation. You will see inflammatory change. You will see nodular tissue around it. So, almost a chronic - the best way I could describe it is a host versus graft reaction that you would see, say, in transplant surgery, where there is an attack of the body on the product. That's the sort of change I can see. So, it's induced that response.

We've got some meshes that I've seen where they haven't crumbled, that would be the wrong word, but they've sort of - almost snapped on themselves. So, you've got slightly movement - but they are rare. You don't see that often. You tend to see much more either the very inflammatory change or the mal-position or misdirection of a particular part of the mesh.

Simon Whale: But the majority of the problems you're seeing are caused by insertion issues rather than by inherent?...

Sohier Elneil: I think insertion is definitely a factor. We have got, of course, a proportion of patients where it's in the perfect position, it's in the mid-urethral point, et cetera, but still, they've got problems. So, in that particular group, we think it's the inflammatory response which is not always visible to the eye, but it is when you remove it and send off for histopathology. It shows very chronic, bad inflammatory change.

Simon Whale:: Can I also ask about translabial scans? There seem - many women have to almost fight to...

Sohier Elneil: To have it, yeah.

Simon Whale: ...access to a translabial scan, but amongst the clinical community there seems to be a split of opinion on how useful translabial scans are in determining whether mesh is present and where it is and so on.

Sohier Elneil: Yeah.

Simon Whale: What's your view on translabial scans?

Sohier Elneil: So, up until 2016, we never used them. Then - that was mainly because we didn't know how to image the mesh. We kept on trying to find ways. We tried MRIs, it didn't do that. I think as physicians we always want to know as much information as possible before you enter a difficult arena. So, what I have found is that subsequent to when my colleagues started doing this, it has helped me understand more why the patient was having a problem.

So, it gives you clarity on the position of the mesh. It tells you whether the mesh is breaching the muscle, the mucosa, the urethra, the bladder, so you are prepared for the type of surgery that you might need to undertake. You also can prepare the patient better, so you can say to the patient look, you're going to need to have a catheter for 14 days. You're going to need to have a cystogram, et cetera. So, you're better prepared.

I think there is a resistance by some to the understanding or to the role imaging has, but I think also for clarity, for me as a surgeon, the more information I have the better I think the decision and the surgery potentially will be because I know what I am dealing with rather than not what I am dealing with.

So, we've had occasions where patients had a perception that they had a retropubic mesh when actually they had an obturator mesh. So, that kind of changes your scope of approach. We've been told - patients have come and told us we've had two or three meshes, but they actually might have one. Or vice versa, they thought they had one and they've got three.

So, in situations where the mesh is physically easy to see, feel, you know it's there, it's eroded through, that's slightly different to the case where the pain is the factor, we don't know why. I find it very useful then.

Valerie Brasse: Is there no alternative? So, you couldn't have found that information any other way than by the translabial...

Sohier Elneil: Yeah, it can be - so, my colleague, I spoke to her - who does a lot of scanning, she uses an endovaginal technique. You don't need to necessarily use translabial, but you just need to know what you're looking for and how you're looking. So, she uses an endovaginal process. She usually uses a 2D probe. She doesn't use a 3D necessarily. But it just gives you clarity of where everything is.

Because it's a difficult arena and it is a fraught arena, I think you do need as much information as possible before...

Cyril Chantler: So, the problem isn't the equipment. That's generally available.

Sohier Elneil: No.

Cyril Chantler: It's the operator.

Sohier Elneil: It's the operator and the operator who knows what they're talking about. So, I get more information from my colleague who is also a urogynaecologist as well as a detailed scanner, because she's got that experience, than I do from somebody who doesn't necessarily have the urogynaecology background. They can tell me that the mesh is there, but it's not always as helpful to me as a urogynaecologist. But that's something that can be worked on.

Cyril Chantler: But you can pay X-hundred pounds and go and have one privately, can't you?

Sohier Elneil: Yes.

Cyril Chantler: That's being done by somebody who is not...

Sohier Elneil: ..Exactly.

Cyril Chantler: ...working in a multi-disciplinary team.

Sohier Elneil: Exactly and so the information I - unless - because I see a lot of patients who have done that, the information I gather from that source has not always been helpful to me at all.

Cyril Chantler: Okay.

Julia Cumberlege: Mrs Elneil, I'm afraid we've got somebody else coming now.

Sohier Elneil: Okay.

Julia Cumberlege: But can I thank you so much for coming. I'm very conscious we could go on a lot longer...

Sohier Elneil: Oh, not at all.

Julia Cumberlege: ...but if we have further questions, perhaps we could put them to you, and if you have questions to us...

Sohier Elneil: Sure.

Julia Cumberlege: ...we would welcome them.

Sohier Elneil: Sure.

Julia Cumberlege: But thank you so much.

Sohier Elneil: You're very welcome. Thank you. Thank you.

END OF TRANSCRIPT

Session 3: Myra Robson

START OF TRANSCRIPT

Julia Cumberlege: I think it would be helpful perhaps if you could start by saying who you are so we've got that on the screen. I don't know if you've brought a statement - if you'd like to start with that and then take a few questions from it.

Myra Robson: Yes, that's fine.

Julia Cumberlege: Okay, if you'd like to start, that would be good.

Myra Robson: My name's Myra Robson and I'm a specialist pelvic health physiotherapist. I work in Lewisham and Greenwich NHS Trust in South London.

I'm also involved in other public health initiatives and created Squeezy app, which is a pelvic floor exercise app. It is that led me into Mesh in the first place when Kath Sansom contacted me about Squeezy and about conservative measures for pelvic floor problems.

As a result of that, I became involved in Kath's work and in the Sling the Mesh group. She invited me to join the group and over around about the last two years, I've been involved in the group as the situation has escalated. My role has been to help with clinical advice and answer questions when they come up, and also to act as a bridge between the mesh-injured community and some of the medical professionals, and to try and start the conversations going about the way forward and how we can improve the current situation.

Julia Cumberlege: Thank you very much. Have you got a statement you want to make?

Myra Robson: What I was going to say with my statement was that I feel that the role that I've taken is quite an unusual one. I don't think there's many people who've got a foot in each side of the camp so I think I've got quite a unique viewpoint in understanding how the mesh-injured community - particularly women because it's mostly the gynae mesh I'm involved with - are feeling and how they're responding to changes that are happening, both in the news - such as the news we've had this week about the devices - and about the progress that gets made with the mesh situation, with the review body and so on.

I'm really keen to use my position to help support the path going forwards in any way that I can.

- Julia Cumberlege: Thank you very much indeed. I think the last time we spoke you did actually say that you are supported by various organisations. I'm not talking about - I'm talking financially - is that right? Have you got any...
- Myra Robson: The only support I have is for a group called Pelvicroar which I run with two other physiotherapists, which is a social media group for pelvic floor issues. We have some sponsorship for running our website and for our trademark by Living With - which is the company that makes Squeezy app - and by two other product companies.
- Julia Cumberlege: Thank you very much indeed. Can I ask you from the point of view of - I mean, you've declared your interest which is great, but do you find that there are other conflicts of interest within the whole of this area? Perhaps conflicts of interest from the pharmaceutical industry or surgeons being influenced, or the MHRA? Are there any issues there which you think we should explore?
- Myra Robson: Not that I have seen. In the hospital I work in, I worked with a consultant for a while [inaudible] when it was at its height, probably about eight to 10 years ago. I'm not aware of any conflicts of interest but being a relatively small hospital, we don't see as many of the reps or receive as much of the financial support as some of the bigger hospitals. So, for the work that I've been involved in, I haven't seen that.
- Julia Cumberlege: Thank you very much. Can I ask you, you talked about two camps - if you'd like to say a little more about the camps and about whether you feel there is some consensus albeit that you've described two camps?
- Myra Robson: I think gradually over time that the majority of the mesh-injured community and healthcare professionals, are starting to see that actually there are more problems with mesh than we had first realised.
- A lot of the mesh-injured community have huge amounts of anger and also anxiety and fear - and I can understand that position - because they feel that they have had a treatment that was perhaps unnecessary, perhaps not consented for or not consented for fully - was offered when they could have had an alternative such as physiotherapy or pessaries. These were either not offered or not explored fully enough and some of them have expressed feelings that they've been operated on for reasons that were just incorrect. Perhaps financial incentives, or the surgeons were just in a position of power and using that in a way that was inappropriate.
- I think over time that the work the review body has done, which has been extremely positively received by the mesh community, and the latest

research on mesh and medical device in general, is helping them to see that actually although there is a problem it wasn't necessarily coming from the wrong reasons - that there have been some genuine mistakes that have been made.

From the terms of the healthcare professionals, I think the same thing is happening. When it all started, I think a lot of the mesh-injured community were viewed as being perhaps hysterical, creating a buzz on social media that was unhelpful, and perhaps some of the symptoms - because the reported symptoms can be quite unusual and difficult to objectify - that perhaps that they were exaggerating or making these symptoms up.

I think as time has gone on, the volume of women, the volume of symptoms that were being expressed and the evidence coming forward is helping the healthcare professionals to see that there is more solid evidence for what's being reported. I can see that there are moves being made to bring the two sides together and to get a little bit more mutual understanding.

Julia Cumberlege: Is there a greater warmth now towards physiotherapy?

Myra Robson: I think it's getting there - yes. I think more of the pelvic health physiotherapists in the UK are gaining an understanding of mesh and I'm trying to make sure that the message is spread wherever possible.

We still have a big challenge in educating the musculoskeletal physiotherapists which may cover a much larger body of the profession. One of the problems is that women with mesh complications may go to their GP as a first point of contact. They often will present with symptoms such as groin pain or back pain and then they're being referred to a physiotherapist - not necessarily inappropriately, it's a good place to send someone with back pain - but those physios may not be fully understanding of mesh, and again that's not unreasonable.

Then these patients are perhaps being treated in a way that although it would be completely appropriate for an average back pain patient, it's flaring up a mesh-injured woman quite considerably. That is still causing some concern but I've worked with the group - particularly the Sling the Mesh group - to help them to see that actually it's a specialist pelvic physio that they would want to see and to be open and discuss their mesh problems with anybody else, with the idea that if a physio is not familiar with the topic, that they can then come and speak to me, look it up, become familiar with it. I think we're starting to avoid some of the flare

ups that were happening. I think that situation is improving but I'm working with my professional body to try and find ways of spreading the word further and educating everybody.

Julia Cumberlege: That's very encouraging. Thank you.

Cyril Chantler: How many schools of physiotherapy are there in England?

Myra Robson: That's a question. I really don't know, but pelvic health physiotherapy is not taught as an undergraduate subject for the majority of schools. It's a post-graduate training and that's partly why there are far fewer of us than there are generalised physiotherapists.

Cyril Chantler: Is there still one at Kings?

Myra Robson: There is a school of physiotherapy at Kings, yes.

Cyril Chantler: What connection would you have with that because that would be your local one, so to speak, won't it?

Myra Robson: Yes, at the moment I haven't made any connections with any of the schools of physiotherapy. I've been working with the professional body to try and get information out more centrally.

Cyril Chantler: How would the training take place then? Will the professional body do it or will they do it through the schools?

Myra Robson: In terms of mesh, what we think at the moment is that it doesn't actually alter any of our assessment or treatment options. We work on treating the individual and that's exactly the same position no matter what the complication is - with mesh or whether post-removal, et cetera - so it's about understanding what mesh can do to the body, what presenting symptoms may be, how irritable the condition is and how easily flared up symptoms can be. Then working around that, rather than specific techniques. It's much more of a theoretical training that's needed which is why I'm keen to use websites, journals and so on.

Cyril Chantler: But there will be clinical interventions to be researched and outcomes to be measured...

Myra Robson: Mm-hm.

Cyril Chantler: ...and the usual way of doing that is through some sort of academic base. Correct?

Myra Robson: Yeah, that's a very good point. At the moment, one of the problems I've got is that all of this is done in my spare time, rather than...

Cyril Chantler: [Unclear].

Myra Robson: ...as part of my job. The list of things to try gets longer.

Cyril Chantler: But your professional association is the - what is it?

Myra Robson: Pelvic Obstetric Gynaecological Physiotherapists.

Cyril Chantler: What connection do they have to the big professional body?

Myra Robson: It's a subsidiary of the Chartered Society of Physiotherapy.

Cyril Chantler: Right, so do you have any connections to the Chartered Society?

Myra Robson: Yes, and I am in discussion with the head of the POGP and also, she's in discussion with the CSP. I've made links with another training person at the CSP.

Cyril Chantler: Do we need a national strategy?

Myra Robson: I believe we do, yes.

Cyril Chantler: How we can help to review - develop that - shall we meet the Chartered Society? If so, who do we meet, how do we do it?

Myra Robson: Yes, I think that would be really positive and also, involving the POGP in discussions would be a very positive move too, and supporting some time to allow some of the specialist physios to spend some time planning this out would be good.

Cyril Chantler: We only make recommendations but we have to make practical recommendations.

Myra Robson: Yeah. I think some time is important, so there are several of us who are interested in the mesh complications and has some experience of it, and having any support with that to put guidelines together, I think would be very positive.

Cyril Chantler: Thank you.

Simon Whale: Can I just ask about the relationship with surgeons and consultants, so if you take a situation where a woman doesn't have a physiotherapy intervention but ends up in front of a surgeon discussing surgical options for SUI or prolapse and mesh is a consideration in that context, how likely in your experience is it that the surgeon would say, actually you ought to try physio first before I go anywhere near you?

Myra Robson: My experience is it's very individual. I think we're getting more towards referring to physiotherapy as a first line but there are some surgeons who, even now, still don't really believe that physiotherapy is a good option. Partly because of the adherence to it, so we know that for SUI, for example, that the evidence suggests you need a three-month programme of exercises and you need to be exercising up to six times a day. Understandably, the adherence tends to be quite low but we know that it works.

We also know that waiting lists can be long and not all hospitals will have specialist pelvic physiotherapy access. That does make it more difficult for some of the surgeons to choose it as an option.

I think with all of the mesh issues we've had, and obviously it's the first line in the NICE guidelines for SUI, I think we're getting more interest in it and more women are educated as well and asking for physiotherapy as a first line treatment.

Simon Whale: You don't see a cultural problem amongst surgeons?

Myra Robson: I think there's an element of it still. I've certainly worked with consultants who are not particularly interested in physiotherapy and even in my own hospital, some surgeons will never refer to me despite all the work that I do trying to get them to use us as a first line, but I think it's improving.

Julia Cumberlege: Can I ask then, if a woman does ask for physiotherapy, what's the waiting list like?

Myra Robson: At my hospital, it's about two months at the moment but it varies. At Kings College Hospital, there's no GP direct access to pelvic physiotherapy so they're already referred into the consultants before they can get to physiotherapy. Really, we should be first line from a GP rather than going into secondary or tertiary care.

Julia Cumberlege: How big is the private sector in terms of physiotherapy?

Myra Robson: It's quite significant, yes. There is a lot of interest in pelvic health physiotherapy in the private sector, partly driven because women can't access as much in the NHS as they would like and the nature of the work makes it very suitable for part-time physios, physios working unusual hours that fits in around family life which a lot of the patients want as well. It's quite a thriving area at the moment but expensive.

Julia Cumberlege: It is. Thank you very much. Valerie?

Valerie Brasse: I'm just curious about that gatekeeper role, to access specialist pelvic physiotherapy - I mean, I'm not sure of the numbers but as you say, you turn up at a consultant who may have a waiting list of months and months before you get to see them - that's months by which you haven't had access to the specialist physio that might have been necessary before a consultant even really looked at you.

Myra Robson: Yeah.

Valerie Brasse: The option for the GP to make those referrals - presumably that isn't happening - they're not being able to access specialist pelvic physios?

Myra Robson: Not routinely, no, and some GPs are not aware of what services are being offered in their area. In my area, we set up GP direct access which is great but we still have GPs referring straight into the urogynae team and we're trying to establish a much clearer pathway for that because it's not necessary - it's a waste of time and money.

I'm also really keen that we look at new and inventive ways of getting the physiotherapy information out to patients so out of around 44,000 physios in the UK, there's only around 800 of us who are pelvic health physios. Clearly, without a huge investment of time and money, that's not going to change any time soon. We need to be much more creative about how we go about this which is partly why I created Squeezy because that makes sure that you've got good evidence-based information that patients can access.

My professional body has leaflets - information on its website that patients can download as well - and yet despite the amount of information on the internet, people still don't know where to go or where to get their quality information from. I think there's still work that can be done in making sure women are aware of the pelvic health problems that can happen, how common they are, that we can treat them, not to suffer in silence - all of those aspects also need to be dealt with so that we are clearing up some of the minor problems before they become bigger problems.

Valerie Brasse: The obstacles to setting up GP direct access, is that a result of or because there are so few of you? What are the obstacles?

Myra Robson: I think, yes, partly it's that and partly it's educating GPs and getting the information out to them - understanding that pelvic health physiotherapy is a thing, that it's different from general physiotherapy and often in the NHS, that we're so busy ticking off the boxes and meeting our targets that

actually taking that time out to plan a service and plan a change, becomes very difficult.

Simon Whale: Could I just ask about whether there is in your mind a distinction between preventive pelvic floor physiotherapy on the one hand and management of a condition - whether it's SUI or prolapse, or whatever? Firstly, in terms of what you see, what is the balance between the two, and secondly, when should the preventive message be getting through to people? At what time in a woman's life should they be introduced to the concept of good pelvic floor health?

Myra Robson: I think it should start at the teenage years. We learn about our eyes and go to the opticians, our teeth and go to the dentist but we don't even think about the pelvic floor most of the time. I think when girls are reaching adolescence, the same time we're doing sex education and periods in schools, we should be talking about pelvic health. For boys as well - I think everybody should be aware of this - then when they're going through the post-natal period, we want good quality information. There is a drive towards every new mum should be seeing a pelvic physiotherapist and I think that's a really excellent principle, but again in practice, I can't see how we could achieve that at the moment. Again, we need some more creative ways around it.

The biggest area is the stigma and we need to be talking about this more. My group #pelvicroar on social media is all about getting people to know about pelvic health problems, so that they're coming forwards at an earlier stage. If women are doing their exercises and doing them correctly before they have children, we know from the evidence that we can reduce the risk of stress incontinence, for example.

If you pick up a problem quickly and then go and get treatment, we know again from the evidence that we can have a significant impact so it's starting at the grass roots of basic information and making sure it's accessible and that women are encouraged to talk about their problems and get help as soon as possible.

Sonia Macleod: I mean, one of the questions is that if you're saying adherence is quite low because people have to exercise every day rigorously, is there a way, and how do you improve adherence?

Myra Robson: I think there's a number of ways. We're looking at - we would like to set up a trial with Squeezy app, for example, because we know from the surveys that we've done and the subjective data that it improves people's adherence. We know that smartphones are the way forward for so many

things, and Squeezy is designed that you can set reminders, it keeps an exercise record and so on.

We know from the literature there are other ways of making contact with people, for example, and one study showed that if you rang a patient every day, their adherence went up hugely. Now that's not practical for most of us, but there are developments that we've made, for example with Squeezy, that will allow your app to be connected to a clinician platform. There are ways that we can use the technology to further that.

We're also looking at ways of having online consultations or questions and answers with the professional. What I've seen in the Mesh group is that women will often ask questions that other women are answering because they don't know where to go and get a professional answer. Sometimes it's something really simple, but it's getting them an answer from a source or a person that you trust that's really important when there's so much out there.

I think if women understand the importance of what they're doing then I think that will help adherence. If they understand that these conditions - particularly incontinence - are treatable, which a lot of women still think they just have to put up with it or it's a normal part of having children, or a normal part of ageing - getting rid of those myths I think will take us a long way forwards to getting adherence.

Sonia Macleod: Are there products as well as apps that will help?

Myra Robson: Yes, there's a huge variety of products. For stress incontinence, you can use incontinence pessaries such as Contiform, which will help support the urethra. Use those in the vagina so patients can put them in yourselves as they're doing sports or exercise, for example.

When it comes to prolapse, the range of pessaries is phenomenal and yet we hardly use them in the UK. There's still a massive amount of misunderstanding around them. 70 to 80 per cent of women can be successfully managed with a prolapse with a pessary which again they can sort out themselves. The most expensive pessaries cost £50 and last for up to 10 years so it just seems complete madness that we're not exploring this option more.

Julia Cumberlege: Why do you think that we don't use that option?

Myra Robson: Again, there's a lot of myths around them so traditionally they were used if you were waiting for surgery. I still hear patients say, my doctor says I'm too old for a pessary, I'm too young for a pessary - so I'm not sure what

the golden age is for a pessary - and doctors traditionally haven't used them so much because they're a conservative tool. But physiotherapists aren't trained to use them - and I fit pessaries but it's considered to be an extended scope role for physios. If it's a conservative role for the surgeon and an extended role for the physios and the nurses, who is supposed to be fitting the pessaries? We need to be addressing that and that's something else that I'm looking at with my professional body - how we can introduce that more for physiotherapists.

Patients don't like pessaries often and I see so many patients who say, but I want it fixed, so they're not understanding that if you operate on a prolapse, there's still a 20 to 30 per cent chance of recurrence. But we're still seeing surgery as being the answer in many cases - obviously less so now. Again, it goes down to education.

We know that pessaries are a degree of guesswork and it takes on average two to three attempts to get the right pessary but often it's, try a ring, it falls out, you're not suitable for pessaries. It's something else that needs a little bit of time taken to set it up and get some clear training, guidelines, understanding of it.

Sonia Macleod: But if you're saying that's not a surgical option - so surgeons don't do it - physiotherapists is an extended option, who does it? Where does that fit?

Myra Robson: I think it should be physiotherapists and nurses. I think we should start with it being gynae specialist, getting guidelines clearly established - we don't have any good guidelines in the UK but they have excellent ones in Australia which I'm basing my work on. Then we need to be training and spreading out to GPs and practice nurses.

Julia Cumberlege: I think we've got to draw this to a close sadly, because I'm sure we could go on longer, but I just have to say, Myra, if you've got things you'd like to ask us we're always available and open and accessible. Certainly, there may be questions we want to come ack and ask you and I hope that will be possible.

Myra Robson: That's fine, yes.

Julia Cumberlege: But thank you for all the work that you're doing helping women in this way. Thank you.

Myra Robson: Thanks very much.

END OF TRANSCRIPT

Session 4: Dr Wael Agur

START OF TRANSCRIPT

Wael Agur: So, thank you for inviting me. My name is Wael Agur, I'm a consultant urogynaecologist, working in Scotland. I would like to thank you for giving me the opportunity to provide evidence today, and also thank you for suspending these procedures after meeting with the mesh-injured women. I would like the review to know that you cannot meet all the mesh-injured women, because there are women out there who do not know that they had mesh procedures, there are women out there who had mesh procedures, but do not link it to their current problems, and there are women out there who know they had mesh procedure, they link it to their current problems, but they are too private to speak to your team.

Also, it's important for the review to know that you have not met - the majority of the people who receive these procedures are absolutely happy with it. That is the majority of the women who receive these procedures.

So, I'm a surgeon and a clinician and a researcher, and one of my duties is to reduce the risks of the treatment I'm providing, including the surgical procedures I perform. So, it has been a learning process for myself, and for many of my colleagues as well. I used to perform all transvaginal mesh procedures, and I used a variety of mesh devices during these procedures. I gradually stopped performing these procedures, or, in other words, suspending these procedures in my own practice, with the realisation that there are risks associated with these procedures using these devices that are largely out of my hands.

So, as a surgeon who performed continence procedures, it's my duty to reduce the risk, to mitigate the risk - to identify it, to prevent it and to address it when it happens, and to reverse it if possible. I've been largely successful in doing this, with the non-mesh procedures, with the native tissue procedures. However, with the introduction of mesh procedures, and after a few years of doing these, I started to hear about complications that happened with my colleagues, that I thought it's important to learn from. So, rather than - well, life is too short to learn from your own mistakes; you must learn from others.

So, I started to suspend these procedures in my own practice, because I thought the risk is - or cannot be accurately predicted, cannot be prevented, it can be absolutely serious, it's a lifetime risk, it's a cumulative

risk, and it cannot be reversed in the majority of women who develop it. Giving my opinion that this risk is avoidable, because there are alternatives that are not associated with mesh-related complications, then in my opinion, in my opinion for most of my patients, this actually is an avoidable risk. So, that was the main reason that I do not perform any procedures at all just now, of the mesh type. I continue to do the native tissue surgery, or the non-mesh procedures.

I'm also a researcher, I led some research groups into looking into mesh procedures in comparison with non-mesh procedures, and while there has been significant improvement in our understanding of the risks and the comparative risks between mesh and non-mesh procedures, I found serious shortcomings in the research, and I believe this is at least in part contributing to the perception of clinicians of these adverse events. Or, you could say the significant difference in perception of these risks and their seriousness, between the medical profession and the patient group, and the public on the other side.

So, from the review of the literature, it was very clear to me that there has been a significant focus on short-term outcomes rather than long-term outcomes. There has been a focus on efficacy, on the success of treating incontinence, rather than the adverse events. There has been some research, or academic practices that are - can be called outcome switching, where the researcher looks at certain outcome. This has led, in my opinion, in confirmation bias, where the research team inadvertently wanted to reach an outcome that conforms with the current thinking, or the direction of travel of everyone.

Yes, there has been influence from industry, sometimes it's declared, sometimes it's not declared. Sometimes, embarrassingly, declared at a later stage. But what really strikes me most in some of the publications I've read, is the perception of the researchers or the authors of the reports of the pain itself. So, you will find in the literature reports of research studies that describes them as chronic pain. So, at one year, there is a percentage of chronic pain. Some studies say one per cent, some say two per cent, some say three per cent. But you will find the conclusions that this procedure is safe, even though there are two per cent or three per cent of women who are suffering chronic pain at one year follow-up.

So, very, very little was done to find out what happened to those two and a half per cent, how much pain killers they are taking, how much impact on their quality of life, how much impact on their - if there is any disability. I think, because the risk is cumulative, we are now seeing these

complications that were hinted at in the research a few years ago, but because there is no long-term evidence, the evidence only coming from patient campaigners and the society.

Having said that, I strongly believe that the mesh procedures were not created equal. There are mesh procedures associated with much higher risks compared to others. I put in my written evidence that there are perhaps two procedures that should be suspended, or to continue with the suspension of these, and perhaps there are two procedures that need to be restricted to situations where previous surgery using patient's own tissues were not successful, or if the patient cannot have the native tissue surgery. The procedures also need to be restricted only to surgeons who can perform both mesh and non-mesh surgery, for balance and for prevention of directive counselling, and to be performed only for patients who are fully informed of all the risks and their consequences. Thank you very much.

Julia Cumberlege: So, can I ask you, and I would like to go into the conflicts of interest in a minute. But can I ask you the two procedures that you think should be suspended, which are those?

Wael Agur: So, this is the trans-vaginal use of mesh for women suffering from pelvic organ prolapse. That's the first one. The second procedure is a transobturator tape for stress urinary incontinence.

Julia Cumberlege: All right, thank you very much. You talked a bit about conflicts of interest and the influence of industry, et cetera. Could you say a bit more about that? Who are they influencing, and how?

Wael Agur: So, it takes several forms, and the medical device industry and the mesh manufacturers are not the only part of industry that is influencing medical research. That also applies to pharmaceutical companies. This is a - there's a wider picture of influence. So, there are studies that have been solely, 100 per cent funded by industry, and there are studies that were partly funded by industry. There were studies where the researchers doing the research were - have competing interest with industry, or being personally and non-personally funded by industry. Sometimes in relation to the project at hand, and sometimes in the relation to other projects.

In one case that has been widely publicised, it was revealed that the manufacturer has actually reviewed the report before submission to the peer-reviewed journal, and in fact, it appears that the manufacturer did make some changes to the report, before submission and before

publication. That was not declared at the time, but it was declared a year, or I think maybe two years later.

Julia Cumberlege: Thank you for that. Have you any views about the regulator? Because clearly, we need regulation in this, and whether you feel that's been adequate, or whether you feel it should be strengthened.

Wael Agur: The regulation must be strengthened. The - it was quite surprising to me how soon the mesh devices came to the market. I was not a urogynaecologist when the first device came to the market, so I cannot tell you a lot about that. But I was a practising independent urogynaecologist in 2009, where there have been several mesh devices that is called TVT lookalikes, and me-too devices, where other manufacturers wanted to create competitors for their own device in the market.

These devices were represented to us by medical reps as exactly - will do exactly the same as the previous devices. So, this is an equivalence. But there is something that is additional, for example, it is less price, or it will give less complications. It was quite surprising how little research, in quantity and quality, was done before these devices were marketed.

The regulators must do more to tighten the rules around the - before approval of devices. There are steps going in the right direction in the States, but it appears that the European Union and the UK is a bit behind the FDA at the moment.

Julia Cumberlege: So, strengthening the regulator would be to address this issue of equivalence.

Wael Agur: Yes. I think the FDA has proposed very recently to update the 510(k) process where devices are approved on equivalence, rather than they are - its own merit. The famous example that we know that the most commonly used or the prototype classic mesh device has been approved on the back of another device that was subsequently removed from the market, but the current one continues. So, there is certainly problems with the regulation.

Julia Cumberlege: Thank you very much. Cyril.

Cyril Chantler: Could you - it has been suggested to us that there are no circumstances where mesh should be used, because there's always a better alternative - or an alternative. Can you describe a patient in whom you would recommend mesh?

Wael Agur: Okay. So, again, mesh devices are different. There are - some of them are associated with seriously high risk, and almost no benefit, or no benefit whatsoever. So, I will answer your question four times. For the use of mesh in prolapse, I cannot see any circumstances that a woman would certainly require the use of mesh vaginally to correct prolapse, rather than any other option. So, that's why this is one of the procedures that I suggested that the suspension would continue.

For the transobturator tape, it's very similar to the use of mesh for prolapse. The only - what we could say, an absolute indication to this procedure would be if there was a woman who had the very rare vascular graft procedure that, where there is a vessel, large vessel going behind the pubic bone, so she cannot have a Burch colposuspension, a retropubic TVT, or an autologous fascial sling, because they all require going behind the pubic bone. So, if there's a large vessel to go in there, then that would be a contraindication.

However, there are still other procedures that can be done vaginally, for example, bulking agent injection. So, that's why I suggested that the transobturator tape should not be used except in very rare, exceptional circumstances. But I believe that the vascular surgeons have largely dropped this procedure in their practice anyway, so there will not be a lot of women with a retropubic big vessel. So, that's why I believe the transobturator should not be used. Especially if it's associated with the highest risk of chronic pain, of any continence procedure.

So, for the abdominal placement of mesh, yes there is evidence that it is the procedure with the highest efficacy for prolapse, because it's abdominal and pulls the prolapsing organ right up through the abdomen. However, to me, it seems that the incremental benefit of reducing the recurrence rate does not justify going through the abdomen, with all its associated risks. It does not justify implanting a mesh device. However, there may be women who will have several vaginal procedures, and they were not successful, using native tissues, and in those women, perhaps the only way forward would be to place mesh abdominally if they accept the risk, compared to the recurrent prolapse they already have.

Cyril Chantler: Would you do that as an open operation, or a laparoscopic operation?

Wael Agur: So, there is no difference in efficacy, or there's no significant difference in efficacy between the open and the laparoscopic approach. However, the laparoscopic approach, in the vast majority of situations, requires the insertion of a second medical device, which is a fastener to fix the mesh to the lower back. It is difficult to take a stitch in this area, it's a very

strategic area, very difficult to take a stitch as we would do during the open procedure. So, if laparoscopy is employed, then a second medical device is required. Sometimes this medical device added another layer of risk, which is disruption of the intervertebral disc by inflammation and infection.

For the last procedure, the retropubic tape, that was the classic TVT that was the procedure that the vast majority of surgeons, gynaecologists and urologists would say it's the gold standard, and it has replaced the colposuspension, which is the previous native tissue gold standard. There are significant risks associated with it, but it appeared to be - it is not the worst offender. It is the mesh procedure that we could say that it is the mesh procedure with the least mesh-related risks. That does not mean it is safe. There are women who are - who developed serious chronic pain and chronic problems with it. However, there will be women who have tried all other continence procedure using their own native tissues, and their incontinence is still persistent and very bothersome. Some of those women may opt to accept the serious risks associated with the TVT.

Cyril Chantler: So, it would be a last resort, as far as you're concerned?

Wael Agur: Exactly.

Cyril Chantler: You'd go through all the other possibilities before that.

Wael Agur: Yes. So, I proposed in my written evidence that the retropubic procedures be used as a second line surgical treatment. So, the - after conservative treatment does not work, the first line surgical treatment for incontinence would be the native tissue surgery, or the bulking agent injection. If these don't work, then it would be the retropubic TVT procedure.

Simon Whale:: Just to pick up on that point, so if the first line surgical procedure fails, the native tissue first-line procedure fails, and you then resort to your second-line mesh procedure, does the fact that the first has failed in any way increase the risk of failure of the second line of treatment?

Wael Agur: Yes. If the first procedure is a colposuspension or an autologous sling, the second procedure, inevitably, whatever it is, the risk of its success is lower than the quoted 85-90 per cent. It will be probably in the range of 75-80 per cent. However, if the first procedure is a bulking agent injection, then there is a consensus among surgeons that it does not compromise the patient's chances of having the background success rate as everyone else.

Simon Whale: So, the success rate of the second-line mesh procedure is only marginally reduced, it's not substantially reduced. Did you say, 85 to 80 [unclear].

Wael Agur: Yes, yes. The same applies for a second native tissue surgery.

Simon Whale: Yes, okay.

Wael Agur: So, this is not something inherent to the mesh procedure.

Simon Whale: Can I also ask a question about - you mentioned earlier that when you were doing transvaginal procedures with mesh, you used various different types of mesh, I think you said.

Wael Agur: Correct.

Simon Whale: Did you notice a difference in terms of risk of complication, as between different types of mesh for the same procedure?

Wael Agur: I did not do them enough to be confident, to be able to confidently answer that question for you. However, I did move to - from one device from a certain manufacturer to a different device from another manufacturer, hoping that I will get less complication, or my patients will have less complications. But that hasn't happened.

Simon Whale: So, to put it crudely, you wouldn't say there was a good mesh versus a bad mesh scenario?

Wael Agur: They are all bad.

Julia Cumberlege: Right, okay. Valerie.

Valerie Brasse: Yes, you've obviously looked at the NICE draft guidelines that have come out, so it's interesting in your point about not using mesh for transvaginal prolapse. I've been looking at it, and my reading of it suggests that currently, we have a restriction that it can't be used unless it's for research trials. But that seems to have gone in the last guidelines. It's possible, if you were not suited, or not suitable to have transabdominal, actually you may take the transvaginal approach, or that's what they seem to be recommending. I don't know whether you've read in the same way.

Wael Agur: I did read it in the same way. I totally agree with you. I'm not sure how a committee of NICE reaches a conclusion that restricts a procedure to research only, however another group within the same - under the same umbrella, reach the conclusion that it can be offered, out with research. I've seen that, and I...

Valerie Brasse: What would you be saying?

Wael Agur: I've already - what would I be saying to my own patients?

Valerie Brasse: To NICE, if you were responding, I don't know, to the draft guidelines. You comment about that?

Wael Agur: Yes, yes. So, we - yes. We've sent comments on this, and we said that the recommendation from the interventional procedure advisory committee, IPAC, which was published on 17 December, 2017, stands. In my opinion, it should be restricted to research only. In fact, it should be restricted full stop, until we find out from the largest research study on prolapse, that has completed three years ago, which is the PROSPECT study, we should wait for the long-term outcome from this study before using any mesh, either within or outwith research.

Valerie Brasse: Again, that's now - how old is that study? When are we likely to see the next round of results?

Wael Agur: So, the two-year results were published in December 2016, and I believe the team now is preparing to publish the long-term results of the PROSPECT study. I think the five- or six-year results.

Valerie Brasse: So, that's coming out quite soon?

Wael Agur: I don't think - it will be in early winter '19. But you could check with the team.

Valerie Brasse: We will do, thank you for that. Can I just go back - obviously you had this sort of change of heart about how you used mesh, or decided not to. Are you alone in this? I mean, one doesn't get the sense that the rest of the profession similarly took that view. So, I'm just wondering how that came about, that you observed, and you heard, and you learned from what you've been hearing on complications rates elsewhere, but the rest of the profession took a different line. How do you explain that?

Wael Agur: Well - that's the impression you get, and I understand that. However, there is an increasing number of surgeons who already stopped doing, or using prolapse mesh, and stopped using the transobturator tape, even before I stopped. There are surgeons who never used prolapse mesh, and there are surgeons who never used transobturator tape, because they did not think it was a good idea at all. However, I think in my case, things were a bit different, because I was part of an independent review, and that did not end up very well, and I had to resign from the committee. Then I had to express my views, why did I resign from the committee. But

I'm not alone in this. There are quite a large number of surgeons who stopped doing this, but perhaps they didn't speak in public.

Valerie Brasse: I suppose one of the issues is the - sort of breakdown in relationship, if you like, between medical professionals on the one hand, and the mesh-injured community on the other. It's probably the relationship is at an all time low. How one might repair that, going forward?

Wael Agur: We had that, in the Scottish group. So, there was a significant split, and we managed to - so, from 2014, and up until the second half of 2016, for two full years, we managed to get the mesh-injured women, or the representative of the mesh-injured women, and a representative from the clinical community, including the college, and including clinical societies, we managed to get them on the same table. We managed to broker an agreement, and publish an interim report that everyone signed up to. The Scottish report at that time, in October 2015, was the first authority in the whole world to express concerns about the transobturator tape. So, the group was leading the world.

I strongly believe, if you bring a group of dedicated clinicians and mesh-injured women around the table, look at the research, and with the perception of women who have good outcome, and the women who had bad outcome - this is what we've done in Scotland - I think eventually, the truth will come out, and you will get everyone to agree on the way forward.

Julia Cumberlege: Excellent.

Sonia Macleod: It was just a quick question. You were supplying your evidence to the patient decision aid, which I thought was fantastic. How did that develop, and how did you implement it, and how widely used is it in Scotland?

Wael Agur: So, the idea of the decision aid came after the publication of the Scottish report in October 2015. It took us a few months to develop it. We - development started with the local continence multi-disciplinary team, so that involved physiotherapists, continence nurses, fellow surgeons. We also had significant help from an improvement advisor with Healthcare Improvement Scotland, we also had an academic from Glasgow School of Art to design the PDA for us. We started using it in September 2016.

The theory behind it was patients are still not well-informed even after they read the leaflet. Some patients do not want to read the extensive leaflet. I suppose the idea first came up during one of the Scottish government meetings where we said, okay, we've developed this information leaflet on mesh tapes. It's 24 pages long. Who's going to

read it? It's just too long. Yes, it describes all the risks, but who's going to read it? So, the idea was that we summarise the comparative benefits and risks of all the four procedures in one A4 page, in a nice table that says this is adverse, this is the advantage.

So, we've designed this, it took us a few months to design it. We've got version one out. We started piloting it in my local area. I spoke about it in national and international meetings, and every time I speak about it, lots of surgeons come to me and say, that's a great idea, could you please send us the link? My hospital published the patient decision aid on the website, I think that was September 2017, in all its nice and glossy format. I also run training courses for surgeons on native tissue surgery, and I always mention the PDA. So, the form has been used in maybe two or three centres in Scotland, and perhaps, as far as I'm aware, maybe six or seven centres in England.

I did speak about the form in the Royal College, in a meeting of the Royal College last - earlier this month. The Royal College is very enthusiastic about developing the patient decision aid, and I've been working with a representative from the clinical society and the Royal College to develop version two, which will be easier for patients to read, and will have more explanation on risk and comparison of risk. So, version two is expected to be published by the College soon.

[Aside discussion]

Julia Cumberlege: Can I...

Simon Whale: Yes.

Julia Cumberlege: What you were saying at the very beginning is absolutely right, that we cannot see all the patients, and that some are too ill to visit us, others probably don't know they've had mesh inserted. Others are very happy with the mesh, and don't actually want to talk about it, and we absolutely understand that. I just want to ask you, though, some of the patients we've met have been 70 years old. So, that was - mesh started about 20 years ago, so they are now 70 and really suffering from the mesh, because things have happened to the product, as it were. I just wondered if in fact, this plastic that is introduced - is there a certainty that it will disintegrate? Is there a certainty that it will cause problems, or can it actually be inserted and people be very happy with it till they die, and die, perhaps in their 80s, 90s?

Wael Agur: I wish I could answer that question. I cannot answer it with certainty, unfortunately. Having said that, I can only speak from my own personal

experience, because the research is very deficient in this area, and there will be basic science research in how - what the mesh does in vivo, inside the human body, years and years later. But that's not my area of expertise. Having said that, I can tell you, from my own experience, from my own clinical experience, not the lab experience, is that I have seen patients who had mesh for over 10 years, and they come into clinic with something completely unrelated to this, and I found this by chance only, when reviewing the records, that they did have a mesh procedure. But what they're presenting with has nothing to do whatsoever, I'm confident of that.

I've also seen some patients who had mesh 10, 15 years, and been absolutely fine for 10, 15 years, and all of a sudden, they are presenting with all sorts of problems, that are not just in their head, it is actually something physical. I cannot tell 100 per cent which one will have the best outcome, and which one will have the worst outcome and be in a wheelchair. Because I cannot tell, and I cannot reverse it, I stopped.

Julia Cumberlege: Well, thank you very much. Simon.

Simon Whale: Can I just ask you about translabial scans, because in your evidence, your written evidence, you pose the question as to whether they are a useful investigation tool. I just wondered whether you had a view on that yourself, that you could share with us. Bearing in mind that, as we've heard, and no doubt, you have, women often struggle to get access to an NHS translabial scan, and they end up, sometimes, in many cases, paying privately for a scan, which doesn't always help the diagnosis or decision making that follows. Bearing in mind also, that there seems to be a disagreement within the clinical community about the usefulness of translabial scans. So, what are your thoughts on using them?

Wael Agur: So, yes, there is disagreement within the medical community about the usefulness of the translabial scan, or the transperineal scan, or whatever scan to find where the mesh is. Some clinicians do an MRI scan to try and find where the mesh is. So, there has been effort to try and identify where it is, before the surgeon goes in and takes it out. So, I am not a mesh removal surgeon. I have not removed any mesh at all in the last, at least, three, four years. I did attempt, and some of the attempts were successful, others - some others were not successful and required a repeat so I stopped. When the national centres were recognised in Scotland, then I refer to the national centre in Scotland for mesh removal.

So, a woman who would require a translabial scan is a woman who is considering removal of the mesh. The idea is to identify where the mesh

is, to guide the surgeon to remove it. It seems that the... there is agreement - well, there's not agreement, but there is a view which I support, that it is not costly, and it can show something that the surgeon did not know about, and needs to know about. One example for this, is if the mesh device has been inserted in an unusual place, or if the mesh device has moved inside the body to an unusual place. However, surgeons who are experts in mesh removal, and they have the documentation of the type of the device, they do an examination, and they can feel the device, especially if it's eroded, there is no need for a scan.

The other side of the argument is, if the notes are not there, if the patient does not know whether - how many mesh devices she had, then perhaps an ultrasound scan would be guidance. So, patient selection is perhaps key. What is certainly needed, is a pathway for treatment of women who develop mesh complications, to identify which one would require a translabial scan and which one - I think NICE, the draft guidance, has formulated a really very interesting table on what investigations are required and what their uses are, but there's no stepwise direction.

There is a meeting of the mesh removal surgeons next week, where, I have no doubt that this issue will be discussed, which is how to create the pathway which should be, I think, open for both the clinician and the patient, so the patient should read - I think the pathway should be written in a language the patient understands, and that is along with a specific patient information leaflet. So, we need a national information leaflet for women who suffer from mesh complications, and a very clear pathway to guide both clinicians and patients.

Julia Cumberlege: Well, Dr Agur, thank you so much for coming, and I'm sorry it's such a trial getting here. But we are delighted you managed to make it. Maybe we'll see you in Glasgow. Thank you very much.

Wael Agur: Thank you very much for having me.

END OF TRANSCRIPT

Session 5: Professor Carl Heneghan

START OF TRANSCRIPT

Julia Cumberlege: If you would like to start.

Carl Heneghan: I'm Carl Heneghan. I'm Professor of Evidence-Based Medicine in the Department of Primary Care Health Sciences in the University of Oxford. I'm also Director of the Centre for Evidence-Based Medicine in the University of Oxford. I'm also an NHS urgent care GP, which is generally a weekend job - keeps me busy. I'll be there Saturday morning. I am also an NIHR senior investigator. Just from a conflicted point of view, I'm also a clinical advisor to the All-Party Parliamentary Group on Surgical Mesh.

Julia Cumberlege: Thank you very much. It's over to you if you have some things you want to tell us.

Carl Heneghan: You've invited me here. I guess the position is - do you want me to start on Primodos? That's what we said we'd start with first. I get asked a lot now in the public by context to look at evidence by members in the public, particularly where they consider there are adverse events or harm has been caused. In fact, I was approached four years ago by Justice for Kids, but at the time said we had no resources or no funding and I couldn't do anything for them. But I was approached by Marie Lyon and the Association for Children in November after the Expert Working Group. I don't normally do this, but she's a very persuasive woman. I think you've met her and you can probably say that.

Julia Cumberlege: We know.

Carl Heneghan: I listened to her for about an hour and I said, I will go and look at the evidence working group report for you, and based on the comeback - because we work in a zone of neutrality where we don't have preconceived ideas, but we bring our particular skills in epidemiology and evidence-based medicine - how do you apply decisions to actual patient care as opposed to how do you discover new interventions and so forth? That's a very important distinction. The epidemiology of discovery is in animal studies. The epidemiology of decision-making is about human studies.

I looked at the report, which I have in front of me - when I do this I tend to read stuff with a glass of wine or whatever and go over the report. When I read the EWG report it was very clear to me there were omissions in the report and the way it was put together was not what I would consider as consistent with systematic review methods.

There were a number of errors within the report. One is they combine oral contraceptives and hormone pregnancy test. Not asking a clear question right at the outset presents you with a problem. That's always been - it's like saying we're going to look at two drugs in one go in a systematic review. It's combining apples and pears. Second is, they didn't use standard methods for appraising the quality. But more importantly, they didn't summarise the effect estimates in a meta-analysis, which is what we've done in the report I sent you.

In the draft report, it is clear though they did do that but they removed it from the report, because in the forest plots it says, we used a pooled relative risk to do the analysis. So, somebody somewhere in the EWG did perform a meta analysis; they just didn't report it.

The standard method is to present - in a systematic review what is important is, you take all of the evidence, you appraise the quality and then present that evidence. Then you take the studies that are at high risk and remove them. That's what's called a sensitivity analysis. In doing that, you see if the effect is stable to that result. If you remove them and the result disappears, becomes non-significant, you get concerned that the quality of the study is affected and the result.

So, when you look at our paper, which you've got a copy of, you'll see that when we did the sensitivity analysis it didn't affect the results. For a number of conditions, it is clear the evidence shows there is an association with congenital malformations, all congenital malformations, congenital heart disease, musculoskeletal, urological and [syndrome factual] but not for gastroenterological. That's what the evidence shows. The question is, why wasn't that done in the first place. For me and my team when we sat round a table like this and looked at the report, we just were slightly flabbergasted to go, why wasn't that done?

If you understand that basic principle of systematic reviews, you're sat in front of you with evidence of association. In the past, it's clear to me why that wasn't done. Systematic reviews were not established methods. In fact, the Cochrane Library came into establishment in 1994 to particularly overcome the problem of significant and not-significant results.

The best example is the Cochrane logo, which looks at the use of dexamethasone in pre-term labour and its effect on respiratory distress. There are seven studies in that logo. Five of them are not significant; two are. Most of the historical arguments are saying, oh, there's a positive study; oh, but there's a negative study, and playing that out in the literature. So, it doesn't surprise me in the past that these problems

persisted. You can see why. That's exactly why we established systematic review methods.

Now you come to a position - why did the evidence working group not do the correct study? I don't know the reason for that, but I shared - you should ask them that. Why did they do a systematic review and a meta-analysis and remove that? Why did they combine two treatments which are completely different? Why didn't they do the sensitivity analysis? We're left in a position that, if I was sat in a court of law now presenting this evidence, I would say there's a clear association in the evidence for an increased risk with hormone pregnancy tests.

Julia Cumberlege: Can I ask you about your study that you've done? What is the status of it now? Is it in general public - is it published?

Carl Heneghan: Yes, it's in the general public. It's in *F1000*. There are two new emerging areas of publication. One is pre-print publications where - they're important and I've done reports on pre-prints for organisations like World Health Organisation. You can understand in something like an Ebola crisis you need to make the evidence available irrespective of its peer-reviewing. *F1000*, it is put in the public and the peer review is in the public domain.

It's had a first review which has approved it. I'm aware that the second review is now in. Once that is in, it will be approved, and that means then it will be indexed on PodMed. Based on the peer reviews, we will make some minor changes to the document. We've had one or two errors pointed out to us, but the overall message won't change.

Cyril Chantler: Who peer-reviewed it?

Carl Heneghan: David Healy peer-reviewed the first one and approved it. The second one, I don't know, because it's out to seven peer-reviewers at the moment. We'll keep taking it...

Cyril Chantler: I know Michael Healy. Who's David?

Carl Heneghan: David Healy is a professor of pharmacology or pharmacovigilance in the University of Cardiff in Wales.

Julia Cumberlege: Will it be published in things like the *BMJ*?

Carl Heneghan: *F1000* is a publication in its own right. The Wellcome Trust publish through the *F1000*, so that will be the publication we use now.

- Simon Whale:: What would you expect the Expert Working Group to do when your paper is available to them?
- Carl Heneghan: What would be really nice is - I'm aware that one or two members of the Expert Review Group have sent emails to some of my colleagues saying, where did we go wrong? They haven't sent anything to me, but I'd be quite happy for them to email or even review - they can leave comments, where did we go wrong? We were prepared to answer any issues based on systematic reviews that we've done. Just to say, I've done in excess of 100 systematic reviews throughout my experience.
- Cyril Chantler: I'm very surprised that when they set up the Expert Working Group they didn't set up a publication peer review committee to look at the report before it was published. Certainly the National Academy of Medicine always does that.
- Carl Heneghan: I think there are two distinct problems, and I've been on the record saying this. If you're asking the same people who oversee safety to then look at the problems when they occur, I can't think of another area or public body that allow themselves to look at themselves and come up to an opinion. I think there's a need for independence within this to separate out the evidence production, which is what we've done in effect. If somebody had said, come to us and do the evidence, we'd have just done the same thing.
- You might not like the result, but we're independent. In the same way as you say, some of the structures then present to an independent panel who go, do you know what, on the balance of probabilities here's what we think went wrong. You're asking the same organisation who oversaw safety to police themselves. We know that doesn't exist. If we ask the police to do that, we just say this is a whitewash. We haven't fixed - we haven't understood this.
- Continually what will happen is - I've been here and I'll be around, and your Review - no offence - will come and go in the same way as directors of the MHRA. In yesterday's *Panorama* I felt sorry for the guy they put up who was trying to defend - I thought it was embarrassing for them to put up somebody who was so junior to defend really important issues. In defending it, we're not moving forward the status quo. If we accepted there are structural problems and we need to fix these, it would be like as a clinician. If I get a complaint I have to reflect and look at what I've done and think about it. I don't defend myself. I'd be in front of the GMC for that.

A recommendation is to separate out these investigations from the body that oversees safety, because they are the people who have to say - if it's a judgment that there's an association, they have to say, we got it wrong. I just don't see a public body ever admitting that. Just to be clear though, your point about the *BMJ* - one of my other jobs is editor-in-chief of *BMJ Evidence-Based Medicine*, to add to my list of jobs - you shouldn't judge the quality of a publication by its impact factor or the peer-reviewers, because that's an onerous mistake. We teach basic epidemiology to say, just because it's in the *Lancet* and *New England* it doesn't mean it's any good.

What I would be welcoming, if anybody would like to write to me or write directly and comment on the paper - and you should ask them to do that - specific issues, I can answer them in quite some detail and I'd share that. But the benefit now is, it's all open peer-review, so everybody gets to see the answers. Whereas, if it was in the *BMJ*, you wouldn't get to see it. This is the future of publication that's coming right now.

Sonia Macleod: As part of our evidence submission, we have had evidence presented to us that other statisticians have looked at the available publications with a view to doing a meta-analysis on them. They have decided that they were not sufficiently robust or of sufficiently good enough quality to allow the meta-analysis to be done. What is it about what you have done that differs?

Carl Heneghan: But that's not established systematic review methods. I don't understand that. You can't decide, we don't quite like the quality of evidence, we're not going to put it together, otherwise you would invalidate the basic principles of systematic reviews. I'd have to - there's no publication out there that can point me to say, a methodological approach is, if you don't like the quality of the study - because remember, quality assessment is a subjective judgment. It's not objective. So, depending on your conflicts, you could make it good or bad. What you do in systematic reviews, which is across the board, you publish all of the studies and then you remove the ones of low quality and see if the effect is stable. That's standard method...

Sonia Macleod: But how do you grade the quality? Because the grading of the quality has to be subjective, surely.

Carl Heneghan: There are two established methods. We use the Newcastle-Ottawa scale, which is a 9-point scale with 10 questions. That's a validated scale that's been out - there are some criticisms of that scale that exist. Most of the criticisms exist on the basis - if you are untrained then you'll come to

wildly different areas and disagreement. At the moment, the Cochrane promotes Newcastle-Ottawa scale. We promote it. They are bringing in a new scale called ROBINS-I, which is for observational studies, but the guidance is not there yet and it's not guided for case control. But they all do a general thing. There is no right answer when it comes to quality. We could slightly differ in our subjectivity.

We assess the overall quality of evidence as moderate. But there's a very important point to understand. If you assess the quality of evidence in randomised trials for treatment effects, low-quality trials overestimate benefits and underestimate harms. That's very clear. If you look at our review, that's what low-quality trials tend to do. They underestimate harm, because there are no benefits here, but they underestimate harm. You can't have it both ways.

There is a bit of a methodological gap. You can't say, low-quality studies overestimate harms, because that would go against all the empirical data. In fact, if you look at studies like the [Lensa] study in figure - they tend to have lower effects. If you look at one of the - Lawrence 1971 study would have a low score on the Newcastle-Ottawa scale. In its nervous system outcome, its effect size was nearer the normal effect.

Sonia Macleod: Yes. I suppose my question is, if you look at the individual papers, first of all there are papers that don't get included because when you do your searches for whatever reason they don't match the criteria. So, there are odd studies missed out. So, no meta-analysis is ever complete, if you see what I mean.

Carl Heneghan: I don't understand the premise of the question. It's not complete whether you've set out prespecified methods and you stick to them.

Sonia Macleod: Yeah, it [unclear] specified, but it doesn't necessarily find every single paper.

Carl Heneghan: Are you saying this one or - yeah.

Sonia Macleod: Yeah. This one there are...

Carl Heneghan: Yeah, that's fair comment.

Sonia Macleod: But also in terms of grading the individual papers within the meta-analysis there is an element of subjectivity in the way you do that presumably. I'm looking at the Gal '72 paper, and it says, were the controls adequate? One of the queries over that paper has always been whether the controls were adequate or not.

Carl Heneghan: Yeah, okay.

Sonia Macleod: So, there is an element in there that has to be a subjective judgment.

Carl Heneghan: Okay, so your question is - but the incorrect thing to do is to not include it. The correct appropriate - let me just explain. The correct method is to do a sensitivity analysis and remove Gal from the analysis and see if the effect is stable. If it's still stable, you feel confident. We could run that effect - we can run that analysis for you tomorrow if you want that. If you say to us, we'd like you to remove single studies at a time, see if the effect is stable, you can do that.

You can carry on doing this and this, but do not get hung up on - there's an exact correct judgment of bias, and if we can't find that we can't find an association. That's flawed thinking. That's flawed thinking in what the EWG did, and that's, I consider, a group that didn't quite understand systematic review methods. As opposed to coming from a discovery or epidemiological background, you might do these things. But having done a lot of systematic reviews, that's a standard approach. Otherwise you lead to publication bias and reporting bias, and you reduce the power of the effect. So, you just get an underpowered effect all the time.

It's very clear if we get hung up on that, which people will do - you'll get a conclusion like the EWG, and you're in a different remit. You're not in the epidemiology of making decisions. You should use all the available evidence in making a decision, not a bit of it. Because we know we're littered with examples where that's been done, and generally what's been shown is the positive results and the negative results of it all.

Sonia Macleod: I guess my question was, when we're looking at your sensitivity analysis, you're saying, okay we need to remove the papers that we are worried aren't as robust, that aren't as reliable.

Carl Heneghan: Yeah, so the ones that scored lower on the Newcastle-Ottawa scale.

Sonia Macleod: Because there is an element of subjectivity in scoring, how do you balance your analysis for sensitivity when of the papers you're dealing with a lot of them aren't terribly good quality and they all have inherent issues?

Carl Heneghan: You're using words like terribly good quality. What would define a high-quality case control study to you, is something that meets nine of the nine criteria of the Newcastle observational scale. You use two independent reviewers who are highly skilled in their job, and they come to a decision. If you judged it, you may be out either side by one, but I suspect across the whole lot you'll balance out. We could take 10 experts

if you want. We'd get to pretty much the same answer. That's what would happen.

You could argue single points here and there, and I think that's okay. What you do then is, you have a third person who's a consensus to discuss them. But we're not talking the difference between nine and zero; we're talking the difference between four and five or five and four. That's all you're talking about here. And, yeah, you can get hung up on that, and a lot of people I work with, statisticians, get hung up on these issues, because they're trying to say, there's a certain answer. There isn't. By default you define it as subjective.

We can only get to an approximation of the truth. In fact, I'd say many of the studies were well done when you look at them for case control methods. The other important aspect is, it's a mistake to believe that randomised control trials are the top of the evidence for harms. That's an incorrect fallacy. There are about three reasons why. The first is, if you think that's something is harmful, it's unethical to expose an individual in a randomised control trial. So, you can't give people - expose them to [unclear] biomass or smoking. We know that. That's a flaw.

Second is, in the time period randomised control trials weren't done, so that's another flaw in the thinking. Our levels of evidence, which are cited over 300 times in the CBN, would put a systematic review of case control studies at the top of the hierarchy. So, it is the right approach. Some of them were well done. The major problem was the reporting bias, the way they were reported in a non-standard way, makes it difficult to extract the data. There's a possibility we made one or two data errors. That's why we want people - and we accept that's a part of science. You will make errors when you try and discern.

The hardest thing was to decide the population that had hormone pregnancy test and, could you extract the data on them alone? Very difficult to do. But even if you went over that, found the one or two areas, the material elements of what we showed won't change very much. The associations are there.

Cyril Chantler: Can you draw a conclusion as the EWG didn't that there is a causal association, or put it the other way round, would you say you can't exclude that?

Carl Heneghan: I think there is a very interesting issue in language, and this is where people get tied up a bit. We very clearly will say there's an association with hormone pregnancy testing and congenital malformation, and the

evidence is clear. The homogeneity about the effect sizes is important. There's zero heterogeneity for many of the effect [testaments]. That's an important - and the direction effect is positive.

Causation to me is really an issue for the courts, because you are trying to say, in this individual did X cause Y? I think this is where we get in a bit of a problem, because to definitively say cause, you've got to look at individual cases and say, in this case, did this person do X, Y and Z? You'd want more information about that individual. If they, for instance, weren't at high risk in the first place, they weren't taking other substances like alcohol and smoking, they didn't have some predetermined genetic risk or family history. I think if you take them, and an individual didn't have them, you would then say, based on this association, on the balance of probability this caused my pregnancy - that's why...

Cyril Chantler: I don't want to put words into your mouth. Would it be fair to say that you cannot exclude a causal association?

Carl Heneghan: You certainly could not at all. You would have to have the evidence to disprove the other way.

Cyril Chantler: On what you have presented, you could not exclude a causal association.

Carl Heneghan: No, and nobody could. If they did, they would be not taking the evidence to...

Cyril Chantler: Would it be also fair to say - and I am putting words in your mouth - that your work does support a possible causal association?

Carl Heneghan: Probable is probably a better word.

Cyril Chantler: Probable causal association?

Carl Heneghan: Yes, because that's what you were doing - on the balance of probability does hormone pregnancy cause malformations? yes. Does hormones cause malformation?, That's a difficult statement to make.

Cyril Chantler: We've got that. What you said, which I think is very interesting, is that causal has to be a matter for the law, because they have to balance the individual. Is that right?

Carl Heneghan: Yeah. In the absence of hormone pregnancies, do congenital malformations occur? Yes, they do. You can only say it's causal in the complete absence of something it would definitely not have happened. That's my mind of...

- Cyril Chantler: So, you can't put the total numbers together and say, it [suits] the one, two per cent we expect.
- Carl Heneghan: You can say it doubles your risk of this event occurring. The question is, once it's occurred, was that caused by this? That's a different question, and that's not what we set out to do with the evidence in the first place. Once somebody has had an event - but for this you would say yes.
- Cyril Chantler: I remember Martin [Bogra] doing one at Seascale over radioactivity. They came to the conclusion it wasn't - there was certainly an increase in congenital - no, it was I think the development of Hodgkin lymphoma or something. There was an increased prevalence, but they didn't think it was related to radioactive - it seemed to be more when people moved for some reason they were more susceptible.
- Carl Heneghan: This is very interesting. If you go back to causation and where we are, if you go back to the Oxford childhood cancer studies in the '50s, that was a single case control. What's the lady's name, the woman who knew everything? The book is called *The Woman Who Knew Everything*. It's an excellent book. It's gone from my mind. She was an Oxford researcher. They did a case control study of children with leukaemia and pretty much like these came to the conclusion that it doubled your risk if you'd had an abdominal x-ray for childhood leukaemia.
- It was pretty clear for everybody it was a good idea to stop doing abdominal x-rays, but because there's no manufacture or business involved, I think we could understand to do - it took us a bit of time though. There is a significant time lag between harms and when we understand where we're going to go. Twenty-four years for cigarette smoking.
- Julia Cumberlege: Can I stop you there? We actually have the expert on cigarette smoking. I know we could go into that area in some depth. I'd like to move on now, and thank you so much for what you've told us already...
- Carl Heneghan: You're welcome.
- Julia Cumberlege: ...on the whole question of mesh. One of the things I wonder - is this: conflicts of interest. We've heard a bit about conflicts of interest concerning perhaps the industry, perhaps the MHRA, perhaps doctors or whatever. Have you any views on that?
- Carl Heneghan: You're really touching on a difficult subject in medicine. You're talking about an industry where there are significant amounts of money and a process that relies on - I wrote this yesterday - it's a process where the

problem is, you have to get your device to market as fast as you can, because there's no funding prior to approval and getting your device out there. The whole system is built around sales.

The fundamental issue I've always gone on is the problem of equivalence which allows you to bring devices to market with no evidence requirements. Our piece in *BMJ Open* showed for 61 devices there wasn't a single one had ever - a trial done for any single mesh device. On average, when trials occurred for the small proportion it did, it was five years after it had been on the market.

Are you asking me, is there a system in place where people are paid as surgeons? The answer is, yes. Are they flown around the world to become world experts very quickly in the latest mesh device? Yes. Is the MHRA funded by industry? Yes. Is the whole system commercially conflicted? Yes, it is. We asked even the GMC - I wrote this recently [inaudible] asking why at the time of GMC registration should I not have to at least make a declaration of my interest? Our members said it was not in their interest. So, you're asking the people with conflict of interest.

In America, there at least is a *Sunshine Payment Act*. You're probably aware of that. I think it would be for this review group a step forward to say there's a mandatory declaration particularly for clinicians and surgeons. I think it's important that if I'm treating you, you know who's paying me.

Cyril Chantler: The GMC used to say that. I was chairman of the standards committee. We set that, but it may have been changed.

Carl Heneghan: The problem is, who can police that? I can only see one group, which is the GMC, because every year I have to make an annual declaration and it would not be that difficult to say, oh, by the way, here's - you'd have that timestamped.

Cyril Chantler: You should put it on the appraisal form.

Carl Heneghan: Yeah, and on your GMC, which you can look me up, you should be able to see - you might want to say, hold on a minute, is this chap being paid by anybody right now? There's no other way we will be able to do that. The second problem I think that's happened is that the ability to sell products in the market is helped by uncertainty. The major reason I got interested in mesh is, I couldn't quite understand why anybody would let a lifelong implantable device on the market with no evidence beyond one year. This was very clear from 2005, and it's not changed at all in that period. You're seeing emerging problems at 9 and 10 years.

The other problem we've got is our approach to data. We have a huge amount of data in the NHS and most of it is inaccurate. There's no sense that we are going to change that. So, one of the pieces I wrote recently with Fiona Godley was to say, a fix is, in Sweden they have a compulsory post-marketing registry that the government funds and then all the societies enrich it. But the spine has to be correct.

So, whoever presents you data from a retrospective database, not a single one of them has tried to validate the data. Some of these people are convicted and some are not, but they are taking it as though it's validated data, so when NHS Digital produces its reports, we're clear this is how many operations have happened and how many reoperations have happened. That's unknown, because we haven't validated it.

If you don't do that, we have no chance of fixing the problems going forward. For implants, we need a mandatory registry that is funded by the central core government or the Department of Health and then enriched for extra questions to, say, phenotypes. That would be in our interests, and it would be in our economic interests as well. We just don't quite understand it.

The second thing is, also with the conflicts - there is an inherent conflict in the NHS now, as somebody who works in it - there's not an open forum for mistakes or errors or things going wrong. There's too much blame for individual clinicians and surgeons. I wouldn't want to be a surgeon right now in this current environment. It's a nightmare.

Cyril Chantler Or an obstetrician.

Carl Heneghan: Yeah, definitely an obstetrician. But most of these should have come through an era of research. It's outrageous for NICE to say in 2017 vaginal mesh should be used in research when it's been on the market for 20 years. That's what they should do at the end - so, NICE is a problem here. The regulations are the regulations. It's highly unlikely we'll fix the regulations. I don't know how expansive you want to be in solutions, although you could reinterpret the wording in the regulations if you were outside the European Union. At the moment it says, clinical evidence can be something like a clinical investigation. It's not defined in the regulations.

Sonia Macleod: Do you think new MDD regulations coming in 2020 will improve that?

Carl Heneghan: No, they don't, and I've just written about it two days ago. It's got the same language, so it will create more work for notified bodies, more manufacturers - but it creates more conflicts of interest because it relies

more on experts. I'm happy to send you that piece. It's got the same problem. You can use equivalence, and it's not defined clinical investigations.

The Swiss do this all the time. They reinterpret definitions and say, we are going to interpret that, meaning a clinical trial with a control group that should be reported in full within one year of completion. You've solved the problem. That lack of specificity presents as a problem with the regulations. Taking the regulations aside, the people who then give a position is NICE. NICE approve devices all the time.

I have to say, I was slightly shocked when I did read this the first time that in 2003 they approved mesh but said, we want a 10-year post-marketing study. But they have no legislative powers, so why do we let them approve without fundamental requirements that are part of the approval? So, if they're not met, that approval is removed. NICE need some legislative powers, don't they, to be able to say, this is part of the approval.

If we accept the regulations are the regulations, NICE then has a huge role. But they tend to be - since about 2009 their remit has shifted to being too pro-industry. They let devices through on very lax bar and a low approval. That is an issue. But they should be doing what they did in 2017, saying we will give this expedited approval, however, we need a two-, five-year study, and if they're not done, it will be withdrawn from the NHS. That would be a solution for us that could help.

Sonia Macleod: But do you think that would help? I'm thinking of the US in terms of the 5-2-2 studies that were requested for mesh. The result there is an awful lot of the mesh products were recalled from the market and most of the studies weren't actually...

Carl Heneghan: I agree. It's not a perfect fix and it's a good point. Essure is a good example, because at least with Essure they did ask for the two- and five-year studies. There have been some examples like [PIP] implants that didn't get out there because they said, we want studies. So, I agree - still the US is not perfect. I don't quite understand their 5-2-2 system and it's supposed to be mandatory but it's not. But this is after the horse has bolted.

Sonia Macleod: Yes.

Carl Heneghan: At least you could go, once at the point of approval in NICE they have legislative power to say, if you don't do X, this approval is rescinded in the NHS.

Sonia Macleod: My other question is in terms - the UK is a relatively small market. If we shift our emphasis so we're not in alignment with either the European or the US system, assuming post-Brexit that we end up with a slightly different framework which none of us know, we are going to be such a small market that are we actually going to get devices on the market?

Carl Heneghan: That is a very interesting viewpoint. If you were writing a review that says, we made all these problems but there are some fixes, the concern is if we fix it and then we end up with no economy, no industry and no devices. But I think you could incentivise a high-quality performance system. My position is to think of the Formula One industry, because they rely heavily on high-quality data. That's why I think the post-marketing registry is fundamental to this.

What you do is, when you get a NICE stamp at five years, you've got high quality that goes round the world. They may come here, chance and go, we accept some devices will have to go, but if we get a winner we will let it out in the NHS and get on with optimising the intervention. At the moment, we're left in this area where with mesh nobody really has a clue who's got what in them and which device is better than any other, so let's just carry on with the status quo. So, I totally agree with your point. I think these fundamental nuances could create a system that incentivises high-quality evidence, which is my job, and not the low-quality stuff that keeps us in this mess.

The other bit that - to come back to your conflict of interest point that we need a point on - is the private industry across the board, not for these three but across the board. There's no data collected in there and there's no data. So, many people who are having devices like mesh or having them removed could be having them done in the private sector. We have no understanding of what's going on. That can't happen. They have to interlope their information...

Cyril Chantler: Just to interrupt you, I happen to be on the Private Health Information Network which the CMA set up to deal with that problem. We are linking into HES data. We can talk about HES data but I'd rather not. But I hope that will get round that problem.

Carl Heneghan: The bit you point - I've not seen anybody who's not got a goodwill to fix the problem ever in the last 20 years. Everybody is trying to fix it, but when we have fixes they tend to run out of steam and get kicked down the road, because they don't get legislated in some way.

Cyril Chantler What we're thinking about - we've spoken to - and another meeting on the registry tomorrow - is the notion that when a surgeon completes an operating list, he does it digitally and has all the information that you and I might require, including a bar code for the device that goes in, and it goes on a central registry - I think they'd rather call it a database - that then organised registries can access information doing that. We used to do that with the European Dialysis and Transplant Association register, which was small. We had to do it on paper, but this will be digital.

Carl Heneghan: Using the unique ID is perfect. The problem is - or just to say it seems to me absolute common sense. Some organisations get that, so you see the orthopaedics fix the problem and obs and gynae not fix the problem. What I'm saying is, across the board that has to be mandated for in all implants across...

Cyril Chantler: I agree. Surgeons are up for that, as you saw there last...

Carl Heneghan: Yeah, I was amazed. If you'd have said that two years ago they'd have been throwing you out the room, but now they're shifting the emphasis because all the issues are appearing. I think as a safety review - but it needs funding and legislation to make it compulsory. Then you can have the added value of enriching it with more data to make it research-active, which will drive the economic value of it.

Cyril Chantler: I read your editorial.

Carl Heneghan: I always think the one mistake I've always made is, I said BSI, when they see the metal hips, which is a bit like mesh, and when they test it, they obviously could have looked at these issues. They came back and said, we never saw the device. We never even do that. We don't test devices. We just see the documents. In the old days when we used to have a kitemark, it used to mean something. At the moment, there is no stamp that says, this has been through a system that we say is safe and effective. That will slow down the early phase development but lead to longer benefits.

Setting out these positions will help the thinking of where we're at now. My concern is, some of this will get kicked down the road like it has done in the past unless we have some very concrete- like that saying, this is not just for mesh; this illustrates across all implants; this is what we require.

Simon Whale: Don't you think if you take that kind of approach that you've just outlined - which I think we probably all see the merits of that - the risk of one country in isolation - I keep coming back to this point that you were discussing with Sonia - one country in isolation divorced from the opinion and divorced from everywhere else in the world standing alone doing

that. Whilst it may be great for us, and we may be able to incentivise people to still bring products to market here, if you were the manufacturers sitting where they sit, what would you be thinking?

Carl Heneghan: They're slowly coming over. About seven or eight years ago, companies like Medtronic were starting to see the writing on the wall. You're talking about, will manufacturers carry on incentivising poor-quality products? The world is shifting in our understanding of what determines a high-quality product, and they can only take one or two more big problems that people will just lose faith in this business model that says we're going to keep selling you stuff that you don't really know if it works or not.

Simon Whale: It needs an international approach to it, doesn't it, to maximise...

Carl Heneghan: Not necessarily, because not all countries have the datasets and the approach to data like a national health system like we do. There are countries who've done it. South Korea is another one who has taken an approach to the data that allows them to understand what's going on. Many systems are fragmented because they're all private-insurance-based. So, when we look at our data, we've got a better opportunity to really go somewhere different than everybody else.

There are only a few countries in the world who can do this. Sweden has some advantages, because it's got a single ID number. We have too many ID numbers, so there are things you could talk about. We've got social security, NHS. They've just got one number. But I wouldn't - the argument from business is, you'll lose out. The long-term, medium-term view is, I think it will be a huge win, because it will be a high-quality performance system.

Your argument suggests why do we have Formula One industries, half the Formula One here in the UK? I don't understand it. On that basis, you should just go to where it's cheaper and the market is bigger. It's because of that high-quality product. That's where we're at. When we produce a system for mesh that's free of conflict and produce the evidence that we need. The point is, you will never be able to afford for devices the clinical trials of sufficient length. So, if you don't have a post-marketing system, you just perpetuate the current problem.

You need this short-term trial - tell you what you need to know. Then the long-term follow-up that can remove those devices that are ineffective really efficiently and quickly. If we don't have that, we'll just end up with the same system going forward. At the moment, we've got a new mesh which is composite mesh, which is basically saying the old mesh is bad,

this is new. It's the same problem. There's no evidence to show it's any better. When we do look at the evidence, it doesn't get reported, and it's going to emerge on the market and say, we're fixing all the problems of the past. It's exactly the same issue. It's used equivalence, and it's in the same cycle.

Julia Cumberlege: You have these huge organisations, perhaps in America and in other parts of the world, and they must surely look to places like China and India and all those who have huge populations. Surely for the marketing people, that is a great incentive to sell the product. Why should they be interested in ensuring that the product is of the highest quality? If they try and market here, then perhaps we put in so many barriers that in the end you lose some of the initiatives, some of the new products that could be introduced.

Carl Heneghan: You're arguing for a race to the bottom, which is what exactly is the discussion going on in America.

Julia Cumberlege: No, I'm just concerned about this country.

Carl Heneghan: America has the same discussion going on now at the moment saying, all the innovation is happening in Europe where you get the approved devices. So, it happens there, but it doesn't mean their industries are located in Europe. They're just doing the approval here in Europe and selling it in Europe first, and then getting on with making the right evidence back in America to show it's a high-quality product.

The problem is, we always get there in the end, as we've done with mesh. It's just whether we can get there in a quick enough time. It's not like you can carry on selling devices and they're useless in healthcare and everybody is, like, carry on. China hasn't got a massive budget, by the way. It's the same as us. It's got an aging population, so it has to have a value-based approach. We can't just say, go and sell stuff. If you look at what's happening, oh, my gosh, look at how much harm we've added in and extra cost.

We just looked at the outpatient appointments with about £250 million. We're now trying to look at the cost in primary care for mesh. It's going to be in excess of £1 billion probably. So, what we're saying is, yes, we will move some small, medium enterprise businesses, but over half of the clinical trials are done in two countries: Germany and America. Most of the drug trials done in America - is because their regulations are tighter not laxer. If you get US FDA approval for a drug, you've got access to the

globe. If you sell a drug in China, you don't have access to the world; you're probably just going, let's see if we can get away with it.

I see the dichotomy, but you have to sell it as a high-performance system. That has economic advantages in a huge way, because we are world-leading in knowledge. That's why we have two out of the six biggest journals. That's why we have the Cochrane collaboration. That's why we have a functioning NIHR like nobody else does; we just don't know how to use it in applied health sciences. I get the economic argument, but we've got to shift the emphasis for people.

Simon Whale: Is the MHRA the right organisation to provide the device regulation of a high-performance system?

Carl Heneghan: The MHRA is the right organisation to oversee patient safety, but it's not the right body to oversee when it goes wrong or to set out if it is going wrong. They need separating out. That's the problem. That's been a clear problem...

Cyril Chantler: You mean the patient safety of devices, don't you?

Carl Heneghan: Patient safety of devices is about reporting system and how they're reported in, sending notices out to hospitals. They do an okay job of that, but I think because also you're asking them to oversee when it goes wrong and all these other functions, they're scared to death. So, they put out people who defend the system and then they leave.

Cyril Chantler: But they don't have to relate directly to patients at all. I asked them that last week at this other meeting, and they said, no, our responsibility relates to the industry.

Carl Heneghan: Yeah. That's their function and what they should be tasked with. Everything else needs to be rethought and said, in terms of what's happening in actual clinical practice, is that NICE's function? Possibly, but it isn't the MHRA's. This is why you understand devices don't get withdrawn. The only reason they can get withdrawn is if they're not functioning as specified. Nothing to do with patient harm. That's not - there's no legislation to remove them for harm.

Cyril Chantler: We've got the...

Carl Heneghan: These two bits are not well understood. America doesn't get this either. I think there are needs for some new bits of the system that say, we are responsible for what happens in the health system, the harm caused, and we look into it. I have to say, one of the things that - I don't know if

anybody has mentioned this - the only people who keep us on path at the moment is the media, because they are really understanding their role in the public health. They bring these to the fore so that we're aware of them. But I don't get MHRA or NICE or the government telling me about implant failures.

Julia Cumberlege: Any other questions?

Cyril Chantler: I have one more. It goes back to Primodos. It's not directly what you've been doing. Have you done any work on the teratogenic effects, or lack of, of oral contraceptives in its various dosage?

Carl Heneghan: Not in terms of the various dosage. You're dichotomising the basic sciences versus the applied health care, aren't you? My reading of the basic sciences is, there's not much of it. It doesn't really help you in much, because there are only two things that really basic sciences and animal studies help us with: either there's a dramatic effect or there's an absence of a mechanism.

Cyril Chantler: I actually wasn't mixing those. I was thinking in terms of its application in population. There must be vast amounts of evidence.

Carl Heneghan: In terms of contraceptive pills?

Cyril Chantler: Yes.

Carl Heneghan: Yes. One of the things which I said right at the outset to Marie Lyon - I said, we don't - that is a bigger study for us, a significant study. If you task that, you'd have to go to the NIHR and fund us, because it's not something I can do in my spare time. I'm aware the evidence is there.

Simon Whale: There is evidence there.

Carl Heneghan: There is evidence out there.

Simon Whale: But you haven't analysed it.

Carl Heneghan: No, and there's much more of it than this. Nobody funded us to do this. This is my team in their spare time. But if you looked at the contraceptive pill, it's a very - but your position, and you've said it really succinctly, was to say, are we at a position that we can rule out a causative effect for contraceptives? The answer is, no. The question is, is it a big enough question that we should continue to pursue and be vigilant about it? The answer is probably, yes. But we don't portion some of the funds to safety in the health system. So, we end up in this cycle of, we don't quite know.

I think it's a very important question to ask. If you take contraceptive pills and you're pregnant, in about windows four to seven, does it affect you? I don't know the answer to that. There is lots more - the problem is, the files for that are about that big, because there is a huge amount of evidence for contraceptive drugs.

Julia Cumberlege: There we are, Professor Heneghan, you've got a future today, I can understand.

Carl Heneghan: I'm not going out of business any time soon, I can tell you that.

Julia Cumberlege: Can I thank you so much for coming.

Carl Heneghan: You're welcome.

Julia Cumberlege: It's been a very interesting session. Thank you for that. If there are questions you want to come back and ask, please do so. Perhaps we have the freedom to come back to you if there are things that we want to investigate a bit more.

Carl Heneghan: Two things from my point - I'm particularly keen that if the MHRA or anybody wants to send us a response and ask us questions or anything about the review - could you re-do any analysis - we can do that or explain any points. I'm happy to do that.

Julia Cumberlege: Thank you.

Carl Heneghan: The second thing is, I'm in the process of putting forward what I think are some fixes or solutions which we have discussed some of them here, which I'm going to publish, which I'm quite happy to send.

Julia Cumberlege: We'd be very glad. Thank you very much indeed.

Carl Heneghan: You're welcome.

Cyril Chantler: Thank you.

Simon Whale: Have a good day.

END OF TRANSCRIPT

Session 6: Professor John Abraham

START OF TRANSCRIPT

Julia Cumberlege: So, if you would like to start just by saying who you are and where you're working, that would be really helpful.

John Abraham: Right so I'm John Abraham at King's College London. I'm a professor for what it's worth. So, I've been working on testing and regulation of pharmaceuticals for - it's 30 years now I'm shocked to say. I'm a somewhat unusual academic in the sense that I work on pharmaceutical testing and regulation from the location of a social scientist and a political scientist but in the course of doing it, or at least doing it the way I do, I have become an expert in all sorts of aspects of drug testing including toxicology, pharmacoepidemiology, clinical trials and all these sorts of things. But I don't actually do any of them.

So, I'm not a white coat scientist, if you like. But I review a lot of evidence that is submitted to the Food and Drug Administration because it's the most transparent in the world I think still. But also, there are regulatory agencies, Sweden, the UK and so on. So, I review the evidence and the claims that are made by various stakeholders and scientists including the regulatory scientists, including the industrial scientists and so on.

When material comes into the public domain through court cases, I also review internal pharmaceutical company evidence and communications and scientific data which otherwise would not have become publicly available. So, I don't know if some of you here might remember the big Halcion controversy, the controversy over the safety of Halcion. It wasn't very good news for the BBC because the BBC Panorama programme was sued by Upjohn the manufacturers for the claims they made in a programme. But the consequence of that libel case meant that absolutely masses of evidence came into the public domain because the court case of course was in the public domain through the Royal Courts of Justice.

So I analysed all of this material and then made judgments about the quality of the regulatory decision making. I've done that in the Opren controversy which is a big drug disaster here in the UK in the 1980s and also the Practolol disaster which some of you might remember from the 1970s. Of course, we're all aware of the thalidomide case but it's rather different because it pre-dated any formal regulatory system and of course that's also the case with the initial approval of Primodos which is, I guess what we're here to discuss today.

So that's what I've done, that's what I do, that's my expertise. So, I was asked by various people involved in the Primodos controversy to review the expert working group report of the MHRA. Is it okay to call these things by their acronyms or do I need to - everybody knows that the MHRA is, good.

So, I did that and that's kind of most of what I submitted to you in my written submission. Maybe I'll just summarise my view and then you can ask me more if you want to, but - so my feeling is that there is - in the content of that expert working group review, there is evidence of toxicological problems with the drug. So, there is animal toxicology evidence suggesting harm from taking Primodos, teratogenicity evidence to be precise. There is also evidence of toxicity and teratogenicity in the epidemiological studies. There is also evidence of it in the spontaneous adverse drug reaction reporting and there of course is evidence which is the claims made by the alleged victims who claim to have been injured by taking the drug.

So, we don't have perspective randomised controlled clinical trials which is the golden standard for trying to impute causality between a drug and an adverse event. But it seems to me on the basis of the evidence of the expert working group reviewed, it was wrong to conclude that causality should be ruled out. So, the conclusion that there is no causality was an incorrect conclusion, which is not to say that there was definitive evidence of causality, because I don't believe there was definitive evidence of causality, in the material that they reviewed.

The other point I would say is that since that review, there have been some developments which shouldn't be ignored. One is Neil Vargesson in Aberdeen has done some studies claiming that Primodos is toxic - teratogenic I should say to be - teratogenic to fish and there has also been Carl Heneghan's meta-analysis, who obviously you've heard from because I met him coming out the door. His meta-analysis - which I've looked at and which seems sound to me - is saying that, as far as I read it - and of course you've heard his own evidence so you should take his evidence on that above mine, but as I read it, he's saying that on the balance of probabilities, there is a causal link which is a stronger statement than I made when I reviewed the initial expert working group analysis.

There's another observation I would make, and again you can ask me much more about this if you want to, which is that, it is certainly the case that of course there was no formal medicines regulation in the UK when Primodos was first introduced onto the market in the 1950s. But it is true that it was possible to do teratogenic testing at that time. It is also true in my view that there was sufficient ethical sense and ethical intelligence to suggest that the drug company should have done animal teratogenicity testing on the drug before putting it on the market to be given to humans.

Now when I looked at the expert working group of the MHRA's report and its references - and of course nearly all, if not all, of its references to the

company's teratogenicity testing were not published and - but we'll come to that in a second but - so I only - I can only refer to the reports - to the report itself but even on the basis of its references to those studies, it looked as if there was no animal teratogenicity testing done until the 1960s. In other words, this drug was put on the market before it had ever been tested in animals for teratogenicity. I regard that as appallingly unethical, even by the standards of the 1950s.

There is then the question of whether or not it was illegal. As I said in my written submission, clearly it was not in violation of medicines regulations law because none existed at that time. Whether it was illegal by reference to general consumer product safety law, and the duty of a manufacturer to care about such things, is something I don't know the answer to, but I certainly think it should be investigated and it should have been investigated by the MHRA.

The other issue I think that concerns me and it's sort of implied in my written submission, is that I wasn't clear, and I certainly didn't derive any reassurance from the MHRA's expert working group report which I'm just going to call EWG from now on. It certainly wasn't clear from the EWG report that they had made strident efforts to ensure that the company had submitted to them all the relevant data. There was no discussion of that issue. There was no discussion of what steps they had taken to ensure that the company had not submitted merely a selective set of data. It wasn't clear that we had comprehensive data and it wasn't clear why the data that was submitted was continued to be protected for - on commercial grounds and withheld from public view, for two reasons, first, given that the drug is now off the market, what possible justification could there be on commercial grounds? Secondly, in cases like this, the public interest should always - the public interest and safety should always override the commercial interest of private companies.

I make a more general observation, which is that this happens in the context of decades upon decades of extensive and undesirable secrecy within the UK pharmaceutical regulatory system. You probably know that when the *Medicines Act* in 1968 was first introduced the work of the Committee on Safety of Medicines and various other experts - all in fact, all of their expert advisory committees to the Department of Health at that time were covered by, not only by the *1911 Official Secrets Act* but by *section 118 of the Medicines Act*. So, there was a double blank of secrecy preventing any public discussion or public disclosure of the workings of the regulatory agencies.

The MHRA - I think it was 2003 that Tony Blair gave us the UK *Freedom of Information Act* - and so the MHRA has come some way since then because of the UK *Freedom of Information Act* but the UK *Freedom of Information Act* in my view remains too weak. It's too easy for the regulators still to retain evidence and data that should be in the public domain, so that we can have proper scientific evaluation. One of the fundamental principles of science is open ability to scrutinise the claims made by fellow scientists, whether they work in industry or in the government. So, we have a real problem in this country. It's not confined to this country, it's better in some other countries and it's worse in some others. But we have a real problem in this country with, not just transparency, but the idea of science, particularly industrial science and government science, being publicly accountable. I think that's to some extent characterised some of the issues that, in a broader sense, that we have, to do with in the Primodos controversy.

The final point I'll make is the one of justice and that is, irrespective of whether or not one can definitively identify a causal link between Primodos and very severe adverse events for the people who took it, there is clearly a responsibility upon the government and I would argue the manufacturers as well to deliver justice in these cases because of the inadequacy of the testing of the product before it was given to these people. Now you might argue well the government can't be blamed for the fact that there were no - there was no regulatory oversight at that time because we didn't have the *Medicines Act* and we didn't have any formal regulation. But from my own research, which has been published in a few locations some years ago, it's clear that the British Government knew about the problem of not having any drug safety regulations, particularly in the light of the 1937 elixir sulfanilamide disaster in the United States which prompted the US Government to introduce drug safety regulation.

It's clear that the British Government knew about that and decided to do nothing, and I think in that sense, historically, the British Government has a duty of negligence in terms of justice towards these people because it did not introduce drug safety regulation at that time. 1968 was far too late and then we waited three years for it even to be implemented.

Just a final, final comment because I'm sure you're fed up listening to me. Thalidomide happened in 1961. In the United States, the FDA strengthened their regulations by 1962. It took us until 1968 to get the *Medicines Act*, and then we gave the industry three years to get used to the idea by saying it wouldn't be implemented until 1971. All this is lax,

and it points to an inadequate response to the problems of drug safety by the British regulatory system and the British Governments over some historical time. I think to understand what's happened in this controversy you have to have some understanding of this more fundamental problem that the British Government has had with transparent and publicly accountable drug safety regulation.

Julia Cumberlege: Can I just say, I mean, I think one of the worries with Primodos was when it was first introduced. I think there was a difficulty wasn't there, that it was also used for abortions and for family planning and for all those issues. Wasn't there a concern that if they made it very public, then the population would be extremely worried and that actually it could result in adverse effects for a lot of women?

John Abraham: There may have been that concern but in my opinion, that sort of concern is always unfounded.

Julia Cumberlege: Yeah.

John Abraham: So, one hears, and you can see it in the internal documents of governments when they come out into the public domain, you can see experts, governments scientists and regulators frequently saying things, well we shouldn't tell the public about these risks because it will alarm them - and the argument you're making it might even cause them harm. But my view is that's never an adequate argument. It's better that the public knows what the risks are and that they can then make decisions on the basis of those risks. Assuming the drugs going to be left on the market. Remember this is a - I mean it would be a slightly different argument with a sort of breakthrough cancer drug, but this is a pregnancy testing drug. I mean so the benefits are really minimal for that indication at any rate.

Sonia Macleod I think as well as that though the two core ingredients were used in oral contraceptives and I think that was one of the concerns at the time, as Julia was saying, is that oral contraceptive use people will be concerned. So, although yes, as a pregnancy test absolutely. However, the active ingredients were in other preparations as well.

John Abraham: But it remained on the market into the 1970s, into the mid '70s...

Sonia Macleod: Yeah.

John Abraham: ... being used, even if not recommended, being used as a pregnancy test. The fact that it was being used by the - as a pregnancy test way into the 1970s is something that would have been recorded and certainly should

have been recorded by the - what was then the medicines division tracking system, post marketing surveillance systems. They must have known people were taking those pregnancy test. So, in that context, it's clear that the warnings...

Sonia Macleod: How would they have known people were taking it as a pregnancy test as opposed to using it for its other indication?

John Abraham: Because - well, it would be...

Sonia Macleod: Because it was prescribed for secondary amenorrhoea as well.

John Abraham: Yeah, it would be - okay, so it would be an unusual tranche of yellow cards that didn't inform about why the drug was taken. So, when doctors - can I assume people are familiar with the yellow card system? Okay. So, when doctors fill out a yellow card system - ah sorry a yellow card report which is a suspicion about the drug has caused the adverse event, they will generally - if not always but I couldn't swear that they do it always, but they will generally specify why they were giving the patient the drug. So, their tracking systems would have that data and they would - and given that they had that data, they should have been much more proactive in warning against its use in that way and indeed withdrawing it from the market for that indication, and really being much more proactive about it.

Cyril Chantler: Can I just ask you ethically to go a bit further on something you said?

John Abraham: Mm-hm.

Cyril Chantler: Suppose that giving publicity to its possible teratogenic effects led to complete withdrawal of all the contraceptives across the world, the consequences of that would be pretty horrendous for women wouldn't it?

John Abraham: Okay so - but - so why would one decide to?

Cyril Chantler: Because they both contain progesterone and oestrogen.

John Abraham: Yeah, yeah but they're being used for different purposes. I mean this is like saying if you have an ingredient used for one disease where there's no evidence that it's a - I mean so - I'm trying to think of an example.

Cyril Chantler: I can't.

John Abraham: I mean if you think of - well, you have - so you have drugs that are developed for - to treat some diseases, right, but actually subsequently they're found to be effective to treat another disease and that's how they

market it. So, the idea that it would be okay to keep marketing for the diseases for which there is no efficacy, it would be absurd.

Cyril Chantler: No, I agree with that bit of it.

John Abraham: Okay, the same argument applies to safety.

Cyril Chantler: It's that if you know that - if you say well, we're withdrawing this drug because we're using as a pregnancy test and we don't need to - but we're really concerned that it might have...

John Abraham: And we think it might have...

Cyril Chantler: ... some teratogenic effects, then, people are going to say well it contains norethisterone and ethinylestradiol so what does this pregnancy test contain? I know the dose is entirely different. I'm just concerned that if this was to go to social media and all that - I'm interested in the ethical argument that's all.

John Abraham: Yeah, no, I mean, I don't change my view on the basis of that, so what I would say to that argument is it's up to the regulatory agencies to up their game in terms of precise and adequate communication. In particular, if, in relation to contraceptives - so the first thing I'd have to say is the Committee on Safety of Medicines in the '70s was doing reviews about the carcinogenicity and the teratogenicity of contraceptives. So, they were already concerned about that issue anyway and with some contraceptives, there is reason to have some concerns. So, my view is that you should tell people about what the evidence says.

Cyril Chantler: No, I agree. So, it's not a valid argument basically.

John Abraham: No, I mean, it's only a valid argument if the regulators' review is trying to communicate the risks, are really rubbish communication and scare people because they don't make proper distinctions and so on between things like dosage and benefits and use. Actually, this is something that we really need to improve on as well.

Cyril Chantler: I'm trying to put myself into the minds of the people who as you said are recorded as saying 'well we mustn't worry the public'.

John Abraham: Well, no, I think that's something that has been said by regulators at that time. It's still said by regulators today about many of these sorts of issues. I think in some cases we can take it at face value as a genuine concern. I think in other cases one could take it as a rationalisation for inaction which is motivated by other concerns and other interests and so on. But if

we take it at face value then so okay, sometimes that's a concern, what I would suggest from my own research is it's not very persuasive as the underlying explanation for many of these problems because in nearly every case I've looked at, those sorts of concerns are marshalled to protect the maintenance of the drug on the market.

So, I think there are other kinds of forces at work. I think that the secrecy I think is largely about protecting commercial and industrial interests and the institutional interests of the regulators. I don't believe it's primarily about protecting the interests of consumers and patients though I don't discount that as a possibility in some minority of instances.

Julia Cumberlege: Can I just say that I think - I'd be very surprised if people did not agree totally with you, but we have to be open and honest and truthful and we absolutely agree with that. I think the majority of the population do and we would certainly want to think deeply about that when we're doing our review. But I just was trying to think about what it was like in the '60s, '50s whatever, when this particular medication was introduced.

I really think at that time, there was a tremendous feeling, especially among very concerned clinicians, GPs, others, and I can think of a very personal instance where someone was dying and the clinician said 'we mustn't ever tell them they're dying, they've got to have hope'. So, we're actually going to go on talking about how they're going to live their lives when everybody, family, everybody else knew. So, there was a feeling I think in those days of a very different attitude, from clinicians to the individual patients and that may well have gone across to whole populations.

So, it's difficult for us because when we're dealing with something that is so historical that we have to think about what were the attitudes and users' sociologies - we certainly know a lot about that. What were the attitudes at that time? So, we are searching for the truth of what happened then, but I think we have to think a little bit about the context of what the attitudes were like in those years gone by.

John Abraham: I agree we should put it in a good historical context and particularly we're looking at something that happened in the '50s, '60s and '70s in - well not all of it happened then of course, some consequences happened later. But - so first of all, my heart is warmed to hear that you think that most of the population agree with my analysis. But, since we're talking about history, I would say to you that in the '60s, '70s, '80s, '90s and 2000s - I guess all counts as history - the UK regulatory authorities and the pharmaceutical industry have fought tooth and nail, tooth and nail, at every turn to

prevent greater transparency and public accountability of the pharmaceutical regulatory system.

So, it's not - so that goes right through the decades. So that section of the population certainly doesn't share my view. I think even to this day the UK regulatory authorities would resist the kind of extensive public access to regulatory decision-making that exists even in the US. The US system falls far short of what I'd like to see. So, in the US system, the regulatory decision-making process enters the public domain once the decision is made but it is essentially secretive before that except - with the one exception of expert advisory committee hearings which happen in public. Now, that would be vastly more transparent than the US system.

Coming on to attitudes of clinicians, okay, so, clinicians and their interaction with patients and consumers. If that - if we're talking about those kinds of clinician practitioners, then maybe they did have these sorts of different attitudes that you're referring to but - and I don't mean this as any disrespect to clinicians, but I'm not sure how much that matters.

The people who know, who really know about pharmaceuticals are the drug manufacturers and all the clinicians that they bring into their purview to conduct clinical trials - which of course didn't happen with Primodos. But all the people in the purview of the company developing the drug that they get to help them develop the drug, they know a lot about the drug. The people who work inside the regulatory agencies, either as expert advisors or as full-time civil servants, who review the data submitted by the companies. They're the people who know the data about the drug.

Doctors prescribing stuff hopefully read what we call in Europe the summary product of characteristics, what you call in the US the label. Hopefully they read that, if they're good doctors and that's pretty much all they know except for their - over time, their experiential knowledge of prescribing, which is partly why actually on the whole, older drugs tend to be safer than new drugs because there is this additional knowledge that doctors gain through experience.

So, the clinician's attitudes, I'm not sure how significant they are to the decision-making process here. Course you can argue that many of the expert advisors to the regulatory agencies are themselves clinicians, but they're clinicians who have come into that position from a particular perspective.

So, attitudes have changed, but when you look at the cutting edge of decision-making by the companies and by the regulatory authorities, and I refer you back - and I can send you my published work on Practolol if you want, I refer you back to the Practolol disaster which occurred in the 1970s. The view of not being very transparent, and the view also of not being proactive in warning the public, the view of acting slowly, in a nutshell, giving the drug the benefit of the doubt. In other words, saying, well you know, it's probably better to keep this drug on the market. There are these claims about it has benefits and so on and so maybe they are [unclear]. This is a really pervasive problem and it flies in the face of the objective scientific evidence.

Sonia Macleod: But hang on a second, Practolol was on the market for quite a long time afterwards because it did take quite a long time for the sclerosing symptoms to appear in some of the patients and it wasn't instantaneous.

John Abraham: No, it wasn't instantaneous, but it was on the market for a long time after...

Sonia Macleod: And they were quite...

John Abraham: ... the very severe adverse events were identified, and they were very rare types of adverse events.

Sonia Macleod: They were very rare and I think that was why it took quite a long time to - as my understanding then there was not a lot of information about Practolol out there, but my understanding was it took quite a while to attribute because it was both rare and because it wasn't necessarily [perhaps] instantaneous in terms of time of taking them.

John Abraham: It certainly wasn't instantaneous, but the fact that it was rare, I think many pharmacoepidemiologists and people involved in spontaneous adverse drug reaction monitoring would say that actually that should help you identify...

Sonia Macleod: In terms of [unclear].

John Abraham: ... because rather like thalidomide, it was really clear that this was specific to this drug and - so there were - and I would argue, and I've published that the UK regulators should have acted to withdraw Practolol from the market much faster. You see in many of these cases and it's not actually - I don't think this is true in Primodos, it's a more complex kind of argument, Primodos, but you see the argument that yes there are these safety

problems but maybe the benefits outweigh the risks. But actually, that's not what the evidence showed. It didn't show it in the case of the Opren disaster. It didn't show it in the case of the Practolol disaster and it certainly hasn't - doesn't show it in the case of using Primodos as a pregnancy test.

Julia Cumberlege: Thank you very much. Any questions?

Simon Whale: Can I just ask one thing about - back to the EWG?

John Abraham: Sure.

Simon Whale: I think in your - when you wrote to us you talked about conflicts of interest...

John Abraham: Yes.

Simon Whale: ... and non-personal conflicts of interests in particular, I was interested in that, what - would you be able to briefly expand on what you said?

John Abraham: Sure. Well I mean these things are - I think they're - I mean I think the categories are fairly reasonably defined. So personal interests would be, if you hold consultancies in a company or shares, so you receive consultancies from a company, or you hold shares in a company or something of that nature. So essentially, money that you can put in your pocket. Non-personal interests refer to, for example, you might be in receipt of a grant from a pharmaceutical company so you can't put that money in your pocket, but it's good for your position probably within your institution. It's probably good for your career and that sort of thing. So, these would be non-personal interests.

But then you - and this is where - this is the thing that I raised in my written submission that I wasn't clear about, what people were asked. It wasn't clear to me whether people were asked do you have conflicts of interest with Bayer, the manufacturers, or do you have conflicts of interest with the pharmaceutical industry? Obviously, these are two different questions. So, you can say 'no I have absolutely no conflicts of interest with Bayer', but you might have huge conflicts of interests with the pharmaceutical industry more generally.

I think it's inadequate merely to ask do you have conflicts of interest with Bayer because - now I'm not imputing anything specific to the members of the expert working group by saying this, because I would need to have more detail in order to analyse that, but I will make a general observation

that it is often the case that people who have conflicts of interest with some companies in the pharmaceutical industry may quite likely have such a conflict of interest with a specific company in the future or expect to have such a conflict of interest in the future.

Or, more generally, hold a sympathetic view of all pharmaceutical companies relative to somebody who has no conflicts of interest with the pharmaceutical industry at all. You understand what - the point I'm making? So therefore, we need to be - we need to ask the right questions about conflicts of interest. That's not to say I'm arguing conflicts of interest determine one particular conclusion or another of the expert working group. But we need it to be precise and clear and the expert working group appendices about conflicts of interest did not offer that level of clarity and like they should have done.

Julia Cumberlege: Anything you'd like to ask of us?

John Abraham: I suppose yes. I'm curious to know how much you are going to investigate the sort of adequacy of our drug regulatory system around things like public accountability and secrecy. Is that something that you will...

Julia Cumberlege: I'm sure there are a whole lot of issues that we're going to be exploring when we're coming to write our report. Clearly, today has been very helpful to us. Thank you so much for coming. It's been really, really useful...

John Abraham: Great, okay.

Julia Cumberlege: ... and thought provoking. Thank you very much.

END OF TRANSCRIPT

Session 7: Professor Neil Vargesson

START OF TRANSCRIPT

Julia Cumberlege: I'm not sure if you want to make a statement first, but what we would like would be if you could say who you are, and what is your interest in this area, and if you have got a statement, that's fine by us; otherwise we'll ask you some questions, perhaps. Is that alright?

Neil Vargesson: That's absolutely fine. Yeah. So, I'm Professor Neil Vargesson. I'm from the University of...

Julia Cumberlege: Hang on, I think it's just got to pick up your...

Neil Vargesson: Okay.

Julia Cumberlege: Yes. Now, go for it.

Neil Vargesson: Okay. So, Professor Neil Vargesson. I'm from the University of Aberdeen. I'm a developmental biologist. I have been all my life. Fascinated by how you grow from a single cell to us, and particularly interested in why that goes wrong and why you get birth defects. So my main research interest has been Thalidomide, and more recently Primodos; trying to understand how the drugs work in the embryo and understand their mechanisms, and then with Thalidomide, particularly, to see if we can make forms of the drug that don't cause birth defects, but still have clinical relevance, because those drugs are still relevant today.

My interest in Primodos came about four or five years ago. I saw a newspaper headline called *The Forgotten Thalidomide*, and anyone that knows me, knows I'm a bit OCD about Thalidomide, so anything mentioned about Thalidomide, I'm going to go off like a gun. And I thought if we could understand how Primodos works, maybe that would shed a light on Thalidomide.

And so we started work on zebrafish embryos, because that's what my lab works on mainly, and we used those as a drug screen, because they're very useful for screening drugs, and the idea of the study was really to get an idea of what the drug's capable of doing, and is it worth following it up. And the answer is it does do some things, and yes, it is worth following up.

Julia Cumberlege: So I think you've probably been interviewed by Jason Farrell, were you? Did he...

Neil Vargesson: Sky News. Yes. Last year. Yes.

Julia Cumberlege: Yes. And I do remember then seeing some of the zebrafish that you'd been working on, but even then you were saying you've got to do more research, and this is obviously the research that you're now undertaking. But, can I ask you on the zebrafish, how has that particular research project - how has that been received?

Neil Vargesson: In the community?

Julia Cumberlege: Yes.

Neil Vargesson: Quite well. I've not received any negative comments from the scientific community as such. It has an Altmetric score - I'm not sure how much faith you put in these things - but an Altmetric score is this way of measuring an article's interest, and it's set up by Nature Group, and they do it for most articles, and it's an Altmetric score is something like - over 600 - which means it's in the top one percentile of articles published since it was published, in terms of people hitting or clicking on the link to it; downloading it; talking about it on Twitter, Facebook, that sort of thing; citations, that sort of thing. So that's been excellent.

The study was never meant to be a definitive answer, despite what Jason and some other groups may have thought. It was always meant to be - I work on fish and chickens, and we wanted to see - I have these assays in my lab right now, they're very easy to use, what does this drug do in those assays and is it worth taking it further? A fish is not a human, so we need to go into a mammalian system, with a placenta, ultimately, to then say, well, how does this drug work?

But the idea was to get some idea that this is worthwhile following up. And it is. And I think that's how the community see it; there is something going on, we can't explain it at the moment, so that's what we'll try and do. Now - so that's why we're now going into the mammalian, in the human side.

Julia Cumberlege: How about the scientific community? Have you had any response from them?

Neil Vargesson: Nothing negative.

Julia Cumberlege: No.

Neil Vargesson: It's been cited a few times, although once by [card]. But it's only been out, what, seven months, so we needed to give a bit more time to see how many times it's cited. But I've not received any negative - the MHRA were - they had some criticisms about the dosage that we used. That's

fine. You know, this is a human synthetic hormone you're adding to a zebrafish embryo. We don't know what the kinetics of it are. We don't know what the receptors are that would take this up in the fish, if they're the same ones as in a human.

It's very likely that you'll only get a small amount of drug into the fish, and that's all it takes to cause problems. We know that other zebrafish studies, if you look at Thalidomide, you have to use quite large doses to reciprocate the Thalidomide effect you would see in a human, or in other species. So a study came out last year looking at estradiol itself in fish, from Dan Gorelick's lab, that showed you have to use supraphysiological concentrations of oestrogen to get a physiological response in fish, or a physiological-like response, like you would see in a human, in a fish.

So, again, it's a - you know, fish are not humans, so it's a combination of use higher doses because you see a response at a higher dose, but we don't know why -if it's because of the right receptors, or kinetics, the breakdown products; that sort of thing. So I'm happy with that.

We've done some more work, following on from the MHRA meeting. They suggested that we do a full range of concentrations and different time points and my student started to do that. If you look for subtle damage, as opposed to the gross damage that we showed in the paper, you can find problems with the heart at very, very low doses, even as low as one microgram. And she's going to go lower to, sort of, see if we can fine tune when you start to see the - find the really, sort of, subtle damage. So, yeah, it's a start, and I'm writing a grant right now to try and get money to get it all done.

Sonia Macleod: Can I just ask, with the sort of damage that you're seeing, one of the criticisms of the EMA was that there wasn't any systematic morphological assessment that they could see. Are you, sort of, doing those (with the finder) the damage that you've done with the gross damage?

Neil Vargesson: Yeah. We did do systematic morphological damage. As I say, they never asked - they never came back to me to ask me to...

Sonia Macleod: They said they'd spoken to you.

Neil Vargesson: They spoke to me on the phone. They invited me to talk to them. They gave me four days' notice of a telephone conversation which lasted 15 minutes at the very start of July, and in their report they said they didn't choose to come back to me because they'd already made their decision, but they had all these questions which the MHRA asked me, which I've answered. Yes, we use a set criteria...

Sonia Macleod: They did say they didn't think speaking to you would make a difference to the outcome.

Neil Vargesson: That's fine. I have no problem with that. I mean, it wouldn't have changed - as I said to a few other people, the overall conclusion I don't have a problem with. More work needs to be done. That's fine. Yes, we use a standard criteria. We use the OECD Guidelines for Toxicity as well, and with the new data that we're producing right now, yes, we will be comparing it to control groups, as well as double blind.

Simon Whale: So, in terms of the expert working group, I presume you're not surprised - I don't want to put words in your mouth - but you're not surprised that they didn't change their 2017 opinion.

Neil Vargesson: No.

Simon Whale: They encouraged you to move towards the chicken, mice and human tissue research, did they? Or not?

Neil Vargesson: Okay. So, I was quite clear to the MHRA and to the EMA when I spoke to them on the brief phone call that this a preliminary study and more work is needed, and to me this now allows me to put my hand on my heart and say, we can now go forward and do some more work research, based on some evidence that it is doing some damage in a fish. I don't know what the answer will be when you do it in humans, mice and chicken, although it does cause problems in chicken, but the mouse and the human is what we're really interested in, and that's what we need to be doing the research in.

The MHRA - no I was going to do this anyway. So the hearing we went to - I went to - I wasn't surprised by their conclusion that more work is needed.

Simon Whale: I'm only asking because you'll be at least as aware as we are that there's been some criticism of the EWG in relation to the way they've interacted with you, and it's just helpful to understand your perspective.

Neil Vargesson: I'm getting confused. Do you mean the EWG that did the 2017 report audit?

Simon Whale: Yes.

Valerie Brasse: That's the original.

Neil Vargesson: The original one.

Valerie Brasse: The 2017 report there was some criticism that they hadn't taken into account all of those up-to-date studies and they were actually specifically talking about your study, the brown paper on the zebrafish. Then of course we had this secondary MHRA meeting, [unclear] working group, and then the referral to the EMA. I suppose the question for us is, as a result of what you presented to them, has the science, sort of, moved on? Were you expecting to be able to shift their opinion about the state of the science around this? Or, were you never intending to do that?

Neil Vargesson: As I said, the work we did was never going to be - it was never going to say, it does or does not, it was for us to say, this is worth following up. I went to the MHRA originally, I think in October 2016, and presented the unpublished findings at that time, which they liked, but because they were unpublished and not peer reviewed, they couldn't include it in their report, and I don't have a problem with that. That was - you can't put non-peer reviewed science into a government report.

My criticism of that report is that they then did that, using articles from Schering, and that was - my criticism of the report was that - why did you do that? Some of the conclusions that were based on those reports, I felt uncomfortable with, which is why I then made - I wrote an article for theconversation.com and Sky News did a report on that. But it wasn't that I disagreed with the overall conclusion that more work needs to be done; it was more that it did seem that they were using non-peer reviewed articles to base some of their conclusions on.

Some of the science, you know, you're looking at studies from the sixties, seventies and eighties. If you want to find a study that says it does cause problems, you'll find it. If you want to find a study that says it doesn't, you'll find that one too. Some of those studies were flawed anyway because it wasn't clear how much the drug got into the animal. Was it the full dose? Was it a smaller dose? Was it a mild dose? I was arguing that perhaps what the MHRA might want to do is to actually fund some more research, to nail it either way.

I've made it quite clear to various groups, including Sky, that I'm not going to - I am on the middle of the road - I'm not going to predict what this will do in humans and mice. I don't know. But I think - I also can't tell you that it doesn't do it, so I would like to see more research, to be definitive.

Valerie Brasse: And your sources of funding?

Neil Vargesson: Well, I'm applying to the MRC - Medical Research Council - but I don't know how - well, I'd like to think given the paper that came out it's got a

lot of interest, given the government enquiries that are going on, I'd like to think that that would be taken by the MRC to see that that's something in the public interest; it would be seen to be a worthwhile cause.

Sonia Macleod: Can I ask, Primodos obviously has two constituent ingredients in it - you've tested them in the ratio within the original formulation?

Neil Vargesson: Yes.

Sonia Macleod: Have you tested them individually?

Neil Vargesson: So, ethinyloestradiol, you can put as much on as you wish to the fish, and the fish are quite happy, and it seems to be the norethisterone acetate that's causing the issues. In fact, we've got some preliminary evidence that when norethisterone acetate is with ethinyloestradiol, the effect of the norethisterone acetate seems to be reduced.

Cyril Chantler: Reduced?

Neil Vargesson: Yes. So, it seems to be that the damage is less, so you still get damage, but it doesn't seem to be as great as when you put nor on its own. But again, we're following that up, just to make sure it's not user error or...

Cyril Chantler: Are you surprised by it?

Neil Vargesson: Yes.

Cyril Chantler: Well I thought progesterone was the same.

Sonia Macleod: Certainly in humans the studies for prevention of early miscarriage indicate that there's no malformations [unclear] large doses of progesterone to fairly early stage pregnancy.

Neil Vargesson: Yes, but this isn't progesterone; this is a synthetic progesterone, synthetic...

Sonia Macleod: That was synthetic and natural progesterone.

Neil Vargesson: Sorry.

Sonia Macleod: That's my understanding of it, but obviously that would be something we will check.

Julia Cumberlege: Is there anything you'd like to ask us?

Neil Vargesson: So, I was going to - I did prepare a presentation which I sent yesterday...

Julia Cumberlege: Thank you.

Cyril Chantler: I received it.

Neil Vargesson: ... and I - no, it's fine. I didn't know if you wanted me to do a presentation or not, so this is fine, but there's one thing I wanted to mention, and the [Polkonin] study from 1984, it's slide 23...

Cyril Chantler: Slide 23.

Neil Vargesson: ... yes.

Cyril Chantler: Thank you.

Neil Vargesson: Both the MHRA and the EMA use this quite a bit, and this is the only study I'm aware of where components of Primodos were given to pregnant women and then the plasma levels of the components were looked at. My criticism of that paper is that they say that 17 out of 35 drug exposed pregnancies had haemorrhaging, and then they dismissed by saying this was normal, or no different to women with non-drugged pregnancies.

I have to say that that's just not true. Women that have haemorrhaging in pregnancy would be seen by the clinicians, and haemorrhaging in embryos, particularly in mice and chickens, usually indicates vascular disruption, which then leads to birth defects. So that paper seems to be one that a lot of people refer to as a standard, but I have a concern about it on the basis that they're actually saying, when we added this to women, we saw haemorrhaging in their pregnancies, but they didn't actually tell us what happened to the foetuses; whether they were normal or not.

That whole product study was to look at what Primodos is doing in the pregnant women. They did the maternal plasma levels which shows it peaks and goes down, and takes 48 hours to go to zero, but didn't tell us what happened to the fetuses.

Cyril Chantler: Why did they give it to the women?

Neil Vargesson: These were women that had chosen to have elected terminations and the drug company asked permission if they could then give the women Primodos.

Cyril Chantler: In twice the dose of the normal Primodos.

Neil Vargesson: I think it...

Sonia Macleod: The standard dose [unclear] plasma [unclear].

Cyril Chantler: Yes. So they were giving them as a single oral dose. I thought they normally give 10 milligrams of norethisterone and 12 hours later another 10 milligrams.

Sonia Macleod: They do, but they did just a single dose.

Cyril Chantler: So it's actually twice the dose.

Neil Vargesson: They gave - I'm assuming that they gave the dose that a pregnant woman would have taken; two tablets, so they gave it in one dose

[Over speaking]

Cyril Chantler: They gave it all at once, because they normally give them 12 hours apart.

Sonia Macleod: Yes, they do...

[Over speaking]

Cyril Chantler: That's right. So you're going to do it.

Neil Vargesson: That's right. But it's - that paper's - I've got so many question marks about this paper, anyway, given what they were doing, but otherwise the only other thing I was going to say was...

Sonia Macleod: Can I just ask on that paper?

Neil Vargesson: Go on.

Sonia Macleod: If you're saying vascular disruption - you can attribute malfunctions and birth defects to vascular disorders, what kind of malfunctions and birth defects would you see?

Neil Vargesson: It depends on its stage, but in the time that Primodos would've been used, it would be minor; it wouldn't be loss of limbs, it would be digit tips, things like that - eyes; ears; internal organs, but it wouldn't be like the Thalidomide thing. So I go back to my story about the forgotten Thalidomide. When I heard about the forgotten Thalidomide, I was desperate to find this and see what it did, and I was expecting to see...

Sonia Macleod: [Unclear].

Neil Vargesson: We didn't see that. We never have seen that. The damage is, even with the gross malformations in the fish, they're still quite subtle when you compare it to Thalidomide on the fish. But I would expect to see digit tip loss; peripheral damage to noses; eyelashes.

Sonia Macleod: When you give Thalidomide to the fish, is the damage bilateral?

Neil Vargesson: Yes.

Valerie Brasse: And when you give Primodos components, is the damage bilateral?

Neil Vargesson: Yes.

Sonia Macleod: So, do you ever see unilateral damage?

Neil Vargesson: We have seen it with Thalidomide once in a while, and with Primodos, sometimes, yes, because sometimes the fish develop movement problems and I imagine because if they can't move around very well, if one side is flat on the surface, they may not get as much drug, but normally the damage is on both sides. I don't remember seeing just unilateral side damage, no.

Cyril Chantler: When - how many weeks were these women having terminations who got this combination?

Neil Vargesson: I can't remember.

Simon Whale: It just says, early pregnancy.

Male 2: Oh.

Neil Vargesson: I've got the paper on my computer. I'll see if I can find it.

Cyril Chantler: So they then did evacuation of the uterus and examined the fetus. Is that what happened?

Neil Vargesson: No. Five to nine weeks. Five to nine weeks old. No, they didn't tell us what happened to the fetuses at all.

Cyril Chantler: So how do they know there was haemorrhaging in the developmental phase?

Neil Vargesson: They did a scan and said there was haemorrhaging on the scans, and then that's it. We're not told what actually happened to the - and it might be because there was nothing they could look at.

Sonia Macleod: I was about to say by the time you've done that I suspect it wouldn't have been terribly easy.

Simon Whale: Nine weeks, no, it wouldn't actually.

Cyril Chantler: Are there any other papers like that?

Neil Vargesson: Yes.

Julia Cumberlege: Anything else?

Neil Vargesson: Unless you've got any questions about the presentation that you've there?

Julia Cumberlege: If we have, perhaps we can come back to you on that, and the same for you, if you want to come back to us on any questions, please do that. Otherwise I'd like to thank you very much indeed for coming today.

END OF TRANSCRIPT

10th January 2019

Session 1: Dr Frances Elmslie

START OF TRANSCRIPT

Julia Cumberlege: If I could just perhaps start by asking you to tell us, who you are, and your position and what your organisation is and what you do?

Frances Elmslie: I'm Frances Elmslie. I'm a clinical geneticist at St George's. I'm currently Chair of the Clinical Reference Group on medical genetics for NHS England. My background is originally in paediatric medicine, but I became interested in the genetics of epilepsy way back in the early 1990s and completed my MD thesis on genetics of epilepsy.

It's really from that work that I then started to see patients who had been exposed to sodium valproate in the womb. It's really an offshoot of my primary line of work that I have developed a bit of interest. I haven't ever done any research in the area, so it's very much a clinical interest, and I've seen patients through my general practice with fetal valproate syndrome or at risk of fetal valproate syndrome.

Primarily, my main interests now are really in paediatric neurodisability, which includes epilepsy in children and adults. I see families with a strong family history of epilepsy for example, and an interest in their management. Also an emerging interest in how understanding the genetic basis of their disorder may allow us to offer better treatments. I also have an interest in brain malformations that have - that can be predisposed to epilepsy and intellectual disability, and particularly tuberous sclerosis which is a particular genetic disorder.

Julia Cumberlege: Right, well thank you very much. Today, we're concentrating on valproate and the issues surrounding that. I just do have to ask you, do you have any interests, conflicts of interest, things that we ought to know about?

Frances Elmslie: Not regarding valproate, no.

Julia Cumberlege: No, alright. Thank you very much. You've sent us some very good written evidence and thank you very much for that. In that, you're describing the features of fetal valproate syndrome, or fetal valproate spectrum disorder, which I know terms are - both terms are used. I just would like to ask you, what degree is there an agreement on these features? Are there any areas of difference? Are there any differences internationally?

Frances Elmslie: I'd say amongst clinical geneticists there is very good consensus on these features. I think clinical geneticists, because we have been used to describing malformation syndromes for - that's what we've done forever, I think we were really the first group of people who were describing valproate consistently in the medical literature.

But they were very ad hoc and they were very single, many, many single case series of people who had presented to clinical geneticists, so I would say there is a very good consensus amongst the clinical genetics community, and a growing consensus amongst other health professionals. In particular, the malformation risk is very - now very well established and very well recognised, and there is consensus in that area.

I think the area that has been more difficult has been that of autism spectrum and neuro, the effect on neurodevelopment. That has been because there were definitely issues of bias ascertainment in those early case reports, because some of those, the children that came were the children that presented to clinical geneticists for evaluation. There were a whole host of children that had not presented.

A lot of that has been ameliorated through prospective registries, of which there have been a number in - there's the Belfast registry, which is the UK registry, a European registry, an Australian registry and a US registry. All of those have shown similar degrees of malformation.

In terms of neurodevelopment and autism there's been much less work in those. Those prospective registries have not been focused on picking those things up. They've been on - very much on looking at the physical outcomes. There is definitely now an acceptance that there is an effect on neurodevelopment and an increased risk of autism spectrum. But that has not been so well studied.

Julia Cumberlege: Can I just pick up the bit about registries?

Frances Elmslie: Yes.

Julia Cumberlege: Are they really comprehensive? Are they - is there any mandatory requirement to put things onto the registry or are they more voluntary?

Frances Elmslie: They are voluntary registries. I don't think any of them that there's a mandatory requirement. But I may not be completely up to speed with the non-UK. The UK registry is one of - that health professionals are encouraged to report pregnant women with epilepsy to the registry. Then those women are then contacted after birth to ask for the outcome of the birth and the health professionals also contacted. There is no mandation

to actually put people on the registry as far as I'm aware, and obviously the follow up is also voluntary.

Julia Cumberlege: They're useful but they're not comprehensive?

Frances Elmslie: They're not completely comprehensive, no.

Julia Cumberlege: Alright, okay thank you very much. As you will know, Sir Cyril Chantler is very much into the medical field and everything else.

Frances Elmslie: Yes.

Julia Cumberlege: He's now going to take on the questioning.

Frances Elmslie: Okay.

Cyril Chantler: Thank you very much. Carrying on the conversation that Baroness Cumberlege started, we've struggled to understand how many children are affected within the families.

Frances Elmslie: Yeah.

Cyril Chantler: We've learned that there is an effect on the IQ, there's a general effect. If you include that as part of the disorder, then we've been told that as many as 40 per cent of children may be affected. Would that be reasonable?

Frances Elmslie: I think the recent prospective studies have been suggesting, yes, that there is a general effect on IQ. If you compare the IQ of children with - who've been exposed to valproate and compare that, particularly, with the maternal IQ there does seem to be a difference between what one would expect and what one sees.

In general, and actually there's an inaccuracy in my report that I should correct, that that does not take people into the learning disability range, although some children are within the learning - the intellectual disability range.

Cyril Chantler: Yes.

Frances Elmslie: There's a decrease overall in general, if you're looking at cohorts, in IQ compared with the expected IQ. Yes. I would say 40 per cent is actually probably a reasonable figure. The numbers are still quite small from these prospective studies. We don't have huge amounts of data. But that seems like a reasonable ballpark, yes.

Cyril Chantler: Thank you. We've discussed before and you've included in your written evidence the anxieties, which we've had expressed to us across the country...

Frances Elmslie: Mm-hm.

Cyril Chantler: ...when we've met families about the possibility of grandchildren...

Frances Elmslie: Yes.

Cyril Chantler: ...being affected.

Frances Elmslie: Yes.

Cyril Chantler: You said there is no current evidence that that has occurred.

Frances Elmslie: Yes.

Cyril Chantler: There's no current scientific evidence that it could occur, but that doesn't mean that won't emerge in the future. Is that a reasonable...

Frances Elmslie: I think that's reasonable there. The way in which it could occur is through an epigenetic effect on the next generation.

Cyril Chantler: Yes.

Frances Elmslie: There is - I've done a little - well a fair amount of reading around this, and there's some evidence, scientific evidence that valproate may have some epigenetic effects in vitro, in animal models. When I talk about animals I'm talking about Zebra fish, so very simple organisms. Whether that would actually translate into an epigenetic effect in humans I think really it's quite far a way down the line scientifically...

Cyril Chantler: It's a big leap.

Frances Elmslie: ...to suggest that. Say again.

Cyril Chantler: It's a big leap.

Frances Elmslie: It's a big leap, exactly, exactly and we don't have any evidence from human studies to suggest that that is so.

Cyril Chantler: Could I ask if anybody else has a question in this area because [unclear].

Sonia Macleod: In terms of saying that we don't have the evidence at the moment, so going forward how do you think would be the best way to gather that kind of evidence?

Frances Elmslie: It would - I suppose there are two main lines. There would be increased scientific work looking at the effect of valproate probably in higher organisms directly. The other way would be family follow- up. There are lots of confounding variables that would need to be taken into account, but really these - the recent studies have been much more robust than previous studies. I think the scientific methodology is there, though we just need to very robust.

Sonia Macleod: But that would require you knowing who your affected cohort were.

Frances Elmslie: Of course, of course.

Sonia Macleod: We've heard going through that there is difficulty in terms of actually tracing.

Frances Elmslie: Yes, I think so, and obviously the group who have had obvious malformations would be a group that would be good to study. You would need to make sure that they had a good robust genetic assessment to ensure that there weren't alternative causes for their malformations, and a need to ensure the family history is looked at properly as well. But that would be a group to look at to see if there was an increased risk of malformation subsequently.

Cyril Chantler: Thank you.

Julie Cumberlege: Valerie, do you want to...

Valerie Brasse: I just had one question, because I noticed from the MHRA evidence that we've received that the email the PRAC Committee as they call themselves, the Pharmacovigilance Risk Assessment Committee, have said that they were going to prioritise this area of research going forward.

Frances Elmslie: Okay.

Valerie Brasse: Which is exciting news...

Frances Elmslie: Yes.

Valerie Brasse: ...as it's all about the transmission of this intergenerational effect.

Frances Elmslie: Yes.

Valerie Brasse: I just wondered how the clinical community feeds into that programme if it does at all. Because obviously it is a golden opportunity to be able to influence potential from your own clinical expertise what you think can help [unclear], I don't know whether you have any insight into that.

Frances Elmslie: That's the first I've heard of it. I would imagine actually neurologists would be a good place to start, because they would be actually managing and seeing women who've been on valproate and therefore have an idea of the children who are coming through. But it's going to need a group consensus. We need clinicians to get together, because as clinical geneticists we are often the people who are diagnosing, we're not following those children. We make the diagnosis but then those children will be followed by paediatricians and potentially neurologists because some of them will have other features as well.

Valerie Brasse: Well, we are meeting with neurologists so obviously we can put that to them.

Frances Elmslie: Yes.

Valerie Brasse: Can I just follow up on that one question actually, because as you say you aren't following the children. What we've been hearing from the patient groups is, and as they're getting older, more and more different effects come through. Also they see - also they perceive and their worry is always who's monitoring longitudinally this group this cohort...

Frances Elmslie: Mm-hm.

Valerie Brasse: ...the smartest children who develop all sorts of other effects through their lifetime.

Frances Elmslie: Yeah.

Valerie Brasse: They have a real concern about that, what is the answer?

Frances Elmslie: Yeah, I think it's a particularly common issue with disorders that are diagnosed in childhood, and it stands for a whole range of genetic disorders as well as multi-system disorders. As clinical geneticists often our role is essentially in diagnosis. But we often then hand over care to paediatricians and paediatricians are great at coordination of care. That's what they do. But then the children come to adulthood and it all falls apart, and we see this time and time again.

Actually, at that point quite often they come back into clinical genetics, because we are - I always describe myself as a GP for rare disease. We are quite good at that overview. At the moment no such services really exist for people with this particular disorder. They do exist, but very, very piecemeal for other conditions. I run a clinic for people with tuberous sclerosis and this is exactly what I see, there's people coming back in aged 18 because suddenly the care becomes very fragmented.

I think we talked about this before, but that is one possibility is that there would be centres of excellence for these patients to be seen through adulthood and dip into, and ensure that management and coordination of care happens.

Valerie Brasse: I think my colleagues might want to follow that up.

Julia Cumberlege: Simon just has one.

Simon Whale: Yes. Can I just ask a question about what you said earlier about the UK registry?

Frances Elmslie: Yes.

Simon Whale: The registry it can - captures data that's entered by a range of healthcare professionals does it?

Frances Elmslie: Yes.

Simon Whale: That includes GPs as well as neurologists, geneticists?

Frances Elmslie: Yes, so anybody can actually refer to the registry. Essentially, as a health professional, if you see somebody who is pregnant with epilepsy, whether they're on medication or not, you can report them to the registry, obviously with their permission so you would seek their permission.

Simon Whale: Does it - is it able to or does it already contain any information about whether that woman's on or been aware of the pregnancy prevention programme?

Frances Elmslie: That's a very good question and I don't know the answer, because that's new. The registry's been running for a good over 10 years, and so I don't know what the up to date information would be.

Simon Whale: But structurally there's no reason why it couldn't [contribute] to that?

Frances Elmslie: No, no I don't think so, no not at all. It's coordinated by a neurologist called Jim Morrow who is based in Belfast. I can contact him and ask him about that specifically if that would be helpful.

Simon Whale: Thank you.

Julia Cumberlege: A pregnant woman would be on the registry if that is the system that works and that she gives her consent...

Frances Elmslie: Yes.

Julia Cumberlege: ...and all the rest of it. Then when the baby's born that then is followed up...

Frances Elmslie: Yes.

Julia Cumberlege: ...using the registry.

Frances Elmslie: Yes.

Julia Cumberlege: Yes.

Frances Elmslie: It's only actually followed up at three months of age, so this is very focused on malformations that are immediately evident within the first three months of life.

Julia Cumberlege: Right.

Frances Elmslie: It is - so it is not a prospective registry looking at long-term outcomes for children.

Julia Cumberlege: Because things like cleft palette, which could be caused by this valproate, that actually occurs - appears much later doesn't it?

Frances Elmslie: You would hope that most children with cleft palette are picked up in the neonatal period.

Julia Cumberlege: Right.

Frances Elmslie: You would hope that most of them would be picked up by three months of age. There are some that have a much more subtle cleft palette that are even - I saw a child the other day who was diagnosed aged seven with it, but that was with a very subtle cleft palette, so most...

Julia Cumberlege: If the baby's not feeding then you...

Frances Elmslie: Yes, yes exactly.

Simon Whale: Sorry can I, just one more question on that. For how long does the registry maintain or follow the progress of the child?

Frances Elmslie: It actually doesn't, so it just gets the data at three months. Does this child have a malformation or not.

Simon Whale: That's it, it stops at three months?

Frances Elmslie: That's it, that's it exactly. The other studies that have been going on, and the Liverpool Manchester study linking, which links in with the States that has been specifically a prospective study looking not only at

malformations but at neurodevelopment. That is the one I get, I passed the reference on last time. The last report was, Meador was the first author. That is an ongoing study, so they are looking at this cohort of children prospectively to look at neurodevelopment and other aspects.

Julia Cumberlege: Perhaps [unclear].

Cyril Chantler: Can we go back to the idea that you've referred to, and we've taken on board, about a limited number of centres which provide expertise which would cover all ages.

Frances Elmslie: Yes.

Cyril Chantler: The point you've made. We have been told that sometimes they've been referred, patients have been referred to clinical geneticists who have no experience of valproate, and so these limited number of centres would have clinical geneticists who were experienced, like you are, in valproate?

Frances Elmslie: Mm-hm.

Cyril Chantler: How many centres would you think would be appropriate in England?

Frances Elmslie: I think it would need to be based on geography.

Cyril Chantler: Yes.

Frances Elmslie: To ensure that people have easy access. I would say probably a couple in the north of England, one in London one in the Midlands and one in the Southwest, something like that.

Cyril Chantler: Something like that, okay

Frances Elmslie: We need to be thinking the UK of course. I keep thinking NHS England, so we'd need to think about Scotland...

Cyril Chantler: Yes.

Frances Elmslie: ...and Northern Ireland and well, so probably a centre in Scotland and one in Northern Ireland would be appropriate. We're probably talking about eight in the whole of the UK something like that.

Cyril Chantler: Yes. The question then arises would they also take on the role of looking at women who might have suffered damage from other teratogens in pregnancy. Primodos for instance has been very much part of our enquiries. People who are the children of mothers who took Primodos also have similar anxieties and problems in coping.

Frances Elmslie: That's an interesting thought actually, because obviously as a geneticist we do have some expertise in teratogens in general.

Cyril Chantler: Yes.

Frances Elmslie: We tend to have different expertise depending on the effect of the teratogen, and our clinical practice. One of my colleagues is an expert in skeletal dysplasia, and therefore has seen lots of people who have been exposed to thalidomide for example.

Cyril Chantler: Yes.

Frances Elmslie: But you could suggest there may be centres of excellence for teratogenicity instead. I think you may end up having to have different individuals within that centre.

Cyril Chantler: Yes.

Frances Elmslie: Or you - we are at the cusp of a change in the role of clinical geneticists as well, so you may have people who then develop expertise in teratogenicity specifically. I don't think that's an impossible suggestion. I don't think it would be only Primodos and valproate I think we would certainly be saying how about clinics for people exposed to teratogen, so alcohol would be - that's a common referral to clinical genetics.

Cyril Chantler: Yes.

Frances Elmslie: I think that would be quite an interesting proposition actually.

Julia Cumberlege: We'd rather introduce this just now...

Frances Elmslie: Yes.

Julia Cumberlege: ...talking to you, but could you describe for us a centre of excellence? Who would be there? I imagine in your particular field geneticists are actually pretty rare people.

Frances Elmslie: Yes there are about 200 of us in the country.

Julia Cumberlege: Two hundred of you.

Frances Elmslie: Two hundred in the UK, yes, just over 200.

Julia Cumberlege: Oh right, so this includes Scotland and Northern Ireland?

Frances Elmslie: Yes.

Julia Cumberlege: Yes, okay. Could you just paint a picture for us about this centre of excellence?

Frances Elmslie: Yes, so I think the most important thing would be to think of it as being more of a coordinating centre rather than a centre that delivers absolutely everything, because it becomes impossible for some of these services to be delivered centrally. I would say one of the most important roles would be a clinical nurse specialist who acts as the coordinator for care, and making sure that the patients can actually access the right care for the individual aspects of the condition, because they'll all be different from one another. Ensuring that that where possible, is delivered locally, because what we don't want is people driving 100 miles to see a clinical psychologist or whatever.

I would say in that clinic we would need also, obviously clinical geneticists to talk about diagnosis. But in addition some people who are interested in neurodevelopment, so autism spectrum disorder. That may well be either a psychiatrist with an interest in learning disability or a psychologist with interest in learning disability. There aren't that many of those people either, but there are people out there and it's recognised as being a growing need as well.

From the point of view of the medical aspects of care, then I don't have a feel for actually what may be present still in adulthood that has not been managed already. Things like cleft lip and palette will have been surgically corrected. Doesn't mean there's not always some problems but hopefully they would have - been under a team that would still be managing those sorts of things.

Spina bifida is a complex area, and they do have their own teams that generally follow people up into adulthood, because they have ongoing medical needs. I think it would be, needing to have a bit of a flex to ensure that you all - you are able to communicate with local teams.

I would say a core of a clinical nurse specialist to act as the coordinator, a clinical geneticist and then a psychiatrist/psychologist with an interest in learning disability, autism spectrum. Then flexing to be able to involve other health professionals as needed, would be off the top of my head.

Julia Cumberlege: The coordinator is very important.

Frances Elmslie: I would say the most important person.

Julia Cumberlege: Could you have another sort of clinician? Could you have a nurse being a coordinator?

Frances Elmslie: Yes.

Julia Cumberlege: Yes.

Frances Elmslie: That's what I would favour, yes.

Julia Cumberlege: Yes.

Frances Elmslie: Somebody with clinical knowledge...

Julia Cumberlege: Yes.

Frances Elmslie: ...who is able to give some clinical advice, but whose primary role is to make sure that everything is happening.

Julia Cumberlege: Right, thank you that's very helpful. Cyril [unclear]

Cyril Chantler: Yes, thank you. Moving on then, one of the questions that's arisen is hyperextensibility.

Frances Elmslie: Okay.

Cyril Chantler: We did discuss that before, but it's come back to us again.

Frances Elmslie: Okay.

Cyril Chantler: The families who do believe that a child with fetal valproate does have a problem of hyperextensibility.

Frances Elmslie: Mm-hm.

Cyril Chantler: But that is not genetic, so can you explain all this to us please? Can you help us?

Frances Elmslie: Yeah, so we usually use the term hypermobility.

Cyril Chantler: Right.

Frances Elmslie: Hypermobility is of the joints, so people have increased mobility particularly of, well it can be large and small joints. But that can affect things like fine motor skills, being able to hold a pen, and so that often has a particular impact on education and requirement for occupational therapy and that sort of thing. But also there can be an effect on just physical actions, so exercise tolerance can be affected by hypermobility and joint pain as well. Often it just contributes to fatigue and children complaining of joint pain.

Now it is - in the medical literature there isn't, I don't think I've come across anything actually that has been specifically written about fetal valproate and hypermobility. For hypermobility it is quite common in the general population, but is also often associated with other things. I see a lot of children with chromosome problems for example, and a lot of those children would have hypermobility in relation to their chromosome abnormality. I can totally believe that it could be part of this neurodevelopmental profile. How - the aetiology of that is another question.

Cyril Chantler: But it doesn't fall into the spectrum of genetic conditions that are associated with hypermobility?

Frances Elmslie: What this wouldn't do you mean from our - the fetal...

Cyril Chantler: Yes, for people with fetal valproate syndrome, they - there is no genetic course of hypermobility with them.

Frances Elmslie: For them I wouldn't say so, no, in this particular group. There are genetic causes of hypermobility.

Cyril Chantler: Yes, that's right.

Frances Elmslie: Yeah, but they are - they're separate and they're specific gene changes that we would consider looking for if there were other features not just hypermobility by itself, because that's a common feature. But we would look at the skin we would look at - think about blood vessels and all those other things, yeah. But I - it would not make me consider specific genetic disorders unless there were some other associated features.

Cyril Chantler: Okay.

Frances Elmslie: Is that clear?

Cyril Chantler: Yes, thank you, that solves that problem, thank you.

Frances Elmslie: Okay.

Julia Cumberlege: Can I just ask you, when we've spoken to patients some of them are quite reluctant to be referred to geneticists.

Frances Elmslie: Okay.

Julia Cumberlege: Now I'm just wondering whether there's something that your profession can do. Do they need to do it? Obviously people have got freedom to choose how they want to look after their children and to have them

diagnosed et cetera. But I'm just thinking that it's very hard for us to get a real handle on the numbers.

Frances Elmslie: Mm-hm.

Julia Cumberlege: For us that is quite important as we think through the rest of the review, and I wondered if you had any thoughts on that.

Frances Elmslie: Yeah. I think quite a lot of people just find the whole idea of genetics a little bit scary and don't really understand what we do. I think there is also potentially - there are pros and cons to a diagnosis, and of course we may come up with an alternative diagnosis, which we may be saying well actually we think this different diagnosis has caused your child's problems which may be something that people don't want to hear.

Even in my clinical practice sometimes people say, if you think my child's got a syndrome I don't want you to tell me about that. Other families would say actually we have found this very empowering, because we've been able to either meet other families who've got children with the same thing, or it's enabled us to be able to access things that we would not have been able to access otherwise. I think that's the area that I would try to emphasise is that first of all we don't force diagnosis on people. We would discuss that during the consultation whether this is something that they wanted to explore, how much information do, they want from us.

I think the - what we potentially could do as a profession is to think through our professional societies, is there anything we can do in terms of good publicity to put out a bit more about what our role is, and a little bit more about consultations.

Now, what we already do is if somebody's already referred into genetics they get some information about what the consultation would be like. But that means they have already been referred to us and they've actually already said they'll come into an appointment. We can maybe think about our systems and whether we should be sending out proactively some more information through paediatricians, through GPs potentially about what we do.

I do - one of my other roles I work with the Clinical Genetics Society, so that's something I can certainly discuss with colleagues and see if we can potentially do some publicity about what's good about going to a clinical geneticist.

Julia Cumberlege: That's helpful, thank you very much.

Frances Elmslie: Okay.

Julia Cumberlege: Anybody else want to ask anything?

Sonia Macleod: Can I just say, when you said about alternative diagnosis, one of the things I was interested in was there's been some evidence to say there's possibly - potentially shared genetic aspect behind both autism and epilepsy.

Frances Elmslie: Yeah.

Sonia Macleod: I wondered if you could tell us a little bit more about that.

Frances Elmslie: Yeah, okay. I think the link between autism and epilepsy is particularly noticeable if there is also intellectual disability. We know that there are quite a number of genetic disorders that predisposed to all three, and probably that is what is accounting for the association between those three things.

If you take out intellectual disability there is still an association, probably at least a four-fold relative risk of each, if you have autism of having epilepsy and if you have epilepsy having autism. But if you have intellectual disability as well that increases the risk very greatly of having both. There are quite - now many, many genes that predisposed to all three of those.

Amongst the other group I think - I suspect there is a shared genetic basis for those, but we have made much less progress with that.

Julia Cumberlege: Right, Simon.

Simon Whale: As we've been round the country talking to parents and people directly affected children, young adults as well, they very often talk to us about the struggles and the barriers they encounter in terms of the education system, but primary care as well and social support, the welfare system. Those barriers have stemmed from, they tell us they, stem often from a lack of recognition or understanding of fetal valproate spectrum disorder...

Frances Elmslie: Mm-hm.

Simon Whale: ...and the symptoms of it. I just wonder from your point of view how do you think it - do you recognise that? Do you see that from the patients you see, do you hear that from them? How does it impact on the management of the disorder?

Frances Elmslie: I would say I totally recognise it. I think, unfortunately, it's not completely unique to fetal valproate. I think there are particular aspects that would make it more difficult in fetal valproate and possibly other exposures to teratogens that they are poorly understood, and we haven't got really good robust evidence for it.

I think one of the problems is that there is no test. I think that's something people often struggle with particularly in the medical profession. As a geneticist we struggle with it less, because we - going back 30 years we didn't have tests for genetic disorders. We just looked at somebody and said you have Noonan syndrome. I know that because of all the features that we put together. We don't have so much of a problem without being able - of not being able to prove it with a test.

But I would say there is often an issue for children who have non-specific learning disabilities, enabling them to be able to access the right education, the right social support the right inputs in general. I think once you have a proven genetic diagnosis often those things become easier. That's around educational priorities I would say they probably go, oh yes, I know something about that I will prioritise my resources towards that individual. Where you just have a condition where there is - it's a subjective to some extent, diagnosis it's - and relatively poorly understood, I think it's just given a lower priority.

I think the second half of your question is about, is this something I recognise in management is a difficult one. Because if I'm honest with you I don't really manage these patients, because what we do is diagnosis, and so in a way we're guilty that's the way our service is set up. We say, yes, you've got fetal valproate and usually we say off you go, but I'm happy to give you that as a diagnostic label.

Simon Whale: But we talked a bit earlier about the special centres, centres of excellence.

Frances Elmslie: Yeah.

Simon Whale: In what way do you think they might be able to deal with some of these - this kind of problem this lack of recognition, and a knock-on effect on that support for the individual or the family in education for example or in welfare?

Frances Elmslie: I think partly being a specialist centre you'd have some kudos. If you are a child, and you've been seen by a specialist centre that is designated as a centre for diagnosis of teratogenic disorders or whatever we decide, then you would - that would be - carry with it much more gravitas than it

maybe currently does. That would be one thing. I think also in terms of the coordinator specifically that would be part of their role.

The other thing actually that I haven't - just coming into my head is the other thing that I've seen work really well, and I'm sorry to keep going back to tuberous sclerosis, but that's where I have a lot of experience, is that the charity itself has a support worker who comes to our clinic now. But she is the transition between the clinic and the community, and she often is able to support families out in the community.

It may be worth thinking about somebody in that role. How that is funded is a separate issue. But somebody who can cross-link between the families, seeing the families at home, helping them, sit down fill out forms which is very much what she does, but also picking up the phone and talking to education, going into schools that sort of thing. I think a clinical nurse specialist would struggle to do that on top of everything else, but a person that's linking in between community and clinic would be really useful.

Valerie Brasse: I wonder if I could follow that up, because of course it seems to me once you were referred into such a centre actually life could be made a whole load easier for you if it was set up as we were talking about.

Frances Elmslie: Yes.

Valerie Brasse: The issue for me is getting referred in...

Frances Elmslie: Yes.

Valerie Brasse: ...and if the portal is the GP practice presumably.

Frances Elmslie: Yes, usually.

Valerie Brasse: Are you finding, by the time people get to you that some have been months if not years of frustration about just being able to access the help that people need. There's something about that link back to the first point of entry, which is the GP practice, and understanding that this person needs to be referred on. Do we need to be thinking about that side too?

Frances Elmslie: Yes, I think we do. Obviously if children get to a paediatrician often they're referred in then. But often it is a couple of steps before they will end up in clinical genetics.

Valerie Brasse: Because we hear from the patient groups that they're having to educate if you like the GPs as to, look, this is what we think we have.

- Frances Elmslie: Yeah.
- Valerie Brasse: That seems a rather sorry state of affairs, because obviously first access and fast access. The other thing that we were told is that, if you don't get it right then what can happen is that a child is diagnosed with something wrong, and the treatment given to them that could actually impair their health condition even further because they're not getting that immediate right access right the first time.
- Frances Elmslie: Yeah. I would say that that is - it is a common frustration actually. One of the other things that has happened, and I think hopefully it will be beginning to have an impact, is the rare diseases strategy which would - this would fall under, because this is still a relatively rare condition, and that is looking at provision of care for all people with rare disease.
- One of the things that's been suggested is a sort of flag to say this is a person who's at risk. How that's actually going to be definitely implemented I think is not quite clear. But we do actually have an implementation plan for England now published last year, so that's something that could be used as ammunition I suppose. It's there in black and white.
- Julia Cumberlege: Dr Elmslie, can I just ask you, one of our difficulties has been to actually find the figures that are appropriate for the number of children, now adults that have had - suffered through sodium valproate. Have you got any handle on the figures that are in population, the numbers of people?
- Frances Elmslie: I absolutely haven't actually. I think that's a really difficult one, because obviously the children we've been diagnosed, many of them now will be adults. But I don't think - and you know we've had valproate around, so there should be a significant cohort of adults, but I suspect there are people who have just missed out on being diagnosed.
- I imagine it is under-diagnosed, particularly in the adult population. It would only be the children that have been diagnosed that have come through. I can't - I think if we're thinking of 40 per cent may have something within the spectrum, we would have to do some calculation. I don't know how many people have been given valproate over the years, and I really don't have a handle on that at all.
- Julia Cumberlege: No, right, anyway just sort of thinking about support.
- Frances Elmslie: Yes.

Julia Cumberlege: We need in a way - with something like Primodos we know roughly the numbers.

Frances Elmslie: Yes.

Julia Cumberlege: But with sodium valproate it is much more difficult.

Frances Elmslie: I would agree with that.

Julia Cumberlege: Yes.

Frances Elmslie: Yes and prescribing practices have changed over the years with an increase in valproate, now a decrease in valproate being administered. I think you need a good health economist an epidemiologist to have a look at prescribing over the years and what the theoretical number may be.

Julia Cumberlege: Right.

Frances Elmslie: I think that's quite a complex calculation.

Julia Cumberlege: Thank you. I'm going to ask my colleagues if there's anything further they would like to ask you. Then I'm going to ask you whether there's anything that you would particularly like us to think about within the course of the review.

Frances Elmslie: Okay.

Julia Cumberlege: Cyril.

Cyril Chantler: I've asked all that I wish to ask.

Frances Elmslie: Okay, good.

Sonia Macleod: Just a quick question. You just mentioned differences and changes in prescribing practices. Have you seen a decrease in the number of children affected with sodium - fetal valproate disorder recently, and have you see anything to do with other antiepileptic drugs that's increased or [unclear].

Frances Elmslie: That's a really good question. It actually comes back to what we were talking about earlier, is that of course the children have to be referred to us for us to see them. I would say I have actually seen fewer children referred in to me recently. Whether that is because they're being managed elsewhere or because there's a real decrease in them actually being affected, I don't know. What I would say is that I have not seen an increase in malformations, or seen children who have malformations related to other antiepileptic's at the same time.

Sonia Macleod: Okay.

Frances Elmslie: That's probably all I can say about that.

Julia Cumberlege: Alright, thank you. Simon.

Simon Whale: Just a quick, very quick follow up to that question. The children that you see are they typically in one particular age group or is it anything from very young children to teenagers?

Frances Elmslie: Yeah. They're usually younger children I would say, under the age of 10...

Simon Whale: Right.

Frances Elmslie: ...most of them, yeah.

Julia Cumberlege: Thank you very much. It's over to you. Have you anything particularly you think that we should be thinking about during the course of the rest of the Review?

Frances Elmslie: The inquiry, I think one area that we really need is better research actually.

Julia Cumberlege: Better research.

Frances Elmslie: Better research and I think it's the prospective follow-up of children that is still lacking. There are a couple of very good studies that are going on. But I think the whole reason this area is so difficult is because we haven't had good prospective studies going forward. I think the only way we can answer the question about the next generation would be through good well-funded prospective studies. That will be my key message.

Julia Cumberlege: Well thank you. That's very helpful I'm sure there are other questions that may come up before we produce our report, so do come back to us we're open and accessible.

Frances Elmslie: Okay.

Julia Cumberlege: If there's anything else you think that we really should be thinking about that would be very helpful. Congratulations on the work you're doing now, and thank you what all you are doing for people who are suffering in this way. Thank you for coming today.

Frances Elmslie: That's my pleasure.

Julia Cumberlege: Thank you.

Frances Elmslie: Okay, thank you.

END OF TRANSCRIPT

Session 2: Action against Medical Accidents (AvMA), Private Healthcare Information Network (PHIN), NHS Resolution

START OF TRANSCRIPT

Julia Cumberlege: So, if I could just start off by introducing ourselves, and then I'm going to ask you to introduce yourselves. So, I'm Julia Cumberlege, and I'm chairing this review. Sir Cyril Chantler is my vice chairman, he's on my left.

Cyril Chantler: May I just say, at this point, it's a good time for me to say, I am a non-executive director of Private Healthcare Information Network, and that needs to be declared.

Julia Cumberlege: All right, thanks very much indeed. Okay. Simon Whale is on my right, and Simon is the third member of the panel. On Simon's right is Valerie Brasse, and Valerie is our Secretary to the Review. On Cyril's left is Sonia Macleod, who is our key researcher in this. So, that's us. I just think it would be helpful if you could say who you are, and I know today that we do have an observer from one of you, welcome to you. Thank you for coming. There are other people in the room today who are just helping us run this event. So, perhaps we could just work along the line, is that all right?

Matt James: Certainly, so, good afternoon, I'm Matt James, I'm the Chief Executive of the Private Healthcare Information Network, usually referred to as PHIN. We are an independent not-for-profit organisation holding a government mandate from the Competition and Markets Authority to collect and publish data in the private health care space across the UK.

Julia Cumberlege: Thank you very much, very succinct, thank you. Peter.

Peter Walsh: I'm Peter Walsh from a charity called Action Against Medical Accidents, known for short as AvMA. We are a UK-wide independent charity. We provide independent specialist advice and support to people when things go wrong in healthcare. - explaining people's rights, helping them with investigations, and whichever avenues they choose to pursue as a remedy for what they've experienced. We work in partnership with the NHS and with private healthcare, with health professionals to seek to improve patient safety.

Julia Cumberlege: Thank you very much indeed. NHS Resolution.

John Mead: Hello, I'm John Mead, I'm technical claims director of NHS Resolution. We are a special health authority operating a number of indemnity schemes on behalf of the Secretary of State for Health and Social Care.

Julia Cumberlege: Thank you.

Denise Chaffer: Afternoon. I'm Denise Chaffer, I'm director of safety learning at NHS Resolution. I'm a midwife and I'm a nurse by background.

Julia Cumberlege: Thank you very much, indeed. So, I'm going to just ask any of you, are there any interests you need to declare? Interests in terms of financial interests from other organisations or anything? No? Right, thank you. So, I would like to start with you, Mr James. As I understand it, and you've explained it very succinctly, that certainly you are not working for the private sector in any way, except that you are collecting information and disseminating it.

One of the things that I think has concerned us, or certainly concerned me, is that solely private work is not - rather, complaints are usually handled by the private provider. I'm just wondering, private providers have their own policies, when it concerns complaints and so on. I'm just wondering, should there be a centralised complaints litigation handling for the private sector, in the way that there is for the NHS?

I think the difficulty comes when the private sector is doing work, transfers to the NHS or vice versa. There seems to be a bit of a lacuna there, and I don't know if you'd agree with that.

Matt James: Well, I should probably state initially that complaints handling is outside the scope of PHIN's remit, so it's not something with which we are directly involved. There are some other organisations which I'm happy to signpost, who should certainly get involved in giving evidence about complaints handling in the private sector. So, I will speak personally as to what I know happens, from a number of years of working closely with the private healthcare sector.

Essentially, my understanding is that complaints, as distinct from claims, are handled within each provider, certainly at first and second stage complaints, but that an independent organisation exists for handling third stage complaints, that to which most independent hospitals subscribe. That organisation is ISCAS, Independent Sector Complaints Arbitration Service, who should probably be called to give evidence on this point. They now work, I think, with one of the main dispute resolution organisations, I want to say CESR, or something like that.

Female: CEDR.

Matt James: CEDR, thank you. C-E-D-R, thank you. So, that's my main understanding of how complaints are handled in that sector, and there are different processes, of course, for claims, where again, those are usually handled within legal processes that are administered by the individual hospital providers.

Julia Cumberlege: Right, okay, thank you very much, indeed. I don't know if you two groups, whether you want to come in on this, or we'll move on to another subject.

Peter Walsh: I'd like to, Baroness Cumberlege, if I may. We have experience of advising, supporting people with complaints, both in the NHS and the private sector, and we do notice a very stark difference between them. Patients in the private sector do not have the same rights as NHS patients. For example, if you're an NHS patient, you have a statutory right to a standardised complaints procedure. If you are not satisfied with that procedure, you have a statutory right to take your complaint to the ombudsman.

The arrangements that exist in the private sector are an attempt to provide a second stage review, but it's not in any way the same, or even similar to the role of an ombudsman. Also, people in the NHS have access to paid-for independent advocacy. Certainly, in England and in Wales and in Scotland. That doesn't exist in the private sector. So, what we tend to find is that, generally speaking, people who have experienced problems, harm, in the NHS get to find out about where they can get independent specialist help and advice. There are leaflets, there are posters, there are people whose job it is to sign post people.

In the private sector, people are much less aware of their rights. They don't have automatic rights to the independent complaints advocacy service. They often don't get told about us. So, by the time people have got to us, they had a very, very difficult journey and gone to various places and been told, well, no, we can't help you.

For years, we haven't been alone in calling for a single complaints procedure for private and NHS. Also, improvements - whether it's a single agency, it's difficult in the private sector, because you have lots and lots of autonomous organisations of course. But, again, with NHS, say in England, we've got NHS Resolution, you can get detailed statistics, you can get reports, analysis of what's going on. In the private sector, and even with the primary care practitioners, it's almost impossible to get any reliable data about what's going on. How many incidents have happened

in which organisation, and what's being done about it, what follow up has taken place?

Julia Cumberlege: Yes. So, your solution then, to this, is...

Peter Walsh: It would be a complaints procedure that's common between the NHS and private, access to a statutory right to go to an ombudsman, funded advice and information, independent advice and information for people in the private sector health system, similar to that which is available in the NHS, and some tightening up of the indemnity arrangements.

A common problem we come across is this confusion about who is liable, if there is a liability issue. You get independent doctors working in private institutions, and the private hospitals say, well, it's the consultant you need to sue. The consultant will be saying, it's the hospital you need to sue. If they've got a contract with the NHS, there can be arguments about whether this is an NHS indemnity, or is it a private indemnity. So, it needs to be tidied up and regulated better.

Julia Cumberlege: Well, thank you very much. I'm not quite sure if this is really your field?

Denise Chaffer: Well, it may be just worth adding that at NHS Resolution, we do provide CNST cover for some independent sector that are undertaking NHS work that's commissioned. So, part of - John would know more detail about than myself, but the - in terms of the safety learning aspect of claims, we do produce what we call scorecards, which is getting back to organisations their own claims data, and that includes the independent sector that are in membership. So, we do do some work with the independent sector, alongside the work we do with NHS organisations, particularly in the safety learning space.

Julia Cumberlege: I know you've made great strides in that field, so, thank you.

Matt James: May I - can I just add a couple of observations that may be helpful. The first is that the issues of indemnity will be looked at, I understand by the Bishop of Norwich's inquiry into the issues surrounding the case of Ian Paterson. So, it may be relevant to have some cross cooperation with that inquiry, on that basis.

The second, just to pick up on Peter's comments, is, in common with our mandate from the Competition and Markets Authority, the issue of private healthcare is one where people are both consumers and patients. So, to the extent that protection exists and complaints processes exist in private healthcare, they're possibly more oriented around a consumer

approach to protection, than in the NHS where they're oriented around a patient and medical approach to protection.

It's possibly worth considering how those two things overlap. Because unlike in the NHS, people also are consumers and have that commercial and financial aspect to consider as well. So, in some ways, the process needs to be more than that in the NHS, but arguably, certainly not less.

Julia Cumberlege: Right.

Valerie Brasse: Sorry, can I just follow that? The interface is actually between privately funded care in a private provider unit, as opposed to NHS funded care in a private unit. So, if you are an NHS funded patient in a private provider, you are following the complaints procedure which is the NHS mandated one.

Matt James: That would be my understanding.

Valerie Brasse: So, as far as the provider is concerned, they can end up - and a clinician working in both, ends up dealing with two different complaints processes. That's how it works.

Peter Walsh: Yes. Also, the indemnity - some private organisations use the CNST under NHS Resolution, but it's optional. They can choose whether or not they join that scheme. So, you can be an NHS patient - in other words, private healthcare funded, under contract by the NHS. If something goes wrong, and unlike any other normal NHS patient, you find yourself having to sue an organisation that's using completely different scheme, with different cultures, different approach, different systems.

Julia Cumberlege: Thank you. Can I go back, I'm sorry, to you, Mr James. You don't appear to be receiving all the data that's mandated by the Competition and Markets Authority, particularly on the adverse events data. So, are you doing anything to rectify that?

Matt James: Well, I think it's fair to say that this is still a relatively young program, and that implementations on the scale of PHIN take a long time to get right, and that we could undo an awful lot of potential for good by making small errors as to accuracy in the publication of adverse events information. So, we've essentially taken the approach of working with provider organisations, with the relevant authorities, with the medical professions to try to build momentum in the way that we approach this, and to approach it responsibly.

Now, that means that it's taking slightly longer than was originally envisaged by the CMA to bring into effect the reporting that is mandated. But I'm confident we'll get there. Certainly, PHIN remains fully committed, fully realising the scope of the CMA's order, and the CMA remains fully committed to realising the scope of the CMA's order. But I think there's also a general recognition that you progress carefully. That's particularly true when it comes to information being reported about consultants, individual consultants, and I think it's also true for hospitals.

So, the first stage that we've looked at is really to gather information on activity, and being able to count things. I know that should be straightforward, it sounds straightforward. It's not entirely straightforward, either in the NHS or in the private healthcare sector, or certainly the interface between, where historically, those two [unclear] systems have used different methods of counting, and we've had to really bring the entire private sector back into using the same basis of counting activity as the NHS.

It's essential that we've done that first, because you have to know how many of things are happening, before you can make any sort of intelligent comments or data about the rates of incidence. So, we do receive adverse events data from a large number of the larger providers. What we haven't been able to do yet, is necessarily take that through to the point of publication, to have assured ourselves of the robustness of that data. But it will come.

Julia Cumberlege: How long do you think that's going to take?

Matt James: We'll progress to publishing the first adverse events information later this year, and that will be some of the more straightforward adverse events, for which it is not common to risk-adjust the publication. So, for example, in never events, the never event within the NHS would tend to be reported as a bulk number, or a number as a rate against either a number of admissions, or a number of bed-days, or something similar. Similarly for infections. So, we'll be able to publish that data later this year for the majority, I think, of private hospitals.

Then there's a range of complexity through the adverse events, through to those which we've stated we will achieve and are putting an enormous amount of effort, not just internally to PHIN and the other organisations, but now in close cooperation with NHS Digital, NHS England, CQC and other parties, under a broader program called the Acute Data Alignment Program, or ADAPt, to bring to bear measures which simply could not have existed before, and would not have existed without this program,

which rely on close connection between the private data that we are marshalling, and existing NHS data, particularly on unplanned admissions, unplanned transfers of care between hospitals, and unexpected deaths.

So, there's an awful lot of complexity required to bring that information into existence. We've been working on that for five years, to be honest, but that will still take at least another two years to come to fruition to a publishable point.

Julia Cumberlege: All right, thank you very much.

Simon Whale: Can I just ask a question which is for all of you, I suppose. As the Chair mentioned at the beginning, we've met many, many hundreds of people around the country who have been affected by the three interventions that are specifically within the scope of the Review. One of the things they've often said to us, is that there's a disconnect between the adverse event report and the intervention itself. So, someone may well report an adverse event, but it's not always accepted that it's linked to the specific intervention. Do you recognise that problem, and if so, what's the solution to it? In the NHS and in the private sector.

Matt James: I would say that's enormously complicated.

Julia Cumberlege: Sorry, you'd say what?

Matt James: That is enormously complicated. So, if we take something as simple as never events, I tend to propose a relatively hard-nosed view of it, which is that if it happened, it should be attributable both to the hospital and the consultant where it happened, without necessarily attaching fault or blame, but simply as a matter of fact, that there was an adverse event associated with an episode, and that our first event, therefore was associated with the hospital and the consultant that provided the care.

However, the history of reporting of incidents across healthcare, particularly in the NHS, because that's where it has happened, rather than in private healthcare where it hasn't historically, is that people can't divorce that from a notion of blame and legal liability and other factors. So, there is extreme nervousness about the idea of any automatic association of that publication, and the effect that it would have on reporting rates, honesty, transparency, disclosure, therefore the ability to manage the issues within a hospital, at a clinical governance level, and at a national level, and how those things would affect. So, that's one aspect of it.

There are also issues around definition, because it won't surprise anybody to know that there are many different definitions of any given type of adverse event floating around the system, and you pretty much have to pick one and go for it. I think there are complications around the way that patients and the public and the media will receive and interpret publication of those - of information which, as you might imagine, given the role that I've chosen to do, I'm a great advocate of transparency and getting the data out there. But I also do recognise that information put into the public domain is often not used responsibly, or is easily misunderstood.

I think there are a range of other complexities also to consider, and procedural factors. So, for example, in this Review, you're looking at some very specific interventions, and very specific adverse events that attach to those. PHIN's work takes a much more general approach to adverse events, because we're trying to cover all specialties, all interventions, 500 hospitals, 15,000 consultants, 20 different specialties, both surgical and medical, at least 11 different types of adverse events across those. It has to be a relatively generic approach.

Now, sometimes, you will see the same answer from two different directions. Say, for example, a specific failure may lead later to a readmission to a hospital. Clinically, and for the purposes of this Review, you may want to consider the specific failure. PHIN's data would look at readmissions to hospitals, and then ask what was the reason for that readmission. So, you might get to the same answer, but from two different directions, and again, that sort of complexity needs to be understood.

So, none of that is to say that we shouldn't be doing it, none of it is to say it shouldn't be done. We are absolutely 100 per cent committed to getting through those issues, and that's why we set up the organisation, and are pursuing this course of action. But I do also recognise the complexity in it, and I recognise the frustration that would be experienced by patients, because those things don't seem [unclear].

Cyril Chantler:

Yes, it often goes beyond frustration, it's desperation. Because, if you take, as an example, we could apply this across each of the three interventions that we're specifically looking at. But if you take as an example, surgical mesh, if a woman reports severe chronic pain, abdominal pain following a mesh operation, we've certainly been told in many cases, where that woman was being told, well it can't possibly be due - anything to do with the mesh that's been inserted in you.

It takes that woman months, sometimes years before someone actually says, well, perhaps it is. Then the story changes, and her experience changes. But the emotional stress of going through that kind of journey is extraordinarily difficult.

Matt James: I would recognise that completely, because I think in order for people to be able to recognise that the mesh may be associated with the chronic pain, there would need to have been a certain amount of data collected to say that mesh can be associated with chronic pain. But there also needs to have been a process that comes before that, that finds a way of recording chronic pain as a complication potentially of that kind of intervention. So, there is a clinical and governance iteration that can take years, frankly.

We can imagine that following this Review, or as a result of things which we now know have happened, people might be able to collect data in a way that could identify the same issue in the future. One of the problems, I think, we'll face, is that there are a million different issues that could occur, and so, you need a corresponding number of processes to identify every possible thing in order to be able to catch things as they're happening, or prospectively, rather than simply after hundreds - dozens or hundreds or thousands of patients have suffered adverse consequences in things which weren't well-understood, and therefore weren't well-measured.

Julia Cumberlege: I - sorry, go on.

Cyril Chantler: I was going to wonder whether other witnesses wanted to - would NHS witnesses like to say anything?

Denise Chaffer: Well, probably from a slightly different perspective, I think, responding to my colleague, is the whole area around incident reporting and the reason for incident reporting, particularly serious incidents, is based on learning. So, the actual national reporting learning system, it's what it is there for. So, therefore, we need clinicians to report in that context. I think some of the issues around the understanding about why it's so important to (a) report, secondly, to do that in partnership with families, and involve them, is absolutely the philosophy of what we all need to be working towards.

That's certainly what NHS Improvement's safety teams' view is, that's certainly what NHS Resolution's view is, and I'm sure that's what my colleague in AvMA would be. I know we're talking about an ideal, but actually, there's a whole lot of work that's needed to be done around

people being able to trust the system. I think we have made significant progress. There is a hugely improved reporting culture within, particularly, the acute NHS sector. Less so, in probably primary care at the moment.

I think that's the way we need to work on, the focus of the whole reason that we want people to report, is so that we can learn and improve and take immediate action where it's needed. That's absolutely positive that we are working with - certainly, within my own team, we've been doing some workshops around improving understanding around what must happen at the point of incident - the point of a moment an incident occurs. What is the support that should be put around that for families, whether it is around immediate(media?) meetings, avoiding having people go into some adversarial complaints processes, involvement in investigations.

We've seen some gradual improvements, but some of our most severe [unclear] around maternity, the importance of involving families through the investigative process, and feeding back. I think that has got to be the critical driver, for driving reporting. I think when it gets viewed in a negative way, or punitive way, it tends to just push reporting underground. That's absolutely the reverse of what we need.

John Mead: If I could just add to what Denise has just said, we've been on public record as an organisation since as long ago as 1998 to the effect that we will not withdraw cover from any of our members if they provide explanations to patients, if they apologise when things have gone wrong. Duty of candour. We will not withdraw indemnity if our members do that. Hopefully, that is an encouragement to the reporting that Denise has described.

Cyril Chantler: But they're still underreporting, would you say?

Denise Chaffer: Well, I think it's the variation in reporting, I think that's absolutely a fact. I think organisations, the way they - you often hear quoted, the organisations are fearful of litigation. Actually, what we hear when we speak to front line clinicians, is they're fearful, sometimes of their own organisation's response to the way in which incidents will be managed. That is the area of learning that we're working, probably hardest at.

I brought with us, actually, we've got our Saying Sorry leaflet, which I'll leave you a copy. So, it's absolutely in print that saying sorry is absolutely the right thing to do. It is what we would expect. So, I think our common messaging across all of the arm's length bodies is the first point is

openness, recognition, transparency, apologies, support for investigation. We've got a journey to go on. Although I think we have made significant progress in some areas, that we're getting much better at it, but there's a long way to go, as we've heard.

Julia Cumberlege: Peter, do you want to add anything? I mean, I particularly want to ask, actually, about the duty of candour, which of course is a relatively new law, whether that actually has increased some of the reporting, or whether it has decreased it?

Peter Walsh: On that specific question, it's too early to say. But anecdotally, the feedback I'm getting, I don't know if my colleagues at NHS Resolution would corroborate this also, despite teething problems with its implementation, with people understanding what has to be done and how to do it compassionately and well, by and large, things have improved, since the statutory duty was brought in in England. People are having conversations with patients, with their families, that before the duty of candour came in, simply wouldn't have happened. Or they're certainly having fuller conversations than they would have done before this was brought in.

It never was going to be an overnight fix, but our perception is that it's begun to change culture, and make the kind of openness and honesty that we and colleagues are espousing much, much more common than it used to be. However, it's going to take time. It needs more than fine words, it needs proper regulation as well. So, the CQC needs, for example, to be seen to be taking stern action against organisations who are not complying with this duty. So, it's a carrot and a stick approach, where it's not all about threatening people, but it's demonstrating that it's not just a paper rule, it's going to affect organisations if they don't comply with it, coupled with training, support and understanding that this approach is in everyone's interest. Not just the patient's, not just the family, but the individual health professionals, and the NHS or private institution who are doing it.

But, in practice, it's still the case that an awful lot of people who come to us have not had that open approach. I mean, there's two kinds of reporting, I suppose, there's the proactive reporting that you can only do if you know about it anyway, you understand that something has gone wrong, you report it into the system for learning purposes.

But even when people present with an argument, a complaint, a suggestion that their abdominal pain is due to something, and other problems, all too often, the response that the patients and families we

speak to have, initially, is more often than not defensive. It's first of all, starting off, how can we make the case that this isn't due to anything that could have been avoided, rather than, let's really get to the bottom of this and find out, what is the root cause. Not to blame or punish anybody, but to give a proper explanation, a factual explanation to people as well as show compassion, and move on to learn.

Cyril Chantler: Can I now extend the conversation into system failures? Because we've met an awful lot of people who have suffered in all three areas that we've been asked to consider. One of the things we have learned, is how long it can take for the problem to be actually recognised in the system. So, one of our tasks is to consider how could that be better in the future? We're not blaming people, we just want to try and understand why it is taking so long for problems of women that have actually taken sodium valproate to be heard about what's happened to their children? The same problem with mesh and Primodos.

What can we do as a system, and it's not - I'm not saying any of you are responsible, because there are others who we are going to see, like regulators, and they're in the same business. But all of us, together in it, and it's not working. So, what would you think we should be doing to try and make the system better?

Peter Walsh: Shall I - who wants to go first, shall I finish off?

Denise Chaffer: You go first.

Peter Walsh: Okay, thank you. I'd say - it's not an easy question for any of us, we haven't got a complete answer, of course. My two suggestions are, (1) around culture. We have begun that journey of having a more open and honest culture. When I say open and honest, I'm not suggesting that people are always being dishonest when they bat problems away. I think it's part of human nature not to want to believe that we've been harming people. Not to want to countenance that lots of people have been harmed who needn't have been harmed. It's overcoming that sort of culture by not having a blame-orientated approach, by showing people aren't going to be inappropriately hung out to dry as individuals.

So, there's all that can be done around culture, but also, it's the regulation and the robustness of investigatory procedures. Again, I think that there's light in the tunnel, because we now have the healthcare safety investigation branch, a properly specialist dedicated unit, albeit very limited in capacity, who can look at issues forensically and come up with learning points for the system.

If we can have much more of that - I mean, Denise mentioned that one of the weaknesses we all recognise that's been across the system is the quality of investigation. It's been very, very inconsistent, to say the least. Sometimes appallingly bad. Anything that we can - I think that in itself is the single biggest thing, improving investigations when problems begin to get recognised. Thank you.

Denise Chaffer:

I think what I would add - I agree with what Peter said - is the fundamental issue there is around clinical medical professions seeing families and patients as partners, and I think it starts with that relationship. That people are equal partners in this journey, and therefore they're entitled to adult level information that gives all of the risks, and people can have those conversations. I think whilst - and same with the duty of candour, we've got areas where there needs to be huge improvement. We have got pockets of excellence as well, around the country.

We have got organisations where, particularly, they've been assessed as being well-led, there are features of that that are shown in some of the CQC reports, that show something different is going on. So, there are different types of relationships with patients, and I'm talking specifically from a hospital point of view. I can't really speak with expertise around primary care, apart from my own personal experience clinically, is that where patients are seen as partners, and the organisation's focus is patient-centred, you tend to see that those kind of relationships, around people being listened to, and being heard, and being met with when they've got concerns happens a lot more swiftly.

I think one of our biggest challenges, and certainly the work we see across the whole of England is variation. What we found that does help, is to encourage improvement by shining a light on what good looks like. Some of the conversations that people need confidence to have, the difficult conversations around explanations when things haven't gone well. Staff need training and support of how to do that.

We've been providing some having difficult conversation training, for example, in our maternity early notification scheme, to help clinicians have those conversations. We have assumed that people are able and confident to do that, and that's a bit of a journey. But from our experience, we run a number of conferences around the country, and what's different and unique about our conferences, is that we try and get - where we see good practice, we get the organisations to present to each other. We avoid having keynote speakers, and we get an organisation

that's really made progress in a particular area to share what it is that they've done.

We recently had a very successful conference on understanding consent, and we had Nadine Montgomery speak. I think hearing the person behind that whole piece of work around consent legislation, from the heart, say why did that happen? What was the journey of that? But that changed the views of people in that room, and they went away, and the whole way in which they're going to practice and have relationships with families will change.

So, we can't change it all overnight, but I think by shining a light on what good looks like, it gives organisations confidence to see that they can do the same.

Sonia Macleod: Can I just ask, we're all saying since duty of candour came along, you think it's made a difference. You're saying, you're doing education of staff.

Denise Chaffer: Yes.

Sonia Macleod: What's the follow up to actually make sure that things change?

Denise Chaffer: Well, I think - I mean, that's a really difficult question, because that's a measurement question, isn't it, what's the impact of all of this. I think what you see, I mean, there are some measurables where organisations are getting this right. I think - going back to the well-led domain, that's one example of. You see the way in which an organisation is viewed by the users of it, in a much more positive way. The way they can access the services, they can get hold of senior people.

One example is, there's one trust that's been in the well-led domain who has a 24/7 email direct line to the senior executives, if there's any kind of problem, and they will commit to resolve that very quickly. So, I think, where - the problem with duty of candour is, what we mustn't do is have a policy and miss the point. The point isn't what level incident this was, this is what would I want, if I was a family member and something's gone wrong. I don't want to say, does this meet the duty. Actually, every area of care, if somebody wants to have a discussion about that, it should apply across the board.

In terms of whether we're seeing progress in that, it's impossible to say. But what we can say, is that there are some organisations who are ahead of the game on this, and where that's happening, there are other measures externally to us, where we're seeing improvements. Particularly around the complaints side of it, unresolved complaints.

Some of the work that's been done with complaints in particular is - one other measure is repeat complaints. So, when a complaint's not been resolved, it comes back and comes back.

Whereas actually, if you have a philosophy that the moment you have a complaint, you meet with someone face to face and you resolve the problem, or aim to, it then avoids people getting into the adversarial relationship and approaching Peter's organisation because of the frustration that they haven't been able to get an answer, which then goes further down the line, is that the only way I'm going to get an answer here is to take a claim, because I'm not feeling that I've been listened to. So, I think it's a complex question to answer.

But I think it's upon all of us, across the whole system. I think the question was about the system working, how do we work collectively across all of the system, whether it's ourselves, NHS Approval, Academic Health Science networks, how do we do it with one purpose, which is actually to make it far more partnership for families, and they're feeling equal partners in this.

Sonia Macleod: But I think the question is how do we know that the interventions are actually working?

Denise Chaffer: Well, I think - well, the only way you would know is the feedback that you get from families that use their services. That they feel that they're open, they're accessible, they're listened to, and you're not having a - if you yourself analyse complaints, your complaints are not all in that space, around feeling that they're not being listened to.

Cyril Chantler: Can I go back to this question of a system? When things begin to go wrong, it seems to take an awful long time before the system understands they're going wrong and can do something about it. At least that's the experience in these three areas that we've been hearing about. So, is there not something where all of the people who are collecting information could actually have a central intelligence unit that can bring together and go - you talked, Peter, about the HSIB. Who decides what they're going to investigate? How do they know that? A service with a memory, and going back 10 years and so forth.

Peter Walsh: I think the short answer to that is they do. They're very clear that they're completely independent, and they'll identify...

Cyril Chantler: Yes, but how do they - how do they get to know there's something to investigate? It seems to take an awful long time before the people suffering terrible pain because of mesh had their voice heard. Or the

mothers with children affected by valproate had their voice heard, and Primodos likewise.

Peter Walsh: That resonates with our experience of dealing with the families and the patients as well. But I also really echo and understand Sonia's point, that even if there's recognition that something's going wrong, and even if the investigation is exemplary, and comes up with an action plan, sometimes the action plan isn't implemented, and there isn't a follow up. There isn't someone standing behind that action plan, external, saying has it been done? We've had families who have gone back after a year, after having been satisfied there's been a thorough investigation, there is going to be learning, it's going to be stopped from happening to someone else, and they find out...

Cyril Chantler: But if you see a pattern of people coming to you, or NHS Resolution, you see a pattern of things coming your way, and you think, oh, that seems to be a cluster. Where do you go immediately in the system to say, hey guys, you need to be thinking about this. Then they can use other intelligence, and CQC or MHRA or whatever.

Peter Walsh: Well, we would go to NHS Improvement, and say, this is a pattern we recognise. It's far less likely on our numbers that we'd be sensitive enough to get those. But NHS Resolution might. But the one part of the system problem I think you've identified, Sir Cyril, is - it's the follow up, it's the oversight. Okay, you've done a good investigation, you've got an action plan. (A) have you done it, and (b) is it working, or do we need to try something else? That's a bit of a missing cog in the system.

Julia Cumberlege: So, if you tell NHS improvement that you're seeing a trend, and that you're very concerned about it, what do they do?

Peter Walsh: I think what they do, is that they take it into consideration along with all the other data that's coming into them. So, they certainly wouldn't jump because we reported a small cluster of things that we think is the matter. But they would put it into their system in the same way they do the other issues. If I might take an example of this is, they do, from time to time, issue patient safety alerts. Often, they're about drugs, medicines. This has been happening for some time, and it's really good that it happens.

But studies we carried out a few years ago showed that the problem was, although the advice was good and being disseminated, there wasn't a follow up to check that hospitals and other people were actually following the instructions that they'd been given. Again, it's that follow up, that oversight.

Julia Cumberlege: I think it's very...

Peter Walsh: People are going to send it out, and say, okay, we can tick the box, it's done.

Julia Cumberlege: It's disappointing that the system is not sensitive to these things that are coming forward. Because if you - the purpose of this Review was set up, the terms of reference were agreed by the Secretary of State. The Secretary of State set it up because of all the political activity from members of parliament and their constituents. Also, the all-party parliamentary groups. Each of these three elements, Primodos, sodium valproate, and surgical mesh, have a parliamentary group. Now, that is not a good way of actually finding out what's happening, what's going wrong, satisfaction for patients.

I was very interested in what you were you were saying about places of excellence, or really good places. I'm just wondering, if you're seeing this good practice, what do you do with that? Do you disseminate it to others? Because we do know in the NHS, there is often the sort of feeling, not invented here. So, we're not actually going to listen to that. But it seems to be a terrible pity if we've got gems, if we've got places of good practice, that that actually isn't disseminated widely.

Denise Chaffer: So, there's a number of approaches that we take. So, what we tend to do with wider claims data, is we look at it through a lens of high value or high volume, and what might our action be in those areas. We've appointed clinical fellows over the last two years to deep dive data and pull out and interpret that data, and work across the system. So, both our reports, the cerebral palsy report, and more recently, the Learning from Suicide report, is wider than NHS Resolution, so it does work across a number of other stakeholders that are in that space. Because one of the things we want to do in our organisation is to give a unique contributor, not duplicate. It does highlight best practice, so if you look at those reports you can see areas of good practice.

Then we, throughout our regional and local stakeholder events and conferences, we shine a light on, give opportunities to people to speak on those areas. But I think in your wider conversation, I think around how does the system know, and how do they communicate - it's always been a challenge around, is there a national database that we could put incidents, complaints and claims all in one place? It's possible, and it's being worked on through [unclear] NHS Improvement to ask more around what they're doing with their new patient safety management information system going forward.

The problem with claims, is they're time lagged. It's also around - and also with the complaints through the Ombudsman, obviously, they're very high-level complaints, it's not everyday complaints, and how do you theme them? Our work has been much more at local levels. So, getting organisations that are looking at their own incidents, complaints and claims in the same space. Because the contributing factors would be similar. So, there's local work and ownership to be done there.

But NHS Improvements – national patient safety, it would obviously be better to speak to them than me, I can't speak for them, but I have worked with them. They do collect in, as you know through the National Reporting and Learning System, clinical incidents that are reported on a daily basis, they do theme them, they do look at the very rare national events. They do produce safety alerts. From an organisation's point of view, and having worked in a number of trusts, there is a process within an organisation, when you see the safety alert, and the way in which it's distributed, and there is - there are assurance processes, and there are governance committees that review those and talk about the actions.

The monitoring responsibility sits specifically with an organisation's own boards and governance boards, but also with the clinical commissioning groups. So, that is their role. So, all clinical commission groups will, through the contract, have regular meetings with their trusts. They should be following up Serious Incident Report action planning and overseeing those. Certainly, overseeing other events in that way. So, there are people in the system doing this, and I think very similar to how we spoke earlier, there's variation. There are some places where that's being done in a very sophisticated and advanced way, and others where there's a way to go.

Simon Whale: One of the messages coming through from this is that there aren't - there are several organisations, perhaps more than several organisations who have a responsibility in this area.

Denise Chaffer: Yes.

Simon Whale:: Both within the NHS and separately, in addition, in the private health care sector. Is that part of the problem, that there's all this overlap and/or confusion about whose responsibility - it's patient safety ultimately, that we're talking about here - whose responsibility patient safety is? Is the solution to that to create yet another body which is the body responsible for patient safety?

Denise Chaffer: I think it is one of those cases, patient safety is everyone's business. But it's no one organisation's sole responsibility. I think the responsibility - I can speak for NHS Resolution, our responsibility is to work in partnership and alongside those other bodies, for exactly the reasons that I've spoken about.

Our examples of that are in the maternity space, particularly we've got a new initiative where we are receiving point of incidents around potential - babies that may have potential brain injuries, so we are knowing at the point they happen now, whereas in the past we wouldn't have known until we received a claim. So, we're able now to work with those bodies, CQC, NHS Improvement, NHS England, Royal Colleges, around things we're seeing happening this afternoon. So, in the past, we wouldn't have known.

So, I think there's progress being made. There's progress being made in learning from deaths, in the inquest work, which we've certainly been linked up with AvMA. So, I think there has been huge progress. It's not all - there are such a lot of areas we need to improve on, and get the system working better together. But I'm not sure it's because there's - it's been clear though, all of those organisations, exactly what their role is, and not taking away the absolute [unclear] responsibility for the individual organisations who are ultimately responsible for care of patients.

Cyril Chantler: There's a - I get all that. But there's a sort of - another perspective for that. If you're the person who has suffered harm, is it clear - I mean, do you think it's sufficiently clear to an individual in that situation where they should go, who's responsible for helping them?

Denise Chaffer: I think - I mean, the question, I suppose, the real test of that question is to ask the patient or the family.

Cyril Chantler: When we've asked people...

Denise Chaffer: Yes, so the families...

Simon Whale: We've got a very clear answer from the people we spoke to.

Denise Chaffer: The families, their first port of call would be the organisation where this has occurred. I think what they would then look to do is go to external bodies that may - if they've not had a good response from the organisation responsible, they'll go to other bodies. I think that's where it becomes confusing for families, and I think, clinicians themselves are also confused about the different bodies and their roles, particularly as there's quite a lot of change going on at the moment. It does make it much more

difficult to navigate the system. But I think that's upon us all our role is, going back to partnership with patients, is to help and sign post them, and not to send them off somewhere else, for people to hold the ring and try and resolve things for them, and say, well, it's not my organisation, go and talk to X.

Certainly, we don't do that. We've had cases where we had people come to speak to us, where it's not specific claim-related, and we will pick up the phone and get somebody to support them, rather than just say, oh, it's not us, go and talk to someone else. I think that's all about responsibilities to not do that.

Julia Cumberlege: I have to say, maternity services - we've had real pressure put on us from the clinicians to have a single portal. Because they are just fed up, having to put in the same information to so many different bodies. It's inefficient, it's wearing, it's not good for the clinicians, and it's not good for the patients.

Denise Chaffer: I mean, we would all agree with that. There's a shared ambition to resolve that completely.

Peter Walsh: Yes. I mean, I agree with Denise, in that patient safety is everybody's business, and it's really good to see the way that NHS Resolution is evolving into being much more involved in patient safety, rather than simply the claims-handling side of things. However - NHS Resolution are also very good, in terms of telling members of the public where they can go to for independent advice and help. So, we get people coming to us, because they've been told about us, or found on NHS Resolution's website, information about us.

The Duty of Candour guidance for all registered organisations clearly says that those organisations should be telling people about us and other forms of independent advice and support. Now we - some of them do. But we know that a huge number of them don't. So, in theory, everyone who's been part of a duty of candour process should have been handed some information about where they can go to get an independent view on what they've been told, and whether they need further help. It isn't happening consistently.

So, it's another example of - things are moving in the right direction, but they could move much, much faster, and be much more consistent if there was a tougher requirement to follow the guidance and the systems that exist.

Julia Cumberlege: Right. Any questions? Sonia [unclear].

Sonia Macleod: It was just one question. That is, that we have heard from an awful lot of people, a huge number. Yet, in the evidence that you submitted to us, in terms of pelvic mesh claims, I think you said you had 160. Now, compared to the hundreds of women we've heard from, that's a very, very small number. There seems to be a discrepancy there, I wonder if you'd like to elaborate a little bit more about that.

John Mead: Well, the 160 are the women who have actually made claims. There are a lot of reasons why individuals choose not to make claims. Some of them don't want the hassle, some might not be able to get appropriate funding, some might not be able to find the right solicitor. Litigation or making claims, certainly litigation, are very tiring and trying processes. So, many people who have potentially valid claims do not make them for one or other of those reasons, and many others as well, I'm sure.

So, I'm not surprised that we have a relatively small number of claims, because that is common across all types of claim, not just mesh.

Sonia Macleod: Yes, absolutely. I mean the valproate [unclear] because I think we had up to 24,000 affected individuals, and thus far, you've paid six claims. The discrepancy is huge. But what it does raise is a question, if we are looking for mechanisms to detect class wide problems, those numbers don't seem to do it. So, how do you do it?

Julia Cumberlege: Perhaps you'd like to write to us on that.

[Laughter]

Julia Cumberlege: Valerie.

Valerie Brasse: Well, just a specific, actually, if you think about the three interventions that we're looking at, predominantly they affect women and/or their unborn children. I'm wondering, what you were just saying about the difficulties of going through litigation, and what your experience might be. Do you find that that's a problem for women who have gone through these experiences, and actually they're less likely to bring the claims, they're less likely to seek the help, than maybe others who have experienced an adverse event going through the system? It's just for comment.

John Mead: That might be one that Peter would have better insight than me, actually.

Peter Walsh: I have to say, we haven't recognised that. But it's perfectly possible. I suspect it's got something to do with the complexity of the issues, about it not being clear that there is a winnable case, if you like, to take forward.

But I think you also need to see this in the context of - the numbers are surprisingly small. It's already incredibly difficult for anyone to bring a claim against a healthcare organisation. It's going to become tougher. Unfortunately, the government's position so far, has been to say, we're going to make it even tougher.

So, even if you can identify a solicitor who now would be prepared to take your case on and try and get you justice, already, we've had legal aid taken away. The only way you can go forward, is you find someone prepared to do it on a so-called no-win, no-fee basis. Soon, we're to have something called fixed legal costs, which would put a limit on how much work lawyers could do on your behalf. So, hypothetically, you could have an organisation that continued to defend, up to the point where they know that people aren't going to be able to afford to take the case any further.

So, it would potentially take us back - I mean, the culture in this area has improved a lot over the years. It used to be, literally, a hard 'deny and defend' culture. That's begun to change, for the reasons that we've heard. But now, with the financial constraints and the pointing finger of what's the bill for litigation, it looks like easy pickings to say, well, look, let's attack that area.

But one of the unintended consequences is that - is (1) we don't get that learning, because the system doesn't hear from those cases in the same numbers as one would if people could actually challenge an initial denial, as to some extent, people are able to now. So, it's bad for patient safety. Also, it would change the culture once again to incentivise a 'deny and defend' approach. Because if you deny and defend long enough, no one's going to be able to take you on.

John Mead: Well, if I could say two things in response to that. First of all, that the proposal, the government's proposals in relation to fixed recoverable costs are only in relations to claims worth up to £25,000. Secondly, as Peter knows, we do not adopt a 'deny and defend' approach. We have a duty from the department, from the Secretary of State, to pay justifiable claims, and that's what we always attempt to do.

Peter Walsh: I wasn't suggesting NHS Resolution does, John. What I'm saying is that inadvertently, an unintended consequence of the fixed cost regime might be that it would have the effect of incentivising individual organisations to go back more to the 'deny and defend' approach. Fixed costs of £25,000 at the moment, but many organisations, including yours, I think, have

argued it should be much, much bigger, and draw in many, many more serious claims. So, it starts small, but beware.

Those so-called small claims are very serious cases, some of them. We're talking about stillbirths, we're talking about deaths of older people, and other fatalities, and life-changing injuries. It's not always borne out by the size of the claim, how serious the effect has been on people's lives.

John Mead: Certainly. I agree totally.

Denise Chaffer: Can I just add something to that? I think it's worth noting we've recently commissioned some research about motivation to claim. I think it's worth - we can probably sign post you to that document, it's on our website. That was around low value claims, but it's very interesting insights in that. So, what we don't want to be in the place where people are taking a claim because nobody will speak to them, or give them an answer or an explanation. Where we are in the place is that people due fair compensation, that's the process. There is an NHS indemnity scheme for that purpose. So, some of this is around good signposting of families, right from the beginning, not, go see a lawyer, because they're going to listen to you, but actually, you've got a case, and this is the process. So, there's something around all these conversations around that.

I think, the answer to some of the things you said, Peter, I think our example of what we do in learning and education is the reverse of that. We're trying to meet the families very early, avoid them having to get into adversarial positions, admitting liability early. So, I think there is some progress to be made and we are - we're on that journey. I think nothing is perfect yet, but I think there's a motivation to try and improve the system. Our organisation is very much behind fair compensation [unclear].

Sonia Macleod: I don't think anyone's questioning yours, but the trusts don't have to go to resolution, do they?

John Mead: CNST is not compulsory, that is correct.

Sonia Macleod: It's not compulsory, it's voluntary.

John Mead: Every trust in the country is a member.

Sonia Macleod: I know you have all of them, I know they do. But what - I mean, I think there has to be a space to look and say well, it is voluntary, it isn't mandatory, there is the option to step outside and do something else. There is potential to consider that as well. I think it's unlikely, because you had 100 per cent of them for a very, very long time.

John Mead: Twenty years.

Julia Cumberlege: I'm going to draw this to a close now, but I'm going to ask my colleagues if there's anything finally they want to say, then I'm going to ask you the same, if there's a final thing you think we ought to be discovering, thinking about, in the course of the Review. So, Sonia, anything?

Sonia Macleod: Nothing.

Julia Cumberlege: No. Simon, no. Valerie, no. All right, so, it's over to you. Matt, I do appreciate you've had to be quite quiet on this, but we did appreciate very much what you were saying at the beginning.

Matt James: Well, I think we have a second evidence session as well, we'll just be still thinking about data and how to pick up on some issues there. But it struck me through that last conversation, starting with Sir Cyril's original question about systems and improving the time, that we are at a point where we are still applying 20th or even 19th century processes to problems which arguably could be addressed in a different way these days, if we can collect information, understand what that's telling us, and react appropriately better.

Because the process of legal recourse via an individual taking action through a lawyer against an organisation has been part of English justice for hundreds of years. The process we've talked about, about joined-up information being available, again, as I started to explain earlier, rely on a certain iterative, very gradual, very slow building up of evidence. Now I think some of those factors are addressable through better use of modern technology and better reporting if we choose to do so.

Whilst we don't have time to get into it now, I will flag one counterpoint to that, which has been a massive inhibitor to us in our process of bringing better information forward, that I would strongly encourage the panel to consider, if you haven't done already, which is the factor of how data privacy rules interplay with the desire to protect patient safety. Because I see those things operating in opposite directions, with massive inhibition to proper authorities' ability to properly protect patient safety, because information can't even be moved around the system and analysed.

I know we don't have time to get into that now. I'd be happy to pick it up in the following session. But if we don't get time at that session, I would encourage the panel to look at it.

Julia Cumberlege: There's always an opportunity for any of the panel opposite us here to write to us, if there's anything you feel we've missed, or we ought to be exploring. Peter.

Peter Walsh: There is one thing we haven't had a chance to discuss that I'd like to say. It's around the transparency about trials and other information about drugs, medicines or devices, which at the moment doesn't have to be volunteered. So, people are able to choose the successful results and put them forward. They don't have to publish all of the information, all of the evidence that they hold. That seems to me to be a very, very serious gap in the system that could be plugged.

Julia Cumberlege: I think when I was at St George's, it was called grey material. Because that - yes.

John Mead: Nothing specifically from me, thank you. But we are very happy to assist the panel in any further way possible.

Julia Cumberlege: Thank you. Thank you very much.

Denise Chaffer: I just - I'll leave you our leaflet we've got on consent, and our Saying Sorry leaflet. That might help you. I actually agree around the data-sharing challenges. But I think there's huge motivation. The only thing I would add is, NHS Resolution's - predominantly CNST covers secondary care, not primary care. So, I think, that's just to keep the context of that, in terms of the way we've been speaking about, that's the trusts that we have in membership, are predominantly in that space.

Julia Cumberlege: Well, thank you so much, thank you for your time and thought you've put into all of this. We look forward to seeing some of you again. Thank you very much.

END OF TRANSCRIPT

Session 3: Medicines and Healthcare products Regulation Agency (MHRA)*, Drug Safety Research Unit (DSRU)

START OF TRANSCRIPT

Julia Cumberlege: We are the people that want to listen to what you've got to tell us. We are very interested in these particular areas that we've invited you to today, the areas in which you work. We will be asking you questions but if you could first of all, as I've suggested, start by introducing yourselves. So, Dr Raine, if you'd like to start.

June Raine: Good afternoon. My name is June Raine. I'm Director of Vigilance and Risk Management of Medicines. My responsibility is to monitor the safety of medicines in clinical use in the UK. The operation of the Yellow Card Scheme falls within my division.

Julia Cumberlege: Right.

John Wilkinson: I'm John Wilkinson. I'm Director of Devices at the MHRA. My responsibilities extend across the whole gamut of devices regulation in the UK.

Julia Cumberlege: Thank you very much indeed. Hello.

Mick Foy: Good afternoon. My name is Mick Foy. I'm Head of Pharmacovigilance Strategy in June's group, the Medicines side and part of my day to day responsibilities are the running of the Yellow Card Scheme.

Julia Cumberlege: All right, thank you very much.

Liz Lynn: Hello, I'm Dr Liz Lynn from the Drug Safety Research Unit in Southampton. My role there is Head of Scientific and Educational Development.

Julia Cumberlege: All right, thank you. Other people in the room here today are our staff who are just helping us to run this session. So, that's really what we are. So, as I say we are focusing on adverse events and complaints herein. That's the purpose of this session. So, perhaps if I could start off and ask you, Dr Raine, you mentioned the Yellow Card System. It's something that I know has been in the front of your mind and certainly at the front of ours, because when we've been travelling around listening to patients, hearing their stories, there's a degree of mystery about the Yellow Card System. People do feel it's very limited.

Some of the patients we've spoken to have said they've submitted something to you about an adverse event et cetera and in fact the

response has not been very quick and in some cases, it hasn't been there at all. So, I think we're probably all at one that it's a system that needs improving. Perhaps you'd like to tell us your thoughts on that, what its limitations are, and how we could improve them. Thank you.

June Raine: Thank you very much, Baroness Cumberlege. I would like to begin though by thanking the Review for the invitation to come here today to give you some of our thinking in relation to the important issues you've just spoken about, what goes on with the Yellow Card Scheme and how quickly and responsibly we react to patients' concerns. I would like first though to say that the MHRA wholly supports this review, its aims and objectives. We're wholly committed to strengthening the Yellow Card Scheme and the way that we listen to and respond to patients who raise concerns with us about the safety of medicines and medical devices. It is a very important opportunity for us to learn from the experiences that you've just delineated. To reset our plans certainly

Julia Cumberlege: Thank you so much for that. I've omitted in my introduction to ask you whether any of you have got conflicts of interest, because we need to know that.

June Raine: I can confirm for the Review that none of us have any conflicts of interest on the MHRA.

Julia Cumberlege: No, that's fine, all right. Sorry to interrupt. Please go on.

June Raine: No, not at all. I hope it's acceptable to the Review today if I spend a little time telling you about how MHRA addresses some of the issues you've spoken about. No effective medicine or medical device is without risk. That's the normal starting point for a discussion on safety. We fully appreciate that behind that is the truth, that a medicine or a medical device that is given with the intention of doing good has in fact resulted in harm. That harm on an individual level may mean something that is really quite tragic, as we've just said. We appreciate this. It could be one of us, it could be one of our families, and we owe it to this Review to demonstrate our commitment to change and in particular to improve and strengthen the Yellow Card Scheme.

We are not complacent. So, I would like to just say to you that we aim to promote and protect public health by making new interventions and treatments available to patients without any unnecessary delay. It may be transformative for them and their condition but we need to uphold high standards of safety, and quality, and efficacy or performance. We work closely with other regulators because we don't regulate health

professionals or the health service. We need to liaise closely with the General Medical Council, the General Pharmaceutical Council, those who produce clinical guidance such as NICE and those that deal with compliance, the Care Quality Commission in particular.

We aim to listen to and respond promptly to patients in all aspects of our work. We have helplines, we have consumer and customer liaison points, but importantly we involve patients in our committees so that they have an important voice in safety decisions. We also have a patient group consultative forum. We set up, when necessary, special groups, networks. For example, in one of the cases you've talked about. Our belief is that when a patient comes to us with a safety concern that in itself is important, but when they go beyond that and profess to want to change the future system for other patients, we treat this as being something of enormous altruism and courage and we are resolved to do something to fulfil that expectation.

So, I will turn now to the Yellow Card. It's the focus of our discussion, it's our vital early warning system which detects safety issues with devices and medicines. It is recognised as a leader, as a scheme for protecting signals, but we are not complacent and we fully recognise the need for some really very important change. I'll come onto the areas of limitation in just a moment. If I may, I would like to tell you how patients are helping us achieve that improvement. We obviously encourage reports from all branches of the healthcare professions, but patients are now our single biggest reporting group, more than GPs, more than pharmacists, more than nurses.

What they give us is enormously valuable information on how an adverse event or a side effect affects their lives and that of their families. That information is woven into an assessment process including our patient clinical record database, the CPRD. So, patients' information is vital. Just to perhaps give you an example, looking back to 2018, out of 74 new signals, 16 of those were triggered by a patient and 30 more, and that's over half altogether, had valuable information from patients. So, it is a patient's scheme, it is their hotline to us. I think the other point to emphasise before we talk about the limitations that we're going on to is that patients have driven the evolution, the journey of Yellow Card.

They have helped us design the electronic reporting and the app, and they're using it more than the health professionals do, in some ways leaving health professionals behind in the way that they're helping us to move forward. We do look at the link between our app and the NHS app as a key development to bring this system forward. Let's talk though

about the limitations. I'd like briefly to highlight three. The first is awareness of the scheme. If you don't know about it, you can't use it. The second is under-reporting, particularly by health professions who are aware of adverse incidents but don't tell us, and we don't know what we don't know. Thirdly, that it is essentially a reactive scheme. It's been called passive, but it's essentially reactive.

On awareness, we continually promote the scheme. We've just had, I think as one of your attendees told you, a massive social media campaign that's mirrored in other countries that has driven up reporting by 20 per cent. That's not a permanent increase. Education of healthcare professionals is supported by CPD points for modules of training in vigilance, and there are PSHE modules for school children now to start that process of education early on. On under-reporting, we feel this is a really serious issue and we have constantly worked with the professional regulators to make sure that their membership, the GMC, the GPHC, are in no doubt that learning from adverse incidents is part and parcel of a healthcare professional's duty.

I've already mentioned that linking our app with the NHS app should be in the pocket of every health professional, informing every aspect of their work. The third limitation of course is the reactive nature of this scheme. That may lead to some of the delays, although patients often report quicker than the health professional. We have to strengthen signals using other data sources and increasingly link between data sources, so our CPRD is linked with cancer registries for example, and other datasets, ONS, so that we can look at those trends in the context of healthcare and rapidly strengthen or refute a signal.

Much is going on, particularly with NHS Improvement to make sure that a safety issue that comes to us is rapidly available to all those who need to know about it. So, I've tried to highlight three main areas of limitations and the direction of travel. We're working closely with the CQC. Reporting is very variable across the UK and we want all the local audits to be as informed as possible about the vigilance that's going on in that locality and hence be able to strengthen. We have heard from the patient groups how important it is to them that we revisit the issue of mandatory reporting. We are already beginning to consider this and we'll be happy to talk to you more about what that might look like moving forward.

So really, in conclusion we know that healthcare is changing. How healthcare is delivered is changing. The patients' role in that is changing. The NHS plan talks about protection. We are a vital part of that preventative regime. We want the Yellow Card Scheme to take advantage

of all the advances. Personalised healthcare - we want to have a Yellow Card Biobank so that your genetic makeup can limit your risk. We need to use these tools, but will it be enough?

That is why we're looking at this opportunity of the review to really test our thinking, to look at our plans and priorities, and to look at the vision that Yellow Card will be the go-to system for patients that will be a responsive two-way system that they rely on, and patients deserve nothing less. We're looking forward to discussing that and to answering your questions. Thank you.

Julia Cumberlege: Excellent, thank you very much indeed. Before we go on to the other issues that are here, can I just say, I'm interested that you say the Yellow Card System should be mandatory. What does that mean? How do you mandate it?

June Raine: There would be various levels of mandatory. We are looking to strengthen, through the Care Quality Commission work, the audit nature of looking locally when inspections happen at how adverse events, side effects, are picked up and reported. That would have a very strong effect, if you like, on a level of mandatory. Ultimately, a legal requirement for a health professional to report, and we have looked at this in the past, may or may not be productive. Other countries have gone in that direction and it hasn't improved their ability to pick up signals.

Times change, and we would wish to look at, if you like, what levels of mandatory and whether organisational mandates as opposed to individual mandates would serve us best. Our plan would be, and is, to consult other stakeholders, our Yellow Card Centres in Scotland, and Wales, and Northern, and Midlands to see their views on this and to take the views of patients themselves. So, I hope that has given you an idea of the consideration that we're undertaking at the moment.

Julia Cumberlege: Yes, that's very interesting, thank you. Who would like to [take this]?

Cyril Chantler: We've met an awful lot of people across the country who have suffered terribly. What we have heard is how long it has taken for the things that have gone wrong to actually be acknowledged. I mean, you know more than pretty well anybody in the country about this in relation to valproate. The same thing in relation to surgical mesh. It has taken actually the patient groups working with parliament to actually bring this to the public's attention and led to our Review being set up. The system has failed those people, because it's taken so long. What can we do - it's

not blaming anybody, we're all doing our best, but what change can we make within the system?

There are a lot of people involved. You are one player, the GMC, the CQC, hospitals, GPs. What can we do as a system to actually make sure or reduce the risk of this happening in the future? Why was it necessary for the patient groups to draw this to our attention? Why didn't we spot it?

June Raine: Thank you, Sir Cyril. I think you've put your finger on the heart of the issue that we need to address. There are many aspects to bring to this discussion. The role of the MHRA as a scientific organisation, fact-based judgements, is to have, in order to inform those judgements as rapidly as possible, the best possible sources of evidence. If I could briefly speak from personal experience in charge of safety of medicines, it is that looking at the right data at the right time may inform prompt decisions most appropriately. There are other examples such as the analgesic co-proxamol, for example. So, Yellow Card isn't going to give us an answer on certain things.

What we need to think about is generating the right evidence. For example, the valproate issue was of neurodevelopmental delay and whether it was a persistent issue or not. It was the cornerstone of being able to focus on the proportionate risk management. In terms of the system working together, the key point is coordination and timeliness of appreciation of priorities and it has taken huge efforts, and I pay tribute to our former minister and others, to bring the relevant bodies together for an appreciation of the priority for action. Last but not least, you mentioned the women themselves whose work has brought us to this position.

We owe it to them to learn the lesson at system level about the necessity for coordination so that the SPC or [as our tool] the licence changes, the NICE changes, the CQC puts this as a priority, et cetera. If we chart the progress of this, it has been too much stepwise and not enough simultaneous appreciation and coordinated action.

Cyril Chantler: Can I specifically - I'm told - and again you may know more about this than I do. There's a system the FDA have called MAUDE and there's another one...

John Wilkinson: Yep.

Cyril Chantler: ...in relation to - what is it?

Valerie Brasse: FAERS.

Cyril Chantler: FAERS. So, it covers both of you. That involves patients very radically, doesn't it, very importantly. Should we have a similar system?

June Raine: I think at this moment all items are on the table.

John Wilkinson: Can I say, that's for devices.

Cyril Chantler: Yes, one is for medicines, one is for devices, so there's more than FAERS.

June Raine: Understanding human factors - if I might perhaps just finish. To understand human factors, which is at the heart of some of the other systems...

Cyril Chantler: Yeah.

June Raine: ...involvement of those affected but actually using tools such as the Behaviour and Insight Unit and studies into implementation science, it is an evolving area but I would say given the urgency of change that we look at all possible approaches.

Cyril Chantler: So, what do you think of MAUDE and FAERS? FAERS is for drugs.

June Raine: Yeah, I know, I'm just trying to decode it now. It's the...

Mick Foy: Federal...

Valerie Brasse: FDA adverse effects.

June Raine: It is, yes. We - there are strengths and limitations, but I think the ultimate change will happen when we are better at understanding what influences human behaviours.

Cyril Chantler: Do we have anything to learn from that system?

June Raine: Yes.

Cyril Chantler: Do you have anything to learn?

John Wilkinson: I think we do. It's an interesting issue. In the context of devices, we are frequently disappointed that we can't disclose information because of the nature of the legislation. When we were working on and negotiating [... in] Europe the new European legislation we were pushing very hard for much greater transparency in this area. We didn't get what we wanted, but the consequence of that is we're now working very hard on a voluntary scheme which sits outside the legislation. That may help to push the system over the edge in...

[Over speaking]

Cyril Chantler: Where does the new patient safety incident reporting system come into this?

Mike Foy: PSIMS.

John Wilkinson: PSIMS.

June Raine: This is the PSIMS development with NHS Improvement.

Cyril Chantler: Yes, you're working with them...

June Raine: Yes.

Cyril Chantler: ...with this too, aren't you?

John Wilkinson: I think PSIMS is absolutely critical, because at the moment clinicians, members of the public, find that there's an array of potential places that you can report to. I think actually simplifying reporting, both from a technology perspective and a route for communication, needs to happen for everybody's benefit. So, I think there's a consolidation. That's what we're working on with NHS Improvement to try and see...

Cyril Chantler: So, who is the leader of this? I mean, I sort of feel when everyone's involved, finding who is involved, who is in charge - is that NHS Improvement?

John Wilkinson: On PSIMS it's NHS Improvement, yeah.

Cyril Chantler: PSIMS. So, you're working with them...

John Wilkinson: Yep.

Cyril Chantler: ...in that area, along with others.

June Raine: It's a very close collaboration.

[Over speaking]

Mike Foy: Yeah. We're meeting regularly with NHS Improvement and other stakeholders who will benefit from PSIMS. It's about to go into beta testing. We're part of that. The historical difference between the NRLS system which is the current system there and the Adverse Drug Reaction Reporting System or the Device Reporting System is the form that is filled in isn't compatible with our forms so we've been working very closely

with them. So, what comes from PSIMS in the future can go from database to database and that will benefit everybody.

Cyril Chantler: Going back to the point that it is the patients who brought this to our attention. It's not the National Health Service, it's not me, I'm a doctor, it is the patients and parliament. I think that means we've all got to ask ourselves some pretty searching questions such as why did we not know about it?

June Raine: Perhaps to look back a little, clearly evidence accrues over time. There are - in the three issues you're looking at, different aspects that are pertinent. You've mentioned valproate, Sir Cyril, and that's a very important example of trying to look at benefit and risk. We know it's a lifesaving medicine. We would never wish to restrict access and I think - and I've mentioned it before in your presence that if our risk minimisation continues to fail some patients, and they are telling us how well they think it's working, we need to go further.

So, in a sense we are learning through this issue how patients input onto what level of risk minimisation is acceptable. That's truly informing the system for the future. They've been our eyes and ears on this. Rather less than the healthcare professionals involved, who are seemingly reluctant in some cases to embrace the challenge of managing these risks.

Julia Cumberlege: Can I ask you, you've spoken about the involvement of patients and it seems to me this has been fairly recent. I mean, in the last decade, last five years. How long have you actually involved patients in face-to-face?

June Raine: Face-to-face. Perhaps start with the Yellow Card Scheme, because we realised in the early 2000s how much society was changing and how patients had much more empowerment over their treatments and conditions. We introduced a review at that time, an independent review led by Jeremy Metters and introduced patient reporting from 2005. As you've seen from my description earlier, patients have been the avid reporters. They've taken up opportunities - the electronic world they've made their own - and now we're seeing more signals proportionately either triggered or informed by patients. The issues around a specific safety matter have been something we look at, depending on the aspect.

So, it may be trying to understand first of all what a patient or a family think is the appropriate response to their issue. I could mention perhaps the drug Propecia where we've looked at updating our product information with patients' and families' involvement. That met their need, whereas with something like valproate it's much more complex in terms

of balancing access and proportionate risk management. So, in a nutshell it's to try to look at the patients' perspective and to weave that into whatever discussion or decision-making process. When we looked very closely at antidepressants it was patients who judged that one particular antidepressant had an unacceptable cardiac risk, and we acted on that.

So, it's about the contextual nature and what the patient perspective is, that we aimed to do, but with, if you like, many thousands of medicines on the market and harms, we need to prioritise and devote the time. We have an engagement strategy that seeks to look at what should trigger a special network, as we have with valproate, or what should be simply an ad hoc fairly focussed discussion that perhaps will lead to an action that the families or others think is the right one.

Julia Cumberlege: So, where does mesh fit into that in terms of priority, in terms of the work you're doing?

June Raine: I need to turn to my...

John Wilkinson: Yes. I mean, I think we get very few reports generally from patients on medical devices. If you like, the portal has been open for a very long time, but people find it difficult to address it.

Julia Cumberlege: The portal being the Yellow Card?

John Wilkinson: No, devices was incorporated - we always had a reporting portal for devices. It was merged with Yellow Card back in 2014...

Julia Cumberlege: Right.

John Wilkinson: ...on the basis that we thought a single approach would more likely attract people to it. I think there's more complacency with devices' perhaps, than aspects of medicine because the surgical procedure and the outcomes are a slightly complex cocktail of inputs. You know, the state of the patient, the surgical procedure, the process, the rehab, a whole raft of very complex issues. So, the patient may not necessarily easily associate the problems they are having with any device that they may or may not know they've had. I mean, in the future hopefully they will all know that they've had devices implanted but historically that would not necessarily have been the case.

I think in devices we would like more reports from patients, but we have to see how we can elicit that and ensure that patients have the information to report. Getting a report about something fairly generic about a surgical procedure where we don't know what devices were used

or what the procedure was don't help us very much. Good information that says, you've got device X and it was implanted in procedure Y gives us something to chew on. So, I think the devices area is more complex but the lessons I think are exactly the same. Patients' voices on outcomes need to be understood. It's interesting looking at the work of areas where we have registries- implant registers for orthopaedic implants -

over the last few years they've increasingly moved to the use of patient-reported outcome measures. Historically you would say, this is a success or a failure on the basis of a set of, if you like, mechanical results. Does the hip work? Does the knee work? That may be okay for the surgeon who can say, yes, I've successfully transacted the exercise but the patient may have a very different view of that procedure and I think that's where patient-reported information adds colour and it will allow us to engage with these issues in a much more transparent way, and a much more effective way. That's relatively recent coming to the table.

Simon Whale: Can I just add something to that?

Julia Cumberlege: Yeah.

Simon Whale: So, the many people we've spoken to about mesh who've suffered as the result of a mesh implant, in a lot of cases what they've said to us is that as far as the surgeon was concerned, the implanting surgeon, there has been a success because it has cured incontinence or it has resolved a prolapse or whatever.

John Wilkinson: Yep.

Simon Whale: It's left the woman, and it's usually a woman, in significant pain and with symptoms of a completely different nature from the original one. So, to your point you've got a situation where as far as the surgeon is concerned, and as far as the data capture is concerned, there's a success. As far as the woman is concerned, her life is ruined.

John Wilkinson: Yeah. I think that is undoubtedly the case in some cases, although I would argue that if patients are suffering the way these patients clearly have, and I've met several of them, then the system needs to respond to that regardless of what the data says in terms of the statistical success rate of a procedure or otherwise. So, I would concur with you.

Simon Whale: The other thing that that they say to us, and I think it's a genuine feeling on their part, is they use the phrase guinea pigs. It perhaps comes back to the point that Dr Raine mentioned earlier about how the system learns, and how - learns about this minimisation and risk threshold. In effect, the

system is learning from people who are going through pain. Pain that wasn't anticipated, that they didn't know they were going to have to suffer, and in that sense was avoidable as well.

John Wilkinson: I think to an extent that is an inevitable result of innovation in medical practice. There will be unexpected outcomes. Most of our efforts have been - and the new legislation is really driving towards trying to improve, particularly in the devices area, risk management around that so that actually you get very early signals if the product, procedure, and they're all entangled with each other, isn't performing as it should do.

Simon Whale: So, in the case of mesh, what do you think went wrong because as far as [unclear] no one I think has got an exact number of people who've been affected. It would appear that we're talking about a very sizeable cohort of people, overwhelmingly women, who've been affected by a mesh that's gone wrong. Presumably you wouldn't say that that's an acceptable price to pay for innovation.

John Wilkinson: No, I wouldn't. I don't think I was alluding to that, really. What I would say is that inevitably there is risk associated with change and innovation and moving forward. That - the trick for us, and everybody concerned, is managing that risk. In managing that risk, we have a significant role in terms of what the manufacturers do and don't do. Equally, the clinical community and NICE also play a role because they have a role in establishing whether a new procedure - the risk profile of a new procedure - is worth exploring or otherwise. They're quite active in that space.

I think we - this is a particular concern for me, that we are - and I think if we'd had a stronger patient voice earlier then probably all of the parties, not just us, would have perhaps intervened in the serial ways that have been recommended by a number of looks at the problem over the years in a more concerted manner.

Julia Cumberlege: I think that patients would say that they've been trying to draw your attention to this actually for many years. It's taken quite a long time for MHRA to actually grab this issue. What I would like to ask you is that you mentioned the manufacturers.

John Wilkinson: Yes.

Julia Cumberlege: Can I ask you what you've done in terms of this particular device that's being inserted into women and causing damage? What have you done with your relationship with the manufacturers?

John Wilkinson: Over the - I think our evidence probably lays a lot of this out. There has been a series of activities with specific manufacturers asking them to review their own evidence, which they have to continuously review. Also, look at the instructions for use so that they are continuously honing those. There has been a series of activities designed by ourselves to handle other regulators to try and ensure that manufacturers are fulfilling their responsibilities. The legislation that we've pushed very hard for will have a significant impact. All of the products on the market with the new legislation will have to be recertified. So, all of - there is no grandfathering, as often happens with new legislation.

Everything has to be re-looked at and the evidence then pass the acid test of the new legislation. So, I think there are serial activities which in the long run will play out and sort this out. The products themselves also have been iterating and evolving across the life of their use as well. So, I think there's constant vigilance in terms of what's actually going on and we've been extolling patients and manufacturers to keep us informed and we've been forcing information and sharing information with peers around Europe and indeed across the world in terms of what's actually happening here.

Julia Cumberlege: So, the manufacturers you say have their own evidence.

John Wilkinson: Yes.

Julia Cumberlege: They are sharing that with you.

John Wilkinson: Yes.

Julia Cumberlege: So, what does that evidence show?

John Wilkinson: Well, the evidence that we've seen broadly speaking is consistent with these products remaining on the market for the purposes for which they're described. You have to bear in mind that the array of applications of these products is quite wide, so given good clinical governance - and I think this is where the other review is looking at the use of these things - in an appropriate use, used according to instructions, we have seen no clear evidence which indicates that these products should be taken off the market per se. There are clinical indications for which there are often applications where there are no better use of...

Cyril Chantler: [Unclear] If there is a product which you have anxieties about, you talk to the manufacturers but you're not allowed by law to talk to the patients, is that right?

John Wilkinson: No, we can - I can. We can talk to the patients, we can talk to any stakeholders. There are no constraints on us.

Cyril Chantler: When I asked that question [unclear].

Sonia Macleod: I think one of the issues is the manufacturer reports into [unclear].

John Wilkinson: Yes.

Sonia Macleod: What's the position on those in terms of disclosing those?

John Wilkinson: That's I think the issue I was alluding to earlier, which is the legislation precludes us from releasing information about adverse incidents and dialogue with manufacturers specifically.

Cyril Chantler: So, when there is an anxiety about a product and you talk to the manufacturer, you can't share that with patients?

John Wilkinson: I think in generic terms if we have a concern, we can share that with patients. We can't with specific manufacturers - introduce issues of our dialogue with specific manufacturers under the current legislation.

Simon Whale: Do you want to?

John Wilkinson: I think there are merits. There are situations where there is merit in full disclosure, real time. There are other situations where we - our job is very specifically to evaluate the information that we have dispassionately without distractions from the outside. I think if you look at GMC's investigation rules or the way the HSIB operates, I think essentially, we have to operate the same way and we have to evaluate as dispassionately as we can the information that we get. That would include information from patients and other parties. That's part of the, in the round, work that we have to do before we would take regulatory action.

Valerie Brasse: Can I come back just to the Yellow Card reporting in relation to medical devices? As Baroness Cumberlege said, the women I know that we've talking to have been very keen to get this information across. Given what we know about the outcomes of some of these procedures for some women, that has been horrendous...

John Wilkinson: Yes.

Valerie Brasse: ...and it has been over a very long period of time. The Yellow Card as it currently exists, is that a suitable vehicle for that particular set of outcome problems? We are talking about someone who would not necessarily know that the operation she had today in a year, two years, six

years, is going to cause the problems that she has. You said, they don't tell us about the particular device put in them. Chances are they won't know and no one tells them at the time...

John Wilkinson: They won't know.

Valerie Brasse: So, it's not their fault, really. Sometime down the line, they've got this problem. Then they're in desperate pain and they go and see a range of people. They want to be able to report that. Some of these adverse events get worse with time and they want to come back and keep on adding information to the Yellow Card. Then they want to get the device out and they go to another surgeon to take that out. What we understand is that we can't link the surgeon's removal procedure, so that's another outcome for that patient, with the original inserting procedure via the one Yellow Card report.

John Wilkinson: Yeah.

Valerie Brasse: Now, I don't know whether I've got that right, that's what we're being told. So, I've asked myself the question, is this vehicle actually working for that particular mesh intervention? Does it work?

John Wilkinson: I think Yellow Card has its limitations in the context of surgical interventions which may or may not have devices involved in them. I think we have our responsibilities which are defined because we are product regulators. I think therein lies one of the issues. That's why the PSIMS integration approach I think will help, because if you have one report which goes to serial organisations, and those serial organisations work together to improve the performance of the system in the context of any intervention or any aspect of safety, then you're likely to get a better outcome than individual organisations trying to do their bit.

Cyril Chantler: Why has it taken so long? I mean, I remember service with a memory, Liam Donaldson, that's a decade ago. Why has it taken so long to set up a system where there's a central coordinating body that liaises with all of the people who have responsibilities in this area?

John Wilkinson: I don't think I can answer that question. June might have a better insight, she's been around longer than me in this particular space.

June Raine: Organisation with a memory, and in the US, to err is human. Well, we're really looking at errors. Things that go wrong. What was a step forward for us was bringing in error into the concept of an adverse reaction. So, that has actually given us the ability to move forward. In a sense it's

looking at how the framework in which we operate needs to be adaptable as things move forward.

Cyril Chantler: There was a National Patient Safety organisation.

June Raine: There was a National Patient Safety organisation and our role particularly was to support that work. You remember the boy that [unclear] into his spine to say there should be never events that should never happen, and that systems had to adapt. That's really where we are at the moment, working closely with the CQC about the kind of things that once recognised should never happen. In a sense I think what we've been hearing about with the mesh, and linking people's reports, that is possible and it's one of the advantages of bringing devices onto the Yellow Card platform which I think Mick might be able to help with how we would link things. In terms of overall...

Valerie Brasse: Sorry, is it being done now? Are you saying it can't be done at the moment?

June Raine: Oh, it can. Yes, we can link - if someone comes back with a follow up on a previous report...

Mick Foy: Oh yes.

June Raine: ...it will all be linked.

Mick Foy: Yeah. So, it's fairly routine practice in medicines that an initial report will come in which will describe the adverse reaction. When we get that we always respond to the reporter saying if you have any further information, please quote the reference number and tell us. Sometimes you can get a series of what we call follow-up cases that we merge into a single master case. That's usual practice.

Cyril Chantler: Do you link it by the NHS number so that...

Mick Foy: No...

Cyril Chantler: ...it's separate reports [unclear] linked?

Mick Foy: ...because people will quite often be anonymised, and the NHS number would be an identifier. So, we link it by an ADR reference number. We do ask healthcare professional reporters to provide a unique ID which is not the NHS number for their reference so they can put it back into the electronic health records.

Cyril Chantler: Why don't you use the NHS number?

Mick Foy: We took advice on that in I think around 2000, and we were advised by the Information Commissioners Office that that would be an identifier and we should not ask for it.

Cyril Chantler: If you ask the patient – we've been here before, haven't we

[Laughter]

Cyril Chantler: If you ask the patient though you can do it, can't you?

Mick Foy: Well, if the patient is the reporter, we've got their full details.

Cyril Chantler: Yes, but do you have a system for linking an initial report from another report coming in six years later if they don't refer to it? How do you link those? So, that was the question.

Mick Foy: Yeah, we do have algorithms that run across our database every week that look at all of our reports for common features. Somebody actually reviews those cases to see if they are duplicates, because quite often...

Cyril Chantler: So, if I had an operation in John O'Groats 10 years ago and then I have a complication in Land's End 10 years later and I put in a separate report, you will automatically link those two events even if I haven't told you about them?

Mick Foy: I would hope that you provided us back with the number, but 10 years later that would be quite rare to be able to remember the number.

Cyril Chantler: If you had the NHS number...

Mick Foy: If you are the reporter...

Cyril Chantler: Some of us were involved in introducing the NHS number. It was in order to achieve that.

Mick Foy: Of course, the patient is...

Valerie Brasse: I do think also the public knows their NHS number. The old system, I'm not sure that they would know that you'd have to look back 10 years ago at the number you gave them. That would be a difficulty.

Mick Foy: It would be, but there are other factors that our algorithms search for to identify duplicate cases such as the age, geography, the drug, the reaction, et cetera. All of these parameters produce a report and as I say, somebody looks down these possible duplicates and makes a decision.

Cyril Chantler: I'm not sure that duplicates - these are the same.

Mick Foy: This would be a follow up case, yes.

Cyril Chantler: It's a follow up, and this is what women have told us.

Julia Cumberlege: I'm very conscious that we haven't actually spoken to you yet. I'm just wondering, Dr Lynn, whether there are any issues you'd like to bring to our attention concerning the Drug Safety Research Unit.

Liz Lynn: I'm not sure you'd call them issues. I realised I haven't actually introduced the Drug Safety Research Unit at all, so could I do that briefly?

Julia Cumberlege: I beg your pardon, yes.

Liz Lynn: Well, that's probably my fault. I think I missed my opportunity. So, the DSRU is an independent academic unit and registered medical charity which was established in 1981. Its aim is to protect patients from unwanted adverse effects of medicines in clinical use. We've been hearing a lot about the Yellow Card System which has been mentioned as a spontaneous reporting system. The bulk of the studies we do use event monitoring methods, and those methods are active systems, so we prompt the prescriber to tell us everything and anything that's happened to their patient following the prescription of a particular medicine.

Then we collate the data from reports from maybe 10,000 prescribers. Then our team of research fellows will analyse the data and they will determine whether or not there is likely to be a link between the new events seen and the drug. So, we're not asking the prescriber or the patient to suspect that there's a link. So, that's the key difference.

Simon Whale: So, how does a drug become a medicine of interest for you?

Liz Lynn: In a number of ways. Sometimes we are approached by the pharmaceutical company. Sometimes we approach them. So we do a continuous process of horizon scanning so we are aware of which drugs are coming through development and clinical trials. We're typically looking for drugs that are going to be widely used such as anti-diabetics, antiepileptics, antipsychotics, anti-obesity drugs, that sort of thing. As I say, so we will get the idea that we may wish to study a particular drug.

We will talk to the company and - I should say that the studies we conduct are satisfying a regulatory requirement for the company, so the company typically would have to conduct this sort of post-authorisation safety study. We are one of the organisations in the UK that can conduct them.

Valerie Brasse: Do they fund the work you do?

Liz Lynn: Yes.

Valerie Brasse: So, the studies are funded by the (MAHSE)?

Liz Lynn: Yes, but we - the DSRU is vigorously impartial and independent. We don't endorse any drugs. Typically, we tend to be the sponsor of a study but the company is the funder. We like to make that distinction. So, we would write the protocol. We would decide which questions we're asking. Obviously, we have to answer any questions a regulator has asked to be answered, but we will design the study. We analyse the data, we will report exactly what we find whether or not it's good for the drug or bad for the drug. We write the study reports, we send them to the company and we also send them to the MHRA and the European Medicines Agency as well.

Valerie Brasse: So, when you're doing this it is because the regulator has asked the manufacturer to run a certain set of tests, so they approach you for the study and say, would you do this as part of this?

Liz Lynn: Effectively, yes.

Julia Cumberlege: So, would you have been involved at all with valproate or Primodos?

Liz Lynn: No. We haven't, I'm afraid. We have not studied any of these three issues.

Julia Cumberlege: Right.

Simon Whale: Would you consider - in the case of valproate, for example where you've got the introduction of the pregnancy prevention programme, is that something that you're able to consider, or do you have to wait for someone to approach you?

Liz Lynn: No, we can approach the company. That would count as a risk minimisation study. We certainly do conduct that sort of study.

Simon Whale: Is it your intention to?

Liz Lynn: It's not at the moment, no, but we certainly wouldn't rule it out.

Julia Cumberlege: So, then we could - can I go back to the words that we've heard from the MHRA? Could I just ask you about registries? I think you mentioned that, Dr Raine, at the beginning. Could you tell us how you think they would operate, what they would be? Can you explain it a bit to us, because I think you felt there was merit in it.

June Raine: Absolutely, and thank you for coming back to this. The effectiveness of registries which capture a longitudinal, greater level of detail in

someone's health journey has been invaluable, particularly when a new class of drugs has been introduced such as the biologics, or it's a patient fraternity such as the haemophilia children where monitoring over a period of time for a specific issue such as antibodies in that case is going to be really helpful in terms of future therapeutic advice. So, these are, if you like, health professional run but now we're looking particularly at how the regulator can make good decisions from registry data.

So, what we're doing, and the European Medicines Agency has been in the lead here, is looking to see, are the existing registries delivering suitable data and can we look at a common operating model whereby we get the evidence that we need in a timely way? You might have heard about some of the very important new medicines for leukaemia, the CAR-T cells where the European blood and marrow transplant databases will be the ones that help to monitor safety, and do it, as John said real time, and it's as close to real time as may be. So, that's the vision that we have. When you come to a specific product, you're not so much looking to the existing health professionals who've looked at a therapeutic area, and key in our minds of course are the antiepileptics.

So, over the years, health professionals have really been able to deliver very important evidence across the class. We're looking at valproate, specifically are the risk-management principles being followed? If there are children affected, what is their future health and life expectation? So, that will be an exceptional registry which is focussed on this drug in this population, women of childbearing potential who are treated with this drug.

Julia Cumberlege: So, you would set up the registry and you would fund it?

June Raine: We're bringing together all interested stakeholders. We've found that a key success factor is building on the professional expertise, the outreach, and if you like the passion of health professionals to do the best they can. So, our stakeholder group includes existing health professionals who've worked in the area of epilepsy and can help us hit the ground running, as it were. We've already had one meeting and we're looking to the next. We've raised the very important question of funding. We know from our discussions with the women and their families that industry funding is maybe not the way that they would see this working optimally, and therefore we are ready to explore other public health funds.

I know from my previous discussions particularly with legal advice that the trading fund to which the MHRA operates can make investment into public health in relation to safety in medicines. So, the options are there.

Until we have an agreed protocol that will answer the questions that need to be answered in a timely way, we will then be able to look at the funding options that meet the needs and concerns of all the stakeholders, the families and the women included.

Sonia Macleod: Can I just check something? When you said, there's a registry of longitudinal follow-up to people who have already been born with valproate exposure, are we talking right back from people born from the 1970s onwards? Are you looking at a limited cohort?

June Raine: The registry would be for women of childbearing potential, or girls, who were initiated on valproate, but our initial stakeholder meeting said, do not forget that the important aspects include the follow up of any children. So, this is for women of childbearing potential initiated.

Sonia Macleod: So, it's prospective not retrospective.

June Raine: Yes, prospective. Let's not also forget, and it might have been drawn to your attention I'm sure, that when a woman is switched to another antiepileptic there could be consequences that we also need to watch very, very carefully indeed. So, we're at the design stage, I have a protocol in my bag. I won't go into detail now but you're more than welcome - if the Review would like to have sight of any of the documentation, we're more than glad to provide it to you.

I hope I stressed at the beginning this is the time to test our plans and priorities, to get it right. Normally when we're looking at an obligation on one drug with a brand leader, we will look to the manufacturer to make full funding available. We are very sensitive in this situation to the views of the women and families.

Sonia Macleod: If you're focussing solely on valproate, presumably that will be excluding the other antiepileptics, so how - as you say, when you have a woman who's on one who has then transitioned onto a different antiepileptic, how would that work?

June Raine: We will need to make sure that working with our stakeholders, including the health professionals involved, that if a woman switches and there are any particular consequences, we have a plan to follow that up too. That's why it's terribly important that particularly with Jim Morrow and others in Northern Ireland who have a lot of experience in this area we get the scope right and then we have the scientific - the parameters that we need to follow. We have had such good value from other registries such as the biologics but we do know that we need in this case to focus on what will answer the questions that we and the women want to have answers to.

Cyril Chantler: You need the consent of the women concerned to set up a registry then?

June Raine: Presumably that will be a key - and they will be key to the governance also, because we will be wanting to capture every woman or girl who was started.

Cyril Chantler: Yes, so you will be building on Dr Morrow's registry that already exists.

June Raine: Very much so. He's been very active in our stakeholder group.

Cyril Chantler: Okay.

Julia Cumberlege: Any other questions?

Valerie Brasse: I've just got two others, if I may. So, one comes back to devices and about when things have to be reported to you.

John Wilkinson: Yes.

Valerie Brasse: At the moment the technical information would say, we would expect potentially inadequate outcomes or something in the range of this percentage. If then that percentage of incidents seemed to be much higher than was originally reported in the technical information that comes with the device, presumably they have to come back and report that to you. The question I suppose I'm asking is, how often is that the case? In other words, the device goes out with, we think there will be an adverse incident this proportion of times. Actually, the feedback seems to be much more. That's being reported back to you. So, I just wonder how often anyone reports that that is the situation and you have to change the technical information and so on and so forth.

John Wilkinson: Yeah. I'm not sure I can - because there are 600,000 products on the market, I'm not sure I can give you a definitive.

Valerie Brasse: Just roughly.

John Wilkinson: There are serial examples where - manufacturers are obliged to trend report. So, if there's an expectation that they will get three per cent of failures and that carries on, that's fine. In a way, it's not fine, because failure is not a good idea, but it is running at the expected rate. So their obligation is if there's a discontinuity in that trend and it steps up, they have to report it to us. That could be indicative of a number of things. Often, it's a manufacturing issue which may be transient and go away. Sometimes it's more sinister than that and requires more substantial [unclear].

Valerie Brasse: Are you seeing more of that, is what I'm trying to get at, looking over a period of time has the proportion of that happens and there's discontinuity...

[Over speaking]

John Wilkinson: I think if you look at the - there are various drivers for all of the reporting that we get. The sheer penetration, increased penetration of complex medical devices, especially implantables over the last 10 years is huge so that's a driver in itself, and the number of eligible patients. The manufacturers have certainly as a result of significant regulatory action become much better at reporting it as well and fulfilling their obligations. So, I think there are a number of drivers. A lot of it is activity based, but some of it - so, I don't think I would be able to draw any conclusions about that.

[Over speaking]

John Wilkinson: There are more problems happening in aggregate with devices than there were 10 years ago. It would be a very difficult statement to make, certainly...

Valerie Brasse: Maybe we can explore that a little bit outside of this.

John Wilkinson: Yes, I'd be very happy to do that, yeah.

Valerie Brasse: Can I just ask one more question of you, Dr Lynn? So, when you do one of these studies, your [unclear] do you rely on the practitioner reporting the adverse drug reaction to [unclear]?

Liz Lynn: No, not at all. We ask the prescriber to tell us all events that have happened to the patients. Sometimes we ask particular targeting questions about particular events that we're interested in that may have been highlighted in clinical trials and we want to know more about. The general aim of event monitoring is to ask about everything. So, whether it's a broken arm or depression or sleeplessness, or anything even if it apparently has no link and then we collate all that data. So, in theory we should be able to detect even very rare side effects.

Simon Whale: Can I just ask a follow up question about spontaneous reporting? So, I think you mentioned, Dr Raine, at the beginning that patient reporting has overtaken reporting by clinicians. Is that right?

June Raine: By the GPs as a group. GPs were formerly if you like our cornerstone, our backbone of our system. Now as of the last year we've had more reports from patients. So, it's as a single group, all nurses as a single group, all

pharmacists as a single group. Overall health professionals if you add them all up will be more. There were about 8,000 reports from patients last year.

Simon Whale: Has the rate of reporting by health professionals declined?

June Raine: We constantly monitor this and look to see how - if we can influence particular groups. Mick will have the latest data, I'm sure. We do look year on year and our Yellow Card Centres look at the local reporting by various health professional groups. We are constantly concerned that GPs should be reporting, should be our main eyes and ears.

Simon Whale: In the interests of time would it be possible to send us that data?

June Raine: Give you that number? Yes, absolutely.

John Wilkinson: Yep.

Simon Whale: I think it's really quite important from our point of view to understand the rate of reporting by health professionals across the piece.

Mick Foy: I can give you the highlights. Over the last 10 years reporting has doubled. Largely that has been down to the electronic reporting system that has been introduced, and the introduction of patient reporting. 93 per cent of their reports come electronically to us. As June said earlier, they've embraced that. No single group has declined over that period of time. Everyone is reporting more year on year. The patients have gone four-fold in that since patient reporting was introduced.

Simon Whale: Yeah, I think if you could send us that...

Mick Foy: I'll send you that.

Simon Whale: ...that would be very helpful.

John Wilkinson: The picture might be slightly different for medical devices, so I think we'll give you a consolidated view.

Julia Cumberlege: As I've done with other people who've come to give us oral evidence can I just ask you, is there one single thing that you really want us to take on board? As Simon said, we're very open to more suggestions if you want to write to us about holes we've left and you want to fill and all the rest of it.

Simon Whale: We are meeting again [unclear].

John Wilkinson: We are.

Julia Cumberlege: We could fill those then, probably. Yes, but is there anything...

June Raine: In terms of Yellow Card, I would really like the Review to know that is an essential component although it's not the only one. It is our hotline and there have been occasions where a report has been extremely important and acted on immediately. So, in the past, one has thought perhaps large databases and artificial intelligence would replace the need, but the health professional or patient who tells us their suspicion or their concern promptly and knows it will be acted on is a vital component of patient safety.

Cyril Chantler: Could you send us one or two examples?

June Raine: Yes certainly, very happy to. Of a rapid and...

Cyril Chantler: Yeah. I mean, [unclear].

June Raine: Yes, absolutely. Well, asthma in a child over 12.

Cyril Chantler: [Unclear].

John Wilkinson: I'd like to endorse what June said in terms of the importance of a portal for spontaneous reporting which is absolutely essential. I would like to come back to you, and I will do with more information on registries in a medical device context because I think it's slightly different. A lot of the principle is the same but I'll come back with some more detail in that area [if that would be all right].

Simon Whale: Thank you.

Mick Foy: I would endorse what June said. I think the Yellow Card Scheme, we could do more with raising awareness of it so people know it exists. I think the key to future success is how we integrate it into the systems that people use day by day so that they don't have to find Yellow Card, that they can report from the tools that they're already using. That integration is part of our plans.

Julia Cumberlege: Thank you, and Dr Lynn?

Liz Lynn: Just briefly, the Drug Safety Research Unit has conducted studies on the reasons why drugs have been withdrawn for various time periods, most recently July 2012 to December 2016. Our finding for that most recent study was that out of the 18 drugs that have been withdrawn from use, 17 of them were due to spontaneous reports and published case reports.

Julia Cumberlege: That's very encouraging.

Liz Lynn: That shows the value.

Simon Whale: Can you send us that, please?

Liz Lynn: Yes, certainly.

Julia Cumberlege: Thank you so much. Thank you for coming. We look forward to seeing you again.

Multiple speakers: Thank you.

END OF TRANSCRIPT

Session 4: General Medical Council (GMC), General Pharmaceutical Council (GPhC)

START OF TRANSCRIPT

Julia Cumberlege: So, could I ask you to introduce yourselves? Just say your name, position, the organisation, and so on, so that other people looking at the recordings know who you are. Also, I would like to know if any of you have a conflict of interest, we need to know that as well.

So, shall we start from this end? Mr Rudkin.

Duncan Rudkin: Thank you. My name is Duncan Rudkin. I am the Chief Executive of the General Pharmaceutical Council. We are the statutory independent regulator for the pharmacy profession and retail pharmacy in Great Britain.

Julia Cumberlege: Right, thank you very much.

Phil Martin: I'm Phil Martin. I'm the Assistant Director for Education and Policy at the General Medical Council. So, my brief covers education matters relating to doctors and the GMC's responsibilities in those.

Julia Cumberlege: Thank you very much.

John Smyth: My name is John Smyth. I'm the Assistant Director for the Case Examiner team in the...

Julia Cumberlege: Sorry, can you speak up a bit?

John Smyth: Sorry. Excuse me. I'm John Smyth. I'm the Assistant Director for Fitness to Practise, with responsibility for the Case Examiner team. My team makes decisions at the end of initial fitness to practice investigations. I should say my background is as a General Practitioner. I don't have any conflict of interest that I am aware of.

Julia Cumberlege: Thank you very much indeed. So, what we're doing this afternoon is to focus on adverse events and the complaint handling of those events. So, I'd like to start off just by asking the GMC - and you must decide who is going to answer this - in your evidence that you've sent us, and thank you very much for that, you are saying that practitioners must report concerns relating to adverse events, or prescribing patterns in the case of the pharmaceutical regulator. I just wondered if you could tell us whether you feel that this requirement should really become mandatory [unclear], and how that would work.

One of the suggestions we've been given is that, in order to get it mandated, it would form part of the appraisal process of clinicians. So, perhaps you've got some thoughts on that.

John Smyth: It's certainly in the guidance already that they're expected to report adverse incidents in relation to prescribing. Making it mandatory, I suppose, is one option. The question for me in terms of appraisal would be how that would be reported. Would you expect the doctors to report it themselves, which they are expected to do anyway? How would you know if they had reported all incidents that they'd been made aware of?

Similarly, I suppose, with the current system, it relies on doctors to report all incidents that they're aware of. The suggestion might be that not all incidents are actually reported currently.

Julia Cumberlege: So, this would come to the Fitness to Practise Committee, would it? Or...

John Smyth: Just to emphasise, I think, in terms of our own remit, obviously our interest is in the fitness to practise of individual doctors. We take action in respect of serious or recurrent concerns about doctors. A one-off incident in relation to a doctor may not necessarily result in action being taken, or in fact in it meeting the threshold for us to open an investigation, because an individual incident may not raise a fitness to practise concern about that doctor.

So, I think it would depend on the context of the incidents and what the reporting ought to have been, what the consequences that were brought to the doctor's attention, as to whether that would ever reach that threshold.

Julia Cumberlege: So, something like the Review into Dr Paterson and all that was happening, is that something the GMC could have done? Or did it require a bishop to chair it and to do the Review?

John Smyth: I can't really speak knowledgeably about the Paterson Inquiry. That's not something I'm directly involved in.

Julia Cumberlege: Sorry, what?

John Smyth: I can't really speak knowledgeably...

Julia Cumberlege: No.

John Smyth: ...about the Paterson Inquiry.

Julia Cumberlege: No.

John Smyth: That's not something I'm directly involved in.

Julia Cumberlege: No. I was just trying to test out how far the GMC can take up issues and how much you feel you have to refer on.

John Smyth: We do take up issues of - that are brought to our attention or that we become aware of through either patient complaints or concerns of a recurrent nature. But it's not necessarily the function of my team to take those things forward so I don't really feel I can comment knowledgeably on that. I don't know whether you'd like to say anything about that?

Phil Martin: I don't think there's much additionally to say. Obviously, I don't particularly want to talk about the case, but it sounds as though this relates to the thresholds that you're referring to. I think there will always be a debate about the exact threshold, but certainly, what we try to do is get involved where we become aware of there being serious fitness to practise - or there being a suspicion of serious fitness to practise issues, rather than necessarily - and the judgement on the threshold for that is taken on a case-by-case basis.

Valerie Brasse: But isn't that one of the problems, really? I mean, here you are, you have the guidance which says doctors should be making up adverse event reports and they should be doing that consistently. I can hear that - you know, obviously, if it's one example that you found out that they didn't report, that would hardly go very far. But if you're wanting to make sure that the guidance around standards of practice for GPs and doctors is being followed, you have to have a way of testing that, don't you? Otherwise, the guidance really is without teeth.

So, this issue about whether it could be picked up on appraisal - so, would you expect a doctor, every time he's reported and made an adverse event report, to have recorded it somewhere so that whoever is appraising them would be able to see a record of these constant reports?

It's sort of slightly worrying, isn't it, that here it is, it's in the guidance, but we don't really know whether they're doing it and don't know how to follow that up?

John Smyth: Well, the guidance is there to inform doctors, obviously. It's there to guide them about what they should do in individual circumstances. But because it's in the guidance and, if they don't always follow the guidance, that doesn't necessarily reach that threshold for taking action on someone's registration, which is the blunt tool that we have to take action.

Obviously, what you're talking about is whether doctors should report every single incident of concern in relation to medication, side effects, unexpected effects. Yes, they should. Do they in practice? I don't know. Obviously, we are far removed from the clinical environment. The GMC isn't sitting looking over every individual doctor's shoulder when they're in the consulting room...

Valerie Brasse: For sure.

John Smyth: ...or surgery. So, there may be a gap in terms of what's reported and what we're made aware of.

Phil Martin: I think there are possibly two issues here, one of which is the way in which our guidance operates. It tries to reflect the fact that there are a variety of different cases and that we're not there on the frontline. So, we try and set principles so that people should. There is also the question of whether, if we were to change that to [being that they] are mandated to, firstly, whether that's within our gift to do, which I am afraid I am not an expert on the topic so I can't speak to, but the second of which is, if that were to happen, would that substantially change the...

Valeri Brasse: the outcome...

Phil Martin: ...extent to which people report?

Again, I think that that's much more likely to happen because of action taken by employers at a much closer level than it is as a result of the GMC's particular guidance of that. I think we've been reasonably clear that our expectation would be, in the event of an adverse event, that we would expect people to note and report it.

Valerie Brasse: So, you would be inclined to say you would be shifting responsibility from the individual to the organisation?

Phil Martin: I wouldn't say shifting responsibility. I'm thinking about the...

Valerie Brasse: Practicalities.

Phil Martin: ...practicality of how - of what, from the position that we sit in within the system, we can affect.

Sonia Macleod: So, would that be in a way similar to the duty of the candour that's effectively an organisational duty but applies to individuals within an organisation?

John Smyth: Well, it is an individual expectation as well for doctors.

Sonia Macleod: Yes, it is. Absolutely. But that's what I'm saying, would there be a parallel there? If you put adverse event reporting onto an organisational level?

John Smyth: I think that duty of candour exists anyway in respect of individual doctors and organisations. But can we say categorically, given our distance from clinical practice in terms of the actual day-to-day delivery of that, that...

Sonia Macleod: Does it work?

John Smyth: ...everybody is candid in every situation?

Sonia Macleod: Yeah.

John Smyth: I don't think we can say that.

Sonia Macleod: Okay.

Julia Cumberlege: Alright. Can I just ask the Pharmaceutical Council - can I ask you, we have been very concerned, and we've heard a lot from women who have given birth to children - as a consequence of valproate - they have been, obviously, epileptic women, and their offspring have been very seriously damaged. One of the things that we really have been trying very hard to do is to ensure that pregnant women are aware of the risks if they are suffering from epilepsy and they are still being prescribed and dispensed Epilim or one of the other drugs.

Can you tell me, where is your role in all of that as a council?

Duncan Rudkin: I think I would first of all want to say we very much share your concern that women and girls should receive the right advice and information, both in terms of conversations with prescribers and also pharmacy and

pharmacists have a key role to play as part of the safety chain at the point of supply. Making sure that the right information and guidance is provided. That appropriate, useful, sensitive, and thoughtful questions are asked to encourage women and girls to access the right information.

So, when we were contacted by the MHRA in the second half of last year about this and were asked to work with them and others on the topic, it was something that we felt was very important and that we should be very engaged with. So, I think there are a number of ways in which we are involved. One is in terms of the standards we set for pharmacy professionals, pharmacists and pharmacy technicians, which make very clear the importance of person-centred care as part of their professionalism with an

emphasis on, I think, dialogue, on making sure that patients have the right information. So, the setting of standards side of what we do, which is obviously directly relevant to this. But, like the GMC, we don't produce guidance on specific medicines, but we will from time to time - and this is an example where, because of the significant nature of the risk and public concern, we felt that, notwithstanding that it's not a topic on which we, as a body, have a role in relation to the medicine as such, it was important for us to use our communication channels to the profession and to the pharmacy sector to support messaging from the MHRA and others in relation to safety information.

So, we have done, and continue to do proactively, a number of messaging opportunities through our contacts with all pharmacists all the register, through emails, through our newsletter to them. Also, because we have - slightly differently from some of the other professional regulators, in relation to retail pharmacy, we also have the responsibility for setting standards for the owners of pharmacies and we inspect those pharmacies - the retail pharmacies.

We are also able, on the ground, to play a part, not in audit, which is not something we do, but in terms of using inspection as a tool to raise awareness and for us to ask questions. So, for example, we in the course of last year added into our routine for our inspectors a specific line of questioning, line of enquiry, around valproate as part of our assessment of whether the standards in relation to medication safety are being met in those pharmacies.

So, there are a number of things we can do, both in terms of standards for owners, standards for professionals and, very importantly, communications. I think with all of those - with all of these interventions,

if you like, it's a case of trying to find and use the right levers at the right moments, in the right way. There is always more than we can actually be thinking about doing in relation to that.

Valerie Brasse: Going down the inspection last year around compliance, presumably with the PPP, what did you find?

Duncan Rudkin: Well, we - because of the way our inspections work, and we're covering a very significant range of issues in a relatively short space of time within an inspection, we don't necessarily have very detailed data on compliance. It is a snapshot.

We're finding a mixed picture, I think is the honest answer. I think there is a high level of awareness of what should happen. There isn't necessarily always that confidence that it is happening. But I think the way in which - one of the ways in which we operate is through using inspection to ask questions and focus attention on issues. So, we're raising the profile of the issue within the profession and the sector as well.

We have some evidence that there are specific concerns about a number of cases. We've got a small number - single figures - of cases that we are at early stages of investigating, where there are specifics that are potentially subject to our due process, actionable in terms of the fitness to practise process.

That's a proportion, what would that be of the total that you looked at?

Duncan Rudkin: So, in the course of a year we did inspect probably around 4000 or 4500 pharmacies. The particular focus on valproate started during the course of the autumn of last year, so it is still relatively - for us, anyway - in relation to us specifically targeting that issue, relatively early.

Sonia Macleod: Have that handful of cases that you think might be actionable - did they all come from your inspections?

Duncan Rudkin: No.

Sonia Macleod: Or did they come from spontaneous reports? Where did they originate?

Duncan Rudkin: We've had a number of matters referred to us via the MHRA...

Sonia Macleod: Right, okay.

Duncan Rudkin: ...that originate through - with members of In-FACT.

Sonia Macleod: Okay.

Julia Cumberlege: Can I ask you - I should know this and I am afraid I don't, but with a community pharmacist, how much information does that person or the people working in that facility - how much information do they get from the GP? I mean would they get a register of women who are epileptic and who are of child-bearing age?

Duncan Rudkin: So, I don't believe that they would have a register. I think it is true to say that it is variable, that in the patient medication record, if that patient has used that pharmacy before - which wouldn't be unusual for a repeat prescription, obviously - then if there's a medication there in the pharmacy's record that is evidently an epilepsy medicine and the woman is of child-bearing age or might be, then the pharmacy is on notice, effectively, that there is an issue that they ought to be exploring. If valproate is - if a prescription involves valproate.

The pharmacies, generally speaking, in the community don't have full access to patient records. It is a patient safety issue, undoubtedly. There has been some progress made with access to the summary care record. There are, of course, then rules about how that's accessed in the pharmacy and the patient's consent is required for that on each occasion. So, there are a number of ways in which the pharmacy might be aware and the pharmacist might be aware that there is or could be a safety issue in relation to valproate.

But I think we've been very clear with them that, on the basis of the information and advice we've had from and through the MHRA, whenever sodium valproate is being supplied to a woman who might be of child-bearing age, then there needs to be...

Male: [Yes, that's right.]

Duncan Rudkin: ...an appropriate conversation, discussion. So, I think you're right to highlight access to records in community pharmacy as an area of potential risk, if the access is limited, and it is in many cases.

There is a much wider issue, of course, about how pharmacy could add more value at the point of supply with - across a range of safety issues, but also in terms of value added on public health and so on, with greater access to records in an integrated way.

Simon Whale: I think we absolutely get the patient safety point you make in relation to access to the medical record of the patient. I suppose - I think what you're saying is that if a patient presents in a pharmacy with a prescription for valproate, whether or not that patient is a regular user of that particular pharmacy, if that patient is a woman and of child-bearing age, the

pharmacist, in your view - I'm putting words in your mouth here - the pharmacist, in your view, should have that appropriate conversation in an appropriate manner. Is that right?

Duncan Rudkin: Absolutely.

Simon Whale: So, he or she - the pharmacist - does not need any further information because the evidence is in front of them.

Duncan Rudkin: Yes.

Simon Whale: The other thing - sorry.

Julia Cumberlege: Please, go on.

Simon Whale: Sorry. The other thing that you mention, this handful of potential FTP cases that have come your way, as it were, via MHRA and In-FACT - it's interesting, so you're saying they may well end up - they may or they may not end up as FTP cases, but it is possible that they will.

Duncan Rudkin: Yes.

Simon Whale: Is there a situation, from a GMC perspective, in which something similar could happen?

John Smyth: So, it would depend on the individual circumstances of the case, and that's not to avoid your question but, obviously, if someone were to prescribe whatever drug it might be inappropriately, ignoring safety concerns about that drug, being well aware of the risks of prescribing that drug in a particular situation and ignoring the guidance, then that might raise a concern about somebody's fitness to practise.

But I'll come back to what I said earlier on, which is an error made on an individual basis in one circumstance that isn't associated with more widespread concerns may not meet that threshold to take action on somebody's registration. So, it really depends on the context in which you're trying to put this.

So, if we're talking about valproate, which is what we've been talking about, a doctor who makes a mistake on one day to prescribe a drug, it may not meet that threshold. If the doctor repeatedly fails to follow the guidance and prescribes valproate, or a similar drug with similar dangers, repeatedly over a period of time, ignoring the guidance that was appropriately available to them, then that would raise a concern in my view.

Simon Whale: But I'm not sure - I'm sure Mr Rudkin can't go into detail here but are we talking about cases where there has been a persistent failure? Or are we talking about cases where a pharmacist has done something on one occasion which has come to your attention and may end up as an FTP case?

Duncan Rudkin: I can't give you that level of detail, I am afraid, but what I would say, it's equally true in pharmacy, of course, as with all the statutory regulated professions including the medical profession, that whether a case amounts to a fitness to practice case with action at the end of the process or not is very fact-specific, very context-specific. It will depend on the seriousness, the context, whether there are repeated and aggravating factors. That's true, certainly, of both of these professions, it seems to me.

Where we have - we've got this - because we've got, through the inspections that we carry out, an opportunity to look at the systems and processes in the pharmacy that you wouldn't have access to through a fitness to practise procedure that's only looking at individuals, it does mean that we can ask questions and look for evidence about what the practice is in the practice. It doesn't necessarily tell you, of course, that that's always followed.

So, there's the difference there between what the standard operating procedures say - that can be different, of course, from what actually happens on a particular afternoon.

Julia Cumberlege: Of course, all of us, I'm sure, are united in the fact that we don't want to see any more children disabled through these sorts of practices. Can I ask you - and particularly, I think, you're a General Practitioner, is that right? Can I ask you, on your systems - and we know that a lot of general practice now has adopted information systems that rely on technology and things like that, make it perhaps more simple - there is, I believe, an alert, is there...

John Smyth: Yes.

Julia Cumberlege: ...that comes up if a woman is taking valproate and she is of child-bearing age. Is that right?

John Smyth: One of the problems at general practice is that there are different clinical systems in operation between different practices. I am not currently in practice so I can't speak about what's happened since the concerns were elevated about the use of valproate. But in relation to other medicines where there are known concerns, if you attempt to prescribe something

you will get a series of warnings that you have to actively click to remove in order to continue to prescribe a particular medication.

So, I can't speak with knowledge about what happens in the case of valproate at the moment, but it may well be that the systems have been altered to include a particular warning in respect of women of child-bearing age. I'm sure your enquiries will lead you to whether that's the case or not.

Julia Cumberlege: So, you're saying some practices wouldn't have that facility?

John Smyth: I'm not saying that. I think most practices now use electronic prescribing systems. There may be individual circumstances in which people still issue handwritten prescriptions but the majority of prescriptions and repeat prescriptions are done through electronic prescribing systems, which do have the alerts that you're talking about on them.

Valerie Brasse: Do you know how many systems are in play in primary care?

John Smyth: I don't, no. Certainly, they've started to reduce the number of systems because some of the older systems have been gradually eased out. So, SystemOne is one of the systems that is now used in a lot of general practices. EMIS I think is still going. Vision I think is under pressure, as it were. But there's nobody - no unified system across the whole of primary care since computers were introduced in the mid-nineties, I suppose, more generally.

Simon Whale: I think the same is true in the case of pharmacies, that there is a - an alert will flash on the screen in the pharmacy, assuming it's all electronic, obviously. That pharmacists will see an alert related to a particular medicine. Is that right?

Duncan Rudkin: I'm afraid I don't know the answer to that question myself.

Simon Whale: Right. I think we've been told that that's the case. But one of the points I was - one of the other things that we've been told is that there is a sort of culture of alert fatigue. That there are so many alerts that there is a tendency to not necessarily pay as much attention to them as perhaps the people should.

John Smyth: I think that's...

Simon Whale: Have you got any experience of that?

John Smyth: That's entirely possible. I can't speak for the people you've spoken to already and what their view is, but my own experience of using websites

that flash things up that say do you want to proceed, people don't read them quite as carefully as they ought to. In respect of actually working as a doctor in primary care, prescribing things that can cause very serious consequences, I would expect them to read them very carefully before clicking off them. Whether that happens in practice, your experience and your conversations suggest not.

Duncan Rudkin: I think the possibility of alert fatigue is something that's been very much in our minds, in relation, for example, to our recent proactive communications around sodium valproate. I don't know that there's evidence that alert fatigue is a real phenomenon and real risk, but I think it's quite - it's not an unlikely scenario, it seems to me.

I think it did come up in a way in the Care Quality Commission report on the safety culture that we saw a few weeks ago. The issue of organisations with good intentions, for very understandable reasons, feeling the need to send out alerts on a range of different topics. But sometimes that must feel to practitioners - both pharmacists and others, maybe - that that's a sort of tsunami of stuff coming at them from a load of different people.

Then, I think, when we're thinking about sending out yet another message we have to think - I think it's incumbent on us all to think, for example, are we doing this because we think it will work and help? Or are we doing it so that we can say we have? You know, it's really important that we are all working in the most effective way to get the right information to people.

So, hence my comment earlier about using all of the different tools, thinking about direct communications, different channels through the owners and people responsible for governance in these - in our healthcare organisations, as well as the individual professionals and their teams.

One of the things that we do when we're inspecting pharmacies is to speak to the non-registered staff: the counter assistants, for example, who play an important part in face-to-face communication and are often, of course, on a practical level involved in handing out medication to patients. We know anecdotally what a powerful role they can play when they're properly trained and empowered in the right culture in a pharmacy. For example, to actually play a key part in safety, both in terms of that immediate transaction but also in terms of spotting opportunities to tighten up systems and things like that.

So, I think it's important we try to communicate with everybody involved, not only the pharmacists, for example, in my case.

Julia Cumberlege: Do you ever interview the users of the service?

Duncan Rudkin: When we are on an inspection we are very mindful of the risk that we get in the way of the service being provided. Most people visiting a pharmacy, if they're there when our inspector happens to be there, wanting their transaction and they want to get on with their - well, we observe - so, what we do at the moment is we observe practice. So, we'll stand - literally stand in the corner and see - watch what's happening. We ask the pharmacy, as part of the standards, to collect customer and patient feedback.

We don't ourselves at the moment directly collect user feedback.

Julia Cumberlege: Cyril.

Cyril Chantler: Twenty years ago, when I was elected a member of the General Medical Council, and responsible through the Standards Committee, for good medical practice, I used to think that one of our roles was to protect and improve trust in the profession, which is, I think, the third statutory duty. Basically, that was about - regulation, was about contract, and it was about conscience. The GMC was the conscience of the profession.

Now, going around the country, we have heard from patients stories which have called into question the trust these patients have in the doctors who have looked after them. Some of the stories have been horrifying. So, I've found myself asking whether the profession - and I'm no longer on the register, I've retired - is doing as much as it should be doing to be trustworthy.

One of the things they've particularly mentioned is conflict of interest. It isn't - I know it has been proposed in the past and I think you've consulted on whether or not the General Medical Council should maintain a register of conflict of interests. Can you tell me about how that went and why you decided not to do it?

John Smyth: I'm not aware, personally...

Phil Martin: I'm afraid that I...

John Smyth: ...[unclear]...

Phil Martin: Yeah, I also don't, but we can provide information - we can take it away and provide information.

Cyril Chantler: Who in the General Medical Council should we speak to, to answer that question? The Chief Executive?

Phil Martin: I would need to find out who was working on that Review. I apologise, I joined six months ago, so it probably pre-dates my time in the GMC. But I will take it away and find a name and provide it to the Secretary.

Cyril Chantler: Because certainly good medical practice used to be very clear about declaring a conflict of interest, that if you had one you had to declare it to the patient.

John Smyth: It still does make reference to conflicts of interest.

Cyril Chantler: Well, you raised the question. It's always been a problem for the General Medical Council, as you say. Good medical practice is guidance. How do you know it's being followed? If you don't follow it and a complaint is made, then you have to justify why you didn't follow it. Otherwise, your fitness to practice may be called into question. But if there is something which is fundamentally going wrong, and this is what we've heard about conflict of interest, then surely you ought to consider whether or not you should be doing more to be trustworthy.

John Smyth: So, I would counter what you've said by saying our experience is that those people who have had bad experiences, where things have not gone well, do have a particular view about the trustworthiness of those that have been involved in their care. My personal view, and my view from my experience of working in the GMC for some years now, is that we see a very small proportion of doctors who are actually on the register. There are over a quarter of a million doctors on the register and in the course of a year, we certainly won't see complaints about all of those. It's a tiny fraction of those that we actually see complaints about.

So, my position would be that there is a lot of trust still and all of these surveys that are done suggest there remains trust. Medicine is one of the most trusted professions amongst all of the professions. That's not to underestimate the devastating effect that individuals may feel - the loss of trust that they feel when things don't go well.

In respect of conflicts of interest, in what context has it come up in these conversations?

Cyril Chantler: This goes back some time ago, when Primodos was given out. It wasn't prescribed, it was given out by doctors. But they were free samples and there was no mention of risk, but then - there wasn't a risk that they knew of at the time, but there was the notion that this was a sample which had

been given and it was part of marketing. That's what we've been told. That was an issue.

There is an issue over surgical devices, as to whether or not there was a conflict of interest because they were being provided with the device by the manufacturer. All these things, if there was a register or it was part, say, of appraisal that you had to declare a conflict of interest - there are ways of dealing with it - would actually be something which would serve to improve trust.

As a researcher now, you always declare any conflict of interest before you give a presentation. It's just routine. So, shouldn't the GMC consider that as being an appropriate action in relation to - well, we know about hospitality but in the use of devices?

John Smyth: I think as my colleagues say, we're not really well-prepared to actually respond to that question, but we can certainly speak to those that were involved in considering that

Cyril Chantler: Maybe you could then give us a response.

John Smyth: Yes.

Phil Martin: Yes.

Cyril Chantler: Thank you.

Julia Cumberlege: Right, anything else?

Sonia Macleod: One of the - sorry.

Cyril Chantler: Oh yes, go on.

Duncan Rudkin: Sorry, just in relation to conflicts of interest, I was involved over the course of a couple of years, from time to time, in some really useful work that was done by NHS England under the leadership of Sir Malcolm Grant on conflicts of interest particularly. I know that GMC colleagues and a range of others have been very engaged in that work and produced guidance for the NHS in England. There is a renewed focus now, the guidance having been produced, on implementation and on evidence of compliance with that guidance.

So, there has been, I think, quite a lot of progress on that front in that way, albeit there is more to do in terms of monitoring and securing assurance that the guidance is being followed. It has, of course, also been

- continues to be in different ways a significant issue for pharmacists, for obvious reasons, in relation to conflicts.

Cyril Chantler: Do you keep a register?

Duncan Rudkin: We don't, no. I think we - it's not something that we've specifically looked at or been asked to consider. But I think if we were, I think we'd be asking whether that was the most - the question for me would be is that the most effective way of actually doing - securing the right outcome? We've, in our guidance - in our standards, which is compulsory, I would say, for all of our registrants, got clear statements about the need to declare and manage conflicts of interest appropriately.

Making that stick in reality and then being able to demonstrate that that's working is obviously a slightly different...

Cyril Chantler: There is a...

Duncan Rudkin: A different challenge.

Cyril Chantler: ...sort of privately-run website, run by a general practitioner, a register, whopaysthisdoctor.org, available. So, there are some doctors who are taking action in this area. But I'm really raising a more general question as to whether it should be a part of the appraisal to recognise your responsibility in this area, because it is set out in the guidance, or it was very clearly set out in my time.

Duncan Rudkin: We've been supportive of - and again, used our communications on occasions to encourage members of the pharmacy profession to engage with Disclosure UK, which is the register that I think has been set up essentially by or with the support of the pharmaceutical industry to - as a voluntary but nevertheless quite powerful tool to provide a forum publicly for various health professionals to declare their interests. That has been very much on the agenda as part of that NHS England work as well.

Cyril Chantler: Thank you very much.

Julia Cumberlege: Can I just ask you, on conflicts of interest, we're seeing a growth now about GPs dispensing as well as prescribing. Do, you see that there is a conflict of interest in that activity?

Duncan Rudkin: I probably should say, and I hope you'll forgive me for taking a sort of technical point, that the regulation of the medical profession is not a matter for me to comment on. It is also true that there are pharmacists who are prescribers. We are working on some guidance ourselves for pharmacist prescribers. In that context, I suspect that we will find, subject

to consultation, that we may well be reluctant to impose an absolute ban, as it were. That it should be unusual. That it shouldn't be the norm from a - in pharmacy, for a prescriber to also be making the supply.

There may be occasions when actually for practical reasons what the patient needs at that moment is actually for that supply to be made. That's probably, I suspect, where we would end up on that topic.

Julia Cumberlege: Can I ask the GMC the same question?

John Smyth: So, the responsibilities of doctors in prescribing medicines are set out in the guidance, in terms of being sure that you have enough information to prescribe safely, making sure that you've made an appropriate assessment of the need for it, explaining the consequences of prescribing, not prescribing. All of that is set out. So, if doctors are in businesses that have pharmacies within them, as long as the doctors are meeting the requirements under good medical practice to prescribe appropriately, the dispensing of that medication is subject to regulation by the Pharmaceutical Council.

Doctors themselves normally aren't prescribing those - aren't normally dispensing those medicines. But there may be dispensaries within their premises. Is there a conflict of interest in that? I suppose, like any business that has overlapping interests, there is the potential for that to be there. Do we have evidence that that is the case? No.

Phil Martin: The only other thing to that - on that is that our consent guidance talks about how doctors prescribing any sort of treatment, whether that's something pharmaceutical or otherwise - we have guidance for how they should discuss that with patients to make sure that they are aware of both the potential benefits and the potential risks involved, and to give them the information they require to come to an informed decision around consent to that.

Sonia Macleod: In terms of consent, one of the things that struck me from the evidence that you submitted is quite how low the number of concerns that have been raised about informed consent are, given that we have been hearing from an awful lot of women who have been saying that at their surgery they weren't properly informed. It wasn't fully informed consent. You were dealing with, I think it's, 175 inquiries in 2018, which seems a very, very small number, and we were very surprised by that.

Phil Martin: Not all of them would come to - not all concerns around that would necessarily escalate to the GMC in regard to that.

John Smyth: No. It perhaps raises an issue around perceptions of consent. So, there are often allegations about inadequate consent or lack of consent that are raised with the Council when we do our preliminary investigations, and it transpires that there is a clearly documented consent process within the medical records. Now, the patient's individual recollection of that consent process may be very different to what's documented in the records, but in terms of evidential proof, it's actually very difficult to get to any allegation that might relate to that matter.

Sonia Macleod: Yeah. So, when you submitted evidence to us and you said you have 175 inquiries related to informed consent...

John Smyth: It may be just that that was the only issue in that particular case. I'm not quite clear on how those statistics were generated.

Sonia Macleod: Okay.

Valerie Brasse: Sorry, does an inquiry mean that it's a complaint that's established?

John Smyth: It's...

Valerie Brasse: Or does it just mean it's the first...

John Smyth: Yes.

Valerie Brasse: I want to talk to you about how I had my consent.

John Smyth: It's a...

Valerie Brasse: Knowledge.

John Smyth: ...complaint that comes to the Council to consider whether or not to open an investigation into that matter.

Valerie Brasse: So, it is already a complaint, not just an inquiry?

John Smyth: It's...

Valerie Brasse: It is a complaint?

John Smyth: It's at the inquiry stage. If it's promoted to an investigation - that's the terminology that we use.

Sonia Macleod: So, those are your first stage...

John Smyth: Yes.

Sonia Macleod: ...complaint handling coming into you, and then they're promoted to the second stage...

John Smyth: Yes.

Sonia Macleod: ...which is investigation? Okay.

Valerie Brasse: Are you surprised by the numbers?

John Smyth: As I say, I'm not sure whether that's - that was the only allegation in those matters, or whether there were others that included other allegations as well. I'm not quite sure how that data has been cooked, I'm afraid.

Valerie Brasse: Because I know earlier you said - what? A quarter of a million doctors...

John Smyth: Yes.

Valerie Brasse: ...on the register? There is a small number of complaints about a small number of those. Do you pick up trends from your complaints? How do you analyse complaints? What information do you draw out of those? Is there anything that you've been looking at in terms of complaints over a number of years that leads you to think there may be something amiss here? Or are they so low that you don't feel you've got a handle on this?

John Smyth: So, that's quite a difficult question to answer because we have a very - a wide range of different allegations that are brought to our attention about all aspects of medical practice, not just primary care but secondary care in all its many forms. So, actually, condensing that into there is a significant concern about this individual thing is quite difficult when you think about the number of encounters that we would never hear about.

So, in terms of recognising trends, I think that's quite difficult. This relates a little to what we're discussing today in the sense of what we could do to identify trends. Given that we're at the very end of the process where it may well be that there has been a local investigation first into a complaint that has been made and those complaints may have been resolved satisfactorily between the individual parties and never brought to our attention, if we're seeing just the tip of the iceberg of things that are out there, or if we are seeing all of the things that are out there, we can't say for sure.

Given the small numbers that we're looking at in the overall scheme of what's out there, it's actually difficult to identify trends.

Valerie Brasse: I suppose it comes back to whether it's a proactive process here or very much reactive. By the sound of it, it's very much reactive.

John Smyth: I think we work in collaboration with others. Certainly, when issues are raised with us about concerns that others have, we can start to look at those things more closely. If we notice trends ourselves amongst particular types of complaint, we speak to other people as well about those things.

Valerie Brasse: But that - but you say that hasn't been happening - actually been noticing any particular trends.

John Smyth: You were asking me specifically about consent, that's what's...

Valerie Brasse: Well, I mean consent was just one aspect, but just looking more broadly at what complaints tell you really.

John Smyth: So, we have been working with other regulators recently around matters of prescribing in other areas, in the online environment et cetera, as well. That's certainly something that we're working hard with other regulators to try and identify trends and think about what we need to do to address those concerns that are out there.

Valerie Brasse: Are you picking up anything in regard to the manner of consultation between a doctor and a patient?

John Smyth: In what regard?

Valerie Brasse: Well, we hear - and obviously you must understand where we start from, but we hear quite a lot of stories of women who have had consultations with their doctors which have frankly been less than helpful and have probably been downright dismissive of many of the women whose cases have come before these doctors. I'm just wondering, they are very vocal on it to us and I just wonder whether they are making those complaints to you.

John Smyth: You won't be surprised to hear that we also hear those kinds of stories. Obviously, our approach is not to say that one person is right and another person is wrong, and there are definitely two versions of every encounter that takes place. So, our view is to try and get to the truth, if we can, of those matters. Those types of situations are actually very difficult to bottom-out sometimes, because there is no independent party present during a consultation. You can't really one take one person's word over another, regardless of how strongly you might feel on a personal level about what has been said by one party or another.

Valerie Brasse: Are they on the increase, those sorts of complaints?

- John Smyth: I don't have any statistics, but certainly from my own experience of looking at cases, they are no more prevalent now than they were some years ago.
- Simon Whale: If, as you say, it's one person's word against another and there is no one else in the room - obviously, that's usually the - often the case - how does a complaint of that nature get treated then? How do you resolve it?
- John Smyth: So, it would really depend on whether evidence could be adduced that would support one version or another. It also depends on what other allegations would be present in that case. So, it's often not just that the doctor was rude to me or the doctor didn't consent me properly, there will be some other aspect of an encounter that would cause concern for the individual as well. That then might escalate the level of concern. As I said at the very beginning, serious concerns or persistent concerns are the things on which we can take action as a regulator.
- Simon Whale: As you may know, we've travelled around the country and we've been to - I don't know, rather lost count of how many places we've been to - a lot of places. In some of them, we've sat and listened to patients who have talked to us about an individual doctor or a couple of individual doctors. Those patients haven't, as far as we know, compared notes before coming to see us, but an individual's name gets mentioned to us in the context of what the Secretary here has described as dismissive, passive-aggressive, egotistical behaviour.
- So, it's not one individual case. I mean, these are anecdotal. We are not taking sides in the sense that we can't prove who is right and who is wrong here. We weren't in the room either. But it does strike us when we hear things like that that hearing a number of people talk about an individual doctor would suggest that there is a problem.
- John Smyth: It goes back to what I said before. Serious or persistent concerns about an individual doctor are things that we can take an action on. So, if the GMC was made aware of persistent, multiple concerns about an individual doctor, that might be something that we could take action on.
- Cyril Chantler: Can I ask, in relation to consent, given Montgomery and the increasing requirement of the consent process, is the Council considering giving advice to the profession about recording - audio recording of consent as opposed to just making a note in the notes?
- John Smyth: I'm not aware of...

Phil Martin: I've not heard that specific suggestion, although I should say it's a colleague elsewhere in my directorate who is leading - we are currently reviewing the consent guidance and I think we will be picking up different views on this as part of that consultation.

Cyril Chantler: So, as well as responding to what, if anything, you think is appropriate to be done about recording conflicts, would you also let us know what you're doing in relation to consent?

Phil Martin: Yeah. We can send that over.

Cyril Chantler: Thank you.

Sonia Macleod: Can I just ask a slightly broader question, in a way. Fitness to practise investigations are about individuals or individual pharmacies. How do you then take the lessons from those and embed them in a system-wide way? Or do you?

John Smyth: So, individual fitness to practise decisions that are made, where action is taken on a doctor's registration, are published. They're available on the register for people to access. So, that's one way in which they're published.

Duncan Rudkin: For example, we report regularly to our council in our published council papers on what's happening with our caseload. Although our - the detail isn't necessarily always there in - at every level that one would want, one can nevertheless see over time in a perhaps not necessarily very scientific way, some trends and things which prompt the lines of inquiry.

So, what we do with those, for example, would be to say well, is there something there that we ought to be monitoring a bit more closely? One of those - a good example that's very topical is workplace pressures. Of course, that's an issue in itself in terms of safety, potentially, but also as an important part of context, could lie behind some of the reasons why, for example, good practice isn't necessarily isn't always followed, if people are feeling for whatever reason that they don't have time - and I wouldn't necessarily accept that concept, but there you go - to do the right thing.

So, our council identified during the course of last year that we'd started to notice a small - and our numbers are very small, but nevertheless a small increase in the number of pharmacies that were not meeting the standards in relation to safe staffing. So, one of the ways in which we could deal with something like that is to track it more closely. Then to use that insight quite organically in a way to then inform our communications

activity, to inform things like targeting communications and expectations of the profession in terms of reflection.

So, for the first time this year, as part of the implementation of a form of revalidation in pharmacy, we will be asking our registrants to submit to us a record of - an account where they have reflected on something in relation to their practice, and a discussion with a peer that's informed their practice. We would use things like what's appearing in the caseload and where the standards are not being met to inform the selection of the standards that we would ask people to reflect on, which then gives it as a sort of focus for communication.

It then encourages others in the sector - education providers, people responsible for journals and so on, and also the owners of the businesses, to then target activity in those areas. So, it's quite an organic and not necessarily very scientific process, but it is starting to - you can start to see the flow a little bit through issues.

Phil Martin: I think the other point on this is that fitness to practices and inquiries are a source of information about what might be going on out there. I think, for the reasons that John has outlined, they are not necessarily the best source, just because the numbers make them - it difficult to assess trends on the basis of very small numbers in a lot of cases. But they can be an indicator of an area where we'd want to - where we might need more guidance, where we might want to push attention.

There are lots of other sources for that. Things like the National Training Survey. Things like the groups that we're involved in with other regulators. So, it's one source amongst many where we might want to focus and attention and think that there might be issues that are coming up.

Julia Cumberlege: Right. Can I just ask, because I think we need to wind up, but - Valerie, have you any more questions?

Valerie Brasse: I just wanted to ask about your inspection reports. Are they made public?

Duncan Rudkin: Well, that's a very good and topical question. They're not currently published.

Valerie Brasse: Can we have one?

Duncan Rudkin: We, for the first few years of our existence, were unfortunately in the position where we didn't have the legal power to publish our inspection reports, which, of course, is a very undesirable position for a regulator to

be in. That was remedied through the course of last year with the commencement of a new power, and we have consulted the public and the profession on the use of that. We have recently made a set of decisions, including confirming the decision that all the reports should routinely be published.

We will, over the course of the first half of this year, be rolling that out. So, it's a very topical question. I think the potential for the publication of pharmacy inspection reports to raise the profile and also raise expectations, which I think is, if I may, Baroness, a point that I just wanted to offer into the discussion. It comes back to the question about - the question you asked my colleagues about the caseload.

The caseload for complaints about pharmacy coming to us is notable for its absence as complaints about advice. In a way, I think, that tells us something about public expectations of what pharmacy is there for, and perhaps an underappreciation of the safety role and the value that pharmacy can add. So, I think part of how we can help to support the work that you're doing, for example, is in relation to that agenda of raising the profile and also raising expectation so that members of the public look to pharmacists and their teams for advice.

We still receive complaints from patients, for example, who are aggrieved at being asked questions by a pharmacist. That tells us something about the level of that expectation in some cases. So, I think there is some work to do in relation to that.

Julia Cumberlege: Thank you very much. Yes, I could give you a lecture on pharmacy...

Duncan Rudkin: I'm sure.

Julia Cumberlege: ...and particularly pharmacists prescribing, but I don't think I'm going to do it right now.

Duncan Rudkin: Maybe do that on another occasion.

Julia Cumberlege: Have you got anything?

Cyril Chantler: No.

Julia Cumberlege: No, right.

Simon Whale: No, thank you.

Julia Cumberlege: No. So, is there anything you particularly want us to take away from today? We have suggested that if there are other things that you think we

ought to have asked about, or there are holes in the questions that we have asked, please come back to us because we are open and accessible. But can I ask you in turn, is there anything in particular that you want us to take away from today?

John Smyth: No, I think we're more than happy to supply the additional information that you've requested. I apologise that we haven't got that available for you today, but we will certainly provide it to you.

Julia Cumberlege: Right, thank you very much.

Phil Martin: Nothing further.

Julia Cumberlege: No.

Duncan Rudkin: Nothing further from me, thank you.

Julia Cumberlege: Alright, thank you very much indeed. Thank you for coming.

Phil Martin: Thank you.

Simon Whale: Thank you.

END OF TRANSCRIPT

Session 5: Professional Standards Authority (PSA)

START OF TRANSCRIPT

Julia Cumberlege: I'd like to ask you just to introduce yourselves, your position, the organisation, what your work is, and ask you if you've any conflicts of interest that might affect your statements to us today? So, Christine, would you like to start?

Christine Braithwaite: I would love to, thank you. I'm Christine Braithwaite and I'm the Director of Standards and Policy for the Professional Standards Authority. I think probably if I allow Mark to introduce himself, and then perhaps we'd just say a little bit about the organisation and our respective roles within that?

Mark Stobbs: Certainly, so I'm Mark Stobbs, Director of Scrutiny and Quality in the Authority. My team are the ones that do the performance reviews of the regulators, reporting on their performance in meeting their statutory objectives. We also have the ability to appeal the findings of disciplinary panels - fitness to practise panels, which are insufficient to protect the public, to the High Court. We also carry out a number of investigations that government or others ask us to do; most recently the Morecambe Bay one.

Julia Cumberlege: Thanks very much.

Christine Braithwaite: Thank you. My team respond essentially to requests from the Secretary of State and ministers in Scotland, Northern Ireland and Wales, to request for advice and matters related to professional regulation. We also encourage and commission research into matters related to regulation and produce policy papers. I have a secondary role, which is in relation to accredited registers and also communications.

Julia Cumberlege: Right, thank you very much. Can I just ask you - I mean clearly you rely a lot on people coming to you with serious concerns and you deal with them how best you feel you should be dealing with them. So there does seem to be really quite - there could be quite a difficulty between the candour that the professionals actually are prepared to state to you. I just wonder - one of the key themes that actually did come through some written work that we've had, is the mismatch between stated attitudes and actual behaviours.

The point about that is that there's a concern, I think, that professionals have to reconcile competing forces when they come to you and you're doing an inquiry, or whatever, into their conduct or whatever the issue is that has been brought to you. It's about, really, the responsibilities that

they have to the profession, to the patient, to themselves, to the community and all that. I presume you try and facilitate that disclosure. But there are various barriers to reporting, and it's the clinicals - clinicians' own negative feelings and attitudes towards disclosure, because they do realise that they are under some scrutiny. I just wondered how you sort of deal with those fears and anxieties that probably come to you?

Christine Braithwaite: I think probably if we divide this...

Mark Stobbs: Yeah.

Christine Braithwaite: ...in terms of answering it. If Mark talks first about our role in relation to complaints and clarifies that, because I think that would be helpful first, to make sure that you've got our position right in relation to that. Then I can pick up the conversation about candour.

Mark Stobbs: Yes, I think it's important to make clear that we don't do investigations directly into registrants or doctors. We are overseeing the way the regulators themselves do that work. So, to that extent, we're rarely seeing - in a position where we are requiring doctors to be candid with us. We may well, however, see how they behave towards their regulator and very often - and one of the things we noted in our annual report for a couple of years, is that we're seeing a number of cases where the regulators themselves aren't necessarily identifying breaches of the duty of candour.

For example, aren't either charging these in front of fitness to practise panels, or fitness to practise panels aren't treating this as an aggravating factor. One obvious case was one where a surgeon had done some wrong side surgery, didn't bother to tell the patient. The patient returns and he says, I'll just give you another operation to put it right. Which - where the duty of candour seemed to have got missed out of the GMC's approach to that. We see other examples from the regulators where this happens.

We obviously do get a number of concerns from members of the public, from registrants themselves, about the way in which the regulators deal with that. We find this extremely valuable from both sides, when looking at the - first the way in which the regulators are carrying out their duties. Particularly the way in which they approach complainants and regulators and dealing with them from a human angle - and actually giving us some clues about where to look at and where the problems are likely to arise.

Also, in particular, with our Section 29 appeals, where we frequently will get the patient coming to us saying, they really haven't understood this. Sometimes they have and the way in which the fitness to practise process

works means that we can't do much. But a number of occasions, we say yes, actually this is something we need to take forward.

Julia Cumberlege: You did a very full inquiry, didn't you, into the Nursing and Midwifery Council?

Mark Stobbs: Yes.

Julia Cumberlege: You came out with some very interesting comments on the way that they were operating as a regulator.

Mark Stobbs: Yes. I think one of our concerns - our main concern there was the way in which they were dealing with patient complaints. Where one of the things we found was that in 2010, one of the main family members there had identified the bulk of the problems that were going on and they did not take it seriously. They preferred the evidence of the trust and the supervisors of midwives, who incidentally had a fairly clear conflict of interest in this. I think this is one where - I wouldn't necessarily say that this was unique to the Nursing and Midwifery Council.

I suspect all of the regulators have problems identifying where a complainant has a strong point. There's a tendency just to assume that the information that you get from the employers, from the trusts is more valuable, is more likely to be true than something that comes from the patient who may not know anything anyway. I think one of the things we - that came for me very clearly out of the Morecambe Bay cases - and something we're looking at for all the regulators - is how they approach complainants, how they deal with them both in a human way, but also actually take what they say seriously.

Those people were in those consulting rooms. They were in the operating theatres. It happened to them. Very often - when you get an account from a doctor or the midwife, saying this is what happened, the fact that the Nursing and Midwifery Council didn't send it to the family member who was there, to say actually does this ring true, struck us as a major flaw in their system.

Christine Braithwaite: Certainly, a lost opportunity...

Mark Stobbs: Exactly, exactly.

Christine Braithwaite:to check the evidence again.

Valerie Brasse: Can I just ask though, is your - you only have a locus then when you're looking at complaints that come in to the regulator. So, one of the issues we've been thinking about - talking about with people who were just here

before you - was, are you getting the complaints you should be getting? Because if people feel that this process is not terribly satisfactory, they may just decide, well it's not worth the bother.

As the PSA do you have any sort of role to play in ensuring the regulators are doing all they should be doing to encouraging the complaints that really ought to be coming for them? I mean, you know, I'm just think about the analogy, I've done a lot of work - as I think several of us have done - around child sex abuse complaints.

Mark Stobbs: Yes.

Valerie Brasse: Actually, child sex abuse complaints, going up was sort of a good thing because it meant...

Mark Stobbs: Yes.

Valerie Brasse: ...it was coming out ...

Mark Stobbs: Yes.

Valerie Brasse: ...the system and people were taking it seriously.

Mark Stobbs: Yes.

Valerie Brasse: So, I'm just wondering whether you have any locus where the complaints don't exist and there's a worry that they should be getting more than they are?

Mark Stobbs: One - we have a number of what we call standards of good regulation, which we use measure the way in which the regulators are carrying out their duties. One of those is about making sure that there are no barriers to complaints and that people can raise complaints easily. There's nothing explicit there about encouraging complaints. Though there is - there are other standards about working with employers, about ensuring that there's proper liaison with trusts with employers to ensure the concerns are raised with them. We look at those. We audit periodically the way in which the regulators are carrying out the work. I think it's always difficult not - to audit what people don't know.

Valerie Brasse: I know, but you can see the point I'm trying to make.

Mark Stobbs: I do, yes. Yes.

Christine Braithwaite: Well I think one of the things we certainly know from our work with the public is that they do find the regulatory system difficult to understand...

Mark Stobbs: Yes.

Christine Braithwaite: ...and difficult to navigate. Of course, with professional regulators, professional regulators are always very specific. They're looking at fitness to practise, they're not - a person may have a perfectly legitimate complaint about their care, but it doesn't necessarily mean it raises questions about the professional's fitness to practise. That can be quite a cause of tension, I think, for people who come forward to the regulator, who then feel disappointed potentially by the way in which it's been responded to. It's because it's quite difficult to explain a fitness to practise process, actually, in a simple enough way. The language is a bit impenetrable to people.

Mark Stobbs: Yes.

Christine Braithwaite: To just return to the candour issue, Baroness Cumberlege, which you asked about at the beginning, and I think you are referring to the report that we did there on the barriers to candour. We did a literature review when we first gave advice to the Secretary of State on - that we were asked for advice on whether there should be a duty - a legal duty of candour. As you know there is a legal duty of candour that's on organisations, and then there is a professional duty of candour on the health professionals. We did identify a number of barriers in the research that we undertook at that time. You alluded to some of those. So, one of those might be conflicted loyalties. Somebody feeling that they've got a loyalty to the patient and they want to their best for the patient.

Mark Stobbs: Yes.

Christine Braithwaite: But then also feeling that they might be letting their team member down, or they might be letting their organisation down. So, there are some quite difficult emotional situations that - excuse me, not long since recovered from a cold - which people might find themselves wrestling with when they're trying to decide what they should do. We have just recently published another report, actually, following up on the progress of the regulators and trying to strengthen the - strengthen professionals - I'm trying - looking for a different word to compliance and I can't find one, so I'll say compliance - with a professional duty of candour.

But we found that many of the barriers still remain. When we put out our first report to the Secretary of State, we recommended that there should be further research into the barriers, to understand exactly what the barriers were and how best to overcome them. That research hasn't actually been forthcoming. What - I think there's still merit in a piece of

work looking at how we could do something in that area. We have found considerable number of initiatives being undertaken by the regulators to try and encourage it through their standards, through education and training. The fitness to practise - Mark mentioned that we were not seeing...

Mark Stobbs: No.

Christine Braithwaite: ...fitness to practise, particularly - sorry duty of candour - particularly appearing in the allegations that the regulators were bringing forward. The regulators have said that they think they are looking at candour but they're not necessarily referring it to it as the duty of candour, but that it's mostly being captured through allegations related to dishonesty.

Mark Stobbs: Yes.

Christine Braithwaite: So, they think they're looking at it...

Mark Stobbs: Yes.

Christine Braithwaite: ...in relation to that. I don't know, Mark, whether you'd have anything further to say on that? It seemed reasonable they don't all categorise their allegations in the same way. So, it can be very difficult to carry out a comparison to see whether they are - actually are identifying all of the incidences of them and picking it up.

Mark Stobbs: I - clearly there is a major link between that lack of candour and dishonesty. I think part of the problem that you face is that it's a very high bar to show that somebody is actually dishonest. So that people will often give registrants - understandably and perfectly properly - the benefit of the doubt. You might want just to say, actually you were not candid. You did not mention this when you should have done, without actually colouring it with the rather higher - more - standard of dishonesty. Which again, raises the stakes for the registrants and makes it more difficult for them to respond and accept.

Sonia Macleod: Do you think that still applies in the same way now the duty of candour is statutory?

Christine Braithwaite: The research that we just undertook with the regulator suggests that there is some confusion that professionals find the legal duty of candour clearer, because it provides a very clear threshold for when it's engaged and when it isn't. Whereas with the professional duty, they found was more nebulous and they would welcome greater clarity from the regulators in that, and suggested case studies would be a way to help

them interpret the two standards and make sense of that. Similarly, although all the regulators signed up to a joint statement, they've got their individual standards and we suggested again it might be sensible to think about having a single standard.

Cyril Chantler: Can I talk to you about culture? The background for me is that I was an elected member of the General Medical Council, but that was 20 years ago and I'm no longer on the register because I retired 20 years ago - almost - 18 years ago. But I've thought about it then and worried about it ever since. We want to encourage people to be honest, open and truthful. To be trustworthy. That means that we want to encourage a no-blame culture because that's the only way you can learn.

I'm on record - along with others - saying that regulators can't improve anything. They - they're there for a different purpose. But it was very difficult to get members of my profession to love the General Medical Council. I mean I tried very hard because I thought it - we were trying to do good things for patients and for doctors. But even when I was on the council, and I used to get letters every day from them about standards matters. Every time the letter dropped through the letterbox, my heart sort of stopped because if you're a doctor, you don't love the regulator.

Christine Braithwaite: No.

Cyril Chantler: Yet we - I understood why it is so important. So, you can - you're getting some measure of my confusion. But one thing I did think was that if the regulator by its processes could be a bit more friendly, then maybe that would actually help the overall improvement of a no-blame culture.

Christine Braithwaite: Yep.

Cyril Chantler: Quite often it is solely holistic. It takes so long to actually get a resolution to the complaint that it's actually the culture of the regulator - mainly for many good reasons - actually doesn't actually help improve the culture. Does that make any sense to you?

Christine Braithwaite: It absolutely does. I mean we completely agree with you. That's exactly what we said in Right-touch reform. I mean we have said that the system has become much too adversarial and it doesn't need to be adversarial. It could be inquisitorial. I think the regulators agreed that there's - the time has come...

Mark Stobbs: Yeah.

Christine Braithwaite: ...for them to move for what they're terming upstream approaches...

Mark Stobbs: Yep, yep.

Christine Braithwaite: ...and to become - and to adopt less adversarial approaches.

Mark Stobbs: Yep.

Christine Braithwaite: There's much more use now to [consensual] [unclear]...

Cyril Chantler: But are you measuring - because in your role as the supervisor - and you're the uber regulator.

Mark Stobbs: Yes.

Cyril Chantler: Are you making any progress in the bodies that you supervise - getting them to adopt your advice?

Mark Stobbs: It's very difficult. Partly because those bodies have legislation which is, in some cases, 20 or 30 years old and which essentially sets these processes in stone.

Cyril Chantler: Yes, and they're trying very hard to get an act to change it.

Mark Stobbs: Exactly. Exactly. I think work that the Nursing and Midwifery Council is doing to try and take things out of fitness to practise panels so that you are talking to the registrant about what went wrong; about whether there are things that they ought to be doing to improve; agreeing conditions by consent, is a much better way of dealing with this. So, you are taking out the formality and legalistic approach.

I think one of the problems that you face, though, is that does depend on the registrant themselves accepting that something had gone wrong and that actually there is something about their practice...

Cyril Chantler: Repentance is part of forgiveness...

Mark Stobbs: ...which needs to improve. It's inevitably - it's a human reaction. If you are saying something went wrong, this is as a result of something you did, you have to be quite a big human being sometimes to accept that that's the case. I think this is - when you have a regulator who can put in conditions, suspend you, stop you earning your living, the stakes are high. You are very well advised to have some legal advice. Even in that legal advice is, you are actually better off cooperating, but not all lawyers will...

Cyril Chantler: But specifically, is there anything that - you're trying to change the way...

Mark Stobbs: Yes.

Cyril Chantler: ...regulators...

Mark Stobbs: Yes.

Cyril Chantler: ...behave, and that's good. But is there anything specific that needs to be done that you can't do, but - which - you mentioned the act of parliament, so can you be specific about...

Mark Stobbs: We...

Cyril Chantler: ...change you want in that act that would facilitate it?

Mark Stobbs: We can certainly be specific about the things that we feel regulators should be - should have greater flexibility.

Cyril Chantler: Which would then be incorporated into...

Mark Stobbs: Yes, exactly. Each regulator has a different...

Cyril Chantler: Have you written - I'm sorry to interrupt - but have you written that down?

Christine Braithwaite: Yes. In Right-touch Reform. Yeah, so in two places really. We did a series of publications. First, we published *Rethinking Regulation* which set out what we thought was wrong with the system. Then we set out - culminating in Right-touch Reform in which we set out a very detailed section on fitness to practise in particular and the changes that we think need to be made. We also responded to the Department of Health and Social Care's consultation on reforming regulation and promoting professionalism. Again, we set out the things that we thought needed to be changed.

Cyril Chantler: Where's that all got too?

Christine Braithwaite: All with the DHSC so we're still waiting for the Department of Health and Social Care's response to the response to the consultation...

Cyril Chantler: Is that public knowledge, your particular recommendation?

Christine Braithwaite: Yes - it's all - all of our things are in the public domain. Yes, they're all published, they're available.

Simon Whale: How long the DHSC had it in their court?

Christine Braithwaite: Over a year now. It's caught with Brexit, essentially. We're - they're ready, we understand. They're ready to respond but they're waiting for a slot to be able to do so.

Sonia Macleod: One of the things...

Male: Thank you.

Sonia Macleod: ...that strikes me is that all of your regulators are regulators of individuals, they're not systemic.

Mark Stobbs: Yep.

Sonia Macleod: If you look at other professions, there are some professions where as well as individual regulations - solicitors spring to mind - you have institutional and organisational regulation as well.

Christine Braithwaite: Yeah.

Sonia Macleod: I know CQC do part of that.

Christine Braithwaite: Yeah.

Sonia Macleod: But I'm wondering when you're talking about fitness of practise, blame and things, often what you're looking at is not an individual fault...

Mark Stobbs: Yes.

Sonia Macleod: but a system one. So, is there a way to bridge that gap?

Christine Braithwaite: Well the GMC have said that they're going to bring in human factors training for their staff, to make sure that they have better understanding of where mistakes - areas and wrongdoing fit within the system. I - we did - we have - we made exactly that point, which is that if you were going to start again today designing a regulatory system for modern health and care, you wouldn't have separate system and professional regulators, you'd join the system together. In terms of the reform that we've called for, we think that's a too bigger change to ask for, to realistically get any hope of change within the time frame that the regulators need to have.

Mark Stobbs: Yes.

Christine Braithwaite: So, we're stuck with what we think needs to happen with professional regulation. But ultimately, yes of course it makes sense to bring it together. That doesn't mean to say that more can't be done as - we say with some imagination and innovation. So, there couldn't be more done between the professional regulators and the system regulators to

coordinate that. I certainly - having worked for the Care Commission - Care Quality Commission in my previous life, could see that it would be possible to design the system regulatory system and assessment processes in a way that would support the professional regulator.

If you want professionals to be candid, if you want professionals to admit to mistakes and to learn from mistakes, then you need an assessment of the systems in which they're working to make sure that those behaviours are being facilitated by their working environment. I think it would be possible for the regulators to work together to design.

Mark Stobbs: I also think there's scope for more work between regulators and Trusts and employers. I think there are a number of cases that we see, which really did not need to go to the regulator. They were either employment matters or they were single issue mistakes, where actually by the time it's got to the Fitness to Practise panel, the registrant has recognised the problem, done the necessary training and really there is no need to do - for the regulator to have looked at it at all, assuming that it could trust the employer to take the steps to ensure that they registrant was competent. I think there's a fair tranche of cases which really need not be in the system.

Julia Cumberlege: But cannot the GMC or whoever is running the fitness for practise, that system - can they not just bat it back? Can they not say, actually this is inappropriate for us?

Mark Stobbs: I think the Nursing and Midwifery Council are trying to do that.

Julia Cumberlege: Does it mean then that they have to have a change in their regulations?

Mark Stobbs: I would need to go and check the details of their regulations to deal with that. I know there is dialogue between the NMC, and the Trust and I think certainly the GMC and trusts about what should and shouldn't be referred. Not all employers understand that. I think once it's referred into the system, probably it has to go all the way through.

Christine Braithwaite: The General Pharmaceutical Council is undertaking work on thresholds. They're looking at thresholds for referral, I think - and we can check this and come back to you...

Mark Stobbs: Yes.

Christine Braithwaite: ...but I think the Nursing and Midwifery Council has more discretion. I think it can do more work with employers to make sure that things are

referred to it are the correct things. I think the General Medical Council has the slight difficulty that it's required to investigate...

Mark Stobbs: Exactly.

Christine Braithwaite: ...something once it's received it.

Mark Stobbs: Yes.

Christine Braithwaite: So, I think they're - it's more difficult for them to reject them, which is why they need to...

Cyril Chantler: They're waiting for the bill.

Christine Braithwaite: ...they need to have the bill to get the...

Mark Stobbs: Yes, exactly.

Simon whale: I suppose - I mean what strikes me is that very often the professional regulator will act when a specific incident is reported to it. Rather than - you know as we've just discussed...

Mark Stobbs: Yes.

Simon Whale: ...rather than a systemic problem. Or necessarily a pattern of behaviour...

Mark Stobbs: Yes.

Simon Whale: ...it's a specific incident that arises.

Mark Stobbs: Yeah.

Simon Whale: I think, as you know, we've spoken to hundreds and hundreds and hundreds of patients, many of whom have told us about patterns of behaviour on the part of the clinician. A dismissiveness, a defensiveness, a feeling that the clinician's always right. The patient, therefore, is inevitably wrong and how that overwhelms the relationship between the patient and the clinician. The patient struggles as - struggles to deal with that clinician, as extraordinarily stressful experiences compound with the pain - the physical pain they're already feeling.

Christine Braithwaite: Yeah.

Simon Whale: So, the issue there, is there is a pattern of behaviour, a cultural aspect in the way that that clinician is behaving.

Christine Braithwaite: Mm-hm.

Simon Whale: It's not just that there was an error or a misjudgement on one particular day. That individual is acting that way often. They may well be the minority, I'm sure they are in the minority, there's no evidence to suggest otherwise. But there are individuals apparently in the system like this because we've heard them. To what extent - I mean I think professional regulators, or GMC specifically, finds that quite difficult to deal with.

Christine Braithwaite: Yeah.

Simon Whale: Have you got any thoughts on (a) the existence of that kind of behaviour, and (b) how it could be better dealt with?

Christine Braithwaite: Possibly. I mean I think that's true, certainly when you look at the major enquiries into some health professionals who've transgressed in the past, ██████ for example, other individuals. You could see that there was certainly noise about them in the workplace. I think the difficulty for the professional regulators is obviously they're not necessarily privy to that. They would only be able to act on the intelligence that they hold themselves.

They are - the GMC - are the most advanced in terms of being able to analyse the data that they hold and start to identify trends in order to be able to either act on that, or feed it through to the Care Quality Commission, for example, for them to be able to act. I think the difficulty comes where information is held at employer level but hasn't been referred through to the regulator, either because the employer doesn't think it meets the fitness to practise - the threshold. Or maybe because those reports aren't being collated and it's just sort of your general discussion amongst people but no one's making formal concerns. I suppose with the General Medical Council's employer liaison system...

Mark Stobbs: Yes.

Christine Braithwaite: ...there is potentially now a better opportunity to be able to join that together. Because clearly if a doctor is undergoing their appraisal and revalidation within a Trust, and there are employment concerns known about it, then I would think that, that...

Mark Stobbs: Yes.

Christine Braithwaite: ...would be dealt through the employer liaison system.

Mark Stobbs: Yes, it would. It should do.

Christine Braithwaite: Then therefore that would now have a conduit through to the regulator. I don't think the Nursing and Midwifery Council for - the council's system of revalidation would quite yet - would...

Mark Stobbs: No.

Christine Braithwaite: ...quite allow that...

Mark Stobbs: No.

Christine Braithwaite: ...in relation to nurses. So, there is more difficulty in relation to that.

Mark Stobbs: They have their own employer liaison service, which is relatively new, but would certainly have the potential to look at that. One of our concerns with the Morecambe Bay cases was that you were getting a number of complaints about the same basic poor clinical care from a number of midwives. It was - that ought to have raised some questions about whether the whole - either the practise of that whole department or the practise of those individuals should have been looked at more closely.

When I raised this with the Nursing and Midwifery Council, they said, well it's quite difficult just to go on a fishing expedition, if you're not sure what you're going to find. This is arguable more repressive for the registrants. It's going to make them feel under pressure and those difficulties there. Personally, I mean I came down to the feeling that this is about proper communication with the employer and the regulator, and the employer being honest with the regulator about concerns. Which may sometimes be tricky for an employer if you have a shortage of midwives.

Christine Braithwaite: I think the real owner of that problem though, is - it has to be the employer.

Mark Stobbs: Yes.

Christine Braithwaite: Because I mean I think the issue is that there are performance - there are performance issues in relation to that individual practitioner that aren't being dealt with properly within the workplace. I think it's less of the regulator's problem to solve and more of the employer's problem to solve.

Julia Cumberlege: The trouble is it takes huge courage, doesn't it? To actually - either for the person receiving the services or for the registrant, or whatever, to - what in my youth used to be called a sneak.

Mark Stobbs: Yes.

Christine Braithwaite: Yes.

Julia Cumberlege: It affects all sorts of relationships and everything else. I just don't know how one can sort of safeguard the courage of those people who want to actually - see things happening, feel it shouldn't go on like that, it's really affecting patient care et cetera, et cetera. You know, so how can we give them some safety, some - safeguard the courage that they've got to come forward? It's really difficult isn't it?

Christine Braithwaite: It is. I think the Freedom to Speak Up Guardians seem to be helping. So, the work that Henrietta Hughes is doing as the National Freedom to Speak Up Guardian and the local Freedom to Speak Up Guardians. I've attended some of their meetings and listening to the local guardians and they were saying - I know it's anecdotal - but they were saying that they were noticing an increase in concerns being reported within the organisation as people felt more comfortable to be able to raise them. The critical point, they said, was then how the organisation responded. So as ever...

Mark Stobbs: Yes.

Christine Braithwaite: ...you know, if you get positive response from an organisation that deals with it properly and it feeds back that they have dealt with it...

Mark Stobbs: Yes.

Christine Braithwaite: ...then people feel that it's worthwhile raising a concern and they feel more comfortable with raising it. So, I think some movement is being made with that through the Freedom to Speak Up Guardians. I have seen it done very well in some organisations and some Trusts. It is where conversations about good things and bad things are held routinely, generally by medical teams, multidisciplinary debriefs. So, this went well today, why did it go well? This didn't go well today, why didn't it go well? It's normalising conversations about care. Where organisations allow that type of culture and that kind of conversation to take place, it's much easier for people to be able to speak up about a concern in a non-threatening and a non-threatening way.

Sonia Macleod: In terms of the Speak Up Guardians, the information that they receive anonymously doesn't go outside the trust?

Christine Braithwaite: The information they've seen anonymously....

Sonia Macleod: So, there's no - what I was trying to - I mean I was thinking of the comparable with the airline industry where there's an independent charity that receives...

Christine Braithwaite: Yeah.

Sonia Macleod: ...anyone that has a safety concern can report into them and they then analyse it. Because they are industry wide, they have far more data and also, they are able to pick up where you have outlier - in their case airlines, I guess. But in this case where you'd have an outlier hospital or trust, or something like that. But if you still contain your complaints within the unit that's being complained about, that isn't a possibility, is it?

Christine Braithwaite: No, they - I mean they can go outside. So, under the PIDA - under the *Protected Information Disclosure Act*, people - provided they follow their internal processes first - can take a concern outside if they feel the organisation isn't acting on it appropriately. Of course, they can also go through to the National Guardian's Office now through to Henrietta Hughes. Henrietta's done a number of investigations now, of assessments of Trusts.

Julia Cumberlege: Right, any further questions?

Simon Whale: No

Julia Cumberlege: No?

Cyril Chantler: No, thank you. It's been very helpful.

Christine Braithwaite: [Unclear] You're welcome.

Julia Cumberlege: Thank you so much for coming.

Christine Braithwaite: Thank you.

Mark Stobbs: Thank you for seeing us.

Julia Cumberlege: Is there anything in particular you want us to take away from this session this afternoon? You can always write to us.

Christine Braithwaite: I don't - no - I don't - thank you. If we do think of anything afterwards, we'd like to - I mean we will obviously like to see improvement...

Mark Stobbs: Yes.

Christine Braithwaite: We think it's difficult. We - all of us are trying to make a change and make a change for the better for the future. We look forward to the results of your considerations.

Cyril Chantler: Thank you.

Julia Cumberlege: Well thank you for the work you do.

END OF TRANSCRIPT

18th January 2019

Session 1: Sanofi

START OF TRANSCRIPT

- Julia Cumberlege: You are going to - I hope - introduce yourselves and I believe you want to make a statement as well at the beginning. So over to you.
- Hubert Bland: Thank you for the invitation Baroness Cumberlege. If we may start with some introductions and a brief overview of why we're all here and what expertise we bring. So, Pascal?
- Pascal Michon: Good morning. Thank you for the opportunity to attend this session. My name is Dr Pascal Michon. I am based in Paris and I belong to Sanofi, I am the Global Established Products Medical Affairs Head. My role is to cover the medical expertise in different hepatic fields including central nervous system and including valproate.
- Hubert Bland: I'm Dr Hubert Bland. I'm the Country Medical Chair for Sanofi UK and I'm responsible for all medical activity in the UK and accountable for the governance for medical activity here for Sanofi in the UK.
- Julia Cumberlege: Thank you.
- Janet Lewis: Good morning. I'm Janet Lewis. I'm Head of Regulatory Affairs for Sanofi in the UK and Ireland. I've been with Sanofi for around about 18 years and valproate has been in my portfolio for - since 2015.
- Julia Cumberlege: Thank you.
- Eric Teo: Good morning. My name is Dr Eric Teo. I'm the Qualified Person for Pharmacovigilance or QPPV of the Sanofi group. I'm also the pharmacovigilance Head of the Regions. My role is the operation and maintenance of our pharmacovigilance system globally, which is to look at the adverse event reporting analysis - aggregate or cumulative analysis. Thank you for the opportunity to come over from Paris to contribute to this process.
- Julia Cumberlege: Thank you. Who is making the statement?
- Hubert Bland: I will. Thank you very much.
- Julia Cumberlege: Okay. Thank you, Dr Bland.

Hubert Bland: I'll begin by reading the prepared statement, but we look forward to having a conversation with you on this important topic and answering any questions and providing any information that we can. On behalf of Sanofi, I want to say that we're acutely aware of the difficult situation that a family may face when having a child with malformations or developmental disorders that may be related to the mother's treatment with medication during pregnancy. We understand the concerns that families - of families that are affected and their need to be heard.

We are pleased to be able to input to the work of this review. We have ensured that we have always been available to assist the review team and when considering the complex issues arising from the use of valproate to treat women and girls of childbearing potential. We responded to the draft terms of reference consultation, submitted written replies to the calls for evidence process and are now attending this hearing. You'll be aware that the issues surrounding the use of - surrounding the safety of valproate containing medicines in women of childbearing age is incredibly complex, and spans a period of at least 45 years. This will be apparent from the volume of information within our written submission and the submissions of others that you've heard.

Notwithstanding this, we hope to be able to answer as many of your questions as we can today in relation to the review's scope. I'd like to spend a few minutes providing a brief overview of the evolving science, our roles and responsibilities and the actions that we've taken. Ensuring the safety of medicines we provide - we provide to patients - is our primary concern, and it's key to Sanofi's mission, which is to protect, enable and support people facing health challenges so they can live life to its full potential.

You'll not need me to tell you of the enormous burden placed on patients with epilepsy. It's a very serious consequence – condition, the consequences of which could be severe and wide reaching. Treatment is complex and careful dosing and sometimes the use of multiple medicines is required to control seizures. The availability of valproate-containing medicines in the 1970s was a very important breakthrough for epilepsy patients, and many have benefitted since then. More than 45 years after being made available, valproate remains of the most effective treatments for generalised epilepsy. Crucially for some patients, it is the only treatment to provide adequate seizure control.

More than 100,000 patients with epilepsy in the UK alone are treated with valproate medicines. Its importance as a treatment option is perhaps best illustrated by the medicine's inclusion in the World Health

Organisation essential medicines list. Epilepsy is a potentially life-threatening condition and patients may need to be on an anti-epileptic for life. The management of epilepsy during pregnancy is particularly difficult, due to the inherent risks associated with the condition and the fact that no anti-epileptic treatment - no anti-epileptic treatment - appears to be completely without risk to the developing foetus.

Knowledge regarding the possible adverse effects of a medicine increases over time, as a result of pharmacovigilance activities in the marketplace. However, clinical trials of any medicinal product in pregnant women are associated with ethical difficulties, and therefore knowledge concerning the effects of the product on the foetus will not be based on robust data. Scientific evidence on the risks of valproate and other epilepsy medicines used during pregnancy have taken many years to evolve. It's important to note that scientific data on adverse pregnancy outcomes can be very difficult to interpret, because of the multiple confounding factors at play.

These include epilepsy itself, other medical conditions, genetics, other medicines, environmental factors such as common toxins.

Pharmacovigilance techniques, safety signal detection and statistical methods have advanced substantially over the last 45 years, together with the technology required to analyse accumulating pharmacovigilance data effectively. Our understanding today of epilepsy and the risks of treatment is significantly greater than it was in the 1970s.

There are four principal participants who develop, consider and act on the information regarding the risks and benefits of valproate in medicines. Firstly, the licence holder. Companies like ours carry out continued monitoring, testing and reporting of adverse events to the regulators throughout the life cycle of the drug. We update the regulators as information becomes available that might impact the benefit-risk profile. We make proposals to the regulator on the information we believe that should be included in the label for prescribers and patients.

The medicines regulator - the EMA at EU level, the MHRA here in the UK - have responsibility for safeguarding public health. They are responsible for supervising the marketing authorisation and ensuring that the benefit-risk balance for use of the medicine remains positive in the context of the developing knowledge and notably pharmacovigilance data. They review the totality of information regarding any medicinal product, including adverse events and information reported by all licence holders, healthcare professionals, patients and published scientific literature.

Based on this assessment they determine the wording of the product information for healthcare professionals and patients which will allow the product to be used effectively and appropriately. Healthcare professionals are ultimately responsible for the care that patients receive. They are in direct contact with patients and are the only ones that have specific information with regards to the health and personal circumstances of the individual patient. Patients together with the healthcare professionals participate in a healthcare plan and take an informed decision on their treatment.

We believe the role of all four groups needs to be considered. Since Epilim was first put on the market, the product information has been consistent with the developing state of scientific knowledge. The first Epilim data sheet in the UK mentioned teratogenic risks - risks detected in animals and included appropriate prescribing recommendations which referred to the use in women of childbearing age, stating that - and I quote - any benefit which may be expected from its use should be weighed against the hazard suggested by these findings.

Over subsequent years the science evolved and further data was collected on the use of this medicine. Sanofi notified the UK regulatory authorities of developing scientific knowledge in a timely way, and we made appropriate applications to update the product information even where the evidence fell short of an established causal relationship. These proposals were taken - were then assessed by the regulators who, as you know, have the final say in the wording of the product information. It was the regulators that had the final responsibility for it - ensuring that the information provided to the healthcare professionals and patients reflected contemporaneous scientific and medical evidence.

It is important to note that pharmaceutical companies are not permitted to interact directly with patients and may not provide medical advice to individual patients. Pharmaceutical companies in collaboration with the regulator play a role in disseminating new safety information and educational materials when the regulator decides that such information is necessary. We have worked and continue to work on a wide range of initiatives to support patients and healthcare professionals in considering the complex issues related to the management of epilepsy and bi-polar disorder using valproate.

This includes working closely with the MHRA to implement recommendations that we made - we made to the pharmacovigilance risk assessment committee at the 2017 European Medicines Agency public hearing. In 2018 alone we distributed over 150,000 packs of educational

materials, including patient facing information, healthcare professional guides and posters. We are currently producing new websites for healthcare professionals and patients.

I've outlined the roles of the relationship between ourselves and the regulator but I want to mention the role of the healthcare professionals and the health service. It's the responsibility of the healthcare professionals to ensure that each patient receives advice on the most appropriate treatment for his or her condition. This includes taking into account the benefits and risks of available treatment - available treatment options, conveying information to the patients which allows them to make an informed choice over the care they receive.

This requires healthcare professionals to keep themselves up to date with the evolving knowledge on the medicines they prescribe. They are required to alert patients to the relevant risks and carefully implement risk mitigation programmes. This can only be achieved if healthcare professionals are effectively trained on the treatments they use as knowledge evolves, through appropriate systems and processes and are given adequate time for the proper implementation of risk minimisation programmes. In conclusion, valproate is a highly effective medicine for a life-threatening condition. For some patients it is the only treatment that controls seizures and they may need to be on it for life.

The management of any long-term condition during pregnancy is very difficult. The management of epilepsy during pregnancy is particularly challenging. However, women with epilepsy should not be treated with valproate during pregnancy unless there are no suitable alternatives. During the European Medicines Agency public hearing in 2017 we heard powerful testimony from neurologists who explained their reasons for recommending the use of valproate in some women of childbearing potential. They argued that it should not be entirely discarded as a therapeutic choice for young women with epilepsy. For some women, it will be their only option to control potentially life-threatening seizures.

Sanofi continues to work with the medicines regulator to implement risk minimisation measures. All participants in the healthcare system - licence holders, regulators, healthcare professionals and patients - have their role to play in ensuring the safe use of medicines. Collectively we must ensure that healthcare systems are able to support the safe use of important medicines such as valproate, based on the latest scientific literature where these are clinically appropriate to the right patient. Thank you. We look forward to your questions.

Julia Cumberlege: Right. Thank you, Dr Bland very much for that, because it was extremely comprehensive and I have to say I think we did know some of that anyhow - perhaps not all of it, but I suspect most of it anyhow. You were talking about - really about the monitoring and the testing and all the other - the processes that you use in order to make sure that Epilim is a successful medication for women of childbearing age. Can you actually confirm that there is a causal link between valproate when it's used in pregnancy and the congenital malformations and the neurodevelopment delay that we've also discovered, talking to patients?

We've been privileged in a way which is not open to you, in that we have talked to hundreds and hundreds of women and their families and we have met some of the young people who have suffered from malformations due to valproate. We've seen all that and I appreciate that is a route that really isn't open to you and I want to explore that a bit further on. If you could just confirm this causal link it would be helpful.

Hubert Bland: If I may, my colleague Dr Teo just to talk about how the causal link and the knowledge around causality has been established over the years. He can explain some of that.

Julia Cumberlege: Right. I mean, it's up to you to choose who you want to answer what questions.

Hubert Bland: Of course.

Eric Teo: Thank you. Individual cases that were reported to the company throughout the last 45 years, each case was analysed and reported to the regulatory authority. Just as a patient would report to the regulator at that time, patients reported cases to the company. Each individual case was analysed, and very often at individual case level, it can be difficult to determine the causal relationship simply because there are a lot of confounding factors. In the 80s, 90s, very often issues were - especially developmental delay - were put down to the disease epilepsy itself and certainly certain forms - certain types of epilepsy - have a genetic component.

On top of that there are other confounding factors, perinatal factors, other concomitant medications, so it is not easy to tease out the causal relationship. Of course, over the years when more cases came in, a pattern began to emerge. For the developmental delay - for the malformation part the causal association was known, and a warning - my colleague can talk about the specific warnings - warnings were put on the very first data sheet right from the beginning. The developmental delay

issue, the causal association, took some years to establish, simply because assessment of a child's development took time and because of all the confounding factors.

By around the year 2000, there was a paper - a draft of which was sent to the company - mentioned that children born to mothers using anti-epileptic drugs, or themselves therefore exposed to the medicine in utero - some children required additional educational needs. That was the first big questionnaire-based survey using additional educational need as a surrogate. When that became apparent to the company, then the company sponsored research in the area. Of course developmental needs is a very broad term. It covers a whole host of issues within it. Again, not easy to tease out.

Certainly by early 2000 and subsequent years the pattern began to emerge. A causal association at the population level was established and the company initially - although the strength of evidence was not high - the company on a precaution, as a note of caution, applied to the MCA at that time to put on warnings which my colleague can elaborate. At an individual case level, just to come back to this, it can be very difficult to establish which factor - whether drug or anything else - was causing the issue, although at a population level there's a percentage risk that was worked out as a causal association.

Julia Cumberlege: Thank you very much. That's very clear, but again talking to the patients, one of the things that they've been very concerned about it how slow it's been to act. Both for you and also for the regulator - act on the emerging risks that have appeared. Although it's true to say - I do accept what you've been saying - that from the outset the information which you gave to doctors for women of childbearing age who were taking valproate, that should only be used in severe cases of those resistant to other treatments. I just sort of wondered if you could tell us exactly really where the great difference was made between the precautionary warnings and then the evidence-based assessments? The time lag is very critical and we - if you could say a bit more about that it would be helpful.

Hubert Bland: Would you like to talk on this?

Janet Lewis: I can talk. As Eric has said, the evidence accumulates over time because it's such a complex area. You don't have an immediate take X, Y happens. What that meant was that we knew from when the product was registered that there was a potential teratogenic effect in animals, and then doing - after the product - it was registered by a company called Reckitt-Labaz in the mid-seventies, and after it was registered they

discussed with the regulators what further studies they should do at that time.

During a prospective study in this group of patients would have been very difficult. The view of the regulator was that it wasn't practicable to carry out a prospective study because firstly, you know there was teratogenic risk, and secondly already we were saying using caution with women of childbearing potential because of that. Data meant - and they couldn't actually suggest any alternative methodologies to Labaz to actually collect those data either. What was agreed between the regulator and Labaz at the time was that Labaz would make sure that they submitted all information that came to them on women who did get pregnant and analysis of those cases.

Sanofi then took over the licence in 1981 and that - I suppose the first data that started to appear was around about 1982 on congenital malformations. There was a study - the Rowan-Alp study - but it was a very small number of patients and there was - it mentioned there were two defects but there was - again, it was individual cases. Again, Sanofi spoke to the investigators at that time and actually spoke to other experts in the field to look what research could be done. MHRA - sorry, it was still Department of Health at that point - they - I'll call them the regulator. At that time, again, those data were reviewed and in the mid-'80s there wasn't enough data to actually say anything substantial.

At that point the information to doctors was updated. Just to say it should be used in caution with women, rather than just consider the hazards. It wasn't until - between the 1982 and late '80s. There were more small studies being done and again, Sanofi sponsored a study that ran between 1982 and 1988 which looked at women with epilepsy who became pregnant. Again there was no conclusive data that came out of that. Also, there was then a number of smaller studies. We have detailed them in our review. I haven't got details of all of them in my head at the moment.

Basically by the late-'80s it was recognised that there was a risk of congenital malformations in women, in humans, and that was - the data sheet was updated at that stage. Then in the early '90s, there was information on neural tube defects specifically added with an incidence at that point of one per cent. Then during the '90s, more information on congenital malformations came to light - the types of congenital malformation, the fact that there was a dose relationship and that if someone was pregnant, it was best to use the lowest effective dose and to use split doses.

As this information became available, there were a number of updates to the product information during the '90s. Now, all that information was submitted to the regulator as it became available and Sanofi analysed those data, the health authority analysed those data and ultimately the final wording that appears in the data sheet is actually for the regulator to have that - to have the final say on that wording. There were small changes made as information became available through the '90s.

Then on developmental delay, it was really - the first real data that pulled something together was in the year 2000, there was the [ADA] paper.

Julia Cumberlege: Sorry, 2000 and...

Janet Lewis: Two thousand. It was in 2000, year 2000. Again, the MHRA had those data and the company actually discussed quite extensively with MHRA - or MCA, sorry - during that period of probably about two years about whether the data sheet adequately reflected the information that was available. There was no causal link at that point. There was - the company wanted to be cautious, so we did suggest updates to the data sheet towards the end of 2002 just to mention that developmental delay had been seen. Again, in discussion with the regulator between 2000 and 2002 it was felt that that update wasn't required, and the regulator said that our data sheet adequately reflected the information available.

Then in 2003, developmental delay was added to the data sheet. What we know now moving forward to today is that for congenital malformations, the SPCA outlines that there is a 10 per cent risk and then for developmental delay, between 30 to 40 per cent risk.

Valerie Brasse: Can we just be clear, you're saying causal association by 2002 was established with neurodevelopmental delay?

Janet Lewis: Not a causal - no. There were cautionary statements added.

Valerie Brasse: Right. When - at what point is there an acceptance there is a causal association in relation to malformations? Just the year or the timeframe in relation to malformations and secondly for developmental delay. What is Sanofi's view on that?

Hubert Bland: Maybe you.

Pascal Michon: Maybe I can answer this question because we refer always to the scientific community conclusions, essentially the scientific literature. When we discussed with neurologists, the scientific community of neurologists said that before 2008 it was not possible to establish clearly

the causal proven association with development - no developmental delay and valproate during pregnancy. However, there was the beginning of a signal as soon as 2004. As said by my colleague, despite these dates - before these dates, Sanofi proactively...

Valerie Brasse: I get that. I think I'm just trying to establish the actual timeframe. You're saying really the community - the scientific community and manufacturers, prior to 2008 would have said there was no established causal link with neurodevelopmental delay?

Hubert Bland: No, I don't think it's as binary as that - as my colleague is saying. I think we all felt that there was a strong signal. I think if you're asking specifically as to the time point in history when we flipped from association to causation...

Valerie Brasse: I am.

Hubert Bland: ...we'll have to get back to you with a report from the scientific literature.

Valerie Brasse: All right. Similarly with malformations, congenital malformations are you in the same [unclear]?

Eric Teo: Again, there were different views because the researchers themselves couldn't agree whether certain malformation types - and later on developmental delay - whether they were attributed to valproate per se or anti-epileptics in general.

Valerie Brasse: I realise this is an evolving picture. I'm trying to establish as of today, are you able to say at what point it was clearly established that this where we were at?

Hubert Bland: I think...

Valerie Brasse: Both congenital malformations and neurodevelopmental delays.

Hubert Bland: I do appreciate the question. If I just might say with a [retrospect meter], looking back, it's perhaps simpler to establish - I think the Heneghan paper suggests that at some point our knowledge flipped from association to causation but one has to reflect on the - it's really important that one reflects on the fact that at the time, the ability to accumulate those information didn't exist. The ability to evaluate that information didn't exist. Methodologies for - cumulative methodological analysis didn't really become routine until the mid-90s.

Valerie Brasse: I understand that you can't now look back and say well you could have done all of these meta-studies then, that's not the question I'm asking.

The question is at what point - if there is a point - are you saying that it was accepted at that time on the knowledge that was available, it had become a causal associations for malformations and then separately for neurodevelopment delays?

Janet Lewis: Yes. We will have that information and we'd have to check where the wording in the SPC actually changed, so I think - Pascal you said it was around 2008 for developmental delay?

Valerie Brasse: 2008 is probably - you'll come back and confirm that?

Janet Lewis: We'll confirm that, yes.

Valerie Brasse: 2008 for neurodevelopment.

Janet Lewis: We'll have similar for congenital malformations.

Valerie Brasse: That would be really helpful.

Janet Lewis: I think what's important is that we actually - and that's why the data sheet evolves, as science evolves.

Valerie Brasse: I get that.

Janet Lewis: That link where you had an association, the wording described that association and then as the data became more available, then those warnings were strengthened appropriately in conjunction with the regulator.

Valerie Brasse: You'll come back and confirm for us a specific time.

Janet Lewis: Yes.

Valerie Brasse: Thank you.

Julia Cumberlege: Thanks very much indeed. Can I just ask leading on from that discussion, thinking that you are a global company, that you're in other parts of the world and presumably also manufacturing and dispensing - not dispensing but distributing I should say valproate, can you tell us - is there a difference in other countries? I mean, are we in the United Kingdom different from say the histories in other countries and indeed were they more cautious, other countries? Were they less cautious? How has the thing developed? I'm trying to get a bit of a comparison.

Hubert Bland: Janet, I think you can speak to this.

Janet Lewis: From a regulatory perspective, the way that the company works is that after signal detection and we have new information, we have a global labelling committee that produces - a company called Safety Information. Then each country is actually sent that same information to be submitted to the regulators at the time it's available. How the regulator interprets those data can vary across countries. I can't really give you information at this particular point because I haven't looked at how different countries have interpreted the information, but the regulators in those different countries have received the same information from Sanofi within the same timelines.

Eric Teo: If I could also add to that, so in our submission to the European Medicines Agency's Pharmacovigilance Risk Assessment Committee - PRAC - back in 2017. We had conducted a survey across several European countries. We also carried out what we call a drug utilisation study to look at prescribing patterns across European countries and the number of pregnancies exposed to valproate in some countries. The results of those interim analyses in 2017 were available which we presented to the PRAC which we then shared with you.

The final analysis is currently under preparation, but in short obviously there are differences between countries - between European countries. Primarily because these countries also have very different healthcare systems. In some countries, they would have - for example in Germany, there would be more neurologists whereas in the UK, although the initiation of treatment in epilepsy is done by a specialist, the routine follow-up may not have been done by a specialist. The routine prescribing and review of the follow-up medication. Again' in Germany, and some other countries, pregnancy planning - counselling for pregnancy - they are different, they are differently set up from the UK.

The UK is known to have a relatively high unplanned pregnancy rate. In some countries, pregnancy counselling is set up differently. There is therefore the opportunity to discuss with women about planning for pregnancy, switching to alternative medications well ahead of the planned pregnancy. Switching can take many months to titrate one medicine up and another down, it's a long process during which recurrence of seizures is a real risk and needs to be monitored very carefully. So, yes there are differences amongst various countries in the usage - in the number of pregnancies exposed, and we would be happy to share with you the results of the - the final results of the analysis of that drug utilisation study once that is finalised, which we hope fairly soon.

Simon Whale: Can I just pick up on - if we think about the things we've been talking about so far, information around risks available to - made available to both patients and healthcare professionals - have you got any observations on where the UK sits on a sort of spectrum of ability to and speed at which it makes those alerts available? We understand the point that the company provides the information, but what we're interested in is your observations on how UK compares in terms of getting that information to healthcare professionals and patients as compared with other countries.

Hubert Bland: Janet...

Janet Lewis: When you look at the UK in terms of how the regulator gets information out to healthcare professionals, I think in modern times - at least when I think going back for quite some time - if you think MHRA has current day practices which they send out monthly, that goes out with information on pharmacovigilance alerts, safety alerts. That goes out on a monthly basis to healthcare professionals. I know as someone in industry I can sign up to receive those alerts and get them. They are widely available quite quickly.

We also have the central alerting system in the UK where we have the ability to almost immediately - the next day - get information out to healthcare professionals via that system. In fact MHRA used that, both after the 2015 PRAC review and the 2018 PRAC review to communicate those risks out to healthcare professionals. I don't know how that compares to other countries, to be honest.

Eric Teo: If I could just - if I could add to that. Again, we did this survey prior - just after the 2014 review in Prague, looking at awareness of risks. The awareness of risks in the European countries including the UK is high. We conducted a survey. Around 95 per cent of physicians in these countries who responded to the survey say that they were aware of the risks and they would only prescribe valproate as a treatment of last resort when other treatments became ineffective or not tolerated.

Again, if you're interested in this particular survey, we can share the results with you. We are committed to carry out a repeat of the survey split down by country - in the principal countries that participated in the survey - later on, once we've had the chance to implement the new raft of minimisation measures. It is there to measure the effects of the minimisation measures.

Hubert Bland: If I may, Eric, I think just coming back to the question. Comparing the UK system's ability to transfer information from, you know, papers and

knowledge accumulated through to the label I think it's always been the case that the UK have been an exemplar within Europe of our ability to process that information from a regulatory perspective. I think direct comparison - I'm not aware of any data that compares - very precise direct comparison.

Sonia Macleod: Can I just ask that when you said awareness amongst healthcare professionals is high at 95 per cent from your survey, what was the sort of response rate to your survey? I'm just wondering did you get professionals who know - who replied to you, or was it a broad sort of?

Eric Teo: That's always a challenge when we run these sorts of surveys, because by necessity surveys are built on a sample size that is calculated on the response rate and we validated this and agreed the methodology with the European Medicine Agency prior to doing the survey. I would prefer to send in writing the details to the survey itself.

Sonia Macleod: Okay, that's fine.

Julia Cumberlege: Right, can I just go on and just ask you about the patient information leaflets? We've been told, until 2003 they actually didn't spell out - sorry, before 2003, the leaflets didn't spell out the relatively higher risk of valproate compared to other drugs. I'm just wondering if you feel that in any way patients are being misled on this? Do you think there were other ways that we really ought - should earlier have warned patients about the risks involved? Because you're talking about surveys, it's quite interesting that a patient group has already done a survey as to what is happening in the country.

It's a small survey because it's a patient group, obviously, that has put these out, and we are still really concerned that these leaflets are not given to patients. Now that's not your problem, because presumably your problem is to ensure that the regulator and the medical profession actually ensure that these leaflets do go to patients. Consent has been a big issue when we've been talking to patients. They have felt they have not been told the full picture. I just wonder if until 2003 we really didn't spell out the problems.

Hubert Bland: I'll ask Janet to speak about this one. She knows all about it.

Janet Lewis: If I can answer that. When medicines were first introduced, the patient information leaflets are a comparatively new part of our society and for all of our drugs. It wasn't until the early 1990s that patient information leaflets were required for medicines. Before that, during the late 1980s, the ABPI - which is the pharmaceutical industry trade body - had been

working on the fact that it should be - you should be able to put patient information leaflets into packs. Obviously under the guidance of the healthcare professional and these needed to be approved and you could voluntarily put the patient information leaflets into packs.

There was quite a lot of work done by the ABPI with different stakeholder groups including doctors, and at the time in the 1980s, it was actually felt by quite a few doctors that patient information leaflets weren't necessarily a good thing. Because very much so there was the interaction between - the personal interaction between the doctor and the individual patient's conditions. They felt that a generic leaflet given to patients with different conditions could actually stop the patient taking their medicine or taking it in a different way than is required for them.

The first patient information leaflets that were introduced, we actually introduced for Epilim in the late 1980s and that had advice on - to tell them to contact their doctor if they were intending to become pregnant to discuss their condition because the drug could affect their condition while pregnant. Then, in the early 1990s, when the SPC was updated actually - when the SPC was updated or the data sheet was updated to show the risk in humans, the patient information leaflet at the time - there was new European legislation that stated the patient information leaflet needs to reflect the information that's in the SPC.

When we were submitting variations to update the information for healthcare professionals, we were also submitting a patient information leaflet to the regulator. The information that appeared in the leaflet reflected the information that was in the SPC. In fact it was in the early 1990s - it was in 1994 there was actually information in the patient information leaflet to say that there was a risk of spina bifida - sorry, neural tube defects and a 1 per cent chance of women having a child with spina bifida. They - and we've submitted these - this information to you, so that's in the pack.

Valerie Brasse:

Actually that's what I'd like to pick up, because I've looked at the information you've submitted and in fact there seems to be a mismatch between what's in the patient information leaflet and then what's in the data and summary of product characteristics sheet. If we were to go back to 1989, and I accept the point that it wasn't mandatory at that point, it was purely voluntary - and I accept also that you're saying you were following the ABPI guidelines - but they conclude that in fact the summary should be a reflection of what's in the SPC at the time or at that time, the data product sheet.

But, as you pointed out, the first PIL just simply talks about tell your doctor if you're pregnant or thinking about becoming pregnant. Yet the data product sheet says an awful lot more, talks about increased incidence of congenital abnormalities in offspring born to mothers with epilepsy both treated and untreated. Talks about neural tube defects and specifically mentions the 1 per cent risk. The PIL does not actually reflect the comparative product information sheet.

Then by 1994 when it is compulsory to have a PIL, you are right, it talks about spina bifida and talks about a percentage increase - 1 per cent risk - but in 1993, 1994, already the product information sheets were talking about dysmorphia - facial dysmorphia - and also making a link with different daily dosages. This point that the patient groups say to us, that the patient information leaflets simply don't actually reflect, there's a sort of catch up going on. Something comes out in the product characteristics and then it's a little while later before it appears on the PILs.

Janet Lewis: If I can go back to the first - the first voluntary PIL - and that was done according to the ABPI guidelines and the ABPI actually did set out particular wording and phrases that should be used in pregnancy. At that time, the legislation - there wasn't the legislation on PILs, there was a lot of concern with the healthcare professionals about the types of information that appeared in leaflets. Specifically there were warnings along the lines - I know, if you're likely to become pregnant, tell your doctor. If you can answer yes to any of these questions, and one of them was pregnant or wanted to become pregnant. Those were the statements that were in the ABPI sort of...

Valerie Brasse: I get that, but it doesn't actually reflect then what is printed in the product information sheet.

Janet Lewis: That was because we - at that time they were voluntary, there was no legislation around patient information leaflets. Once the leaflets became mandatory, then the legislation said that they should reflect what was in the SPC. Again it's in accordance with the regulator. We submit information to the regulator and the regulator decides - has the final decision...

Valerie Brasse: That's your point - that's the point you're making is that it's the regulator.

Janet Lewis: ...on the wording.

Valerie Brasse: The regulator that determines that it wouldn't actually reflect what was in the information sheet.

Janet Lewis: The regulator reviews our data, reviews their data and they look - they have the final say on what the final wording is in both those documents.

Hubert Bland: I think...

Eric Teo: I think another point just to make is that because for many women who stay on valproate, it is an important life-saving medicine for them. The difficulty and a lot of concerns in the past has been that if direct information is put into the patient information leaflet, there is always the concern that it could lead to sudden cessation of treatment, sudden disruption of the medication before the patient had the chance to interact with their physician and get the proper advice. This would have then brought on the recurrence of seizures which in some situations could be quite devastating for the patient.

Valerie Brasse: I fully understand the sort of contextual thinking at the time. I'm just wanting to make sure that we're quite clear that it isn't actually a direct match. There is a mismatch and that really maybe we need to talk about that with the regulators and I'm thinking around what to tell patients.

Janet Lewis: I think that has developed as well. As time has moved forwards, and again - we look in the context of now compared to the context of 30 or 40 years ago and the world is a different place. People get information from so many different places. If you look at the patient information leaflets today, it's so much more information there than you would have had 30 or 40 years ago because now it's all around people being able to make that informed choice. That's - I think that's recognised across society these days.

Hubert Bland: I think importantly if I may, it's Sanofi's position that for all of our medication the information should be equivalent in whatever source or whatever geography we distribute it. We continue to work with the regulators to make sure that happens.

Sonia Macleod: When you say that you provide data to the regulators, you analyse - the regulators have the data, they analyse it. How often do you get discrepant views on what should and shouldn't be included in terms of information and how often are the views fairly closely aligned?

Hubert Bland: Janet, do you know how much interaction?

Janet Lewis: Mostly I would say that they are quite closely aligned. Eric will probably talk at some stage about signal detection and the information that we submit. Obviously we are submitting all our data to the regulator and the regulator will be getting information from other sources as well. I

mentioned earlier around - round about 2000 when the data on developmental delay were becoming apparent and at that stage, the MCA at the time had contacted the company and asked us to carry out an analysis of the data. They would carry out their own analysis with the CSM and I think paediatric committee as well.

At one point I think we were ready to add something on developmental delay and had discussions with the regulator and it was felt through those discussions that - in 2001 for example - that the current data sheet was in line with the information and that it wasn't the right time to update it. By - towards the end of 2002, the regulator was in agreement that we should add something and then we submit some wording, and the final wording was slightly more descriptive than the original wording we'd submitted. Normally the - the understanding of the data is fairly consistent, but the regulator has the final decision on what wording actually ends up in their documents. Does that answer your question?

Sonia Macleod: Yes.

Janet Lewis: Yes.

Julia Cumberlege: Can I just ask about your relationship with patient groups? As I understand it, you really cannot contact or take information or have a helpline or anything like that for individual patients, is that right?

Janet Lewis: That's correct.

Julia Cumberlege: That's because of the law of the land and the regulator and all of the rest of it. One of the things that has been produced - and I'm not sure what your input was to it - is the pregnancy prevention programme, the PPP. The patients have been saying to us that they felt that has taken a very long time to come to fruition, and that they should have had that much, much earlier on. It's interesting what you were saying, Dr Teo, about the importance of keeping epilepsy under control and we absolutely understand that. But, we have heard women say to us 'if I had realised the risks to my baby, if I had really been told what could have happened, I would have gone without the medication. I would have taken that risk. It's my body, my baby. I would take that risk'.

We've been trying to understand better about the pregnancy prevention programme and whether it's really working. What was your input to that and why wasn't it done earlier?

Hubert Bland: Janet.

Janet Lewis:

Okay. In terms of the - there's two things there. There's the pregnancy prevention programme itself and that was actually approved by the PRAC. You're aware what the PRAC is, I don't need to do the - yes. That was approved by the PRAC after the 2017 review. Towards the end of 2017 the company had actually proposed the pregnancy prevention programme to the PRAC because we felt that the earlier PRAC review actually has all of the components of a pregnancy prevention plan without it being called one. There wasn't a contraindication and the pregnancy prevention plan, but all the same information actually was in different parts of the SPC.

There's a bit which has special warnings and precautions, and as a result of this information still not getting to patients, the company proposed that a pregnancy prevention plan was introduced. It has quite a lot of measures both for the patients and for healthcare professionals. It tends to be the sort of last resort in terms of risk minimisation measures. The - we started talking in the UK to the MHRA about the pregnancy prevention plan before PRAC had actually finalised. The actual PRAC review was finished in May for 2018, whereas we started working with the MHRA on the implementation of a pregnancy prevention plan in the February of that year.

I know you'll be aware that MHRA have a broad stakeholder valproate group, and one of the things that MHRA thought was really important and we agreed with was that the stakeholders had an opportunity to input into the materials as they'd be finalised. I've actually brought them along for you in terms of what we had because my feeling is that actually in terms of the timing, that there wasn't a delay in getting these packs out to people. The - we started - we had the final word in from the PRAC even though the PRAC review hadn't finished in February, and at that time we started moving from having an A4 Word document to producing - to producing these documents. Again, with discussion with the regulators and we - the discussions they'd had with the stakeholder group it was felt that some of the PRAC wording was quite complicated. Some of it was quite long and really they wanted some focus on the main messages to get out there.

They asked us to come up with a patient guide that was attractive rather than A4 pieces of paper, so we submitted these to MHRA in February. Then they worked with stakeholders on all of these materials and I don't know if you're aware but there's quite a few materials. There's a healthcare professional guide, patient guide, patient card, we did some posters for pharmacies. There was - obviously the annual risk assessment

form and also we did some stickers for pharmacies as well which I can talk about a bit later.

In terms of timing, because we had consultation back across the stakeholder group it was actually - it was 20 June actually when we had approval for the final materials that were - that needed to be printed. Now, we had - we actually had to print over 500,000 pieces of information, and you'll understand that logistically that can't be done overnight. It took us - what we actually did was we made these materials electronically available the day after we received MHRA approval on the electronic Medicines Compendium. They were available for healthcare professionals electronically. MHRA had already communicated about the materials to healthcare professionals.

Then we started distribution in the middle of July. Sorry - they were printed between June and July, and then it took us eight weeks to distribute to over 150,000 healthcare professionals but 94 per cent were actually distributed within a one month period.

Julia Cumberlege: I do understand the logistics and many of us who've fought campaigns and things like that, we know that - how you have to sort out the printing and the publication and the production and then have distribution. I just - do you not share the patient groups' and the individual patients' frustration at how long all this has taken, and could you not have started earlier?

Janet Lewis: We have to do everything in conjunction with the regulator. Everything we do needs to go through scientific review with the regulator and get their agreement before we can take any action. It...

Julia Cumberlege: But you could have started earlier.

Janet Lewis: Well, we couldn't start earlier in terms of the materials for the pregnancy prevention plan because the PRAC review actually has timelines that need to be followed. Until - because - the PRAC review is a harmonised process across Europe. Until we - we are actually legally obliged to follow a PRAC outcome. We could have done something six months earlier and then had to change the messaging once PRAC had finished which isn't good for communication either.

Hubert Bland: Janet, perhaps if I might interrupt.

Julia Cumberlege: All right.

Hubert Bland: To speak to the things that we did do. You mentioned the earlier PRAC and some elements of pregnancy prevention communication went out beyond these packs. We did start earlier and I don't think we could have started before we were allowed.

Janet Lewis: Can I just add to that, because I will go back to the 2015 PRAC review, but most of the information in - we produced patient guides and healthcare professional guides in 2015 PRAC review, which looked different to this - different colour, et cetera. The same messages about safety were in them at that time. One of the things that we did as well back in 2015 - because again it was - the messages are not getting out there. There was a lot of discussion again that the patient groups were having with MHRA and therefore we were having with MHRA around pharmacists being aware of messages and women getting the information that way.

So one of the things that Sanofi did in 2016 was - we worked with pharmacists to set up a pharmacy alert so when they were dispensing valproate, there was a popup message that actually reminded them that if they were dispensing to a woman of childbearing potential, that they should actually ask them if they were aware of the risks and provide the patient card. We had a patient card back in 2015 as well.

Julia Cumberlege: Thank you very much for that. I really want to move on because...

Cyril Chantler: Can I just say one thing in relation to something that was said? As a doctor, I always felt able to phone the medical director of a pharmaceutical company and seek their advice or pass on information. I found that very helpful. You just told us that you're not allowed to talk directly to patients. Is that a good thing, given how society has changed, medicine has changed? First question. Secondly, are you allowed to communicate with groups of people that are set up to represent patients?

Hubert Bland: I'll take that one if I may. Firstly absolutely. To underscore what you said, there has always been a channel that has been open between physicians to talk to the medical teams within pharmaceutical companies and in fact another route that one should reflect on is that the medical information system for providing that kind of information in a standardised way has been available for a very long time. That was available. We share the frustration that information is not getting to patients and we applaud any activity which amplifies that ability to get it - get the information to patients. There are - you're absolutely right, there are modern methods for disseminating information which is somewhat frustrating that it's not possible.

Reflect for a moment on - and I know that we've underscored it and please forgive me for repeating it - it is - it comes with some serious burden that when one communicates with patients that there might be a consequence which is far, far more significant than - responsible companies like ours might do it properly but if we let this loose and people can communicate directly with patients, that has to be regulated. It is well regulated in this country and I think it's a good system, but we do need to improve how we get the information to patients.

Cyril Chantler: People are getting information from all sorts of different sources in a way which didn't exist when I was practising.

Hubert Bland: Yes.

Cyril Chantler: The world has changed very rapidly. Isn't it better they get the information from somebody who knows, as long as the conversation is shared with the people who are taking help responsibilities like care navigators for the patients, the general practitioner and so forth?

Hubert Bland: Absolutely. We - so there's - Janet wants to say something but in conclusion we do also and are permitted to interact with patient groups and do so with very strict guidance and governance. Janet, do you want to say something else?

Janet Lewis: I was reflecting on the routes of information to patients and I think that is something that should be explored by the whole healthcare profession really. One of the things that's come out of the PRAC recently is the company have proposed to use QR codes so that when the patient receives the patient information leaflet, that they can actually use the QR code to access the risk minimisation materials. I brought along a box of Epilim which now has the warning on the front of the pack, for example.

The warning actually went onto packs again in about 2015 but the pictogram was something specifically requested by the patient groups. After PRAC this time that was introduced onto packs and again, something that quite recently the patient groups have reflected back. It first really came to light after the oral hearings of the PRAC last November was the amount of dispensing in white boxes. Again, from discussions that the patient groups were having with the regulator, the regulator asked us to introduce a 30s pack rather than a 100 pack so that women should at least get one pack which is a complete pack with the patient information leaflet and with the warnings on the front.

One of the things we did while we were moving to introduce that was we introduced stickers for pharmacists with this message on so that they

could actually put those on to the front of the box. I actually - again, applaud that move so that this information should be there as a very specific message to patients moving forwards. These are now entering the markets.

Julia Cumberlege: I just want to say to you that I think one of the things you need to look at again is your website, where you're talking about working with patient groups which you've talked to us about, but you also talk about working with patients. Not patient groups - patients. You may want to just review that. I think. Simon?

Simon Whale: The thing that strikes me about that and about other things are the steps and measures that have been taken including the - as a whole, is this frustration that the patient and patient groups have understandably articulated to us that it could all have happened and should all have happened so much sooner. If you think about the accumulation of scientific knowledge, and you talked earlier about the point at which causality became clearer, that's well before 2016, 2017 and 2018.

Janet Lewis: Many of these messages have been in the SPC for - and in the patient information leaflets - for many, many years. There does come back about the - the only person who can have that individual conversation with women is their individual doctor. We really do hope that the introduction - into the SPC that you must use the annual risk assessment form and have these discussions is really going to make a difference. It's - with retrospect you can always look back, but we have updated the data sheets and the information to patients as information has become available and as it's been approved by the regulator and we've done that in a timely manner within the system as it allows it.

Valerie Brasse: Can I just ask though, you talked about the route back to the doctors as being they can ring the medical team at Sanofi. Has there always been a route - direct route, not mediated by the regulator - from Sanofi to the healthcare professionals?

Hubert Bland: I'm not sure I understand the question.

Valerie Brasse: Cyril asked earlier, when I was doctor I'd be able to ring the doctor and he was saying there was always that channel of communication from doctor to the medical team. Has it worked the other way? Apart from the characteristics form - the summary characteristics form - what is your communication with the doctors? Have you been able to do that without going via the regulator? Do you have a routine channel and how has that changed over time?

Hubert Bland: Yes. There are...

[Over speaking]

Janet Lewis: There's a *Dear Healthcare Professional* communication...

Valerie Brasse: How long has that been in existence?

Janet Lewis: For - a number of years. We've used those over time. Again, you need to do that in conjunction with the regulator.

Valerie Brasse: That's what I'm saying. You've never - are you saying you have never had direct communication to the healthcare professionals without having to go via the regulator?

Janet Lewis: Any written communication - dear doctor letter to communicate new risk information - is done in conjunction with the regulators.

Valerie Brasse: What about commercial information?

Janet Lewis: We do have medical teams who speak to doctors and we do have promotional teams that speak to healthcare professionals with messages as well.

Valerie Brasse: So there is a history of promotional messaging going out?

Janet Lewis: Yes.

Valerie Brasse: Who controls that?

Janet Lewis: Again that's the ABPI code of practice, so that is controlled...

Valerie Brasse: By the ABPI?

Janet Lewis: ...by the ABPI, yes. There's a voluntary code of practice but they have quite stringent regulations so we must promote our medicine in accordance with our licence. There's an internal company review to ensure that we're following the code of practice and part of that is that you are giving a balanced view to healthcare professionals about the risks and benefits of the product, which reflects your current licence.

Julia Cumberlege: Simon, would you like to...

Simon Whale: Yes. Can we talk about post-marketing developments? I think - Dr Bland, you said at the beginning quite rightly that knowledge changes over time and I think you've emphasised that in different ways so far. Obviously therefore post-marketing developments can highlight risks in a way that

clinical trials couldn't. What's the threshold for evidence that leads to action in that post-marketing context? What are the consequences of that action?

Hubert Bland: Eric, would you like to talk about that?

Eric Teo: Specific for drugs that are potentially teratogenic, obviously post-marketing it would be very difficult and indeed in many situations unethical to carry out intervention research or studies. Therefore in post-marketing setting, be that for products such as valproate that has a teratogenic potential, really the system relies on individual reports sent to the company - so individual reports sent to the regulators and there's obviously an exchange of information between the company and the regulator.

All the cases that came in from healthcare professionals, doctors or specialist neurologists or patients - each of these cases is thoroughly reviewed within the company and depending on - all series cases, depending on the threshold - serious cases are all submitted to the regulator within 15 days. Non-serious cases within 90 days. These cases are then reviewed in an aggregate accumulative manner periodically. When there is a pattern that arises then the review is done by a senior physician in the company - in our case a global safety officer located in Paris looking at global data sets, because...

Simon Whale: Who determines the point at which - sorry to interrupt - who determines the point at which a pattern has arisen?

Eric Teo: The global safety officer will take the initial view as to whether there is a pattern and then the initial assessment of the global safety officer is validated or reviewed by the therapeutic area head for the whole therapeutic area in the company which is then brought to a senior committee called the safety management committee of the company that looks specifically at this pattern. It obviously draws in not just individual cases, it will be all the literature that's published at that time - what is known about biological possibility - what is known about the preclinical data et cetera.

Collectively the committee will then take a view as to whether there is a - the signal is valid and if so the committee will then communicate with the regulator and seek their view, saying this is our assessment, what is your view? This is our proposal. If there is a safety signal that is validated and assessed to have a causal association, the company will propose to them measures. I'll give you some statistics for example. We do this regularly

and very seriously across all products. In 2018 there were quite a few - I think 18 total signals derived from cumulative review. There were around 3400 cases related to valproate that were reported to the company.

Obviously the regulators would have a much bigger data set because they receive from all companies. We exchange data. All these were distilled into the 18 signals which were then assessed, communicated with the regulator. Some will then lead to update in the warning in the data sheet, updating the SPC and updating the patient information leaflet.

Simon Whale: So if you take the change in SPC content in the early 2000s - 2001, 2002, 2003 - the summary product characteristics changed and became a bit more specific. Is that as a result of the kind of process you've just been talking about?

Eric Teo: It would be a very similar process. There is a safety officer that looks at all the data set and then goes - subject to the review by her - the therapeutic area head then reviewed by the senior safety committee of the company which then goes through to the regulator.

Pascal Michon: Maybe - if I may - you could also add the support Sanofi provide to independent registries to follow pregnant women and to see the...

Eric Teo: Yes - thank you. Indeed. When - because some of this research requires - and especially signals that potentially arise from pregnancy - such research typically involves a pregnancy register. It's a huge database that is - really requires a mammoth effort. The company contributes - since we knew about this in the late '90s and early 2000 - the company contributes support funding to the UK pregnancy registry, the needs study and the European registry called the EURAP. So we are very active and try and contribute our best.

Currently we are in discussion with the European Medicine Agency to see what more we can do. Beyond the survey that I mentioned before, we are looking proactively with the regulator, the European Medicine Agency, to see whether we can look into what is a good way of switching patients who are currently on valproate - women of childbearing potential, not general population, women of childbearing potential - what is a good practice to switch them to an alternative, prior to planning for pregnancy? That's one strand of research that we are currently involved in.

Simon Whale: One of the problems with signal detection is the unknown unknowns and the fact that if you take neurodevelopmental delay in the case of valproate, it relies on clinicians being able to associate neurodevelopmental delay with valproate. What - how do we - how do

you go about detecting an unknown unknown and does that not also cause a safety issue because there's a delay in the process?

Eric Teo:

You hit the nail on the head. I think that's a really difficult problem that we have been grappling with, to detect developmental delay. The doctor has to wait for the child to grow up through childhood, early teenage. If you look at a paper in the 2001 publication by Adab and Chadwick the children were age 6 and 16. It took a long time. Of course it's also subject to recall. One has to recall what happened several years ago, 10 years ago, whether there was exposure to one medicine or another medicine which could confound the effect of the first medicine.

There are a lot of issues and difficulties in running this type of work. Signal detection inherently is difficult. Of course one could say that do we then err on the side of caution, and again we - the company has a senior committee on labels - called the labelling review committee which then look at - take the information from the signal detection committee - there's two different senior committees - and decide what is a corporate language to put into the label?

We take a step back in the 80s and 90s where therapeutic options are quite limited, all the therapies at that time were more teratogenic potentially. At that time in the 80s it wasn't quite clear which one has a greater magnitude of risk compared with another anti-epileptic. We understand the frustration - we do - but I think there is also contextually it is also awfully difficult for the doctors to decide with the patient which medication to give. Is it monotherapy or is it poly-therapy and what doses?

Hubert Bland:

I wonder if I might add something. You reflect on the fact that it is very difficult and of course we within Sanofi are always embracing contemporaneously what the current best scientific methodology is for this. One of the groups that I don't know whether you have spoken to is the drug safety research unit who you'll be contact with, who will understand exactly what the limitations are around this space a lot better than we will.

Eric Teo:

Of course these days we have much more advanced technology that was not available 30, 40 years ago. Now we have a global database. If we want to look at certain signals, we can go into the computer and use preferred terms and search and go through thousands and thousands of cases and pinpoint what are the cases that potentially could be linked and cross-linked? This type of technology was not available 30, 40 years ago.

Simon Whale: Is that system - there's a system today of reporting adverse events to regulators - is it efficient and rapid enough or would you like to see changes?

Eric Teo: We would think that - we would encourage more reporting. We know that in general, reporting of adverse events are done probably primarily by specialists. There are reports to say that probably 1 in 10 or 10 per cent of adverse events - of serious adverse events are reported. Reports by - we would encourage more reports. Make it easy, make it - facilitate the reporting process by not just specialists but by GPs or by all healthcare professionals, nurses who come into contact - and crucially patients themselves. We would very much welcome. Actually they can - patients can report directly to the MHRA and they can also report to the company.

Valerie Brasse: Do they?

Eric Teo: We hope to encourage more. In my - every case that we get from the patient we will go back and seek permission and say 'can we talk to your healthcare professionals to verify and to obtain further information to what you have given us?' There is a consent process going on there as well.

Julia Cumberlege: Could...

Eric Teo: Clearly any steps that would encourage more reporting...

Julia Cumberlege: You could have a helpline?

Janet Lewis: We do have a pharmacovigilance helpline. Patients can report adverse events directly to the company.

Julia Cumberlege: Direct to the company?

Janet Lewis: Yes.

Simon Whale: How often has that been used in relation to valproate?

Janet Lewis: I haven't got the exact figures about how much patient reporting - we could find out...

Cyril Chantler: But they can't have a conversation with you.

Janet Lewis: They can't have a conversation with us, no - about their specific case, we're not allowed to have that conversation.

Cyril Chantler: If there's a centralised database held for example by the MHRA, can you have direct access to it or do you have to ask the MHRA?

Eric Teo: Actually, since the European set up called EudraVigilance - was called EudraVigilance - we put all our cases into EudraVigilance and so does the MHRA. The - we as a company do daily downloads so it's in agreement.

Cyril Chantler: I was asking the other way.

Eric Teo: Yes, so we download...

Cyril Chantler: Yes, but can you access the information they've got on the yellow card system?

Eric Teo: Yes, we download...

Cyril Chantler: Directly?

Eric Teo: Directly.

Cyril Chantler: Good.

Janet Lewis: The MHRA's yellow card...

Eric Teo: No, the MHRA put them into the EudraVigilance database. We then download. It's direct from them. They put it on and we download it.

Hubert Bland: In fact I hate to bring it up but this is one of the challenges and things that have been discussed around Brexit is ensuring that we still have access to that information, they're able to share information.

Valerie Brasse: Because at the moment you can't get it from the MHRA, you have to rely on them downloading it or uploading it to Eudra - whatever it is.

Eric Teo: EudraVigilance, yes.

Valerie Brasse: Yes.

Julia Cumberlege: I was so hoping this was a Brexit free zone.

Hubert Bland: Quite rightly.

[Laughter]

Julia Cumberlege: All right.

Simon Whale: The - the summary product characteristics has often said over the years, in the timeline you sent to us, that - either said or implied that further research and further evidence is required. There are various examples of that over the years. Did Sanofi take steps to acquire that evidence?

Hubert Bland: Janet?

Simon Whale: Maybe some examples where you did?

Eric Teo: Yes. I think we as a company we worked hard to acquire possible new evidence. I think Janet mentioned before in the 1980s, the company supported a study by Hunter Tell which lasted six year follow up period. The company also provided funding to pregnancy registries and sponsored research into neurodevelopmental delay in the late 1990s and throughout the early 2000s. We have been very proactive in supporting research. Some of the research requires genuine nationwide collaboration and this would be easier in say - we know Denmark, Sweden, they have national registries of patients which we don't have in the UK.

In Denmark and Sweden it's easier to carry out a national survey of how many surveys and then you can crosslink them with how many pregnancies were - can be crosslinked with valproate and therefore look at exposure. You can also look at how pregnancy or the use of valproate was concomitant with oral contraceptive pills, for example. In a nationwide database it would be easier.

Simon Whale: How hard does Sanofi push - has Sanofi in the UK pushed the UK authorities - not just the regulator but policy makers as well - to follow that kind of good example? Do you push them to do that or do you just observe that they don't do it?

Janet Lewis: We know that the MHRA are planning to work on a national registry.

Simon Whale: I'm just trying to understand whether you - whether you take the initiative and say to them, this would be a really good idea. It's something we should be doing because it's working in Scandinavia.

Hubert Bland: I think there are initiatives. Drug companies you can imagine have been keen to have collective data sets available so that we could research new opportunities and pick up these safety signals. The UK regrettably does not have a unified digital system and I think there's - there's a lot of reflection on whether or not this could be significantly improved and every drug company would be keen to support that, that I'm aware of.

Sonia Macleod: So I mean - just to be clear, exactly what are you saying there? Are talking electronic health records, are we talking registries, are we talking...

Hubert Bland: I think everything. For the complete picture in the UK needs to be updated and we'd support it.

Cyril Chantler: Do you have a policy in this area that you've developed and put to regulators as what a better system would look like?

Hubert Bland: I'm not sure that we have, no.

Janet Lewis: I don't think so.

Cyril Chantler: You obviously have a view.

Hubert Bland: Sanofi as a company don't have a view. I have a personal view that I'd like to see a significant improvement...

Cyril Chantler: Would you be able to share your personal view with us?

Hubert Bland: It is simply that. I would love to see - in a world where...

Cyril Chantler: Could you describe what you think it would look like please?

Hubert Bland: I think if...

Cyril Chantler: Not necessarily now, but would you write to us?

Hubert Bland: Of course.

Julia Cumberlege: Actually we are just as interested or even more so about the future than we are about the past.

Hubert Bland: I will - I will make this point in brief. What is currently happening - we're seeing significant positive steps with the Health Secretary focussing on digital, with the systems integrating far more. I can also say this. We are aware that there are pockets of activity within the UK and we can share those with you that we are aware of - where people are getting it right. Where data are being shared in real time and active steps are being made. It's that that we'd like to see.

Cyril Chantler: We're very much engaged with this and so it really would be helpful. Could you bear in mind GDPR when you answer the question? It could be a benefit, not necessarily a barrier.

Hubert Bland: Indeed.

Cyril Chantler: It's a context that we have to be aware of.

Eric Teo: Perhaps if I could just add two points to that. Coming back to the pregnancy prevention programme, so for example the pregnancy prevention programme suggests that there should be pregnancy counselling, and initiation of therapy should be by a therapist and there

should be at least one review annually by a specialist so we have a system - so there's a system that will enable better counselling and pregnancy planning and therefore allowing an opportunity to switch the therapy - the therapy - and whether the system allows annual contact or minimum annual contact.

Julia Cumberlege: I think in future – it would be very interesting if we could see where the boundaries lie, but certainly it would be interesting to discuss with you in future whether you think it would be helpful to you to have the patient organisations - one or two or whatever - actually on to your committees. We - I cannot tell you how much we have learned just going round the country listening to patients, and to hear their stories. It has been gruelling. It has been so tragic what has happened. I just have to say to Sanofi that one of the things that has come out so strongly has been the guilt that the mothers feel, having given birth to malformed children. The emotional angst - the awfulness of all this has been really horrendous.

It is when you hear it first-hand it really makes an impression. You know, we'd like to think about the future, and if you can think of good ways of doing that. Simon, I think you wanted to ask?

Simon Whale: I've got a couple of other things I wanted to touch on. One of the concerns patient groups have talked to us about is decisions on the ways in which risks and benefits of a medicine - valproate in this case - get made and what they talk about is the lack of clarity, lack of transparency around that decision-making process. Do you agree it's not transparent enough and if it isn't transparent enough, what do we need to do?

Hubert Bland: Janet, you could perhaps talk more clearly about what information is available?

Janet Lewis: I suppose there - from a professional point of view, I think there is clarity around the process. I think maybe for people outside the medical profession or outside the industry, there may not be easily accessible information that explains what the process is, because...

Simon Whale: Do you think there should be?

Janet Lewis: Yes. I know on the MHRA website for example they have a very brief introduction to what they do and part of that talks about that they're there to assess the safety, quality and efficacy of the products that are registered in this country. But whether people actually understand what that means in reality.

Simon Whale: It's not - I mean, it is partly about the MHRA but it is also - you are part of the system in that sense...

Janet Lewis: Absolutely.

Simon Whale: How should that - how should change in transparency - improvements in transparency apply to the system including the pharmaceutical companies?

Hubert Bland: I'll ask my colleagues to reflect on what happens elsewhere, perhaps.

Eric Teo: I think perhaps an example is the European Medicine Agency. The European Medicine Agency equally recognise the need to engage the public and make information more accessible - more transparent. In 2017 the chair of the PRAC - Dr June Raine, chair of PRAC at the time - it was - as an engagement tool, the European Medicine Agency held its first ever public hearing. That's to allow information to be shared and views be shared in a manner that is more accessible to patients. That's at the European level. Perhaps that is something that could be considered.

Pascal Michon: We did participate in this public hearing and made proactive proposals in this context.

Simon Whale: What are the barriers? At some point, transparency becomes difficult and may become counterproductive.

Hubert Bland: I think - if we're - firstly reiterate what you said Baroness Cumberlege, I think we genuinely applaud the interaction that you're having with the patients and listening to the patients perhaps is a really, really important step. Anything that can be done to improve that, we support. The second thing is perhaps we can learn from other areas where there have been patient stakeholder groups who are represented on - in previously closed environments like ethical review boards, for example. We now have lay members there. I'm just thinking off the top of my head. Maybe that's one way to help but not necessarily immediately share what is a very, very weighty document - or series of documents.

Julia Cumberlege: Perhaps.

Simon Whale: Can I just change the subject slightly? We haven't talked about Depakote yet, and your written evidence shows that the information provided to patients and clinicians about Depakote is broadly in line with what's available in relation to Epilim.

Janet Lewis: Yes.

Simon Whale: Are there any - I think what's interesting to us is whether there are any approaches or learnings specifically from Depakote that you think we should be aware of?

Janet Lewis: I suppose if you look at Depakote and the current SPC for Depakote, one of the differences between Depakote and Epilim is in the contraindications. What we've seen with Depakote is that during pregnancy there should be an alternative that a patient can take. There's a difference in the benefit risk profile of - of the two patient groups. Maybe it's looking at that as well, maybe it's not just looking at the product - it's looking at the benefit risk in different patient groups and the way the product is used, maybe for different indications - can actually affect the benefit risk.

Pascal Michon: Yes...

Janet Lewis: Go on.

Pascal Michon: Maybe put it in perspective - epilepsy and bipolar are two different diseases and obviously as you said previously it's clear that in epilepsy some subgroups are more difficult to treat, especially generalized epilepsy which represents 20 per cent of all epilepsies and in this group, up to one third of patients could be resistant to all other anti-epileptic drugs. It's identified that there is a subgroup where valproate is the only treatment possible. At the contrary, in bipolar disorder, even - there are several alternatives, pharmaceutical and non-pharmaceutical alternatives and there is no such subgroup where there is no suitable alternative.

That's why - I would say the benefit risk is positive and we assess by the PRAC assessment both in 2014 and in 2018 that it's two different diseases and that's why the contraindication is different. Maybe the epilepsy is certainly a more sensitive - a more tricky disease to be - to be managed.

Julia Cumberlege: I understand.

Simon Whale: You talked about - earlier - about the confounding effects of epilepsy in relation to neurodevelopmental features in particular. I'm just interested in whether you're aware of any studies that look at the effects in the population taking valproate for bipolar in that regard?

Hubert Bland: Are you aware of any studies looking...

Eric Teo: Bipolar disease.

Hubert Bland: Epilepsy, but no. We can come back to you. We're not aware - certainly I'm...

Simon Whale: Yes, if you are able to check and let us know that would be helpful.

Julia Cumberlege: Cyril.

Cyril Chantler: Thank you.

Janet Lewis: Sorry. It's worth mentioning as well that Depakote in the UK wasn't registered until the year 2000. A lot of the time when we were looking at confounding factors, the drug was only registered for epilepsy.

Cyril Chantler: I want to look to the future and the learning that we can acquire from these three areas which we've been asked to review. First of all, research. You mentioned that you are interested in funding research and to find out information that you need - how it affects patients. You mentioned your support for the UK registry, and I think the European registry as well. Are you interested in continuing that activity into the future and are you interested in research - helping researchers in other areas?

The three that have been mentioned to us as concern from patients as we've gone round the country is the question of intergenerational effects and the possibility of genetic changes that might affect grandchildren, that's the first thing. The second is whether or not there is any evidence that men that were on valproate - whether they're affected in any way. Thirdly, the concern about how valproate spectrum disorder develops over a lifetime - the sort of life course. Those are the areas that have been raised with us as areas which require further thought. Is the company interested in looking at propositions in these areas to provide help?

Pascal Michon: Yes, I think we can answer that. After the last PRAC referral conclusion in February 2018, there were several commitments from the company to participate to research programmes. Each topic you mentioned are part of this programme research. As mentioned previously by my colleague Eric Teo, there are some surveys, there are some retrospective studies within existing databases about switching valproate to other medicines. There are surveys to assess the awareness of healthcare professionals and patients on the risk [unclear] and their effectiveness in the coming years.

There are also, as we mentioned, research programme - we've just submitted to the EMA PRAC on the potential transgenerational effect. With a proposal of a protocol - there is a research programme also on epigenetics as we mentioned and this is a commitment from the company to the PRAC to perform this research programme in the future to try to answer these unsolved questions.

Cyril Chantler: Do you work with other funding bodies in partnership in putting forward research funding proposals to the research community to respond to?

Pascal Michon: At that stage what we did, as previously mentioned by my colleague, is to support independent registries that are still ongoing, for example Eudra still ongoing and with also registries ongoing to assess more in depth the - all this research not yet achieved. It's prospectively on observational registries.

Cyril Chantler: But you work with other funding bodies to partner with them?

Pascal Michon: Yes.

Hubert Bland: As a principle Sanofi - definitely, that's the kind of model that we do use often.

Cyril Chantler: Right.

Eric Teo: Some of the studies have - we are working with other market authorisation holders, setting up consortium to co-sponsor studies. That is one thing. The other obviously is we also reach out - we currently - we reach out to the governance bodies of some of the registries and obviously - we need to ensure that there is independence in how these are done so we are waiting to hear back on how best to approach some of this research.

Cyril Chantler: Across Europe, there are public monies available which hopefully we may continue to have access to. There are others in this country. The co-operation between them and industry seems to me to be a perfectly reasonable way forward. That's my own view.

Hubert Bland: No, absolutely. It's one of the things that Sanofi encourages. We are pioneers in sharing the data. We have a very large global data set and one of the things that we're pioneering at the moment is allowing access to our data and collaboratively trying to come up with cumulative discussions.

Cyril Chantler: Good. My next question is again looking to the future. It is apparent to I think all of us, that when a medicine or a medical device is authorised and comes to the market - now I know that there are differences in medical devices which isn't the subject of today's conversation - but things happen when you - the product gets into practice that we didn't foresee. Some of them are advantageous and we can give examples of that. Some are not and the medicine has to be withdrawn in due course.

If it happens in some countries, and I have no direct experience of that, I'm simply telling you what I've been told - so for example in Nordic countries, the industry as a whole takes some responsibility in supporting people who have been affected when - if you like - the unknown unknowns become known and the patients are harmed. Do Sanofi participate in that sort of programme and would the company be interested in looking further into that into the future?

Hubert Bland: Internationally I'm not familiar with that programme but I can say that as - Sanofi's position as it pertains to valproate is that we have always discharged our duty, contemporaneous with the information we had at the time.

Cyril Chantler: I - that's not my point.

Hubert Bland: I appreciate that.

Cyril Chantler: My point - I understand why you make that point - but looking into that future, if there was a new scheme - would you like to explain the Nordic scheme?

Sonia Macleod: The Nordic schemes and also Japan and a few other countries, they have schemes where essentially there is a levy on market authorisation holders into - and that is then used to fund a scheme that provides redress when - as we say, when things that weren't necessarily predicted happen. So, if for example side-effects that either weren't warned about or were more severe than were on the data, there would be redress provided and help and support provided by those schemes.

Hubert Bland: Almost an insurance policy for companies participating.

Sonia Macleod: Yes. They are mutual insurances.

Hubert Bland: I'm not too familiar with it. Personally it sounds like a good system. I think the company would have to evaluate it and executives within the organisation certainly - I suspect currently we'd be having the discussions about it.

Cyril Chantler: Thank you very much. My final question is to actually much more broadly look to the future. We can have different views - people have different views about what might have happened, and some of it's the wisdom of hindsight, but out there there are a lot of people who say to us it's been too little too late. One of our tasks is to think of ways which we - as a system - and we're not blaming anybody for it, we're all in this together. What could we have done looking backwards or maybe what should we

do in the future to try and make sure that we spot things going wrong sooner and we take appropriate action faster? Can you think - thinking system wide from regulators, professionals, patients as well as the industry - what would you suggest we go away to think about?

Hubert Bland: We've all been thinking about that. Certainly I think from my perspective, generally I think we need to utilise what already exists and is already in place far, far better and perhaps greater governance and greater review of what we currently have. I think - Eric, you speak passionately in particular about the yellow card reporting system.

Eric Teo: I think - this is where - I come back to this. I think there should be greater facilitation of reporting of adverse events. Make it easy for not just doctors and GPs but also for patients. Make it less daunting for them to approach a regulator or a company so that all events can be flagged up as early as possible. Of course on the company's side, technology advancements - we also implement more modern ways of detecting signal with proactively looking at what is out there, what is in the media. We treat those very seriously. The system itself - one of the most important things I think we can do collectively is to make the reporting of adverse events more accessible. Not just in the UK but in many other countries because safety topics know no boundaries, we need - the weight of evidence coming to us.

Julia Cumberlege: I think one of the problems that we have created for ourselves across the globe is greater specialisation, and that brings huge rewards because we know more and more. We know more and more about less and less, possibly. The specialists then work in their different silos. What we're trying to do is to look across the whole piece and the whole systems way of working, and with that there are a lot of partners. We understand that. Including of course patients. We have to think how in the future we can work really differently with this new mind-set that we really need. We need the specialists, but we also need to think about a whole systems approach and to draw them in and all the other parties.

Eric Teo: Certainly, going back to training of doctors and governance of doctors for example through the GMC, would - can anything be done to educate doctors about recognising adverse events which can be many years down the line post exposure. Educating themselves and - can something be done to encourage, maybe going further encourage doctors to report adverse events? I think training and revalidation requirements - those could also be considered.

Pascal Michon: Yes, I would support that because at the end we know perfectly that the individual interaction between physician and patient is also the best way to provide information to patients - and the right. If you are the physician, you are the only one to decide with his/her patient which is the most suitable treatment and to give the appropriate information both on the benefits why he or she has to take this medication, but also the risk connected to this. I fully support this point about the training of the physician to improve this meaningful interaction with the patient.

Cyril Chantler: Thank you.

Janet Lewis: One of the things I'd like to add around that is - and we mentioned it, the patient involvement in the process. I'm quite passionate about getting information to patients and it's - when we look at cases like this and the information is there but may not be getting to where it should be, the regulatory system and how it allows us to get approved information to patients and how the system - the whole system itself can provide that information. Again I think technology and digitalisation gives us big opportunities to do that but also one of the things that Sanofi is looking at is involving the patient early on in drug development and looking at what the patient's experience is, how the patient would benefit from a drug et cetera and involving the patient more a stakeholder in the whole process.

Julia Cumberlege: Well, we welcome your passion and we share it. Can I just draw this to a close now? I'm going to ask my panel whether there's any burning question they want to put to you and likewise you to us. So, Cyril, is there anything?

Cyril Chantler: No.

Julia Cumberlege: Simon?

Simon Whale: No.

Julia Cumberlege: Valerie?

Valerie Brasse: Just really a quick one to follow up the other side of what we've just been talking about. Getting the information to patients and then making sure what's supposed to happen actually does happen. Because I think we would recognise that had valproate been prescribed as was intended, i.e. only in most severe cases to women of childbearing age [unclear] were pregnant or because they were resistant to other treatments, we would have less children affected by valproate. The other side of that house is how we're monitoring what was supposed to be going on and actually

that system-wide improvement is as essential in that part of the equation as it were as anywhere else.

Janet Lewis: Yes, I agree.

Julia Cumberlege: All right. Sonia?

Sonia Macleod: Can I just ask, when you came in you said you were currently working on redesigning web materials for patients and for healthcare professionals. Can we have a bit - just a little bit more information about that?

Janet Lewis: Yes. We're actually working - again with the MHRA - we're producing - we're looking at producing two separate websites. One is for healthcare professionals and one is for patients. The one for healthcare professionals, one of the things we're doing there for example is there's a video that's been produced - actually, starring Eric and one of our medical advisors who works on Epilim, to talk about the PRAC review and the outcome of the PRAC review and what doctors need to be doing, what healthcare professionals need to be doing to implement the pregnancy prevention plan.

For patients, what we've tried to do - because we think that you have - you have women who will - when they become pregnant will go out and look for information about pregnancy. I know I did this when I was pregnant. I suddenly read all this stuff that I'd never been interested in before, but by then it's too late. We will have one area with a QR code as a separate website which just links to the risk minimisation materials. What we're trying to do with the patient website is to actually give an environment where people with epilepsy - maybe someone's partner et cetera is looking for other information. Maybe about driving and epilepsy, or other aspects of life and living with epilepsy.

By going to the site it will actually draw them to the risk minimisation measures as well so that they can actually say, 'oh I may not have known about this but I'm not pregnant at the moment but I can see that there's a message here for me maybe in the future or for my partner'. That's the idea behind them. We're working with MHRA at the moment because we do actually get everything pre-approved with them, but hopefully they will be available fairly shortly.

Simon Whale: Is there patient involvement in that second website, patient focussed material?

Janet Lewis: I believe - sorry, I'm not producing it personally. I believe there's been patient association involvement in the development of that but I couldn't - we can definitely find that out for you.

Simon Whale: In the first - in the case of the first one for healthcare professionals. Is that specifically aimed at neurologists or all physicians and does it - is it aimed at pharmacists as well?

Pascal Michon: All healthcare professionals.

Eric Teo: Healthcare professionals.

Simon Whale: It's generic.

Eric Teo: The language used - we tried to make is accessible to all healthcare professionals, not just a neurologist.

Simon Whale: Right. Thank you.

Julia Cumberlege: Would you like to - any of you had any you'd like to do?

Hubert Bland: If I may unless there are any specific questions I'd just like say thank you. Genuinely. We're deeply appreciative that you've included us in this process. It's already obvious to us that as a result of what you're doing, patients are benefitting. Less people are being harmed and more patients will be benefitting from valproate so thank you again. I really appreciate it.

Julia Cumberlege: Right. Can I thank you for - can I say I mean I think you've come to us today with an enormous fund of knowledge and expertise and we really appreciate it, that you've shared that with us. We are interested in the future and we very much hope that you will continue to work with us on that because you are obviously deeply concerned as we are with some of the results of some of the medication that's been given. So, thank you for that. So, for your time and for your preparation for the evidence that you've submitted in writing, and I'd like to also thank your observers who are here today and for our team who have put this on. I'll just say that we hope to see you again in the future, if you're agreeable.

Multiple speakers: Thank you.

Julia Cumberlege: Thank you very much.

END OF TRANSCRIPT

23rd January 2019

Session 1: Dr Vincent Argent

START OF TRANSCRIPT

Julia Cumberlege: I'm Julia Cumberlege and I was asked to chair the Review. When you chair a review, the most important thing is to get the best people around you. On my left is Sir Cyril Chantler...

Cyril Chantler: Hello.

Julia Cumberlege: ...who is the Vice Chairman of the review. On my right is Simon Whale who is also a member of this three-person panel. But next to Simon is Dr Valerie Brasse and she is our Secretary. Then next to Sir Cyril Chantler, who is our researcher, is Dr Sonia Macleod.

Vincent Argent: Hello.

Julia Cumberlege: That's us. We've got other people in the room, but they're here just to help us run the event. I think it would be very useful if you could just say a bit about yourself. Is there any sort of statement you would...

Vincent Argent: Yes.

Julia Cumberlege: ...like to make just for the recording?

Vincent Argent: I'm currently a consultant at Accident and Emergency in Dorchester, because in 2006 because of a back problem, I retired from obstetrics and gynaecology, because I was a consultant actually in Eastbourne, East Sussex. But nevertheless, I do have quite an interest in emergency obstetrics and gynaecology, because many years ago I used to work in a thing called the Obstetric Flying Squad that don't actually exist now. But it was one of the first models of pre-hospital care. That's my background. Perhaps I should just first declare my interests.

Julia Cumberlege: Well, we've got a record of them, but if you need to, please do if you would like to...

Vincent Argent: Yes.

Julia Cumberlege: ...so that we have it on the record...

Vincent Argent: Okay.

Julia Cumberlege: ...because I should have said that we are videoing this oral evidence for everybody who comes to us.

Vincent Argent: Right.

Julia Cumberlege: Then it's put onto our website so that people can see how we're operating and the sort of advice we're being given by others.

Vincent Argent: Okay. It's just that two years ago I was asked to act as an advisor to the all-party parliamentary group on mesh, so I have actually been to some of their meetings and participated in some of their discussions. That's an unremunerated position. Also, I've actually given advice to mainly two of the campaign groups. One was called Messed up Mesh which I think started about eight years ago. Then the more recent one, Sling the Mesh. Otherwise I don't have any contacts with any of the organisations apart from the fact, of course, I'm still a fellow of the Royal College of Obstetricians and Gynaecologists.

My interest in this is really because I, about - it was eight years. I was a member of the NICE Women and Children's Guideline Review Panel. Do you know their role is not to produce guidelines? But it's to check the guidelines when they've been produced to make sure that they address the needs of the stakeholders and also the issues raised in that particular guideline. I was the gynaecology representative for NICE. My colleague, Christina Oppenheimer [unclear], was the obstetric representative for the women and children's group.

During that time, among other - it was a time when things were shaking, because we were asked to give informal advice to SERNIP, the previous Safety and Efficacy Register of New Interventional Procedures. Then I think by 2002 that had merged with NICE as the new Interventional Procedures. Again, the guideline review panel was just asked to give advice on guidelines and some particular guidelines which were quite relevant to the mesh situation.

I have an interest in clinical safety and in medical law. I have a law degree, so I have a bit of a legal background. Also, my first degree at Cambridge was in chemical engineering, so I've always been interested in plastics and other things. I'm still a member of the Institute of Chemical Engineers, because there's a lot of biomedical science which is related to chemical engineering and medicine. It's an interest of mine.

We became aware of the discussions about mesh way back in - just to correct one thing in the submission I made, there was a mistake. On the first page, I put in 1997 I strongly opposed the decision of SERNIP to give

TVT - that's transvaginal tape - a grade A rating because of a limited cohort study's lack of long-term data. In fact, that was in 2000, because I hadn't got - it was quite difficult to get hold of all the SERNIP records. After, I realised that that was in 2000, because what SERNIP did actually in the year 1997, they gave cystourethropexy which is essentially the same operation - they gave it a C rating. Then that was repeated in the next two years and then in 2000 after there was some lobbying [inaudible] to change the rating.

SERNIP had a separate little inquiry and they deemed that it should be given an A rating. SERNIP have actually made it quite clear that they didn't approve products. They basically gave advice. They didn't see their role as approval, though they did say originally when they set up that they would actually hold registers of procedures. But they never really did that, because they were actually quite a small group and they were underfunded. They had committee meetings, but they didn't really go any further than that. There was talk of having registers of different procedures, but it didn't happen.

Then over the years, I've just become aware of the developments in the mesh story and what has happened. I must say one of the things which perplexes me - I like to think I'm fairly neutral, but obviously there has been a lot of campaign groups. There's also been this inquiry, because there seems to be a problem with mesh. Now on the other side, some of the specialist societies and some articles and also some of the manufacturers - perhaps not surprisingly - have used terms that mesh is a gold standard and that it's a quick fix and it's a miracle cure.

Now I can't quite understand why there should be such a dichotomy of views and it's taken 20 years to find that out. That's why I thought one of the main things perhaps the inquiry should do is think about a national recall, similar to the hip recall which is actually under the auspices of the MHRA, isn't it? Patients are followed up every six months or a year or two years as appropriate. But that's not really happened with mesh, at least not from the MHRA even though the specialist societies have actually set up audit processes.

But I'm perplexed because of this dichotomy of views, because it's so important that if a patient, if a woman is being considered for one of these procedures, obviously she needs to be given correct objective information about the immediate outcome, the long-term outcome and about the risks and benefits and pros and cons about alternative procedures and, of course, about the option of actually not having surgery and using other things like physiotherapy or just leaving as you are. I find

that strange. I'm sure the inquiry's been looking at that, why there's such a difference.

Then another thing is, of course, since 2009, just actually now 10 years ago, there have been campaign groups campaigning about mesh. As you know, there have been many reported activities from Scotland and Australia. Of course, there's a new one in France. ANSM, which is the French equivalent of MHRA, is currently conducting another inquiry into mesh outcome. Perhaps I shall stop there.

Julia Cumberlege: Right. Well, thank you. That's really very, very helpful. I'm sure there's bits of that which we would like to explore. I would like to go back a bit to SERNIP and the issue about the reclassification...

Vincent Argent: Right.

Julia Cumberlege: ...from C to A. There was a very interesting article published in the BMJ in October, 10 October last year. In it, the journalist who is Jonathan Gornall...

Vincent Argent: Oh, yes, I've read the article.

Julia Cumberlege: Yes, you know it. Well, I think what comes out very clearly there is that there were a number of people including David Richmond who, of course, later on became the president of the Royal College of Obs and Gynae...

Vincent Argent: Yes. Yes, he did.

Julia Cumberlege: ...who was very concerned about the way the reclassification was made. Also there was Paul Hilton who was another obstetrician, gynaecologist.

Vincent Argent: Yes.

Julia Cumberlege: He said he couldn't really understand the way that the different classification was made when there was no evidence that anybody could actually, well, really look at it in great detail to see why that had happened, how it had happened, what were the influences that actually made that happen. I just wonder, thinking about that - and as I understand it, SERNIP was actually a sort of voluntary organisation set up by the royal colleges. But the Department of Health were advised actually to make it mandatory, that people would have to respond to it and put in their evidence and everything. Actually that was rejected.

Just thinking back to that, could you say a little bit about your view of why the reclassification of mesh was made, and also what impact that had on the current issues that we're dealing with today?

Vincent Argent:

Yes. I was not a member of SERNIP. It was just that there was some contact between the NICE Women and Children's Guideline Review Panel and SERNIP, because we realised we were doing similar things. We did meet up a couple of basically informal meetings when NICE were based in [unclear].

The reclassifications, SERNIP have made it fairly clear, I think, that they were not a body who approved procedures. They just gave classifications. If you like, they gave advice based on evidence. In 1997 when they gave the C classification, that was only to be used as far as the research trials and there also to be a register of the outcomes. That was the case. Then it was I think by 2000 that there was a lot of lobbying [redacted] I understand. I wasn't there when - I wasn't involved in that at all. But [redacted] asked SERNIP to look at the classification, because they felt it was affecting their sales in Sweden and France in particular.

Interestingly, at that time, Sweden was - well, I think you know some of the background of how the procedure, the TVT, was invented in Sweden as - what's been discussed about the various interests there. I think at that time France didn't have a very robust system for checking medical devices, because the precursor of ANSM - which is the current French body - was called AFSSAPS. That was, I think, started after SERNIP did the approval.

Anyway, the reclassification, so there was a review which I think you've probably got a copy of. At least there's a letter from NICE about the SERNIP review internationally. Apparently, there was some extensive discussions, maybe even some differences of opinion about what they should do. I can read it out to you [unclear].

Interestingly, they jumped from a C classification to an A classification, because if they'd gone to a B classification, a B classification is efficacy approved that the procedure works. But there may still be questions about safety. Again, with a B classification, there would be a register of all procedures. But for some reason, it jumped right to an A procedure which was safe to use in clinical practice with no [vital] about registration of procedures and no [vital] about concerns about safety. That was a big jump. I don't think they'd done it for any other procedure, to go from C to A.

I know they did discuss with some detail - just find the actual words they used. The wording was a bit strange. I didn't see this until afterwards, but it was the SERNIP review of January 2000. I think you probably have been given that by the people.

Valerie Brasse: I think we need to check that actually on our database.

Vincent Argent: It's the SERNIP review, January 2000, the tension-free urethropexy, tension-free vaginal tape, TVT. It says, this is a relatively new, minimally invasive method of treating genuine stress incontinence of urine by a sutureless insertion of Prolene mesh under the proximal urethra. SERNIP classed this as a category C in October 1999, when in fact they had classed it as a procedure C back in 1997.

The interesting thing is the third paragraph. It said, the manufacturers of TVT have submitted further reports for SERNIP to reconsider its grading. These included four papers - this is the interesting bit - which had not already been reviewed, but two of these were duplicate publications in whole or part and two were excluded for other reasons. There were also 30 conference abstracts, most of which consisted of incomplete or uninterpretable results. Five reports included patients undergoing concomitant vaginal surgery. The results of, in inverted commas, pure TVT treatment was impossible to deduce. Those with only subjective outcome or follow-up less than six months were also excluded. This left six reports, all conference abstracts of 268 patients with an 86 per cent objective cure rate at six months or more.

Julia Cumberlege: Dr Argent, can I ask you then - you talked earlier on about the discussions that were had when the reclassification was made. Is there any sort of evidence? Were manufacturers involved in any of those discussions?

Vincent Argent: With SERNIP or with...

Julia Cumberlege: Yes.

Vincent Argent: No. It was basically Professor Maran was the chair of SERNIP at that time and I believe the [unclear] person. He was a general surgeon in Scotland, but he was the chair. He came to one of our meetings. It was an informal meeting at NICE. We just had a fairly brief discussion which - I hadn't seen that SERNIP review at that stage. We wrote a letter just saying that we thought it was unusual for a procedure to actually go from a C classification to an A classification. That was it. It wasn't...

Julia Cumberlege: If there had not been the reclassification, would then we have seen fewer of these operations done as they were a category C?

Vincent Argent: Well, yes...

Julia Cumberlege: Really what I'm trying...

Vincent Argent: Yes.

Julia Cumberlege: ...to find out is what is the impact over that intervening period when, of course, NICE came in and took over from SERNIP. But what do you think the impact would have been on the volume of work that was done with mesh?

Vincent Argent: I think it made a big difference, because some colleagues did actually say, well, NICE have given this procedure an A classification or A grading. Expressions were used like, this shows that it's a safe and effective procedure, a safe procedure. On that basis, it became a very popular operation. It has some advantages, because it's a brief procedure. It can be done under local anaesthetic and it can be done as a day care procedure. It was, in many ways, more attractive than previous procedures. Whether it was more effective is debatable. Perhaps some people would say it is more effective, but some say it isn't.

One of the big problems with this is, in general when you introduce new procedures, is what do the regulatory bodies do when they have a new procedure which either might be more effective than the previous procedures and might have some advantage in terms of stay in hospital versus a procedure which may have more complications and especially if those complications turn out to be much more life threatening - life changing, I should say, than the complications of the previous procedure? That's what tended to happen, because the mesh procedures took over, if you like, from Burch colposuspension which is relatively a long procedure and it has to be done under general anaesthetic, and also from vaginal anterior repair which was said to be less effective.

Julia Cumberlege: We appreciate that. We've heard a lot of that from the patient groups. They've told us what they have been through...

Vincent Argent: Yes, right.

Julia Cumberlege: ...as a result of some of these mesh operations.

Vincent Argent: They were not extensive discussions between SERNIP and our committee at NICE, because SERNIP were an independent body and they'd made their decision. We just thought it was unusual to go from a C to A on - especially because the review actually talked about the evidence just being conference abstracts - you see, because at NICE, NICE guidelines are produced on quite strict evidence-based levels. If the only evidence was conference abstracts, that would have the lowest rating of all in terms of evidence. It probably even comes below expert opinion, but it's certainly not level 1, 2 or 3.

Sonia Macleod: Do you think that the way SERNIP was structured, in terms of it being voluntary, impacted on the types of evidence it was prepared to look at and the weighting it placed on the evidence?

Vincent Argent: Sorry, in terms of what being voluntary?

Sonia Macleod: SERNIP was a voluntary...

Vincent Argent: Oh, yes. Yes, it was. Yes.

Sonia Macleod: It didn't have a statutory underpinning. It didn't have the same sort of structure that NICE has, for example, when NICE weights evidence.

Vincent Argent: Yes.

Sonia Macleod: Was that part of the difference between the weighting of evidence or was it just simply...

Vincent Argent: Yes, I think so. I remember, going back to that time, the late '90s, I used to give talks about, if you like, medicolegal matters. I decided a lot of colleagues had not heard of SERNIP. They weren't a very high-profile lobby. Of course, in those days, I don't think there was a website. I may be wrong. There may have been a website. In 1999, probably not. NICE obviously had much better funding to produce the website and easy access. Everyone knew about NICE, but I don't think anyone had - not many people actually knew about SERNIP.

I think that made a difference because - but word got out, because there was - when the reclassification occurred, there was a lot of promotion of the operation by specialist societies and by colleagues and by manufacturers who said this has got an A classification, it's safe and effective. Then it took off. It was a very attractive procedure in many ways. It was thought to be, as I say, a quick fix and miracle cure.

Julia Cumberlege: Right, well, thank you very much for that. Simon, do you want to...

Simon Whale: Yes, Dr Argent, can I ask you something about an issue that's been raised with us by women themselves, women who've been affected by mesh? Many, many of them have talked about how, when they present with what they believe to be mesh complications, doctors are often very dismissive and will instead talk about other women's health issues as the cause of the pain that they're feeling. For example, the menopause.

I'm just interested, given your clinical background, in firstly whether you recognise that that is a phenomenon, that dismissiveness and that desire to link pain to other issues. Secondly whether there's anything that should

and could be done to change that. How do we make clinicians more willing to listen and to take appropriate action?

Vincent Argent: Yes, I think that's been a big problem. It's partly because there was - obviously in the early days, there was a lack of knowledge about long-term complications. There wasn't much evidence and so, to be fair to clinicians, they didn't know what could happen. However, it's probably generally felt that if you're putting polypropylene mesh into the body, that there is a risk of that, because that was the evidence from previous uses of polypropylene mesh for other procedures beforehand. There was no national register. Some of the papers which were published in journals have been criticized as being, if you like, funded by companies. They felt that maybe there was a bias towards not talking quite so much about the complications.

I think to be fair to consultant gynaecologists and surgeons, they would see the patient preoperatively, do the operation. They'd probably have one follow-up appointment maybe after a few weeks, three weeks, six weeks, maybe three months, but then no more. Some of these complications and symptoms actually developed after that, even within a year, a few years later. Of course, they would go to their GP. I think GPs were not well informed at all, because it just wasn't known about quite so well. Perhaps the information should have got through to GPs as well.

Cyril Chantler: You actually said, when you wrote to us, you thought there was a level of denial in clinicians about the mesh issue. Can you expand on that?

Cyril Chantler: I think there was a lot of denial. I think I put that in my report.

Cyril Chantler: Yes, you did.

Vincent Argent: I felt that there was a culture of denial, because it was felt this was the modern operation. It was very successful. It seemed to be effective. It worked for many patients. I think sometimes some of the success rates may have been slightly exaggerated, because they were short-term success rates. But I think there was denial, because I think that patients found that when they went back to their surgeon or when they went to see their GP that they felt they were fobbed off and that the symptoms were caused by something else like, oh, that doesn't happen.

Julia Cumberlege: I think one of the problems really was that when they were faced with this sort of denial, they then went on to another surgeon or another person.

Vincent Argent: Yes. Oh, yes.

- Julia Cumberlege: Actually the follow-up was very inconsistent and not very rigorous.
- Vincent Argent: Yeah. It happens with other types of pelvic pain, too, that patients do get shunted around, because pelvic pain can be quite a difficult thing to manage. I'm sure you've probably - you've heard from the British Pain Society. It has been an emerging sort of subspecialty within pain medicine, because it's very difficult to disentangle the different types of pelvic pain. Yes. If someone presented with some of the symptoms caused by or associated with mesh, I don't think that most doctors really knew what to do. Even now we're learning about the best ways to manage problems. I'm sure there was a lot of denial. They just think, oh, this couldn't possibly happen in my practice.
- One of the problems, I think, is that maybe with the computer age that doctors can now talk about their success rates. They can put it in a public forum on a website and then obviously that makes it perhaps a little bit of bias towards saying, oh, my success rate is such and such, because then they'll attract more patients. That's been quite a big factor in the development of gynaecology in recent years.
- Simon Whale: Do you think, over the years and more recently, clinicians have become better at being able to identify the link between pelvic pain and mesh and more willing to consider that link, or are we looking at a consistent problem that hasn't improved?
- Vincent Argent: Oh, yes, I think the situation has improved considerably in the last few years, because there's now an awareness. There's been information given to GPs. Of course, there's things like the inquiry poster for GPs to actually ask patients to come forward. There have been various campaigns in the newspapers, on television and in the media, so I think women are quite well informed. With things like Mumsnet and the campaign groups, they...
- Simon Whale: It's rather relied on those forces as opposed to the professional or its representative.
- Vincent Argent: Yeah. The professional things have improved a lot. The specialist societies acknowledge there were risks with mesh. Unlike previous procedures, complications - if they do occur - can be much worse in terms of changing someone's life. Therefore they are telling patients just now - a lot of consent and information leaflets now do actually talk about the complications. Some are fairly guarded about what the complications might be. Some of them actually give much more information. But there isn't very - I mean, for instance, problems with walking. I don't think there's any information leaflet I've seen that says you may have problems

with walking afterwards, but that does occur in a small percentage of patients.

Simon Whale: Yes, and problems with sex life and so on.

Vincent Argent: No. I think it's improved. Now because the procedures are - even before this inquiry, the number of procedures being done was going down, because it was realised that this procedure did have some risks. Even at that stage, doctors were beginning to tell patients, well, this procedure, we don't know really very much about the long-term outcomes. Some patients do have long-term outcomes which have been quite devastating.

Simon Whale: Which leads me to another point. You mentioned that phrase gold standard a few moments ago.

Vincent Argent: Yeah.

Simon Whale: We've heard women say that that's what they were told as well, so it's clearly a common theme. What made the medical profession so confident that it was a gold standard?

Vincent Argent: Because they thought it worked. The procedure is effective in 60, 70 per cent of patients depending on who you read. It was probably slightly better than the previous procedures, like vaginal anterior repair, and maybe about the same as a Burch colposuspension. But this procedure could be done - I mean, one colleague basically could do a TVTO operation in seven minutes which is very quick. But it's in one of the promotional literature and so there was some advantage in actually doing more operations more quickly. As I say, it could be done under local anaesthetic and done as a day case. They saw this as a wonderful procedure which...

Simon Whale: Wonderful for them or wonderful for the women?

Vincent Argent: Well, probably wonderful for them. Yeah. There's no doubt there was a lot of promotion from the companies and from websites about this procedure and with individual quotes of success rates of 98 and 99 per cent in the early days, not now. That was obviously not correct. There was very little about the complications. One of the problems with complications was some of the - describing risks of procedures to people should be fairly consistent. You've either got to talk about the national picture or your own personal record. We're not very good at doing that. A lot of vague terms were used like, oh, yes, the procedure doesn't have many problems.

But what you're supposed to use is called the modified Clavien score which is a one in 10, one in 100, one in 1000, very common, common, uncommon and so on. Actually, that's endorsed by the Royal College of Obstetricians and Gynaecologists. They say that when you're counselling someone about a procedure, that's the scale you should always use so you have some consistent - because you could say, for instance, that a risk of long-term unpleasant complications is about - if it's sort of one to two to three per cent, that actually is common in the classification. Whereas terms were used like this doesn't happen very much or this is even rare. The classification rare is really one in 10,000. Yes.

Simon Whale: The motivation was about convenience and speed - is that what you were saying - as well as...

Vincent Argent: I think that had a big effect, yeah.

Julia Cumberlege: Finance too.

Vincent Argent: Yes, so it was attractive for NHS hospitals. Of course, in the private sector, it was attractive because you could do more procedures. Patients would go home quickly. It was a well-remunerated procedure for the time it took. It became very popular with colleagues in independent practice. In some cases, there was a tendency to maybe overemphasise the benefits of the procedure without talking about the disadvantages.

Simon Whale: Can I raise one other point that again women have raised with us? That's about translabial scans. Many women have the view that translabial scans are both important in helping women understand the nature of the complication, or even identifying that there is a problem, but also very difficult to access. Have you got a view on the usefulness and accessibility of translabial scans?

Vincent Argent: I don't have a view on the usefulness, because I wouldn't say I've got specialist knowledge in that field. I understand from colleagues who are actually involved with mesh removal and also with the British Pain Society that it is a useful procedure. It does actually help with surgical planning to see where the mesh has gone and what it looks like. In terms of access, no, I think the access is very poor.

Simon Whale: Why is it so poor?

Vincent Argent: Why is it so poor? Probably because there's so much pressure on the NHS to actually provide those services. But if they're going to be regional mesh removal centres - which there are some already - then obviously they should probably have labial scanning, because as I understand, it actually

- does help with the management of the problems and also the surgical removal.
- Simon Whale: Because the equipment involved is - as we understand it, it's an adaptation to an existing ultrasound machine. It's not a particularly difficult piece of kit to...
- Vincent Argent: No, I don't think so. No, I think it's a fairly standard ultrasound machine with a fairly standard probe. Of course, there's a lack of experience, because if you go to most ultrasound departments, ask them if they can do a labial scan looking for mesh, they'd probably say, oh, I can't do that. I've never done that before. There probably needs to be better training.
- Simon Whale: But you'd expect that expertise to exist in the mesh removal centres or in the mesh medical centres.
- Vincent Argent: Yes.
- Simon Whale: [Unclear] which is currently...
- Vincent Argent: There is a British Ultrasound Society. I don't actually - I must say - I'll look it up afterwards. I don't know what their views are. I'm not sure if they've published any guidelines about it. But they may well have done, because the - it's the BMUS, the British Medical Ultrasound Society, B-M-U-S. They may well have a view about the availability, usefulness and so on about labial scans...
- Simon Whale: Okay, thank you.
- Vincent Argent: ...I expect.
- Julia Cumberlege: Cyril.
- Cyril Chantler: Thank you very much. Do you think doctors should be required to declare their interests on a register every year?
- Vincent Argent: Yes. I think in the modern world, we are expected to declare our interests. If you're employed in the NHS, we do get a letter every year from HR actually asking us to declare any competing interests. It doesn't say what those interests are. That happens in the academic world where the people have to declare their affiliations with bodies which provide finance for research and so on.
- Cyril Chantler: Of course, in the academic world, you are required to make that public whenever you give a presentation, are you not?

Vincent Argent: Yes, it's becoming increasingly so. When you go to a professional lecture so people do declare their most important interests - maybe not all of them, the ones which might be of relevance to what they're talking about.

Cyril Chantler: Do you think there should be a register that the public can access of doctors' interests, which is updated on a yearly basis?

Vincent Argent: Yes, ideally. I think it would increase public confidence in the medical profession and other healthcare professions.

Cyril Chantler: Thank you very much. You talk about recall of mesh. Can you explain what you mean by that and how it could be done?

Vincent Argent: I really mean - because what I said at the start that I am still unclear why - there was a group of people who - they've obviously had complications. They feel they haven't been well served. Then there's another group. There's a group of professionals who feel this is still a gold standard operation. They would push to carry on doing it, albeit with more preoperative counselling and getting proper consent and so on.

I don't think we really know what the figures are, because I think when there are a lot of - one thing I will say, when there are a lot of campaign groups, obviously they're going to concentrate on the problems they've experienced. When you have articles like the Victoria Derbyshire thing in the *Daily Mail*, it makes the public feel there is a huge problem, but it may not be quite as bad as they say. Conversely there seem to be colleagues who think this is still a very, very good procedure, say, oh, I've had no problems with it. You still hear people say that [unclear].

Cyril Chantler: What do you mean by recall? Do you mean that every patient who's had mesh inserted should be contacted?

Vincent Argent: Yes, I think it's important with mesh, because the complications also seem to occur long term. Some of the problems with erosion and pelvic pain can happen five, 10 years after the procedure's been done.

Cyril Chantler: There are 100,000 patients over the last 20 years.

Vincent Argent: There could be.

Cyril Chantler: How do you find them?

Vincent Argent: Well, I think you would do something similar to the...

Cyril Chantler: Because there isn't a register.

Vincent Argent: Yeah, the MHRA hip recall.

Cyril Chantler: Yeah, but that's a register.

Vincent Argent: Yes.

Cyril Chantler: There is a register at the National Joint Registry.

Vincent Argent: Yes, National Joint Registry.

Cyril Chantler: But there isn't for mesh, so how would you do it?

Vincent Argent: No, well, perhaps there should be.

Cyril Chantler: Sorry?

Vincent Argent: Perhaps there should be a national mesh register...

Cyril Chantler: Yes, indeed.

Vincent Argent: ...and base it on the hip register, because then patients have actually been informed about...

Cyril Chantler: I understand that.

Vincent Argent: Yeah.

Cyril Chantler: But I don't know how you can do it when there isn't a register.

Vincent Argent: Yes, I mean, mesh has been obviously a very high-profile problem. In order to actually reassure people, I think a recall similar to the MHRA and National Hip Registry...

Cyril Chantler: Yes, but you can't do it if there isn't a register is my point.

Vincent Argent: No. No.

Cyril Chantler: I think it's a good idea maybe, but I don't know how to do it.

Vincent Argent: Yes, well, I would agree that there should be a register. I think it should be retrospective, because some of the patients may still be unaware that their symptoms may be caused by this problem. Maybe even some GPs or hospital colleagues might be...

Cyril Chantler: I'm not quite sure how you could do it retrospectively actually, because I think you've got to do it at the moment it goes in.

Vincent Argent: Yeah.

Cyril Chantler: Thank you very much. Thank you.

Vincent Argent: Okay.

Julia Cumberlege: Right. Valerie.

Valerie Brasse: Can I just ask a question about the register? We know that a number of registers are funded by the industry.

Vincent Argent: Yes.

Valerie Brasse: Would you have a problem with that if that funding was open and transparent?

Vincent Argent: I wouldn't have a problem with it if it appeared to be objective and not promotional. I think some of the concerns about mesh - and it does happen in other branches of medicine is that some of the activity by the companies were promotional whereas a register should be truly objective. There would need to be independent scrutiny of the register, because that's the way...

Valerie Brasse: The issue is not about funding per se by industry, just the government's process around that.

Vincent Argent: No. I mean, obviously post-marketing surveillance should to some extent be paid for by the company, because it's in their interests to do post-marketing surveillance, because if their product is good and it's successful, then they'd want to be able to demonstrate that fact. But then if it turns out to have certain problems, they do need to be truthful and objective and actually say what those problems are. Whereas there's been a feeling in this particular problem that there's been a certain amount of 'we'll cover-up'.

Valerie Brasse: Thank you.

Julia Cumberlege: Isn't one of the problems with that is that we've met women whose complications only became apparent five, six, seven years...

Vincent Argent: Yes.

Julia Cumberlege: ...after the operation was done? I wonder how one can catch up with some of that, because if a woman has had it today, it probably looks - it may be very successful. But then in five, seven years, whatever, then we have problems emerging. The market surveillance has to be very long term really. I don't believe that happens, does it?

Vincent Argent: No. I'm not sure what happens with hips. The National Hip Registry and the MHRA, that's - I understand is lifelong follow-up. Patients are recalled

every six months or year according to their situation. That probably should happen with mesh. There should be long-term follow-up, five or 10 years. You see, it's [unclear] because it's quite similar to hips in some ways, because they start getting a bit loose after five or 10 years. They might start releasing metals into the body. But with urogenital procedures, as women get older, the tissues change. Therefore, the mesh, which may have become quite hard, will erode through much of the softer atrophic tissues. Intuitively you can see there's a potential for quite late complications. That does seem to be the case.

Julia Cumberlege: In all the research that you've done - and it's been a very useful session. Thank you very much. But in all the research you've done, are there certain meshes that you think are actually more successful in terms of not producing...

Vincent Argent: Certain meshes.

Julia Cumberlege: ...the difficulties that we've heard from women?

Vincent Argent: The answer is, well, probably. Most of the mesh procedures now, most of the mesh is made from polypropylene polymer. That's been around for a long - it's the same as Prolene which is used for suturing, which has been used for many, many years. But it's because of the different physicochemical layout of the mesh because it's sort of criss-cross and there are gaps in-between, so it behaves a bit differently from Prolene sutures. A lot of research is being done into biosynthetic meshes and into biological meshes. There's a lot in the chemical engineering industry and medical plastics industry about development of other types of mesh. Yes, mesh may improve.

I think one of the problems with the polypropylene mesh - Prolene mesh, which was used for most of these procedures, is that we don't actually know very much about the behaviour of it in the body. There's a lot of research being done. It's ongoing to see what the effects are in terms of - especially producing more distant symptoms like immunological reactions and so on, because patients who presented with things like fibromyalgia symptoms have been told, well, that's nothing to do with mesh. But it might be. We don't really know. Because mesh is - well, it's a synthetic polymer. I think more research should have been done into the effects of it in the human body, because it does seem to cause...

Julia Cumberlege: It was quite high risk to put something like that into the body without having the sufficient research.

Vincent Argent: Yes. I think in retrospect the scientific literature on mesh, on synthetic polymers, does suggest that there is quite a high incidence of tissue reaction.

Julia Cumberlege: Thank you. Simon.

Vincent Argent: I think more research should be done into the scientific background for mesh, but it is ongoing. People are still doing research. For instance, when mesh is being removed, it's being looked at to see what its physicochemical properties are, to see what degradation has occurred.

Sonia Macleod: Explant analysis?

Vincent Argent: Sorry?

Sonia Macleod: Are you saying there should be explant analysis done when you remove mesh?

Vincent Argent: When the mesh is removed?

Sonia Macleod: Mm.

Vincent Argent: Yes. Probably when the mesh is removed, it should be analysed just to see what its physicochemical properties are, because we don't know much about that really.

Sonia Macleod: One of the things I was interested in earlier, you said that - obviously the traditional surgery is the colposuspensions and things where you knew broadly what the risks were. When women went to preoperative counselling, there would have been a much better understanding of risk. Whereas with the mesh, I got the feeling you were saying that the preoperative counselling, in terms of risk, just wasn't adequate. Was there a big difference between somebody saying, look, these are your two options, these are the risks for the colposuspension, these are the risks for the mesh, or were surgeons just saying, well, the risks are small on either?

Vincent Argent: I don't think there was a big difference in the preoperative counselling between the two procedures back in the 1990s when mesh came into being, because the standard of preoperative counselling consent in those days was not what it is now. I think you may have a copy. There's a 2003 document from NICE about consent for procedures where the risks and benefits are uncertain. That came in - and it was actually - mesh was partly responsible for that, because having had the discussions with SERNIP, NICE thought they'll produce a document for patients so they

would know that if the risks and benefits are uncertain, they [would] have more information.

But I think generally, if you go back to 1997 when mesh had its first SERNIP rating, that the [unclear] preoperative counselling was nothing like it is now. Things have changed a lot in 20 years in terms of what people are told in further conversation but then also what information they're given in terms of leaflets and also just looking everything up on the internet. There's been a huge change in clinical practice. Now most doctors realise it's an essential part of their practice.

There may have been a difference because the Burch colposuspension, if you like, was in established practice. It did seem to be reasonably effective, but it was a long procedure with a long stay in hospital. There were risks of complications which were known about. Vaginal mesh came along. If we'd been more objective and actually realised this was a new product and given the same advice about, well, we're not really sure about long-term complications, patients would have been better informed. Unfortunately, the focus was very much on saying, oh, this is quick fix. There's no problem. This works and so on and so on.

Julia Cumberlege: Okay. I'm just going to ask members of the team here if there's final questions they'd like to ask you.

Vincent Argent: Okay.

Julia Cumberlege: Valerie?

Valerie Brasse: No.

Julia Cumberlege: [Unclear]. Simon? No.

Simon Whale: No.

Julia Cumberlege: Cyril? No. Right.

Vincent Argent: Can I just show you a picture to finish off with?

Julia Cumberlege: Yes.

Vincent Argent: It was really something - I'm very interested in obturator pain. In the case of a TVT operation - having been a gynaecologist...

Vincent Argent: I just wanted to show you something which had a big effect on me. It's an anatomical picture of the obturator foramen.

Julia Cumberlege: [Unclear].

Vincent Argent: The TVTO operation involves putting a fairly large, sharp needle through the obturator membrane behind the bone on the left of the picture, which is the inferior pubic ramus. Now some women are having problems with obturator pain, even to the degree they can't walk, because in the top right-hand corner of the obturator canal, that's where the nerve artery and vein goes through. It's fairly close to where the needle goes through.

The needle goes through on the left side. But if you look at the fascial fibres, they generally go from right to left, left to right, across. We think that some patients, when the needle's put in, they do get a haematoma or they may have neurovascular damage or they - because of the lines of fascia, there may be some inflammation going along the fascial line. Now of course, the needle's put in blind, because you don't actually see where it's going. Even though the main nerves come out at the top right-hand corner, there could be very, very small nerve bundles which go all over the obturator membrane.

If someone suffers obturator problems, then they sometimes have problems walking, because it affects the adductor muscles of the hip. You can't move your leg quite so easily. Obturator injuries and obturator problems are relatively common in footballers and ice skaters, because they adduct their legs quite a lot. This is one of the problems.

Having seen this, why I wanted to bring it up is because I don't think many colleagues are aware of the anatomy of the obturator canal and if you start putting large needles in through these things that there's a risk of infection, haematomas and so on.

Julia Cumberlege: Right, thank you very much.

Vincent Argent: I just thought I'd show you that, because it had a big effect on me.

Julia Cumberlege: I wish you would teach me anatomy in greater detail. It's very helpful.

Vincent Argent: Yes.

Julia Cumberlege: Thank you. This is very important.

Vincent Argent: I know Dr Baranowski at the British Pain Society [unclear] this picture, too, because he said, yes, that's pretty close. We're talking about a couple of centimetres. Obviously bleeding and infection can crack. That would explain why the risk seems to occur.

Valerie Brasse: He is coming to speak to us actually.

Julia Cumberlege: Right, well, thank you so much for coming today.

Vincent Argent: Okay.

Julia Cumberlege: Very grateful. It's been a really useful session.

Vincent Argent: Yes.

Julia Cumberlege: If there happens to be anything that you feel perhaps you would like to have said differently or whatever, do let us know. We need to know within 24 hours, because we need to then put it on...

Vincent Argent: Okay.

Julia Cumberlege: ...the web so people can see. But certainly, I haven't discovered anything.

Vincent Argent: Okay.

Julia Cumberlege: I don't suppose you have either.

Vincent Argent: Yes, I'm aware you've received a large body of evidence and good evidence from people like the CEBM in Oxford. That's why my submission was very short really.

Julia Cumberlege: Right.

Simon Whale: Thank you very much.

Julia Cumberlege: Thank you. Thank you very much indeed.

Vincent Argent: Okay. Thank you very much.

END OF TRANSCRIPT

Session 2: Royal College of General Practitioners (RCGP)

START OF TRANSCRIPT

Julia Cumberlege: Is there anything you would like to tell us, just in opening remarks? We've had some evidence from you and thank you very much for that. That's been really helpful. I think you've also declared any conflicts of interest that you might have, I think that's on the record too.

Helen Stokes-Lampard: Thank you, yes. So I mean I - obviously, in preparation for this, we've been looking at - we've seen some of the previous videos of people giving evidence. We've had people contact us, and we were made aware of perhaps three areas that I thought I might be able to add some supplementary information as to what we've already submitted in evidence to you.

I have prepared some information in the form of a statement that I can read bits out. I certainly didn't think it was appropriate to read out the fairly significant submission we've already made to you, and obviously, I'm very happy to take any questions that any of you wish to put to me. I do not pretend to have encyclopaedic knowledge of every element of this, but the reason I have brought two colleagues along with me from the College is if there is anything specific that we establish, that you have further information, that someone, somewhere in the College can provide. They're making notes that we can get that and get back and get it back to you.

Julia Cumberlege: That's...

Helen Stokes-Lampard: That's why I have my colleagues with me, if that's okay?

Julia Cumberlege: All right. That's splendid. If I could just start by saying that first of all, my Dad was a GP, so I grew up in a GP's household. He joined the NHS in 1948, so right at the very beginning.

Helen Stokes-Lampard: Very important, yeah.

Julia Cumberlege: Sadly, of course, he's no longer with us. Just thinking about your organisation, it is a membership organisation, and again, I've chaired a number of membership organisations, and they are actually quite difficult, because it's not like something that's statutory and you've got certain rules and things you have to comply with, but certainly, as a Royal College, I'm sure that you do have some of those.

Thinking about the written evidence that you've sent us, I'm just wondering, from the point of view of the College, and I know that you're not a regulator as such, but can you just tell us a bit more about how you promote safety and how you set your high standards of practice that you expect GPs to operate under?

Also, in that context as well, can you say how you ensure that those standards are met?

Helen Stokes-Lampard: Okay. Rather than go through the - because three sections that I prepared were the role of the College in updating our members, a bit of information about the history of Primodos and some feedback on a flu-on-the-wall documentary that was talked about in a previous hearing. Shall I just put those to one side and take questions, or...

Julia Cumberlege: Well, no. If you'd rather...

[Over speaking]

Julia Cumberlege: If you'd like to put that on the record, do, by all means.

Helen Stokes-Lampard: Shall I do that? Because it might...

Julia Cumberlege: Yes.

Helen Stokes-Lampard: ...I think it's probably going to be quite a large degree of overlap in what you're asking.

Julia Cumberlege: Yes.

Helen Stokes-Lampard: Rather than repetition, would that be okay?

Julia Cumberlege: Yes. Do - do that. Yes.

Helen Stokes-Lampard: Thank you. Thank you so much for asking your - asking myself - or asking the College to come along and add to the dossier of evidence we've already supplied to you.

So, yes, I'm Chair of the Royal College of GPs, which effectively is equivalent to the presidents of the other colleges. The Royal College of GPs is the largest of medical royal colleges. We have over 53,000 members, and you're quite right, royal colleges are not regulatory, they're not statutory, they are membership organisations, so we are independent, and our expertise is patient-centred, independent practice.

We're absolutely the largest membership organisation of GPs anywhere in the UK, but we also have members around the world. Over 3000 of our

members are internationally based. Our commitment is to improving patient care, developing GPs' skills and promoting general practice as a discipline. So that's the starting point.

The three issues, if you're happy. This - there was a TV episode broadcast in the autumn. Now, this was brought to our attention by the Foetal Anticonvulsant Syndromes Awareness Group, FACS-Aware. I think they brought it to your attention. I didn't see the episode myself, but I'm now aware quite a lot about it.

Apparently, in November FACS-Aware raised concerns about one episode where there was in one clip a GP seemed to be acting in a way that suggested GPs had specialist knowledge of epilepsy management, which one would not normally expect. So one of our College members, a Dr Judy Shakespeare, investigated this. She contacted the GP involved directly.

It turns out that he's a GP with a longstanding specialist interest in epilepsy, and he was being filmed working in a specialist setting - specialist clinic setting, working alongside secondary care colleagues, and so the portrayal on the TV programme was him enacting very appropriately for the context, but it wasn't made clear in the documentary, and he was actually in consultation with a patient lasting 20 to 30 minutes, which had been carefully edited to about a less than two-minute clip.

So I think he's subsequently provided a very clear and reassuring statement to the FACS-Aware Group, which I've got here. I'm happy to read it to you. I'm happy to give you a hard copy of that statement, but I found it beautifully clear in explaining what was going on. So shall I read it, or shall I just provide you with a copy?

Julia Cumberlege: Yes, okay.

Helen Stokes-Lampard: This was in email form from Dr Andrew Hansen on 27 November 2018. Subject, *GPs Behind Closed Doors*, which was the name of the documentary.

Dear Judy, further to our telephone conversation this morning, thank you for the opportunity to set the record straight, and I would be grateful if you could share this email with other members of the relevant committee. I was very concerned to hear that my consultation, which was broadcast by Channel 5 recently, in their *GPs Behind Closed Doors* series, was being held up by some as an example of poor epilepsy care. As you know, I do not accept this is the case and I hope the following narrative

reassures the committee that ██████ in fact received high quality care and advice.

Having viewed the video footage again, I can fully appreciate why concerns might have been raised, as taken at face value, it does appear to reveal a GP dealing with matters that should be dealt with in a specialist setting.

Unfortunately, the Channel 5 documentary does not provide the context of the consultation, and furthermore, due to the skill of the editor, it's not apparent that a 20- to 30-minute consultation has been condensed to just a couple of minutes. ██████ not a patient of the Ridge Medical Practice - the GP surgery - I was consulting with her in my capacity as GP with a specialist interest in epilepsy in the Bradford Epilepsy Service, BES, which uses GPs with specialist interest and epilepsy nurse specialists to deliver specialist epilepsy care in a community setting close to home. The BES was founded in 1996 and I have worked within that service since its inception. I have done a weekly specialist epilepsy clinic since then.

I also have an interest in general neurology and have done at least two general neurology clinics per week during this time, too. The BES has been recognised nationally as an outstanding model of epilepsy care and is fully supported by the consultant neurologist at our local hospital. One of them in particular provides clinical governance and neuroradiology support to the service.

I'm well aware of the current and previous MHRA guidance surrounding prescribing of valproic medicines for women of childbearing potential. The risks of valproate have been known for many years, and as the evidence about it has increased, we've incorporated this into our counselling and advice for this patient group for some considerable time.

The consultation was filmed before the current PREVENT programme was rolled out, and at that time we were using the old risk acknowledgement forms, which required women to state they understood the need for very effective contraception, but actually fell short of making this a condition of any ongoing prescription. This is consistent with the advice I gave [De-identified] within the broadcast section of the consultation, which represents only a small portion of what was said on the day.

Whilst this may not come over clearly on the video, I'm absolutely confident that I helped ██████ informed decision about her treatment that day.

In the post-consultation interview with Channel 5, which was recorded over the summer, I did describe in detail MHRA advice regarding the need for regular specialist review, to ensure valproate remains essential or to explore alternatives, and the requirement for highly effective contraception. Unfortunately, this was not included in the final edit of the programme, which, in retrospect, would have been preferable. In spite of this, I did feel that allowing the consultation to be broadcast was a good thing, as I felt it would raise awareness of this very important issue.

I've been shocked to hear that it has been perceived so badly by certain people, but trust that the above does provide adequate reassurance about this particular patient's care.

We've contacted the production company this morning to see what their thoughts are about including some further information about the PREVENT programme in a further episode of the documentary. I would hope for a positive response, as their main aim in producing this show is to tell a good news story about the NHS and demonstrate how hard clinicians are working at the coalface to provide excellent patient care. I expect they'll be dismayed to hear these concerns have been raised. Their response is awaited. Kind regards, Dr Andy Hansen. Then there's his GMC number, and so on.

So I can give you a hard copy of that as well. Yeah. In fact, I'll take those out of my file now, to remind me to give them to you. There are a few copies of it here.

So that's - does that deal with that one?

Julia Cumberlege: Yes, thank you.

Helen Stokes-Lampard: Do you want to question anything on it, or shall I just carry on?

Julia Cumberlege: Well, if you've got more you want to tell us, or it may emerge through our questions.

Helen Stokes-Lampard: Well, that was it for the - that particular thing. Then there was the regulation CPD and dissemination of updates on drugs - shall I go on to that bit?

Julia Cumberlege: Mm.

Helen Stokes-Lampard: Yeah?

Julia Cumberlege: Yes.

Helen Stokes-Lampard: Obviously, we - the College is absolutely committed to promoting patient safety and high standards of care and we have a very strong relationship with our patients, and I think in particular with the emergence of the narrative of patients around this investigation, it has been tragic and heart-breaking to hear what goes on. As GPs we develop very long-term relationships with our patients and generally are regarded as the most trusted of doctors. We take that trust very seriously, and so it's heart wrenching for all of us when we hear these tragic stories.

We're committed to working not just amongst GPs, but with all relevant stakeholders, to ensure effective dissemination of relevant and important information, but we are not a regulatory body, as we've said. We do not have a monitoring, investigation or regulatory function, and we're not in a position to assess compliance with any of the standards we set or the best practice we recommend.

Additionally, we do not universally cover all GPs. Once professional examinations are passed and professional qualification MRCGP is obtained, membership of any Royal College is optional - and we talk about members in good standing. Currently we believe around 68 per cent of qualified GPs in the UK are members of our College - 68 per cent. Some of those qualified before it was ever necessary to pass our examinations, so they are - were never members, and others choose not to continue to pay their subscriptions, for whatever reason - lapsed members.

So, in terms of how we raise awareness of members about breaking news or emerging stories, there are many ways that we do this. One of the more popular is - I issue, with my Chair's weekly message to members, my informal blog - and it's of a chatty newsy style. It goes out every Friday afternoon. We have - but we have many other formats for breaking news. We have our news webpage, which is updated almost daily, where we've issued press releases on any issue of topical interest, but also, we have a lot of social media outlets.

We use Twitter, Facebook and Instagram, mainly, as our social media outlets, and we take part in a lot of media and public discussions of - just for the record, so 2018, for example, we're on the record in printed media over 4000 times, with something related to some aspect of healthcare, and over 200 elements in broadcast media. A few of these, as it happens, relate to valproate.

We use all these methods to raise awareness of risks associated particularly with prescribing of sodium valproate of late, but also mesh as well. Some of them were at the request of various bodies, but others

because we proactively felt this was important, topical matter - a hot topic, if you like, that our members needed information and easy access to the relevant links.

Just to be clear, under, of course, general data protection regulations, my newsletter is part of the baseline communication package that members can opt out of receiving, and I checked this week - currently the newsletter goes out to 46,334 people. I think that was yesterday's figure - 46,334 people and that is of the 53,000 members we have, so even within our members there are a chunk who choose not to have any form of email or written communication from us.

So I cannot, and we do not ever suggest that the College can contact all GPs in the UK and we never recommend that the College is used as route for disseminating safety messages or urgent messages about medicines, or devices - that's the role of the MHRA - but of course, we add caveats to our online learning and any resources we've got as swiftly as our resources permit, and once those things are brought to our attention.

As an aside, we've got a flagship research journal, the *British Journal of General Practice* - one of the most highly cited and highly regarded academic general practice journals in the world. That is distributed to all members who want it and the editor of the *BJGP*, Dr Roger Jones, is in contact with FACS-Aware and has previously offered to publish a discussion piece, an article about sodium valproate, and I understand that is scheduled for publication in April '19, and Dr Judy Shakespeare, who I mentioned earlier, our representative, is drafting this at present, with the various action groups, so that's already in hand.

So with ongoing learning of GPs, we have a long history of developing resources and training for our members. We have over 700 quality assured and peer reviewed online learning modules - the joy of general practice is we cover everything. The disadvantage of general practice is we have to try and cover everything, which is very difficult to do.

We have education libraries and we have - we provide educational accreditation of other people's courses and educational materials as well, recognising that we can't do it all.

We have an online learning community, where 160,000 people are registered and signed up, so that's way more than GPs - that's other allied healthcare professionals, working generally in the community setting as well - and we have over 100 other online learning opportunities, outside

of those modules, of bite-size or rapid learning, podcasts, screencasts and videos and so on.

As part of this, we produce learning resources on sodium valproate and the use of mesh, but our ongoing CPD is reviewed constantly and updated whenever we can.

I think that was all I had to say about the CPD, but - so happy for you to ask me anything I've missed.

Julia Cumberlege: Well, thank you very much. That was very comprehensive. Thank you. That's very helpful.

Right, can I just ask you - I mean you made the point very clearly that GPs have to be generalists. They have to cover huge - well, all healthcare, really, for their patients, but I think you do have, and I'm not sure if it comes from the College or it comes from another source - you do have GPs with a special interest in a certain subject. I think they were called GPwSIs, because they were...

Helen Stokes-Lampard: Various names at various times, yeah.

Julia Cumberlege: Yeah. Can you just tell me, regarding epilepsy, do you have GPs who have a special interest in epilepsy?

Helen Stokes-Lampard: The issue of being a GP with a special interest in anything is a very variable thing. There isn't one standard. There certainly isn't a standard package for how we do it, but the General Medical Council, the GMC, is trying to address that in the form of credentials, which are coming in, in the future, but they've been a very slow burn. So credentialing of additional interests is meant to help establish a standard, which is outside the normal scope of practice for any doctor. So a neurologist could develop a credential in something else, and so on, but obviously, GPs, because of the broad scope of where we start from, a lot of GPs are interested.

So historically, you could be - you could call yourself a GP with a special interest. There's no qualification to be a GP with special interest, but good practice with the state, one would normally expect someone to have had further training and further supervision, so if I give a personal example, before I trained to become a GP I worked in gynaecology. I started general practice with a natural special interest in women's health.

So I - when my colleagues were struggling with difficult conditions - difficult management of patients, whether it was menopausal problems,

contraceptive problems, they'd often ask for an internal second opinion, so I was the in-house GP with a special interest, but I never used the title externally, because that wasn't appropriate, but other colleagues would run community-based gynae clinics alongside a gynaecologist and what would normally happen is the consultant gynaecologist would take them under the wing, ensure they had a higher level of baseline training. They would work in partnership, but that was not a formalised qualification.

However, in something like gynaecology, there are additional qualifications that a GP could do to confirm their ability to fit contraceptive implants, or their ability to give contraceptive advice, for example.

So there are lots of historical examples - and I keep getting away from these in particular, to - for the generalist - the general angle.

The credentialing movement is slowly taking off and the College is currently... has a pilot of two credentials, like dermatology and cancer care. At the moment epilepsy care is not on that list. A lot of other medical Royal Colleges are looking at developing credentials, and obviously they're quite interested in whether GPs would like to develop credentials. I've not personally been approached, and I don't know if there's anybody developing a GP for a special interest for neurology care or for epilepsy.

It would be a logical one, but you can see the doctor I mentioned earlier has been working as a GP with a special interest for over 20 years - in partnership with a secondary care colleague. I am quite confident that he's been doing so very competently, and that is why in the revalidation process it is so important that the full scope of one's clinical practice is included in appraisal and revalidation, because in a sense, one is making a declaration to say that you are keeping up to date and achieving a standard that is felt to be appropriate, but there aren't a list of tick-boxes that one can say, that's what a GP with a special interest in epilepsy should do.

Have I answered?

Julia Cumberlege: Yes. Yes, very helpful. Just still sticking with sodium valproate, and you will be very aware of the pregnancy prevention programme.

Helen Stokes-Lampard: Yeah, of course.

Julia Cumberlege: We - from the point of view of the GP, is it something really quite simple that they could ensure that the women of childbearing age actually are

very aware about the dangers of taking medications for epilepsy, which is something that they - presumably people who are epileptic - they take Epilim, or whatever the drug is, and it is very easy for it just to continue, even when they're of childbearing age, if the GP is not aware and gives them some advice. I'm just wondering how that works, that prevention system?

Helen Stokes-Lampard: Yeah. Okay, so if we take - so the generality - anybody with a chronic long-term condition that needs written medication, good practice states that anybody who is put on any long-term medication should be having an annual medication review. We have a quality and outcomes framework that came into general practice in 2004, and epilepsy is one of the diseases conditioned there. It's quite clear that you get flags in the records if somebody hasn't had an annual review of their condition, which includes a medication review. So just for any condition - we could be talking asthma, in that sense.

Within GP computer systems, we've been electronically prescribing for many, many years - my own practice, we started electronic prescribing in the 1980s - but certainly since 2004, when this standardisation came in, the Quality Outcome Framework alerts pop up all the time and with - and there are alerts built into the system concerning the use of sodium valproate in women of childbearing age, and the templates that we use to check is somebody - has this woman had advice on - are there. So they - if the person is there, it's usually they're relatively straightforward.

The normal practice would be that the prescription is issued - so you can get repeat prescriptions for up to a year - unless you need blood test monitoring or anything else more frequently - but that would be a default for about a year. The patient picks up their prescriptions and as that's coming to the end of time, make an appointment for a review. You would either come in and see an experienced practice sister or a GP, who would go through a quick review - have you had any fits? How are things going? In this case, particularly, I know you're on sodium valproate - what type of contraception are you using, and so on.

In general, if there's any doubt at all, we refer to neurology and epilepsy services. As a GP, I do not titrate medicine for epilepsy up and down. It's specialist territory, and always has been, so it's not something that GPs are generally very comfortable - unless we're in a good dialogue with a neurology team and they've said, here's a suggestion - if you get this and that, then go up by this dose or that dose. So you get plans and you get shared care arrangements, but they're written, they're agreed, and usually the patient is very much part of that three-way dialogue - and

more than ever, we ask for signed shared care protocols with secondary care, because the GPs are quite anxious about being left responsible for something they don't feel confident to do.

In terms of the PREVENT programme and the pregnancy prevention plan - obviously we try to disseminate information - I think everybody's been working to try and get that out. What we've encouraged surgeries to do and several times we've encouraged this, is to run simple audits of all the people - all the women taking valproate in your care. Then we've suggested from 10 to 55 years of age, look at those women - who's on? Now then, have they got effective contraception in place? If they haven't, then they should be being referred back to neurologist to get a pregnancy prevention plan in place.

In my own practice, we did this, oh, a year or so ago. I'm now part of a very large practice, and we found 21 women aged 10 to 55. Of the 21, 11 of them had completely cast-iron contraception. They were either sterilised or their partner was sterilised, or whatever, and it was clearly documented. Of the other 10 we went through, six of them actually were also easy to exclude once you went into it a little more carefully, but it did leave four women who we were just not totally happy about, and referred them all straight back to neurology, so that certainly we were - these are people who'd been stable for years on medication. It had been documented that they knew the risks, but they weren't on a modern PPP, so we referred them back.

So, that's an example of what I would expect a normal general practice to have done over the past year or so, as this has been rolled out.

Just to be clear, that's on a baseline population of 28,000 patients, so just - so that was 21 on a population of 28,000. That's an *n* of one, but this is to give you a feel of how things have tended to work - and all those all manner of PPPs - but did that help?

Julia Cumberlege: Mm. So although you have the annual review...

Helen Stokes-Lampard: Yeah.

Julia Cumberlege: ...which actually, of course it's nine months from conception to birth - so the annual review is supplemented by the work that you do with hospital consultants?

Helen Stokes-Lampard: Oh, absolutely. So that's a baseline on any medication, you would tend to do it and you...

Julia Cumberlege: Right. I see. I see. So, going back to my initial question, which was about you're promoting safety - and thank you for your examples - and you're setting some high standards...

Helen Stokes-Lampard: We try to.

Julia Cumberlege: ...within general practice. Yeah, I'm just wondering how you know that there is some recognition of the work that you're trying to do, and although you cannot have a compliance regime...

Helen Stokes-Lampard: No.

Julia Cumberlege: ...presumably you would want your standards to be recognised and to be carried out.

Helen Stokes-Lampard: We would - yeah.

Julia Cumberlege: So how do you know whether that's happening?

Helen Stokes-Lampard: We don't know. We - I've got no way of knowing who reads my newsletter. We don't know who complete the online modules. All we can do is provide it and encourage the narrative - use any opportunity that we have to raise awareness, but we don't have a means of regulating or checking compliance. We just - that - it's not that - the relationship doesn't work that way. Is there something specific that you're looking for?

Valerie Brasse: What stops you? I mean you mentioned just now the audit the you would recommend.

Helen Stokes-Lampard: Yes.

Valerie Brasse: You used to do women...

Helen Stokes-Lampard: Yeah.

Valerie Brasse: ...between the ages of 10 and 55, I think you said.

Helen Stokes-Lampard: Yes.

Valerie Brasse: What stops you doing a survey saying, how many of you are doing it?

Helen Stokes-Lampard: We can ask the question, but of course, you remember the problem with the response to surveys is you get a very biased sample. If I put a question out to say, how many of you did it? The people who are going to respond are those who will have done it.

Valerie Brasse: Well, that might tell you about who's not. I mean, it's just trying to get some sort of sense of putting stuff out there and actually having no idea whether it's doing anything.

Helen Stokes-Lampard: Yeah, I - no, that's a fair challenge. I mean we ask questions of the membership all the time, so we're looking for examples of something - if you're - let us know. Tell us - feedback - but as I said, the sample - the number of people who, in their incredibly crazy, busy lives, take the time to fill something in or return something, is small.

We've just done a massive consultation recently and a response rate of eight per cent to 10 per cent is a good response to any online survey. I guess it's the difficulty of getting a biased sample. If the committee would like us to do it, I'd gladly put a question out. I've no problem with doing it. It's about how meaningful the response would be, I guess, I think, from the academic perspective, but if you'd like us to do something, I'd be very happy to ask the questions.

Valerie Brasse: I guess the issue for you then is thinking, well, we're doing all this, how effective are we being?

Helen Stokes-Lampard: Yeah.

Valerie Brasse: Can we get some sort of handle on this? I mean we can think of it in a lot of other contexts, for example, the obligation on medics, clinicians, to adverse report when they feel they ought to be doing so.

Helen Stokes-Lampard: Yeah.

Valerie Brasse: I don't know whether your organisation ever surveys doctors to say, well, are you doing it? I mean what proportion of you are filling in your adverse reporting...

Helen Stokes-Lampard: The yellow cards...

Valerie Brasse: ...and the levers - the levers for that then, does that appear in the discussion of an appraisal? Does it appear in a discussion around the validation? If anyone's making the checks against the standards you're setting, that you pick it up through potentially the only levers you have.

Helen Stokes-Lampard: I have. That would certainly come under the appraisal schedule. The online e - the electronic portfolios the GPs use for appraisal. There's a very large section on quality improvement, so we take it very seriously. Certainly, we were the first college to be encouraging clinical audit, many, many years ago, of members.

Quality improvement we take very seriously, we encourage, and it's absolutely an important part of an individual GP's appraisal process and the revalidation - but as I said, we don't formally, as a College, seek it. Our members choose to be members of our organisation. We don't regulate them - oh, and I think there's that difference between asking questions and attempting to mandate something where we don't have that authority to do it.

I mean, if there are - as I said, very happy to explore any ideas, and we've worked very closely - when issues come up, I try to be very accommodating. We've worked with the chief medical officer to put things out and to try and get things back, but I think there's also recognition of what is the role of a Royal College, as opposed to a role for other people - certainly not abdicating if it's genuinely trying to be constructive.

Julia Cumberlege: Your appraisals process is through - a technique - a digital system, is it?

Helen Stokes-Lampard: Yeah, I mean, there isn't a standardised system for all general practitioners. There are many electronic platforms. The College used to have one, but in fact there were others that were newer and flashier and so we stopped offering our own electronic platform for appraisal many years, though we have partnerships with various people offering them, but in all of them quality improvement is a key part of it. It has to be included in the five-year revalidation cycle. General practice is one of the first places that really embraced the whole appraisal process.

I mean my own appraisals only go back to '93 was - oh no - sorry, I apologise, 2003 was my first in sort of the modern version of appraisal. I think that was the pilot sort of appraisal before we went into formal revalidation cycles, but from day one, quality improvement was in that - significant events, audit of practice, assessment of self against standards - but that isn't the same as nationally collecting it, as you alluded to, Valerie.

Julia Cumberlege: So who actually appraises what the appraisee has sent in?

Helen Stokes-Lampard: In general practice, we have a series of - so it's a peer appraisal process that another general practitioner undertakes the appraisal.

Julia Cumberlege: I see.

Helen Stokes-Lampard: It's not somebody who works in the same practice as you, so there are general rules, which are - it'll be somebody in the same region as you. It'll

be somebody of a similar experience to you, but it will be somebody who you are not friendly with or don't have conflict of interest with.

I know over the many years I've had - and then there's - that's it - it's meant to be a three-year cycle. You shouldn't have the same appraiser for more than three years in a row, so that you don't build up a buddy-relationship with them, so that they can retain a degree of objectivity. Does that...

Julia Cumberlege: That sounds a good idea.

Helen Stokes-Lampard: It seems - yeah, then there's a responsible officer above the appraiser, so the appraisers are all trained and so on. The responsible officers then nationally are trained and work together.

Sorry, Cyril.

Cyril Chantler: On the same subject, I used to be Chair on the Standards Committee for General Medical Council, but it was a very long time ago...

Helen Stokes-Lampard: Mm.

Cyril Chantler: ...so I'm not quite sure how it works now, but certainly, it was the job of the Colleges to set the standards...

Helen Stokes-Lampard: Yeah.

Cyril Chantler: ...and they did so in conjunction with the General Medical Council, who is the regulator, and certainly in hospitals the appraisal process is actually under the supervision, eventually, of the General Medical Council.

Helen Stokes-Lampard: Yes. Correct.

Cyril Chantler: They have representatives in the hospital, and who are linked to the medical directors and the final revalidation process is approved by the General Medical Council, and you have to be successfully appraised to be revalidated.

Helen Stokes-Lampard: Yes.

Cyril Chantler: Persistent failures in any of the respects that you've just discussed would lead to questions about your staying on the register.

[Over speaking]

Cyril Chantler: How does that work with the College of General Practitioners?

Helen Stokes-Lampard: Almost exactly the same, Cyril. You have to have your appraisal every calendar year. It's a five-year cycle of revalidation, so to be eligible to be revalidated and remain on the general register, you have to have five successful, positive outcomes of appraisal, plus meet other minimum criteria, and as you say, ultimately, it's the General Medical Council that oversees that.

If you have an unsatisfactory appraisal, then there is a process for how that can be remedied. If it is just something technical or something being missed, or if there are other concerns, then other people are brought in to try and help and remedy the situation. Clearly, if there are issues - other issues with somebody's fitness to practise that the General Medical Council is already involved in, then it goes into quite a separate domain of practice, but the standard cycle is that you have to have five satisfactory appraisals to even start the process of revalidation, and each satisfactory appraisal includes an element of quality improvement activity - something every year.

Cyril Chantler: Your standards which the Royal College applies are themselves approved by the General Medical Council?

Helen Stokes-Lampard: Yes. Yes. The baseline standards, of course, are our membership of the Royal College of General Practitioners' professional examination - our licensing exam.

Cyril Chantler: Yes.

Helen Stokes-Lampard: Then the standards beyond that are around what comprises a good appraisal, what should a general practitioner be doing in that? Each year and in each five-year cycle - and we have guides for general practitioners about what should be in that. What we don't, however, do, is have lists of clinical conditions and say, every five years you need to have ticked everything off.

Cyril Chantler: No, I see that.

Helen Stokes-Lampard: It's about personal reflection on your own practice. It's about showing a breadth of clinical updates. Somebody whose pet interests - so if my pet interest is women's health, there's no point in me demonstrating I've gone to 17 courses on women's health in a five-year cycle. Surely what I need to be doing is making sure I've shown all the other aspects of general practice I've been to updates on, so that...

[Over speaking]

Cyril Chantler: Who appraises the appraisers?

Helen Stokes-Lampard: That's where they have the responsible officer, who is responsible for ensuring that (a) the feedback to and from is correct, but that the appraisers are supported, are up to date with the latest guidance, because the guidance on what comprises a good appraisal does evolve too. We have in the College a great colleague, called Dr Susi Caesar, who works with the Academy of Medical Royal Colleges to ensure a degree of standardisation through the whole of medicine, because of course the boundaries between primary, secondary and tertiary care are increasingly blurred and it's important that we're all working in a similar way to support doctors and help them with their professional development.

So the myth-busters' guide to appraisal and revalidations is worthwhile, and it may be - happy to send you this to the inquiry if it's of any use to you, but there are a lot of resources out there, so both the Academy and our own College guides.

Cyril Chantler: Thank you very much.

Helen Stokes-Lampard: Pleasure.

Valerie Brasse: Sorry, can I just ask?

Helen Stokes-Lampard: Please.

Valerie Brasse: If there is a breach then, of the standards you're setting in a particular area of practice...

Helen Stokes-Lampard: Yeah.

Valerie Brasse: ...say around management of epilepsy, or whatever.

Helen Stokes-Lampard: Yeah.

Valerie Brasse: A breach of those would not then immediately lead someone to be taken before the GMC? That wouldn't lead to...

Helen Stokes-Lampard: So...

Valerie Brasse: Yes?

Helen Stokes-Lampard: Okay, so if somebody - say there was - suppose we have a tragic significant event, where somebody ends up having a child who has significant impairment due to taking valproate, in this specific incidence. What would - at a clinical - at a professional level, you would expect that professional to be taking that very seriously. That's a significant untoward

incident in the practice. You would expect that to be reviewed at a practice level, at a personal level, in a case notes review. There's a whole machinery at a practice level for how we would deal with a significant incident.

If however, there was a formal complaint issued against that doctor - so - sorry - as I said, we're talking different things. So the specific doctor complaint, you would go through normal complaints procedures and the complainant could easily go straight to the GMC and raise it at that level. They may go through the practice. They may go regionally. There are a whole heap of ways people complain, but ultimately, the General Medical Council would be looking at that individual's fitness to practise.

Quite separate from that, I would expect every general practitioner, every clinician, to be reflecting on significant untoward events in their practice, in a structured way, using colleagues to reflect on it and learn from it, and show in their appraisal process how they have learned from this difficult clinical experience, or this clinical error.

Those are quite separate things...

Valerie Brasse: Mm.

Helen Stokes-Lampard: ...but that is part of good medical practice. The GMC is very clear about how, as healthcare professionals, we have to be constantly learning and how we do need to learn from mistakes and reflect upon them.

Valerie Brasse: I mean, we've heard from the valproate patient groups on two aspects here, one of which is, we are finding GPs are a little bit lax about the completion of the annual risk assessment form. So that sort of thing, I'm not quite sure - unless the patient then takes it upon themselves to complain to somebody - but of course, they may not be themselves sufficiently well-versed to know what should happen...

Helen Stokes-Lampard: Mm.

Valerie Brasse: ...how that gets picked up.

Helen Stokes-Lampard: I mean, it's difficult without having specifics to know, and obviously, I mean, the first thing is at any point, if any patient is unhappy with any aspect of the care they're receiving, speak to the GP about it. Speak to the practice manager about it. Every practice has a system...

[Over speaking]

Valerie Brasse: ...they need to know. They need to know what they're supposed to have. It puts the onus on the patient to do all the chasing.

Helen Stokes-Lampard: I think with - so with epilepsy care, you know this is very much a specialist territory in terms of the diagnosis and the therapeutic side of things, but there is also reasonably clear frameworks with quality and outcomes framework for what GPs normally do, and that's all available online for anybody to look at as to whether...

[Over speaking]

Valerie Brasse: It's when they don't do that.

Helen Stokes-Lampard: I think - it's difficult to - but if the standards are there and people have been reaching out, it's very difficult to know where the challenges lie, and I guess without the specific it's hard to give you the answers you're seeking, Valerie, but what I do know is that we've got frameworks for good reason.

Valerie Brasse: Mm.

Helen Stokes-Lampard: Frameworks around trying to provide comprehensive wraparound care to patients. We don't just...

[Over speaking]

Valerie Brasse: No, I understand the point of the frameworks. It's when it's not working, I'm trying to get at.

Helen Stokes-Lampard: Yes.

Valerie Brasse: How that gets picked up.

Helen Stokes-Lampard: Yeah. I mean, from a clinical commissioning group level, they have dashboards of how many points people are getting and it's a very simple thing, about the points the practices are scoring in different areas. The challenge practices have is that when they try to [comp] - practices are only as good as the data they have about a patient, so if we don't have the correct email address and we don't have a correct phone number and patients don't respond to the letters, there's only so far you can go, because patients are autonomous creatures and they don't have to come to these things. We have to chase them up to X number of times. What we can't do is force people to attend - and that's always a difficult tension.

So without specific cases to unpick, which I think is a helpful thing to do, at times, it's really difficult to go further, I'm sorry.

Julia Cumberlege: Simon.

Simon Whale: Can I just ask about...

[Aside discussion]

Simon Whale: ...recognising problems when they're presented? So if you take the case of a child whose parents are concerned that it may have foetal valproate spectrum disorder, related [unclear] issues.

Helen Stokes-Lampard: Yeah.

Valerie Brasse: Or a woman who thinks she's got pelvic pain that's related to a mesh implant.

Helen Stokes-Lampard: Yeah.

Simon Whale: How confident are you that typically a GP would be able to make the right connections when they're presented with a patient like that?

Helen Stokes-Lampard: Okay. To be honest with you, a patient who comes in and says, I think I've got a complication of my mesh, or, I think my child has an abnormality related to a drug I took in pregnancy, is actually very easy, because GPs know, right, I'll do that - that is definitely specialist territory - I need to refer this on to a colleague.

What's much more common - and more complex - is when a patient comes in with - so let's take the mesh complications. If somebody comes in with vague symptoms, I don't feel - so, tired all the time is one of the phenomenally commonly presenting symptoms in general practice. Tired all the time has about 2500, 3000 potential diagnostics answers, and so, you know, common things occur commonly.

We start with the, are you run down, are you stressed, are you anxious? We work through a sieve of all the things - you try and take a history to establish what's going on.

So if you've got a clue - I've got discomfort in the area where I've had an operation, or, I think there's something funny going on down below, or - that really does help you home in very quickly. When...

[Over speaking]

Simon Whale: This can be six, seven, eight years after an implant and the woman may well not herself - as you say - may well not attribute it to the implant.

Helen Stokes-Lampard: That's always the difficult thing. I mean, our general practice records are enormous, so a fit, well patient, who has had a hernia actually will flag up quite easily that they've had a hernia repaired, or some sort, because there won't be much in their records. Somebody who's complex, with multiple medical problems, that could be well back in the records and won't necessarily be flagged or alerted, so we're reliant on the doctor/patient communication to try and untangle a diagnostic dilemma. However, once a patient says something like, mesh, pain, site of operation, it helps us focus there, very fast.

There's a huge difference between very vague general symptoms, which could be a psychological disorder or stress condition, a haematological disorder, a physical complication of a procedure, a muscular-skeletal condition. That's where the challenge - that's where the diagnostic challenge happens.

I would say in modern general practice, where things are very stressed and under pressure, we have a 10-minute consultation model, which isn't fit for complex care management - we all agree with that and I don't need to rehearse here the challenges we've got. Lots of people are committed to improving the situation in general practice, but we are thousands of GPs short.

If people are struggling to get an appointment and aren't - and they've got something complex that needs untangling, and they're not able to see the same clinician repeatedly, it can take longer to get to the bottom of it. We know that continuity of care for complex conditions really helps get to the solution faster. So that's a systemic challenge we've got with the whole stressed NHS, which we would certainly recognise.

In terms of the individual, somebody walks through the door and says, I think I've got a problem with my mesh, doctor. That's actually quite straightforward to me, and once I've assessed them to confirm or otherwise - straight to my surgical colleague.

Simon Whale: If they say, I've got pain in my abdomen, and I don't feel right. I've got discomfort. As you say, vague symptoms...

Helen Stokes-Lampard: Actually, pain in the abdomen has narrowed it down massively.

Simon Whale:: It - well, yes, but it's still not - they're not giving you the red flag signal that...

Helen Stokes-Lampard: No.

Simon Whale: ...they're not using the word, mesh, so...

Helen Stokes-Lampard: No.

Simon Whale: What I'm trying to get at is how confident you are that the profession will ask the right questions to get to the right answer as quickly as possible? Or whether the - whether it relies on the patient doing more of the work than the doctor?

Helen Stokes-Lampard: Okay. I mean, within the last two years, I doubt there is a healthcare professional in the country who hasn't heard the word mesh. I mean I think it has been - had such huge profile that I think in recent times people are pretty acutely aware that mesh can cause complications in some patients. I mean, we're also conscious that for 20 years meshes have been used in surgical corrective procedures and people weren't talking about this. So I'm not talking about pre the last perhaps 18 months, two years, but certainly in the last two years, I really don't think there's a GP in the country who isn't aware mesh could equal complications.

So if there is any recognition this patient's had surgery that may or may not involve the mesh, I would expect that to be a red flag if abdominal pain, a malaise has come into it. I mean the biggest thing I see is obviously to say to people, if you're worried about it, tell us. We're not telepathic. Please, give us a clue what you're worried about.

I mean, the joy of general practice is that we usually build these relationships where we can have that dialogue. The frustration is where that hasn't - the patient leaves, thinking, I didn't like to say I thought it was my mesh. That's frustrating for everybody. It's frustrating for the patient. It's also frustrating for the clinician.

Simon Whale: Certainly some of the patients - a lot of the patients who've had mesh complications that we've met and spoken to, will have told us that they know more about their condition than the GP does. I'm saying it's true in relation to families affected by valproate, or foetal valproate syndrome.

Helen Stokes-Lampard: Yes. Absolutely, and expert patients can be phenomenally well informed, and actually, certainly - I mean, in terms of foetal valproate syndrome, I mean, it's - actually, if you have got any anxiety at all that your child has been harmed by anything you've taken in pregnancy, I would have thought that just a small hint of that to the GP is enough to ring all the alarm bells and say, straight - I mean, some things you can look at a child and it's pretty obvious that there is a problem.

Frequently, you have to observe a child over a considerable period of time to establish - particularly developmental problems - I'm sorry, I don't need to tell you that - you're acutely aware of this - and actually, as a GP, if in doubt, you'd be asking for a second opinion. You'd be referring that child on quite hastily, actually, and normally our paediatric colleagues are very good at taking those referrals and working with them and working through the challenge. If we've got any clue about medication and pregnancy - obviously foetal alcohol syndrome - it is more common actually, and a huge challenge. We've got all the issues of people taking narcotic substances in pregnancy and the withdrawal.

So actually, from the children side of it and paediatric referral, that's actually a quicker one that you've got a hint of trouble. I mean, if you've known taken something and it's not been flagged during the pregnancy, and usually we would hope, during pregnancy these were flagged as significant things, I mean, every woman who is pregnant and an epileptic should be under the care of an obstetric epilepsy service, and again, that's pretty clear-cut good practice. So these things should have been flagged and these children should be observed, and these things should be being watched [unclear], but if we're talking historically, which as I suspect is where some of this has come from, awareness has increased a lot over the years.

When I was in medical school, we were all taught pregnancy and epilepsy drugs don't go together. It's specialist territory - beware. That was just a blanket kind of warning. Over the years valproate has become very clear. The message has been stronger and stronger and stronger.

Simon Whale: Do you think - so, again, thinking about valproate and mesh, specifically, the two of them, is there anything more that should be done, or do you think awareness amongst GPs is now sufficient?

Helen Stokes-Lampard: Well, we've got bigger alerts now on the GP records. That's coming up bigger and stronger than it used to, so that was upgraded. The packets of tablets have got it splashed over them large and loud.

Simon Whale: Should have.

Helen Stokes-Lampard: Should have - oh, are they not? Oh. I don't see the boxes. I just heard - okay. I'm sorry, I thought that was already had been implemented, so if it happens, news to me. Sorry - did you - sorry?

Valerie Brasse: I was just going to say, when you said that the alerts are coming up, are you - do you have bigger alerts for more prominent things? Because we have heard about GPs and...

Helen Stokes-Lampard: Yes.

Valerie Brasse: ...fatigue about the alerts that are popping up all over the place...

[Over speaking]

Helen Stokes-Lampard: Yeah, alert fatigue is a challenge, so they are - my understanding is - I've never - I've never been in a consultation where one has flashed up. My understanding is they're now treated the same as methotrexate is in private care. Methotrexate is a drug used which needs intensive monitoring, usually used for rheumatological disorders and a big red box flashes up, bang, in the middle of the screen. You can do nothing till you dismiss this box, whereas most of the alerts pop up discreetly in the corner. My understanding is it was going to be in the format of the methotrexate alerts, but as I've never actually seen a patient - I can check that [unclear].

Valerie Brasse: Going to be, or already is?

Helen Stokes-Lampard: I thought it already was. I thought it had been brought in.

Valerie Brasse: Right. I have to ask.

Helen Stokes-Lampard: I don't know, as I haven't seen one. I can find out for you if you...

Valerie Brasse: Yes please.

Helen Stokes-Lampard:could work. That's one where we can find that out for you. Just call a colleague at the surgery, call up a patient, but yeah, my understanding, it's going to be treated in that way, quite deliberately, because of alert overload. Yeah, that is a challenge, actually, alert overload. It's just the same with the street signs. We have far too many street signs, so people stop reading them, which does nobody any good.

You asked actually a question about, could more be done? I think it is good practice to keep getting these messages out there, so the pregnancy prevention programme - yeah, perfect opportunity. We've got a new GP contract going to be coming in. Each year you can put a national quality improvement activities.

You could ask - it would be a reasonable suggestion that as one of the quality improvement activities that practices every year, every two years, whatever, have to run this audit of all their patients of childbearing age, and demonstrate the patients are under the care of a neurologist and have got an active PPP, or whatever. That would be a good quality improvement activity that, centrally general practices could be asked to

do, and I would like to think that most would be going, cool, that's great - bring it on. That's good and that's straightforward and that's good practice - but you might occasionally pick one up that had been missed over the last year or two, which would be exactly what you're aiming to do. So you could do that.

In England that would be via NHS England. Now, just to be clear, the devolved nations have got slightly different healthcare systems, but this is a four-nation review? Or is this an English...

Julia Cumberlege: No.

Helen Stokes-Lampard: English, okay.

Julia Cumberlege: We cover...

Helen Stokes-Lampard: NHS England then.

Julia Cumberlege: No, we cover Scotland.

Helen Stokes-Lampard: You do cover Scotland? So obviously, it would be the relevant authorities in Scotland, but they've got quality improvement activities in Scotland too, so it would just be...

Julia Cumberlege: I have to say, we're not responsible for Scotland, or for Northern Ireland, or for Wales, because they're devolved countries...

Helen Stokes-Lampard: Mm.

Julia Cumberlege: ...but they have invited us because they've asked us to go and meet their sufferers...

Helen Stokes-Lampard: Good.

Julia Cumberlege: ...and to learn from them, so we've done that.

Helen Stokes-Lampard: I'm really glad, because as a Royal College, we cover all four nations and it's quite frustrating when things are bound by the national boundaries, when actually, the healthcare needs are four nations.

Julia Cumberlege: Yeah.

Helen Stokes-Lampard: I'm also conscious, I have - did you want anything more on Primodos from that...

Cyril Chantler: Yes...

[Over speaking]

Helen Stokes-Lampard: Sorry, did you want to...

Cyril Chantler: Right. Yes. Thank you. One of the things that's been persistent as we've gone around the country is patients' view of conflict of interest - and it's not just in relation to general practitioners.

Helen Stokes-Lampard: Right.

Cyril Chantler: It's come up in relation to other specialisms, particularly surgeons. It's been raised particularly in the context of Primodos, which was a while ago, and surgical mesh, which is contemporary.

Helen Stokes-Lampard: Yeah.

Cyril Chantler:: So, starting at the sort of beginning of this conversation, do you think that doctors should be required to register their interests on a yearly basis and that could then be reviewed through the appraisal process? It might be some central register or some - or in some other way, like, say, members of parliament.

Helen Stokes-Lampard: At a personal level, yes, I do. I think it for the sake of transparency it's a good and sensible thing to do. We're NHS employees. We're servants of the state. The College doesn't have a formulated, official position on it because we've never been asked.

However, centrally, I expect every member of my Council to do a register of interest every year. We expect all the trustees of our College to do a register of declaration every year. I encourage my members of council also - so these are within the College, as a charity, the membership will be, but also, I encourage all members of my council to sign up to *Who Pays This Doctor?* Which is a free, open source resource for people to sign up and update their...

Cyril Chantler: We know about that.

Helen Stokes-Lampard: Yeah. So I mean, personally, I think it's good practice, and I certainly would have no problem with that at all. I think if we have anything - we should be - of all people, we should be transparent - our patients should need to trust us.

Cyril Chantler: Moving on from there, into post-marketing studies...

Helen Stokes-Lampard: Mm.

Julia Cumberlege: ...that general practitioners participate in, do they get paid for that activity?

Helen Stokes-Lampard: Gosh. I don't know that many general practitioners are involved in that.

If you participate in any research, NIHR - National Institute of Health Research - activity, which many thousands of GPs are involved in, and we have very strict codes. GPs get a modest remuneration for the time taken out of providing core NHS care to do stuff - so whether that's recruit patients, mail things, or whatever - very clear tariff-based - doctors don't do it for the money, they do it for the common good. It's meant to be a cost-neutral activity. That's the premise of NIHR stuff.

We encourage all practices to sign up to be research-ready, which is an accreditation, which demonstrates that people are up to date with good medical practice, people understand consent, transparency, good research behaviour.

We have a more research preparedness for practices that take part in more commercial research, so an advanced accreditation system for practices undertaking research. The commercial research is - which I think for post-marketing - so that's within the NIHR, we're very clear of the framework. If it's privately done, then I think practices can participate in it, and presumably do - I don't have much hands-on knowledge of that, though I can find out more if you want?

Cyril Chantler: They get paid for that by the [unclear]?

Helen Stokes-Lampard: Yes. Certainly, in the past practices would have been paid.

Cyril Chantler: Would they be obliged to declare that interest...

Helen Stokes-Lampard: To the patient?

Cyril Chantler: ...to the patient? Say, for example, if they were...

Helen Stokes-Lampard: Yes, and any consent procedure should be. Yeah.

Cyril Chantler: If they were prescribing a medicine, which was part a post-marketing survey and say they were swapping one medicine to a late - a more recent proprietary product, and they were being paid to participate in research related to that product...

Helen Stokes-Lampard: Yeah, in - yeah.

Cyril Chantler: ...would you expect the patient to tell...

Helen Stokes-Lampard: Yes. The clinician to tell...

Cyril Chantler: ...the doctor to tell the patient that?

Helen Stokes-Lampard: I would expect them to tell.

Cyril Chantler: Before prescribing?

Helen Stokes-Lampard: I would, because it should be part of the patient information process, and the consent process. So all ethics committees are very robust on this sort of thing, what needs to be said to the patient, and the patient information that is provided - which is usually, in various formats, in various ways, is accessible to the patient, should be quite clear about anything like that, so I would expect that to be the case.

I don't have hands-on experience of that, because my research and academic activities obviously are exclusively with NIHR studies.

Cyril Chantler: Yeah.

Helen Stokes-Lampard: Again, I can find out more if you've got a specific instance in mind. We've got a clinical information research centre at the College here. I could get a check...

[Over speaking]

Cyril Chantler: I don't have any specific instance in mind myself.

Helen Stokes-Lampard: No.

Cyril Chantler: I am just reflecting what patients have actually...

Helen Stokes-Lampard: Have said.

Cyril Chantler: ...have said to us as we've gone around the country.

Helen Stokes-Lampard: I would imagine that's less - I would have imagined that was less of a big thing in primary care than in secondary care, but if you have a specific instance, we'll try and check it for you.

Cyril Chantler: I rather hope it is now, but then of course, if we had a declaration of interest, this - which patients could interrogate, this would assist us in this.

Helen Stokes-Lampard: Yeah, help.

Cyril Chantler: Certainly in the days of Primodos, which was in the 1950s to '78, there seems to have been Primodos tablets passed out to patients without a normal prescribing process, from what we've heard.

Helen Stokes-Lampard: Right. Okay.

Cyril Chantler: What was the incentive to do that, I don't know, but that's where some of this...

Helen Stokes-Lampard: Okay, so that is...

Cyril Chantler: ...anxieties emerged from.

Helen Stokes-Lampard: I'm so happy - and obviously that is significantly before my time, both personally and professionally.

Cyril Chantler: Yes.

Helen Stokes-Lampard: Yeah. I mean, we can help, if there's any specific question you want us to try and find out more, I'd gladly do that, but it's quite difficult to make going back so far.

Valerie Brasse: It would be interesting to find out if there's any guidance issue to say that a practice can only indulge in, say, one or two of these direct relationships with the private sector. I mean I have no idea whether they're free to just do as many as they choose to, or not.

Helen Stokes-Lampard: Yeah, I honestly don't know, and I certainly don't know what would have been going on 40 or 50 years ago.

[Over speaking]

Valerie Brasse: ...now.

Helen Stokes-Lampard: I don't know.

[Over speaking]

Valerie Brasse: ...now?

Helen Stokes-Lampard: Oh, right. I'll ask the question for you. I am not aware of any, because I think it's not that common. There's not that many practices that get involved outside the NIHR governance framework, which is actually meant to get away from so much of this, to be robust and to ensure that it's all done properly. Certainly, we always encourage people to undertake research within that framework, for all these reasons.

Cyril Chantler: Thank you, that's...

Helen Stokes-Lampard: Is that...

Cyril Chantler: Yes, that's, thank you. Yeah.

Helen Stokes-Lampard: Are there...

Julia Cumberlege: Can I just ask you one on a rather - I'm back in the practice. I'm into the health centre, wherever the doctors are working. One of the things with people who have had mesh complications, it's taken them, the patient, some time to really recognise what the - what the underlying cause has been, and so they come in with other symptoms as well.

Helen Stokes-Lampard: Yeah.

Julia Cumberlege: Some of it's to do with their legs, and all sorts of different symptoms. I just wonder, in the practice I have seen notices that say, will you please stick to one condition to talk to the doctor about. If you have another condition will you come back and make another appointment? Is that good practice?

Helen Stokes-Lampard: That - those signs are an unpleasant and unwanted consequence of the way general practice is being forced to work at the present time in a stressed NHS. Those practices make 95 per cent of GPs feel deeply uncomfortable and they are an administrative way of trying to deal with the massive workload that we have - the patients queuing out through the door. So they are not desirable and what every general practitioner will tell you - every general practitioner will tell you that patients are complex and unpicking what's really going on - I frequently get people coming in with a list of six or seven things, and actually, four or five of them are intimately linked together.

So people are complex. To deal with a medical problem properly involves looking at the physical, the social and the psychological elements of their lives and the condition, which involves exploring it. If a patient is concerned about something and they don't feel it's been dealt with in the one consultation, the [answer] is to look the GP in the eye and say, how can I deal with all these things? I'm worried. A GP will frequently say, let's book you a double appointment to spend longer, unpicking all this. It is in everybody's interests to get to the bottom of a problem and not leave things hanging - it really, really is.

Julia Cumberlege: Does a double appointment still attract the same funding?

Helen Stokes-Lampard: We're not paid - it's a - it doesn't - because unlike hospitals, general practice is funded in a totally different way. We're not funded on the number of appointments. The 10-minute slot is purely a functional consequence of having to see so many patients. We can choose to have longer appointments if we want to. We just get to see less people in the day. It's just the physicality of how many hundreds you need to get through the door in any one day. So there's no funding issue at all related

to a double appointment. It's purely, if you have a double appointment, another patient doesn't get an appointment that day.

Julia Cumberlege: I've got a final question, and I know Cyril has, as well.

Cyril Chantler: Mm.

Julia Cumberlege: Is there anything you'd like to tell us about Primodos?

Helen Stokes-Lampard: Yes. It was just that there was something about *Sky News* and a documentary on *Sky News*. I just wondered if you...

Julia Cumberlege: Yes. We've seen that.

Helen Stokes-Lampard: Because there was a little bit of confusion about that - and there's obviously, as you said, it's a drug that really was before my time, but we did have some material in our archives about it, dating back to the 1960s and '70s, and *Sky News* journalists contacted the College in January 2017 and they asked if they could have access to our archives to look at our material, which we willingly agreed to. They referenced some of it in a documentary that was broadcast on *Sky Atlantic* in March '17 and I think it subsequently - some parts of it have been shown on *Sky News*.

Now, the problem is that documentary conflated two pieces of archived material. They were both written by Dr Norman Dean. The first was an unpublished research study out of Dundee University, which was done in collaboration with the Royal College of GPs in Scotland, and it makes a passing reference to Primodos.

The second archive material was a letter from Dr Dean to the College Chair at the time, a Dr Ekke Kuenssberg, which was specifically about Primodos. In that letter, Dr Dean expressed his personal view that Primodos should be taken off the market, but he acknowledged in that letter that this was not supported by clinical research, including his own research. Now, these things aren't dated, but we know that Dr Kuenssberg was Chair of our College between 1970 to '73, so we can approximately date that letter.

Sonia McLeod: Is that the Dundee University study?

Helen Stokes-Lampard: Yes. I'm just looking - it's the Dundee study, isn't it?

Sonia Macleod: Yeah.

Helen Stokes-Lampard: Yes, it's the Dundee study. Yeah.

Sonia Macleod: That's what I assumed. I just wanted to...

Helen Stokes-Lampard: Yeah. Yeah.

Valerie Brasse: So that study exists? You have it?

Helen Stokes-Lampard: We have the data in our archives, yes.

Valerie Brasse: No one seems to have actually seen the full study.

Helen Stokes-Lampard: If anybody wants to see the - if people want to see the archives, they're welcome. So it's an unpublished - it was never published.

Valerie Brasse: No.

Helen Stokes-Lampard: It didn't show anything definitive, which was why it was never published...

Valerie Brasse: But this was the study...

Helen Stokes-Lampard: ...but the data exists, yeah, absolutely.

Valerie Brasse: It was the study Dean did in consult - in collaboration with Dundee?

Helen Stokes-Lampard: Dundee, with RCGP Scotland.

Sonia Macleod: It's the complete study, it's not just the highlights of it?

Helen Stokes-Lampard: I think it's the complete study. I think we've got about 50 pages of...

Interviewee 2: I don't know if it's complete, but there's a substantial...

[Over speaking]

Helen Stokes-Lampard: I mean it's been looked at...

Sonia Macleod: ...very much like [unclear].

Helen Stokes-Lampard: So we - yeah - and as I said, well, Sky came and looked at it in the confidential, you know, she - obviously, they couldn't take it away, but yes, of course, we will facilitate that as we previously offered to do.

In terms of - yeah - fine. We'll start that up outside - the archive issue...

[Over speaking]

Julia Cumberlege: We may come back to you on that. [Unclear]. Cyril.

Cyril Chantler: This is a question that we're asking quite a lot of people who come to see us, and it is one that causes me quite a lot of anxiety. We're dealing with three things that have really gone terribly wrong, and I'm conscious of the

fact that it's actually taken groups of patients coming together, to get action in this area, and talking to politicians to establish parliamentary health groups. All that has been necessary for us to be asked to review it.

The system, to my mind, seems to have failed, and I'm part of that system and you're part of that system.

Helen Stokes-Lampard: Exactly, yeah, absolutely.

Cyril Chantler: So the question that I'm asking is, can you think of what we might be recommending to try and reduce the risk of something like this happening in the future? If you don't - can't respond immediately, if you want to go away and just think of about that and contact us, I'd be grateful

Helen Stokes-Lampard: Oh, we will certainly do that. I will do that, but I think certainly any device - so thinking particularly about mesh at the moment, but also the challenges we've had over the past years about breast implants - that affected a couple of my own patients - registries. Contemporaneous, high quality, searchable, identifiable registers, really improved. Post-marketing surveillance being as easy and as slick as possible. Also, patient empowerment of the future technology, where patients are being linked with their medical records, making it easier for patients to be able to feed back. All of those have got to be good things for the future and I think the profession would welcome these things.

I think any healthcare professional who believes that their - either their practice or that the system has harmed their patient - that's the worst feeling. That's the complete antithesis of what we're about, as healthcare professionals. So if we can do anything to support and help protect patients for the future, we should welcome that.

Cyril Chantler: It's about being able to hear the patient voice earlier.

Helen Stokes-Lampard: Absolutely, yeah. Absolutely. Just to be clear on - sorry, the Primodos thing. I'm sorry, I just wanted to be - something I was going to say to you it was clear - not about the archive - oh, I'm sorry, it's gone. I - there was something I'd meant to come back at you on. So the archives are not an issue.

Julia Cumberlege: Don't worry, because we are accessible.

Helen Stokes-Lampard: Yeah.

Julia Cumberlege: Always come back to us.

Helen Stokes-Lampard: Yes, thank you. It's just so - yeah.

Julia Cumberlege: Also, in closing this session...

Helen Stokes-Lampard: Oh.

Julia Cumberlege: ...first of all, thank you so much and thank you for bringing your advisor - your friend - your colleagues as well.

If you have any concerns about anything that you've said today that you felt should not be released, perhaps you could come back to us within 24 hours and we'll have a discussion on it, if that's all right with you.

Helen Stokes-Lampard: Of course, that's fine.

All I wanted to say about Primodos, is the archive material, just to be clear, Primodos is only mentioned in passing. It's a study of a wide range of hormones and contraceptives, that's - and Primodos is a tiny part of it, just to be clear - not to get your hopes up about the archive. That's...

Sonia Macleod: No, no. It's just - it would just be interesting because it has always been reported as missing, and not available, so it would be really useful to us to see it.

Helen Stokes-Lampard: Yeah, no, we have something - and I'm sorry, I can't vouch how complete what we've got is, but we have got material in the archive, so we...

Sonia Macleod: Fantastic. Wonderful.

Julia Cumberlege: Thank you so much, indeed.

Helen Stokes-Lampard: A pleasure. Thank you very much. Oh, let me give you these.

Julia Cumberlege: Thank you for all that you do for the College. Thank you.

Helen Stokes-Lampard: Thank you very - can I leave these with somebody? The - that's the statement from the doctor.

END OF TRANSCRIPT

Session 3: FEG Textiltechnik

START OF TRANSCRIPT

- Julia Cumberlege: If you'd like to introduce yourselves.
- Boris Obolenski: [Unclear]
- K Obolenski: Konstantin Obolenski, I've been with the company now for two years. I'm in the Distributor Management and in assistance to the two CEOs, one of which is my father.
- Boris Obolenski: I'm obviously...
- Philipp Schuster: Philipp Schuster. I graduated medical engineering and specialise in textile machinery engineering and I'm Director of Clinical Affairs now at FEG.
- Julia Cumberlege: Thank you very much.
- Boris Obolenski: Boris Obolenski, as my son said, I am one of two CEOs of our company and also one of two founders of the company and owners. I am a mechanical engineer too specialised on technical textiles and that's how we founded our company and that's the company name itself. In Germany it means FEG, Forschungsund Entwicklungsgesellschaft, means research and development company, thank you.
- Julia Cumberlege: Thank you very much.
- B Klosterhalfen: My name is Bernd Klosterhalfen, I'm a Professor of Surgical Pathology now for 30 years, and I am interested for 25 years in the pathology of surgical meshes in particular for how a mesh has to be constructed to be very comfortable. I investigated in this time 15,000 maybe 20,000 explants from preclinical studies and from patients and I have been - served as an expert witness into litigations in the United States and in Australia.
- Julia Cumberlege: Thank you very much.
- Dominic Walsh: My name is Dominic Walsh and I'm the Chief Executive of Hospital Services and we are the distributor for the United Kingdom and Ireland for FEG Textile.
- Julia Cumberlege: Thank you very much because I do believe you actually work with - it's about 50 countries across the globe with your product. So I would like to start only just by asking you a few questions unless there's something you'd like to say first.

Boris Obolenski: Yeah, maybe...

Philipp Schuster: Indeed, we have prepared a brief statement.

Julia Cumberlege: That's fine.

Philipp Schuster: ...which probably will take 10, 15 minutes if that is okay.

Julia Cumberlege: All right.

Philipp Schuster: The idea of the statement is to give you an idea of what we are, what our way of thinking is, what the crucial mesh parameters are because that's the area where we are experts in. These parameters are also important to recognise what the difference is in the meshes on the market. Then we just sat together and thought about the critical analysis of the current situation and potential improvements that we will be put into the statement if that is okay.

Julia Cumberlege: Yes.

Philipp Schuster: So we would just with start. So first of all, thank you very much for the invitation. We are very honoured to contribute to this investigation. A brief remark regarding language, so I'm not a native speaker, if there is any problem on your side on my side then Konstantin is almost a native speaker and will help us out here if that is okay.

Julia Cumberlege: I can assure you it's better than my German.

[Laughter]

Philipp Schuster: All right, so FEG, as Boris Obolenski said, is an owner managed company so we are not subjected any investors' expectations, that is an important point.

Julia Cumberlege: [Unclear]

Philipp Schuster: We are developing and manufacturing mesh implants for the two sectors hernia and urogynaecology but we do not have directors. So in contact with the end users are the distributors which we cooperate with all over the world. The two USPs, what is different, so we do have a fully integrated production line, which means we only buy the granule and then we do the filament spinning on our own.

We do the preparation, the warp knitting, the finishing of the products in-house. That enables a toolbox of parameters which you can adjust and use to adapt the properties of the product. This is an important point. The second USP is the material which we use, so we are the only supplier

of meshes in the market which is PVDF, the polymer. So, to understand our way of thinking and to understand what are the crucial parameters it's important to go back in the history just briefly?

So founded in 1992 as an engineering service provider for technical textiles and textile machinery industry we rather by coincidence got involved into the first project which was to develop a hernia mesh. So this was a project funded by one of the big competitors, an American competitor in the market. We started with the classic engineering approach to set up a requirement profile, checking the state of the art and we came up with a proposal to make a large pore mesh, which at this time was really an innovation.

We also proposed to use PVDF. However, the funding company restricted the choice of materials to only PP, a multi-filament structure, in contrast to our proposal for using mono-filament structure. The reason for this is quite obvious so these were established and registered products which were available at the company, so from that point of view the decision was made. So, in consequence, and deeply convinced that it is possible to make better meshes we started to develop our own meshes, so that was a direct consequence of this project.

Still today we are owner managed and as I said we are not subjected to investors' expectations and this is an important point and a big difference to many competitors. I would explain that on one example. We never developed hernia [plugs] or six arm meshes although technically we easily could have done so. But we were never convinced that these are good products. Meanwhile, there is enough evidence that we were pretty right with this first appraisal we did here.

This is a freedom which we live to decide what we do and what we do not do which is possible because we are owner managed. I would like to come now to the crucial mesh parameters which are important to recognise what are the differences of the meshes available. So basically there are two major tool boxes available where you can adjust the properties- one is the raw material which you use to make a mesh and the other one is the textile design, the textile structure.

Essential requirements for the raw material is a long term stability as long as you do not go for degradable meshes by tension and the low foreign body reaction. So these are the two characteristics that you look at when you choose the raw material. Essential requirements related to the design are mechanical properties of the structure of course. So we always

follow a biomimetic approach, so we're trying to adapt the mechanical properties of our products to those of the host tissue, the native tissue.

That is possible by adjusting the production - the process parameters. The second essential requirement relating to the design is the porosity or effective porosity. The effective porosity is a concept which we established. It describes the porosity after the foreign body reaction, the initial foreign body reaction took place. This is an important difference. Porosity is important on the long term and it's important to reduce the risk for chronic pain. I think this is state of the art.

The third essential requirement relating to the design is the structure stability. So you can design the most nice and beautiful porous but if under tension which is applied in the body the porous collapses it doesn't help. So you need also to check the porosity under tension, under load, this is important. Professor Klosterhalfen did investigations on many, many thousand explants and from his pathologic view he's an expert and can definitely explain the meaning of those parameters which I just sum up, more in detail than I can do. I'm not sure if he'd do that now or a little later.

B Klosterhalfen: Well, after you.

Philipp Schuster: So what is still left is our critical analysis of the current situation so if we can that up front or then Professor Klosterhalfen can tell you a little more on the histology of this - of the meshes.

Julia Cumberlege: Well thank you very much that's been really helpful. An omission from me, I should have told you that this oral hearing is being recorded, it's being videoed and it will be up on our website.

Philipp Schuster: No problem.

Julia Cumberlege: That's true of all the oral hearings that we've been having so I think that's the right thing. I'm very interested in what you were saying about the product. You were very anxious that it isn't degradable. Can I just ask you and perhaps it's in the papers that we have but how long have you actually been producing it and when did you first start to insert it into women's abdomens?

Boris Obolenski: So we developed the first fibres and implants starting in a public funded project by the German Government. So you will find we are very open minded, yes, all our knowledge except some technical special knowledge like spinning machine adaption, our parameters are open to the public.

We learned a lot from Professor Klosterhalfen and his colleague, Professor Klinge who published more than 150 publications.

So all this knowledge we have is open to the public from my understanding and it starts in 1994. So we recognise that there was mainly used not optimal polymers and that was a public project for three years and we developed the first fibres and implants made from PVDF. Started with a lot of technical investigations and animal tests so it took more than six years to really be able to have implants on the market, so that was 2003.

Now so we have 15 years in the market and we have results, yes, even if you do your best and we try really to engineer the best meshes which is possible for every purpose so there is not the single best mesh material. There is a good polymer or a bad polymer but you have to design the structure for the purpose. We call it tailored approach. So the material which is good for a hernia mesh for a special operation technique is totally wrong in another purpose. So that is really essential.

So we have now more than 16 different structures and you shouldn't use mesh A for operation technique C. That is really crucial. Even if you do your best sometimes it occurs that meshes have to be explanted and we offer to all our customers free analysis of all explanted meshes, and that's how we learn best about material structures and so on. All these results are published by Professor Klosterhalfen who can explain better than me.

Julia Cumberlege: So if you're following up after you have inserted the mesh into women and you're ensuring that you get all the information which you need from them and the women are finding it's not as successful as you'd hoped, is it easy to take the mesh out?

Boris Obolenski: It really depends. I have to say it's not easy, it's never easy but it is possible with our meshes especially because our meshes are since 2007 we made a new innovation and now our meshes are visible in MRI. So normally a mesh is invisible, you cannot see a mesh. So what you see if you are a urologist you only see phantoms if there is some water or some air but the mesh is invisible. We offer the mesh - unfortunately not all surgeons ask for it but we offer every mesh as a so called visible mesh and then it is absolutely 100 per cent sure you can identify it, every piece of the mesh and then you can take it out.

Julia Cumberlege: So does it not wrap itself around other organs as we've heard from the patients who have suffered complications from mesh, who have told us how the mesh has actually wrapped itself around the bladder and about

the vagina and other organs and that has made it very difficult to take the mesh out? Does your mesh do that?

Boris Obolenski: Once again we have to explain, what kind of mesh?

Julia Cumberlege: Right.

Boris Obolenski: Do we talk about so called simple incontinence, sling, do we talk about a complicated vaginal mesh technique like these big meshes, six arms, that is totally different? You cannot compare...

[Over speaking]

B Klosterhalfen: But what we know from all of the studies we made from preclinical studies or in standardised conditions and from the patients, from the explants, and here we have insight of explants staying in the body for 20 and 25 and 30 years sometimes. The average is of course - is shorter. So mainly the complications occur after two years in the average but if you talk about slings, or the meshes for prolapse repair we have explants where we have the insight for eight or 10 or 12 years.

What is really important is that you have to understand, every mesh implant produces this foreign body reaction, and this foreign body reaction is a chronic inflammatory type, a type of chronic inflammatory process. You have to imagine what you produce is something which you can for instance compare with a chronic wound with a persisting cell turnover. We made studies on explants taken out after 20 years and if you make special investigations you can see, yes, you have still a cell turnover.

So cells die, cells proliferate so that the tissue around the mesh is remodelled over the years and this is a progressive process. This explains why the shape of the mesh or the position of the mesh can change over years. We know that this foreign body reaction is the main key to understand the complications because the extent of the foreign body reaction correlates directly to the fibrosis. The fibrosis, the extent of the fibrosis directly correlates to the complications of mesh.

There are a couple of complications, what you can call, for instance, chronic pain of the scar around the mesh and if nerves are trapped in this scar or if the nerve is directly traumatised by the mesh you'll get these aromas and the state of chronic pain. If the scar starts to shrink, which is a natural process of the scar, the mesh has to follow the scar and it wrinkles up and then there are folding and this is the reason of erosions.

We know that the foreign body reaction correlates to infection, fistula formation, adhesion, and disfiguration. So the aim has to - or the aim if we want to have biopropital mesh is so that you have to reduce this foreign body reaction to a minimum and to therefore reduce the fibrosis to a minimum. This is exactly what we know and you can correlate it to all meshes. What we know if you have the same mesh structure, make a mesh from polypropylene or PVDF, you can see that this foreign body reaction is stronger than the foreign body reaction of this PVDF.

Valerie Brasse: Sorry, can I just follow that up? So you'll be saying whether it's for stress urinary incontinence, or for prolapse, and if we're talking about transabdominal connected with transvaginal at the moment - a PVDF mesh will have - will generate fewer complications than polypropylene for both those types of procedures.

B Klosterhalfen: Yes, we are always talking about averages and if you want statistical results. You see of course the result of a repair depends on a couple of factors, and also surgeons, and procedure, and of course of the patient and his genetic background. This is very important because there are responders and non-responders so the patients getting the same mesh have different degrees of foreign body reaction.

Valerie Brasse: Well I was going to come to that in a minute because one of the issues that women tell us is that actually there's no women for whom the mesh in any form should ever be implanted. From all your research and your studies would you say that it's possible to define a group of women for whom mesh could have a good outcome, after you've tried non-invasive conservative treatments, that mesh actually would be a desirable next stage? Are you in a place where the more studies you've looked at, the types of women who receive mesh, one can begin to define such a group because the patients who say to us that's not possible?

B Klosterhalfen: That's a very good question. I think you can. You can make tests before whether a patient reacts on these meshes, yes or no. So we made experiments with monocytes which we put into the meshes and we could say how these monocytes are actuated. Basically you can define a patient who reacts low to these meshes but I think you can never say that you're never going to have any complications.

[Over speaking]

Valerie Brasse: ...that. But you've got that group of characteristics in mind have you?

B Klosterhalfen: Yes we do.

- Valerie Brasse: A group of characteristics of that woman who could take a mesh, you're already beginning to think what sort of characteristics, what sort of defining features does that woman present with?
- Sonia Macleod: Can you identify your main responders?
- [Over speaking]
- K Obolenski: [Spoken in German].
- B Klosterhalfen: I think that there is no exact definition what you can have. So basically there are some special patient groups. If you have - if you tried already suture repairs and you have a recurrence and a recurrence you can try these meshes and if the women are older but there is - I think you cannot exactly define [unclear].
- Simon Whale: How important are lifestyle factors for determining suitability?
- B Klosterhalfen: I think if I look at my data for all the meshes for how the meshes react in the body is very similar. In my data pools I have a couple of thousands of these meshes and this individual factor of a patient is a smoker or that a patient has diabetes and randomise out. You cannot see real differences between these groups, yes. Because it's always the arguments during these litigations I say, look, this is an obese patient with a BMI of 35, smoker, she had operations before.
- This is I think - this is randomised out in these data pools because of the high number of these explants. Basically you cannot expect - and this is my personal opinion - the rule of incontinent patient or patients with prolapses are an older group of course and they have a couple of diseases, and I think it is a precondition you have to think about if you sell these meshes.
- Julia Cumberlege: Can I just ask you - I don't know the German system at all - can you tell me do you have patient groups as we do in this country who have taken a huge interest in this area altogether and who have taken on themselves the issue of informing member so parliament, other parliamentary groups, the general public? We've seen a lot of communication through the media, through Twitter, through all the areas that we communicate in now, do you have that in Germany?
- B Klosterhalfen: No, in Germany not so the patients are not pretty good at organising there. I have only [unclear] of organisations in the United States and Australia who have these new mesh device [unclear] or something like that but in Germany it's not like that.

Julia Cumberlege: So how do you do your follow up because we've heard a lot from women who have had these insertions made and then have been very, very ill as a consequence and so they need their voices heard through the parliamentary system? Of course this is why this Review is set up and I just wonder how you get your information of areas where it hasn't been so successful.

B Klosterhalfen: This is a very, very good question and I think in the past we missed to have this quality control in most of the countries where these meshes were used. Of course I think you've got a lot of clinicians and they will say we have to produce this data by clinical studies. The gold standard or the best would be of course prospective randomised studies but we are not a believer because to do a study like that with a particularly good follow up would mean years, even decades and a lot of money.

I think five year especially coming up in hernia surgery is to build up registers is the only chance to get quick - relatively quick results for quality control and surveillance of these meshes what we do. The first step has to be that we can exactly identify the implant or the explant so that you need something like identity card [unclear].

The second step is that we have to know how many of these meshes are implanted in the special time interval and [unclear] service that you have to - [fourth] the companies, or the clinicians or whatever at the hospitals, that they have to send every explant which fails to a registry or a database and then overlook what types of meshes, what products are explanted. What is very, very important that we have not only an overlook after years we have an early warning system.

So I remember mesh types which were introduced or launched to the market and for instance after three months we had a couple of explants back. So you can say it's that and to warn the company or the physician, you can say there is something wrong and this would be what I would recommend in a first step.

Philipp Schuster: May I add a comment here? As a manufacturer we launch the product with a risk/benefit ratio which is on the benefit side of course. But we never can exclude residual risk [unclear] so we do need the feedback from the market. This is the one point. Feedback can come from surgeons to authorities or to the manufacturer himself. If we get feedback we always try and we try very hard to get all necessary information to assess this case and the crucial question is always, is there a clear mesh relation with this event, which is really a challenge since there are so many influencing factors?

It's very rare that you can clearly say, well this is a problem which is really evidence based caused by a mesh. Communication and error culture, these are two points which are of importance here I think. So communication, if we get the feedback from the surgeon, or from the hospital, or from authority, and we try to get all information - it's not rare that we do not get any information, either from the surgeon or from the hospital due to certain reasons.

They simply do not have time or if they do not want to share that information with us, or they say well there's a general data protection act so we're not allowed to share the data with you, so all these problems there.

Valerie Brasse: What about from the patients themselves?

B Klosterhalfen: Very rarely we get contacted by the patients. Although on the implant passport of course we are - it's obvious that we are the manufacturer. It would - what since two years now I'm in charge of this department and we get contacted by patients maybe four or five times and then rather for things like well there is a potential allergy can I have a sample up front to check that. Not really serious events, not reported from patients.

Simon Whale: Is this your experience in Germany or in all countries?

[Over speaking]

Philipp Schuster: Worldwide.

Simon Whale: In the UK.

Boris Obolenski: No, worldwide, absolutely worldwide. You don't get - even if you try hard and I have to say that we have seven people, we are only 70 people in the company, we have seven out of 70 working in that quality assurance. It's absolutely hard and I have to say impossible, yes. I'm personally responsible for this and I want to have the best product in the market and we want to follow up every case we get and believe me we do it but it's really hard. These guys they cannot do it because surgeons don't deliver information, they don't - we deliver to a distributor, the distributor delivers to the hospital, we don't know the patient.

We do not know, never, no. If we ask the hospital they say it's not your information. They don't share it. They don't like it, they are not - they have various reasons and that's why we have some proposals to change this and we would really like it because this is the lack - there is a huge gap, what happens to your mesh? You develop a good mesh and then

you even don't know what happens to your mesh, which procedure was done. In Germany is that one we call it DRG so there is a diagnosis, you know this I guess, I think it comes originally from Australia. They already changed it but the German authorities are very slow.

Cyril Chantler: Diagnostic...

[Over speaking]

Boris Obolenski: So finally it's that way, if you have a hernia okay the hospital is paid to cure the patient from it but you don't know what they do. They get the same amount of money whether they put in let's say the good mesh or a cheap mesh or if they don't do a mesh and they suture. So there are huge financial interests on the side of clinics, hospitals, which are not open to the public.

Julia Cumberlege: I can see that's very frustrating for everyone.

Boris Obolenski: Absolutely you can say so.

Julia Cumberlege: But you are a global organisation and you were talking about Australia, so in Australia do they have registries, do they have very strong databases?

Boris Obolenski: No. The best is - sorry for interrupting - Sweden, there is a hernia register but the actual problem here is urogynaecology so I don't know actually a good registry in this area. That's why we developed our own registry and we offer it to everyone. We did the same for hernia.

Sonia Macleod: So that's open to all manufacturers.

Boris Obolenski: It's open to all our customers and it's open, yes, so for hernia the best example is [Uro HS] called, I think six, seven years ago a large group of surgeons, really international experts independent, we just put some money in it and said do a good job. I think we were the starter company. The big ones first refused, when we stepped in they gave also some money and then this is really the world best registry. It's open to public and it's free and it's so frustrating how less surgeons and clinics are using it. That is the reality, sorry for that.

Julia Cumberlege: Because it's voluntary.

Boris Obolenski: Because it's...

Julia Cumberlege: It is voluntary.

Boris Obolenski: It is voluntary, exactly.

Julia Cumberlege: It's not mandated.

Boris Obolenski: We cannot put force on anyone.

Philipp Schuster: Here another comment. I think registries - you cannot underestimate the value of registries for the post-market surveillance and that is really like - there are so many questions. Even if we get feedback from the market a bit more comprehensive and we would identify a potential mesh relation, we would set up a PMCF study. But really to isolate the impact of the mesh in this entire situation it would be possible or it is necessary to have a vast number of cases. This is in the end and especially in the long term only possible with registries.

Cyril Chantler: But with your registry what proportion of your products have had to be removed?

Philipp Schuster: In preparation of these registries as one of our actions for improved post-market surveillance under the MDR.

Boris Obolenski: For urogynaecology, for the Uro HS, for the hernia sector as an example...

[Over speaking]

Cyril Chantler ...urogynaecology, what proportion of your meshes have had to be removed?

Philipp Schuster: Well this registry is under construction. So the technical part is almost done, we're working on the CRFs together with...

Cyril Chantler: Do you know how many - what proportion of meshes that have been implanted for urogynaecological reasons have had to be removed, explanted?

Philipp Schuster: Only from the feedback from the market from the surgeons because the registry is not working, not yet.

Cyril Chantler: But in your company...

[Over speaking]

Cyril Chantler: ...proportion.

Philipp Schuster: Yes.

Boris Obolenski: Seven.

Philipp Schuster: I know from - maybe six, seven, less than 10 implants.

Boris Obolenski: Less than 10...

[Over speaking]

Philipp Schuster: Out of the information which we've got from the market.

Boris Obolenski: We work hard on it but you know it would be not honest to say only seven out of 70,000 so we sold 70,000 products in the area of incontinence and prolapse but as I...

[Over speaking]

Boris Obolenski: ...mentioned that's worldwide but as I mentioned here you have to look on - for us it's a sling, totally different product, is a vaginal tape, very small amount, we believe in laparoscopic approach for various reasons but I mean surgeons are free. So we offer especially bilateral products now for four years and before we put a product in the market even if we are allowed by CE we always look for some surgeons who use it for one, two, three years just in advance. Because that is our only really safety management because then they deliver because they are interested, they deliver really, really figures and then...

Valerie Brasse: Do you pay them to participate in these trials?

Boris Obolenski: We try not to pay.

Philipp Schuster: It is hard.

Boris Obolenski: Yes, because if you first - to be honest 15 years ago I told the people I cannot pay. We started as a 12 years engineering company working in a field - you know the competitors. So I had to tell really honest to everyone we cannot pay but you get results, we learn and we found always interested honest surgeons. Nowadays certainly we earn some money and that is also our interest certainly but not for every year, not for every year. It is not our main interest, let's say that one, and if we pay surgeons finally it is like a boomerang you know. So then people ask, how did you get this information and if you paid for it it has a - yes, it has a taste?

[Over speaking]

Boris Obolenski: So we try to avoid this and telling the surgeon it's your interest. It's your quality insurance to have good results.

Valerie Brasse:: Does it work?

Boris Obolenski: It works for the legal - actually legal status it works good enough but we are absolutely not - we are not satisfied and we want to change it and we work hard on it but it's not easy.

Philipp Schuster: If you can find a win/win situation, if any surgeon needs this data, needs publications for his personal goals then there might be a setting which works even without money. But I know the situation of the surgeons, they are overloaded with work and I see that it's really hard for them to in addition to what they do put their data into a registry. So this is what we need...

[Over speaking]

Cyril Chantler: ...United States.

Philipp Schuster: Excuse me.

Cyril Chantler: Do you market it in the United States?

Philipp Schuster: No, we do not.

Cyril Chantler: Why not?

Boris Obolenski: In the beginning we got the CE marking so the European market was free for us. Then we decided still being a small company where are new markets? I mean it's easy to understand our main competitors in the global place and we are talking about really global place in comparison to our company, they are in America. So we said, okay, that is the home market we don't understand it. They have large advantages in a home market so we concentrate on new markets.

In that time it was Brazil, today it's not a new market, South America, China which was a very new market is not in our list. India, yes, so we are definitely in all markets but we did not enter the US market for that reasons. It's still - yes, there are many countries to come and the US market was not our first...

[Over speaking]

Simon Whale: ...the UK market. How important to you is the UK market?

Boris Obolenski: We would like to have it more important that's why this gentleman is here.

Dominic Walsh: Yes, it's a market where...

Boris Obolenski: We had a previous distributor in the UK and we were not so satisfied about this situation and so the UK market is for us is I would say important because it's close to us, it's Europe. Whether it's...

[Over speaking]

Boris Obolenski: It's Europe definitely. I mean if you look on the map it's Europe and I have to say I have a strong how you say affinity to England even if my English is bad. My son and my daughter studied in England so we are interested in the market and are interested...

[Over speaking]

Simon Whale: Do you know how many implants you've sold in the UK?

Boris Obolenski: Yes, exactly.

Simon Whale: You do know.

Boris Obolenski: Yes, I think I sent the figures to you. If you're interested I have to look it up, I don't have it in my mind but I think maybe...

Dominic Walsh: Yes, I can comment from being the - dealing with the hospitals [unclear]. One of the differences that we have with some of the other products - Hospital Services is a small medium business - sized business with a turnover of about £16 million, £17 million, [unclear] based in Northern Ireland and we also market in the Republic of Ireland out of Dublin. We have been extremely successful in the Republic of Ireland and we have reached similar sales on the island of Ireland with what all of the GB market has been.

In the time that I've been involved for five years working for FEG DynaMesh we have had one incident where we've had a problem and that's it. There's been one incident and that I think is the - a mechanical engineer, but I'm not a medical engineer and the product is designed for its use. There is also a significant difference in the performance inside the body of PVDF versus other polymers. The PVDF doesn't biodegrade, it doesn't react - it really is flexible so therefore it fits with the patient longer.

[Over speaking]

Simon Whale: Well there are two questions I suppose. Why isn't therefore every single hospital biting your arm off and why aren't other manufacturers jumping on your bandwagon?.

Dominic Walsh: The obvious one is price. There is a differential in the cost. I wish...

Valerie Brasse: How much, what's the differential?

Dominic Walsh: I don't know the price that other big globals are charging but it is significantly different. We're told it could be 300 per cent difference but we're not getting the call back. The product is designed to do what it's designed to be rather than - it is tailored as Dr Obolenski said, it's tailored for the use and it's also this special material which differentiates it. We would love - I would love as a sales person for it not to be called mesh because otherwise we would be saying this is totally different.

Of course there is a label attached to that word mesh which makes it all overall more bad and we have had that debate calling it an implant rather than mesh but it is a mesh. But there does need to be an awareness and we have engaged with some politicians, we have engaged with senior people in the NHS where we did have this conversation. They look at us and go, you've got to get this message across so that the knowledge that mesh is not common, it's not all the same.

Valerie Brasse: Have you talked to the patient groups?

Dominic Walsh: We have talked to some patient groups but we - they can be quite aggressive. I did speak - I met with three ladies from Northern Ireland as arranged by [REDACTED] just to see and it was one-way traffic transmit and it was not going to be constructive and I feel for those patients. Some of the experience they have had is shocking and the one incident that we have had when it was fully investigated and followed up was nothing to do with the product. The reaction change was 10 days, it was a procedure problem and it was corrected very, very quickly.

Cyril Chantler: Can I ask you have you any evidence about systemic immune reactions to mesh? I know all about the local reactions and the foreign body information but have you got any evidence of systemic immune activation leading to the symptomatology in the patients?

B Klosterhalfen: There are some studies showing that there is a type of immune reaction and that's a reaction directly correlates to the foreign body reaction which is produced to measure the extent of [unclear]. In our PVDF I have never seen any case that a physician has asked well there is...

Cyril Chantler: You have had no cases reported to you of possible systemic reactions like fibromyalgia or cytokine activation?

B Klosterhalfen: This is very rare.

Cyril Chantler: Arthritis or skin problems.

B Klosterhalfen: Sometimes I ask, or the patients ask me whether there is a correlation to the mesh or not but I have maybe half a dozen of these cases I was asked. I never have seen in the explants some particulars in the pathology like eosinophilia or something like that.

Cyril Chantler: So none of the cases where the mesh has been removed were related to a body complication they were all related to local complications.

B Klosterhalfen: Yes.

Cyril Chantler: Thank you.

Julia Cumberlege: I'm afraid we've got to draw this to a close because we've got another hearing coming in a moment. But I just wonder is there any final thing you'd like us to hear that we haven't covered?

Dominic Walsh: Could I just because you have - so touched - said something that is actually very close to my heart on this. We would love that part of this process for the differentiation between what we have to offer, which FEG have to offer, what has caused difficulties in the market place...

[Over speaking]

Dominic Walsh: ...so people will realise there is a difference, there is an alternative and that would be great that it was no longer voluntary, that the feedback, the reporting, the traceability which happens with so many other areas within medicine that we actually have that information becomes compulsory. I hate to use that word but that it becomes that we can have the feedback because in five, 10 years' time it's that data which is going to support where we go forward.

Julia Cumberlege: I just have to say if there is any other information you think would be useful to us we are very, very willing to receive it because we want to be open and transparent and people recognise that we are doing a thorough job. So anything else before we close.

Philipp Schuster: I think the most important thing from my perspective for the future is really to establish a reliable registry. So with MDR the pre-market phase gets to strengthen for this manufacturer so I think we will undergo the highest possible standards before approval but post-market surveillance is really a matter of common responsibility. It's something which is...

[Over speaking]

Philipp Schuster: ...is really impossible for a manufacturer alone.

Julia Cumberlege: All right.

Valerie Brasse: If we've got a few more questions maybe we could write to you separately afterwards is that all right?

Boris Obolenski: Certainly, yes, it's a pleasure to help, yes.

Julia Cumberlege: If there is anything you feel that you wish you hadn't said - I can't think of anything - just let us know because we will then look at the video and see. So I do want to thank you so much for coming, it's been a very useful session so thank you very much.

Boris Obolenski: Thank you very much.

Philipp Schuster: Thank you very much for having us.

END OF TRANSCRIPT

Session 4: Dr Mark Slack

START OF TRANSCRIPT

Julia Cumberlege: Can you explain the advantages and disadvantages of the different mesh types?

Mark Slack: Are you referring to prolapse surgery or incontinence surgery or herniation?

Julia Cumberlege: That is what we're interested in, yes. Do you want to say anything about the different types of mesh that are used?

Mark Slack: There is - as I presented to the clinic before and is on my presentation there, there is a simple classification of meshes which is in the literature and there's a slightly more complex classification of meshes which is attributable to myself. You can either divide it into types one to four or types one to six. The type one that I use, they're divided into types one to four. That's based on the material used in the mesh, the pore size, the weight, the porosity and the weave that is employed to knit it. These determine specifically the response in the body - the biological response to the implantation of these meshes.

From the experimentation that we've done in an animal model, it would seem that the safest of the implants is a type one mesh which is a large pore mono-filament open weave polypropylene mesh. I put a reservation around the actual material, because while there are obviously bad materials, there is some debate about whether one or two materials may have advantages. Those would be polypropylene, polyvinylidene difluoride - PVDF by another name. There are ones that are absolutely bad such as PTFE, which is Teflon in common terms.

On that basis we were able in the late '90s to distinguish between meshes that would be considered safe and meshes that were considered obviously incorrect. A range of meshes - those were the types two downwards - we recommended against use in surgery in any form.

Julia Cumberlege: You mentioned polypropylene. Can you tell us really the difference between that and the PVDF meshes?

Mark Slack: Not in the time and constraint. They are both polymers. They - in real terms don't have an enormous amount of difference. PVDF has different surface tensions and possibly evokes a slightly different response within the body. It's a marginal difference and it's a debatable difference. PVDF is promoted very strongly by a team in Germany, who of course have vested

interests as they synthesised and hold patents on it. Polypropylene is a plastic in common use in a variety of domestic and industrial roles, from guttering on your houses to doors, to plastic plates and down to implantables. It is commonly used as an implantable. It is relatively inert, and it is a very stable compound - depending on where it is, and depending on the circumstances that surround it.

For example, there are some fairly weak articles describing its breakdown and degradation within the body. That is in response to oxidation, i.e. the polypropylene is exposed to oxygen in the air so any - a mesh that has eroded becomes available to degradation. Some of the studies that were done looking at the degradation of polypropylene, if you wash the product after the staining process you find that a lot of the degradation disappears because it in fact was an artefact in the processing of the specimens for the investigation.

A polypropylene mesh taken out of the body that has not been exposed to oxidation is usually pretty unchanged from the one that was put in there. A polypropylene mesh taken out of the body after exposure to air, i.e. oxidation, becomes brittle and hard and can break down in a macro format.

Julia Cumberlege: Right.

Cyril Chantler: Why does it break up in the body when it's not been exposed?

Mark Slack: Does it break up in the body? We don't know that it does.

Cyril Chantler: When people try to take it out, they've told us and others that in fact they can't get it all out because it's broken up.

Mark Slack: No. So, the difficulty in taking it out of the body - it depends. If your mesh has become exposed to the air as a result of an exposure, then it will oxidise and the area exposed will become more brittle. That is a reality. If the mesh is intact, not exposed but people want to take it out, the mesh has been largely - almost 100 per cent - incorporated in the fibrous deposition process - in the healing process of the body. Therefore it is both difficult to see and difficult to identify. Therefore the removal becomes difficult, because it is part of the body now.

Cyril Chantler: We've been told that with PVDF there is a product where they can incorporate something into it which makes it see-able on MRI scans?

Mark Slack: All the - all the meshes can do that. You can put anything you want into polymer. You can put radio paint materials...

Cyril Chantler: Is there one on the market with polypropylene?

Mark Slack: There has been, yes.

Cyril Chantler: That can be see-able on MRI scan.

Mark Slack: Yes, yes. We can see polypropylene very clearly on MRI scan.

Sonia Macleod: Is that all polypropylene?

Mark Slack: Pretty much. It depends - so you would need to speak to one of my radiologists, but my specialist radiologist at [REDACTED] is pretty confident about her ability to identify polypropylene on MRI scanning.

Sonia Macleod: One of the things we have heard from patient groups is that the best way to identify...

Mark Slack: Is ultrasound.

Sonia Macleod: ...is ultrasound.

Mark Slack: It's an opinion. It's not necessarily sound. That's open to scientific debate and hasn't been proven. In debate in a scientific forum you would find a body of people that will disagree with that. Trans-labial ultrasound scanning is a modality. It is not perfect.

Cyril Chantler: You told us last time - I think - I want to make sure I got this right. You weren't - I can't say - aware or convinced of any evidence of a systemic reaction causing immune stimulation that comes from the product. You accept there's a local reaction which is actually part of the process why it works.

Mark Slack: Of healing, yes.

Cyril Chantler: But - so we're talking about...

Mark Slack: For an immune response - and I'm not an allergy expert so I say this with caution and I'm moving slightly out of my area of expertise - but for an immune response you should get a sero-response in the body. Development of antibodies, ESR response, alteration in white cells et cetera - which nobody can show yet. It ends up being a sero-negative situation. If you work in the field of rheumatology, you know that one of your biggest problems is the so-called sero-negative arthritis, which crosses over very strongly into whether or not that is an entity. You have conditions like rheumatoid arthritis, have an antibody and you can measure it and you can measure the response to medications.

We have not seen that in polypropylene mesh. We have seen it in biological meshes. Which I remember I think I explained to you. Biological meshes are made of collagen, and if you take a biological mesh and you emulsify it and inject it into the tail of a mouse model, it can and does develop antibodies and can develop rheumatoid arthritis in as short a time scale as 28 days. One of the arguments about avoiding plastics in favour of biologics doesn't stand up very easily. I have as much concern about biologics as I had in the early days of mesh materials.

Julia Cumberlege: Thank you very much. Changing the subject a bit, we certainly have heard from hundreds and hundreds and hundreds of women who feel that the adverse effects that they are suffering from have been caused by a mesh. When they've gone to their clinicians, the clinicians have really been in denial - the surgeons saying that this is not this. They have sometimes talked about the menopause - that is what the women are suffering from. I just wondered if that's something common that you find, (a) this issue of denial and (b) this really trying to put in another reason why the women should be suffering like that? The reason being the menopause.

Mark Slack: This subject is more complex than almost anything we could put together in an open review. Even in groups of experts in a room - I was at a meeting recently in Sheffield which was attended by urologists, colorectal specialists, gynaecologists, pain specialists, all of whom are experts in the subject. It's difficult to gain consensus in their patient groups as well, which I think is terribly important. The complexity goes around the original surgery and the indications for surgery.

There are conditions - so if I go out into the street this afternoon and take 100 women over the age of 40 who have 2 children and examine them, 50 per cent of them will have visible anatomical prolapse. Only 10 per cent will be genuinely symptomatic. When a patient presents to my consulting room and tells me, the opening line is usually 'doctor I've been sent to see you because I have a prolapse'. My response is 'can you tell me how it affects you?' The responses I receive are 'I have pain in my vagina. I have pain with intercourse. I can't hold onto my wee. I can't hold onto my bowels'. That's not prolapse. Those are other conditions in association with a person who happens to have possibly asymptomatic prolapse.

If you therefore - if that is your starting point - with less trained and less experienced surgeons entering into surgery for prolapse, whether it is with or without a mesh - you are about to create a problem. At the end of the five months of placebo intervention, which is about the time period, the patient will return to all the problems they experienced prior to that situation and will 'be disaffected and have a high level of dissatisfaction.

Point one. Point two: if that patient goes along to a practitioner who now responds by saying 'well I'm concerned about your pain and I'm now going to intervene with a range of therapies up to and including opiate analgesia', you're then opening up a second problem.

There is a condition called opiate induced hyperalgesia which is a major problem in Europe and America, due to the misuse of opiates. By the patient then - then comes to my tertiary clinic for removal of the mesh, I am faced with a person where I don't know whether they needed that surgery in the first place, who has had surgery and had inappropriate treatment for it. If you try and remove that analgesia you create an even bigger problem. It is a problem for which I am not convinced I have an answer.

It goes back to the original premise that this is not about just mesh. This is about the type of surgery, the indications, whether it was appropriate, the use or not use of mesh and the anatomic site it is placed in and the route of access that was taken. That gives you seven distinct variables which makes the analysis incredibly difficult. That is one of our real and apparent problems. Now, those patients have pain and discomfort and suffering. My problem is I need to know whether that pain and discomfort and suffering is indeed caused by the mesh and therefore will it be improved by removal of the mesh?

Or, will they be - having undergone a further surgery - potentially worse off because we've undone the potential good the surgery did and threatened them with a surgery and given them other causes for pain. I sit in the camp that I do not know whether removal of the mesh is indeed appropriate or successful.

Julia Cumberlege: What do you do?

Mark Slack: We go through a very careful process. I work in a large multidisciplinary group. We have a lot of experience with mesh materials. I use pain specialists. We use conservative therapy. We use radiology to try and identify - so radiology for example, we can identify meshes that have an inflammatory response around them with fluid. That's easy. Something's going on. There is a passage to the outside. There is a connection or there's an infection. That makes it relatively easy to deal with. We deal with those surgically and I remove those.

If we image them - if we examine them and we can't find anything on examination and their blood tests are all completely normal, and the imaging is neutral i.e. you can just see the mesh line but there is no peri-

mesh inflammatory response, I do not have an answer. We go through everything, we try all the conservative therapy we can, at the end of which I will say to the patients it is your choice. I am a great believer in putting the patient at the centre of their care. If at that point they still want me to remove it, given the uncertainty of success, we will remove them. Or try and remove them. It is difficult surgery.

Cyril Chantler: Can I - I think we saw you before the draft NICE guidelines came out. You've seen them now. There's a sort of hierarchy in there, that - for stress urinary incontinence. This is where you start, with physiotherapy and so forth. Would you think that in that hierarchy, mesh is something that is second line or should you try all the conservative therapy that you know all about before you go to mesh and is mesh the last resort? What would you advise? I know you're saying it's finally and rightly the patient's decision but what is your advice?

Mark Slack: Yes, it's a hierarchy in medicine which is always the same. Do as little as you have to do in the interest of the patient.

Cyril Chantler: I wondered where mesh fits into that.

Mark Slack: Yes. Mesh - before mesh surgery, you do absolutely everything you can conservatively before you intervene with mesh.

Cyril Chantler: Including colposuspension?

Mark Slack: No, those are different things.

Cyril Chantler: Okay, then is it an anti...

Mark Slack: Anti-repair doesn't work.

Cyril Chantler: Okay. What surgery would you do before going to mesh?

Mark Slack: Are we talking about incontinence or prolapse?

Cyril Chantler: Incontinence.

Mark Slack: Okay. So for incontinence your treatment is to give standard advice, which is weight loss. Ten per cent of weight loss is associated with a 50 per cent improvement in incontinence. That's published in numerous journals of medicine, I give it to every patient. I can tell you now that the number of patients that lose 10 per cent of weight I can count on the fingers of one hand. It is not that easy to lose 10 per cent of weight for a variety of biological reasons. So - but we would offer them weight loss. We send them to the physios for a minimum of three months. A lot of

them tell us they have already had their physiotherapy and are therefore not willing to undergo it any further. Then at the end of it we offer them the three operations that are available.

Cyril Chantler: Which are?

Mark Slack: Which is a TVT - we don't at the moment - which was a TVT, a vertical suspension or an autologous fascial sling. In my unit we did not do any TVTs until 2002, because I wasn't doing research in that domain and therefore I wanted to see the results of...

Cyril Chantler: What I'm trying to get to is of the three surgical solutions you've just mentioned...

Mark Slack: They are equivalent.

Cyril Chantler: There's no hierarchy within them?

Mark Slack: No. In that paper I've given you on complications of surgery, you will read for example that a vertical suspension which has no implanting materials, has a seven to ten per cent incidence of severe scar pain for up to two years after surgery. That's real. Due to injury of the iliohypogastric and the ilioinguinal nerves. You cannot avoid that. It has a slightly higher failure rate. It has a recurrence of other problems within it. It is a very difficult discussion for a patient. We give them all three.

The autologous fascial sling I have tended to drop in the hierarchy to a secondary procedure because it has a high incidence of voiding abnormality which itself can be worse than the original position. We tend to reserve that for secondary or tertiary surgery. People who have had failed surgery who have returned wanting something done about their incontinence. I think we must put into this conversation that the patients are incredibly distressed by their incontinence and come and ask us for intervention.

My intervention rate is low and my absolute peak at Cambridge - which is a big unit - I was doing about 50 to 75 incontinence surgical procedures per annum.

Sonia Macleod: Did that include mesh?

Mark Slack: All of them. TVT - we've only ever done the TVT retro-pubic. We have never done a trans-operative because you - the committee knows my views on that operation. We did the vertical suspension, we've never stopped it. We did the autologous fascial sling, we've never stopped it. We have always offered the patients. The patients universally asked for a

TVT, because they are probably victims of a direct to patient marketing strategy.

Cyril Chantler: Can you tell us a bit more about that?

Mark Slack: Direct to patient marketing strategies? It's common in pharmaceuticals. It's - I'm not going to quote you a figure but I think it's about 80 billion a year in the United States.

Cyril Chantler: Is it - you're not allowed to do it over here.

Mark Slack: Yes, but you can do it subtly.

Cyril Chantler: Is it - you're saying that industry would market...

Mark Slack: Magazines internationally - the internet is international.

Cyril Chantler: These are articles in magazines saying you - how wonderful TVT is, is that correct?

Mark Slack: True. I will give you an example. [REDACTED] was an enormous supporter of TVT and promoted it very strongly. At the moment, while they are an enormous condemner of TVT they are a promoter of laser vaginal surgery, which I've put some statistics in my data for you to look at. Which again, would be another devilment which I would consider shouldn't be tried on people at all.

Simon Whale: When we met informally, one of the things we talked about which stuck in my mind was - you shouldn't be putting something into the human body that you can't subsequently get out. You talked earlier about how difficult it is - how difficult removal is. Does that take you to the conclusion that actually it shouldn't be happening at all? It's not whether it should be second or third option of treatment but in circumstances where it is extremely difficult to get out for reasons you've already outlined, should we be doing it at all?

Mark Slack: In medicine, we work on a balance of risks all the time. Something you can't get out easily are certain hips, but we put them in and they make an enormous difference to patients' quality of life. Try to take a hip shaft out of a femur and you will fracture the femur in a significant percentage of people. These are good hips, not the ones that have got into the controversy. The TVT - the incontinence one is the most difficult one to argue about because the results are very good and complications are genuinely probably quite low. That will make me unpopular stating but there are papers I've given you there that look at the removal rates in large databases which don't exceed three per cent.

The major complication rate is probably lower than that. You know, time has evolved since this debate started. We haven't seen the numbers that are talked about. To put into perspective, there are one million polypropylene implants put in per annum in the United States alone from hernias and have been for 20, 30 years. If it was the size of the problem that it was accused of being, I suspect we would have seen a lot more. That's just to put a perspective on it. I hear your point very strongly.

We - in the prolapse, I think what happened there where I think there is irrefutable evidence that putting mesh in trans-vaginally is probably not a good idea and hasn't stood the test of time and doesn't have the evidence to support it. You've got to look at that in the light of the outcomes for traditional prolapse surgery, which are pitiful. Where you have a 30 or 40 per cent reoperation rate in people who have had those operations. Every time you subject a person to an operation you threaten them with a mortality rate and a morbidity rate.

Surgeons aren't a bunch of psychopathic demons. There was a real concern in that there's a quote from 1914, I think, from one of the leading surgeons of this day saying that the management of prolapse of the anterior vaginal wall remains one of the most difficult and complex problems in medicine and it remains the same in 2019. Now, these surgeons started experimenting with mesh in an attempt to reduce that failure rate. They're trying to - and then it becomes again this highly complex discussion. Was the surgeon trained adequately?

I can show you data to show that the better trained the surgeon, the higher the numbers, the less their complications. Was the patient genuinely suffering those symptoms? Do you know what I mean? Would they have been better done abdominally? That's where it's very difficult for me to give you a binary answer. As you all know, I have been highly critical of the method of introduction of mesh and the way it was marketed, sold and used. I am critical of the doctors, of the pharmaceutical companies and of the patients. Patients conspire with their own victimisation.

Why are they doing that? Whether it's because they are subject to direct to patient marketing campaigns or what they've read in the media or whatever, I don't know. But, it is very difficult counselling a patient against something that they want.

Simon Whale:

Ultimately as you say, good doctors give the patients choices.

Mark Slack: Well I - my conversion rate from clinic to surgery is incredibly low. It has always been. I'm proud of that. I am a minimally - you don't easily get a drug out of me either for that reason. That's another whole subject I could bore you with for hours. The NICE guidance you've spoken about has recently declared that for overactive bladder, it should be behavioural modification and drugs ahead of second line treatment which is Botox. Well, the drugs don't work. They have enormous side effects, especially cognitive impairment. They cost a fortune, and behavioural modification would probably do far more than the drugs.

Botox on the other hand has a 50 per cent resolution of problems for between six and 12 months. It's a no brainer.

Julia Cumberlege: Can I just go back to colposuspension operation? There's a very interesting article in the BMJ written by Jonathan Gornall who is an investigative journalist. One of his comments - and I don't know whether you share this or not - but he says that because of the introduction of mesh and it being seen as the best way forward for these prolapses and incontinence and so on, as a result of that colposuspension was then not further researched and improved. He said it was then put into a siding and he felt that actually more could have been done with it in order to improve its efficacy and the way it was done and whether it could have been done keyhole.

Mark Slack: With all due respect, that is a journalistic article and not a medical article. It's very poorly referenced. I'm very familiar with it and I have written to the editor of the BMJ to question why we were moving into the realms of journalism rather than science. I'm very clear on my approach to that set of journalists. The colposuspension has been around since 1961. It is well studied. There are prospective randomised control trials putting it up against autologous fascial sling and anterior repair. The anterior repair was the operation commonly done until about 1994 in United - 1990 - when did I do my fellowship? When I did my fellowship I was criticised for recommending colposuspension over an anterior repair, so in the early '90s.

The colposuspension then took off. The reason it was - it was the more difficult operation to do, so people - there were some of the best prospective randomised controlled trials in the world done, doing open colposuspension against laparoscopic colposuspension and there's one by Carey in Melbourne in Australia which is almost certainly the best designed trial - surgical trial I've ever seen, which showed no difference. Not in pain, not in outcome, not in return to work, not in anything else.

For the people doing it well, but they did it laparoscopically - and that's - I think that data I would probably disagree with.

I think there probably would be advantages now for the minimum access laparoscopic approach. But this is well studied. We also knew that 30 per cent of colposuspension - we knew that over time, the success rate declined. If you did a Kaplan-Meier analysis you would see decline in success to about 60 per cent, and that's published by Stuart Stanton from St George's Hospital. We also know that 30 per cent - a third of patients returned requiring additional surgery to the posterior wall because of the onset of new onsets and prolapse.

We - sorry, can I just send a message. We - I think it was a good operation. We did it commonly. The patients - most of my patients would go home the same day. We - blood loss is next to nothing. We modified the way it was done from the 1961 Burch to the way we were doing it in the 1990s. The TVT came along - I was busy with other research, I didn't have time to do it in a research protocol so therefore I didn't do it. I continued the colposuspension comfortably, in that I believed I was giving a good operation to my patients.

Over time that became very difficult to pursue. The patients rejected it. Ultimately I waited until the Hilton paper on the prospective randomised controlled trial comparing colposuspension and TVT which showed equivalence, effectively. Because of patient demand, I then moved more to TVT. My patients continued to be offered vertical colposuspensions but almost to a person they continued to decline it. Now, we still did some because there were patients that liked the conversation of the more natural operation, but they didn't like the cut. We also do do it laparoscopically.

I think that article is slightly naïve. There is extraordinary data on the vertical colposuspension. It is a much more difficult operation for the average surgeon. It is associated with complications, as I said. Pain alone, 10 per cent. That's a real figure. I didn't make it up. It's published. If you're talking about pain in TVT which is about a similar figure or less, actually - colposuspension has it as well. Therein lies the problem. There is not a single surgical procedure in the world that does not have postoperative persistent pain. Not one.

If a woman has a caesarean section a significant percentage have womb pain and have low sensation around the wound. If you speak to people - the example I use to my patients is if you have your teeth capped, you lose your ability to taste I'm told- if you bite. You don't have - you lose the

proprioception in biting something. Your face is numb. Apparently you lose all sensation in - so the problem we have here is we've put something in the body, so therefore it becomes a focus.

Cyril Chantler: Can you get the TVT out?

Mark Slack: Oh, big operation but relatively easily, yes. You can see it. You can do it laparoscopically and you can do it trans-vaginally or a combination of the two. If you take a TVT out, at least half will not resolve.

Cyril Chantler: What won't resolve, the pain?

Mark Slack: The pain.

Cyril Chantler: Why?

Mark Slack: Don't know. Don't know. It's such a complex subject. The actual removal rate for TVT is low.

Cyril Chantler: Why have we heard...

Mark Slack: Published papers.

Cyril Chantler: We've met a number of women who have had TVTs and have - immediately are unable to open their bladders.

Mark Slack: Unable to open their bladders?

Cyril Chantler: Yes.

Mark Slack: Yes.

Cyril Chantler: Presumably that means the tape is too near the bladder neck.

Mark Slack: That's different.

Cyril Chantler: Why don't people go and take it out immediately the next day?

Mark Slack: You don't actually need to. We evolve in surgery. This is a problem in surgical innovation. Until somebody like health services adequately fund research, things aren't going to change. If you have postoperative urinary retention - the rate of which is 2.5 per cent - you need to divide it into categories. The person who voids not at all, not one drop, needs to have the tape stretched immediately or the colposuspension adjusted immediately. Okay. That's a negligible number. Probably four in my career, which spans 30 years.

If a patient has inability to empty their bladder, so they develop as a consequence of the surgery a voiding abnormality, my practice published is to wait seven days. If by day seven they are still not passing urine well I take them to theatre - by day seven - and I open the skin over the tape and I put an instrument between the tape and the vagina and I stretch the tape. It fractures it, and I close it over again. Almost to a person they void immediately. If you delay that process, you're starting to run into trouble.

Cyril Chantler: So, you've never sent anybody home with an in-dwelling catheter?

Mark Slack: Yes, we do, quite commonly. We send people home for four or five days and they come back and then they have their trial without surgery four or five days later.

Cyril Chantler: I see.

Mark Slack: Or we teach them [unclear].

Cyril Chantler: They don't stay in for...

Mark Slack: No. There is clear management protocol for people who are properly trained which should overcome it. An anterior repair has a similar voiding abnormality complication rate, as does a Burch and an autologous fascial sling has a much higher rate. Which is why we might be - I might reserve it for a secondary procedure. If a Burch goes into complications, it's altogether more difficult to overcome. Can't stretch it. Now, voiding abnormality then just gets into a complex area because you have to work out is it the bladder, have you exposed the underlying problem, have you tried the urodynamics - that's another bit of witchcraft - etcetera.

I think what I'm trying to say is that in the right hands, by properly trained people who are doing - where I highly criticise the TVT is that the industry saw it as an opportunity to mass sell. I almost felt like a pariah in the late '90s and early 2000s for not doing a TVT. I was made to feel like I was doing my patients a disservice.

Julia Cumberlege: Where was the pressure coming from?

Mark Slack: Colleagues, patients and industry. Significant from patients. I had patients leaving me because I was still doing a vertical colposuspension, but that suited me - less work too.

Sonia Macleod: Patient groups talk about dyspareunia being very important.

Mark Slack: In?

Sonia Macleod: An adverse outcome.

Mark Slack: Prolapse repair?

Sonia Macleod: And in SUI. What would you be saying about that?

Mark Slack: Dyspareunia is something that I think - I think we have let our patients down in some respects as well. One of the areas is that not enough money has been spent for research on what is perceived as a woman's problem, and that's my other subject - is that a woman's problems never get treated properly by a male-orientated hierarchy. Money for research. An example: in 2006 there were 100 articles on anterior repair for prolapse and there were 66,000 articles on cervical cancer. Cervical cancer has an incidence of about 0.5 per cent. Anterior prolapse about 17 to 20 per cent.

The research wasn't done. Now, when the woman comes in to see me with a complaint of prolapse - as they will vocalise it - my first problem is to separate out what they mean by it. There is a colleague of mine Steven Radley in Sheffield who has designed a very impressive objective history-taking automated method, which actually they go through and they write it down. It's called the - I'll tell you in a second. Alzheimer's. It's - that distinguishes out, because the patient when they say to you prolapse - the question is what do they mean by prolapse? Do you know what I mean?

Patients will come in and say 'I've got a prolapse' I'll say 'how does it affect you?' 'Well when I have intercourse I have a lot of pain'. That's not prolapse at all. Prolapse does not cause pain. In fact, the minute a patient says they have pain every feeler should go on and you should be saying this is not prolapse. Prolapse - in my lectures to medical students and to registrars, I talk about good symptoms of prolapse and bad symptoms of prolapse. A good symptom is a bulge, it comes out. It gets worse as the day progresses, it reduces when you lie down and is probably better when you're asleep.

Valerie Brasse: You're talking about an extremely...

Mark Slack: Correct.

Valerie Brasse: I'm talking about it post the intervention. Women are saying this is an adverse outcome. It's not being picked up, therefore when people are talking about complication rates they're not getting it right because they're not picking up half the outcomes that we say are a direct result of the intervention we've had.

Mark Slack: When we go back, we identify that a lot of those people had pain before, and they had dyspareunia before and they had constipation before and they had urinary symptoms of overactive bladder before, but they became - with their primary care practitioner - obsessed with it's a prolapse. People want a solution, and they like surgical solutions. It's very difficult to talk people out of it. In the surgery - and I've got it in my presentation - I gave you the results of a prospective randomised controlled trial done in Holland with a seven year follow up, which is much-quoted by the anti-mesh group because of a 40 per cent mesh revision rate.

Which mostly was little snips, because I examined their PhD so I'm very familiar. What everybody's chosen to ignore is that the mesh group had a 35 per cent incidence of pain with intercourse afterwards and the non-mesh group had a 48 per cent incidence of vaginal or dyspareunia afterwards. Not statistically significant, but the pain with intercourse occurs after standard natural tissue non-mesh surgery commonly. That's why it is so important to understand where you are. Where the patient is coming from.

That raises a whole range of - I had an email from a patient today to thank me, because she's feeling so much better now because her hip now has been placed - changed - has resolved her pain that she believed was due to prolapse. Proper history and proper examination, the ability to treat them conservatively.

Simon Whale: If you get the diagnosis right, the process is...

Mark Slack: You're well on your way.

Simon Whale: You prevent the domino effect of catastrophe.

Mark Slack: Correct. The draw about that is we also have - dare I mention it - this would actually - this will get people annoyed for me saying it - there is also an element in surgery - all types, all specialities - of body dysmorphic syndrome. That is the reality. We have to - we do not do that well. We don't really have anything in our history-taking process to look for the person who has focussed in on a symptom pathologically. Male, female, legs, arms, abdomens, vaginas. Now, the vagina is a far more complex organ and is associated with far more complex problems. Added to the mix is abuse - either as children, as adults, abusive relationships, rape etcetera. You start adding a lot into that mix as well.

Now, I am not saying that these people have had any experiences like that. Within these people will be people that have body dysmorphic

syndrome and will be people that have had really bad events in the past who would have been far better treated by a sympathetic ear - a conversation and an attempt to manage it conservatively without surgery. Surgery is the last port of call, irrespective of what you start with.

Cyril Chantler: I have one last question. How many teams should - because you're talking about the need for a multidisciplinary team with lots of people involved. How many such teams do we need in England? They presumably couldn't do all the work that needs to be done, but they could form a hub - a network around them.

Mark Slack: I mean - yes, I can't answer that for you. The concept of practice makes perfect is a very good one. I give a talk with why the operations fail - patient procedure, prodigal practitioner, and around the practitioner everything goes around the relationship between volume and outcome. About 75 to 80 per cent of the world literature - it's about 190 papers - which show a positive result between the more you do the better you get. Both for the institution and the individual.

You can't be a low volume surgeon in a high-volume centre. It doesn't help. You have to be a high-volume surgeon in a high volume centre. You get better diagnoses, better peri-operative diagnostic modalities, you get better inpatient care and you get better outcomes. There is an enormous public pressure not to support that. Try and close a hospital in the United Kingdom.

Cyril Chantler: You don't need to close the hospital if there are plenty of things possible to do.

Mark Slack: The minute...

Cyril Chantler: In my experience we've had 12 centres in the United Kingdom who look after children with late stage renal failure, and it works. For the same reasons you've said.

Mark Slack: Well, you could look at...

Cyril Chantler: I'm interested in how there are going to be a limited number of mesh removal centres.

Mark Slack: As there should be.

Cyril Chantler: As there should be. So, the question is, for the treatment of stress urinary incontinence which is very common, is there any possibility of creating hubs and networks so you can make sure of the standards of care?

Mark Slack: We sort of have been. The first thing is properly trained individuals.

Cyril Chantler: Yes, and presumably then train them up...

Mark Slack: The training system they go through and they train - some of us did an additional three or four years after qualifying.

Cyril Chantler: I'm seeking advice about (a) whether the concept is right and (b) what sort of numbers are we talking about?

Mark Slack: You're speaking conversely. The concept of centralisation...

Cyril Chantler: You just said you couldn't answer the question.

Mark Slack: I believe in the concept of centralisation. Whether you can achieve it, I doubt.

Cyril Chantler: Ah. Well that's our problem, but you could help us.

Mark Slack: I completely believe in the concept of centralisation. It is the entire philosophy of my career. I moved to a big centre, I only do incontinence surgery - I do not do lumps and bumps, I do not do other things which people might think is quite boring. It suits my small head. The point is you get very good at what you do, you get very efficient at what you do. You get very good outcomes, which is massively pleasing. Centralisation, yes. I'm your person for centralisation.

Valerie Brasse: That's about removal, though.

Mark Slack: No, it's about putting it in.

Valerie Brasse: Putting it in as well, is it a specialisation to be around the implant as well?

Mark Slack: Yes.

Valerie Brasse: I'm not sure that the specialised commissioning framework - consultation documents are on the same wavelength.

Mark Slack: No, they don't like it. The literature is absolutely rock solid. It's absolutely rock solid. The more you do, the better you get.

Julia Cumberlege: On that very happy note, I would actually like to bring this session to a close. I would like to thank you so much for coming today. For my colleagues obviously some of it has been a reprieve of what happened before - for me it has been new and I really do thank you for that. I think it's very important that I tell you that if there was something that was - you felt factually incorrect or you've got concerns about what was

inadvertently released, some sort of information - just let us know within 24 hours and we will consider that. Thank you very much.

Mark Slack: One comment before I leave. I think it is incredibly important that the discussion and the debate is more clearly divided into incontinence and prolapse in primary and secondary because they are completely different aspects and I think when we talk about them together, we do make it very difficult to come to a consensus of opinion.

Julia Cumberlege: Thank you very much. Thank you.

Mark Slack: Thank you.

END OF TRANSCRIPT

28th January 2019

Session 1: Expert Working Group on Hormonal Pregnancy Tests

START OF TRANSCRIPT

Julia Cumberlege: So I'm Julia Cumberlege and I was invited by Jeremy Hunt to chair this review in its three component parts. On my left is Sir Cyril Chantler, who is the Vice Chairman of the review. The third member of our panel is Simon Whale, who is here on my right. Next to Simon is Dr Valerie Brasse, who is our secretary. Then on Sir Cyril's left is Dr Sonia Macleod, who is our most important key researcher. So that's us. That's who we are. So I'm just wondering if you'd like to start just by introducing yourselves, just where you're working and who you are and where you're working.

Ailsa Gebbie: Yes, certainly. First of all, I'm Ailsa Gebbie and I was the chairperson of the Expert Working Group on Hormone Pregnancy Tests. We're not going to talk about valproate today, just to pick up on what you said earlier.

Julia Cumberlege: Yeah, sorry, my mistake.

Ailsa Gebbie: Yeah, yeah. Thank you. So I'm a consultant gynaecologist working in clinical practice in Edinburgh. I've worked in women's health all my professional life, in contraception, menopause, general gynaecology, infertility and obstetrics, so I'm very familiar with the risk-and-benefit profile of all the commonly used hormones in clinical practice. I recently stepped down as a director of the UK Clinical Effectiveness Unit of the Faculty of Sexual and Reproductive Health, which is the main body in the UK looking at evidence and translating that into guidance for healthcare practitioners.

I'm also the chair of the MHRA Expert Working Group on hormones in women's health that reviews all products and medicines and drugs related to women. So I will hand - first of all, to Shirley, on my left, to introduce herself.

Shirley Price: Thank you, Ailsa. So I'm Shirley Price. I'm from the University of Surrey. I'm a non-clinical expert on the working group. I'm on the CHM as well. My background is as a toxicologist.

Julia Cumberlege: Great. Thank you.

Ailsa Gebbie: Diana?

- Diana Wellesley: So I'm Diana Wellesley. I'm a consultant clinical geneticist working in Southampton. I specialise in prenatal cases, so I see a lot of babies with congenital anomalies. I ran the birth or congenital anomaly register for Wessex for 22 years and I've been a member of the EUROCAT group or working groups for about 24 years. So I'm on the prenatal committees, [unclear] committees. I'm one of three geneticists that reclassify all the congenital anomalies that are sent to EUROCAT from the 43 registers round Europe. So I'm familiar with congenital anomalies and possible causes.
- Julia Cumberlege: Right, thank you very much.
- Ailsa Gebbie: Stephen?
- Stephen Evans: I'm Stephen Evans. I'm formerly a physicist, turned medical statistician, turned epidemiologist, turned pharmaco epidemiologist. I'm semi-retired, but still employed at the London School for Hygiene & Tropical Medicine. I've been a European Commission appointed expert on the EU Drug Safety Committee. I have been the first statistician involved with the Bristol Royal Infirmary inquiry and I've been involved in other inquiries. But my work is largely on safety of medicines and vaccines these days. I had a brief period where I worked at the MCA, the forerunner of the MHRA, and I dealt with the aftermath of the pill scare of 1995 and also dealt with MMR and autism, for example.
- Julia Cumberlege: Right, well, what a wealth of experience we've got here today. Thank you very much.
- Ailsa Gebbie: So I've prepared a - just a very short statement on behalf of the experts to - just for a few minutes to summarise our position in relation to the report, if that's alright.
- Julia Cumberlege: Absolutely.
- Ailsa Gebbie: Yeah. So we're very pleased to have this opportunity to discuss the findings of the Expert Working Group on the topic of hormone pregnancy tests. So back in October 2015, independent experts, of which we are representative, from a wide range of scientific disciplines, were asked to participate in this group to undertake the very challenging task of assessing a possible association between hormone pregnancy tests and adverse outcomes in pregnancy. Every member of the group came with an open mind and in fact the majority of the group had never actually heard of hormone pregnancy tests. No group member had any association with a pharmaceutical company or conflict of interest.

The group considered the fullest possible data available to us relating to this topic and published its report in November 2017. There was an enormous amount of information to be considered, which the group reviewed with the highest level of scientific expertise and total integrity. The final conclusions of the group were unanimous and in keeping with our terms of reference. We considered all available evidence on the possible association between exposure to hormone pregnancy tests and adverse outcomes in pregnancy and did not find a causal association.

Taking into account all the different strands of scientific evidence, the group, again unanimously, concluded that any perceived effect was likely to be explained by chance alone within a normal population. However, because of the nature of much of the data we looked at, a weak association could not be ruled out or proven with absolutely certainty. That was our conclusion within the report. Hormone pregnancy tests existed in another era of medicine that's very hard to rationalise now. Women's healthcare has entirely moved away from that paternalistic style of medicine that we heard about and now offers, I hope, choice and informed consent.

I would like to emphasise that the hormones within these old hormone pregnancy tests have been used for decades in clinical practice and continue to be used. We're very familiar with them in contraception, hormone replacement and as treatment for gynaecological conditions. For many decades, norethisterone has been one of the most widely prescribed drugs from primary care. The doses within hormone pregnancy tests of both hormones are again within the normal range used in current clinical practice. These are the exact hormones that have shaped women's - millions of women's reproductive lives globally with controlling their fertility, spacing pregnancies, improving gynaecological outcomes and wellbeing with hormone replacement. Indeed, these drugs were used in the past to prevent miscarriage.

So this, therefore, is a very different scenario from the absolute tragedy of thalidomide exposure. The group relied heavily on the input of families throughout, which we hope they felt welcomed. Mrs Lyons, their chairperson, attended every meeting as an observer. But as chair of the group, I was able to facilitate her to question every speaker after every session, which I hope she found helpful. For all of us - and I speak on behalf of everybody here - it was extremely distressing to hear from families who have brought up disabled children into adulthood and have lived with this uncertainty of why their child was born with a congenital anomaly.

In reviewing the scientific evidence, in addition, the expert group were committed to making robust recommendations to the future, which we did. We hope that the safety of medicines used in pregnancy will have a much higher profile now within the UK regulatory framework and reports of possible congenital anomalies associated with use of medicines will be promptly evaluated because we can always learn from the past and do better. But our group did not have any role in commenting on the regulatory actions that took place in the UK at the time hormone pregnancy tests were used.

That's all I would like to say at the beginning, so thank you for your attention. We're very happy now to respond to any questions related to this topic.

Julia Cumberlege: Thank you very much indeed. You did say, of course, that you're independent experts, but I understand none of you - well, I think that you have put forward to us any conflicts of interest you might have...

Ailsa Gebbie: Yes.

Julia Cumberlege: ...and we've received those, so thank you very much for that. Can I just say, you were setting out very clearly the recommendations and everything in your report? Certainly we appreciate the work that you've done with Marie Lyon and her group. But she is very critical, the group is very critical, still, about the findings of the Expert Working Group. Just thinking of the way that you did your conclusions and everything else, do you - and, of course, the APPG, the All-Party Parliamentary Group, has been critical as well. So do you think there's anything you could have done differently, with hindsight?

Ailsa Gebbie: I think we possibly could all come up with some answers to that. It was an enormous task. There was so much evidence that we had to assimilate quickly and efficiently. Stephen may like to talk specifically about the epidemiological aspect of what we might have done differently.

Stephen Evans: I think that we probably were not as clear in our report as we could have been, in retrospect, and particularly with the criticisms levelled afterwards, for the reasoning behind what we said. Now, I've gone through all of that again and I can see that we could have been clearer. We could have perhaps expanded what we'd said, though there is an enormous amount of epidemiological data if you look in the report. But the argument that we had in why we did not wish to put just the numbers together was not made as clearly as we might have done.

For example, there was a big meeting in America where a series of people made remarks about the idea of doing meta-analysis in this area. Sid Shapiro said, if the same systematic biases are indeed present across a range of studies, the only effect of meta-analysis is to reinforce - to produce spurious statistical stability and thereby to discourage further research. Moreover, it is particularly in the domain of low-level associations that the temptation to perform a meta-analysis is the strongest. He was someone who worked at the Sloan Institute, who wrote the key book on drugs and birth defects in pregnancy.

He also wrote a paper called *Meta-analysis, Shmeta-analysis*. He was against it. I wouldn't agree with him totally. There were two others there, particularly Diana Petitti and Sandra Greenland, who agreed with him that just putting raw numbers together from observational data was generally a very foolish thing to do, but that there were sometimes gains from meta-analysis of studies.

I was one of the authors of a publication that came out three years ago, *Evidence Synthesis and Meta-Analysis for Drug Safety*, where we set out, we think, where are the considerations for including observational data. A lot of people think that you shouldn't ever do it. You should only do it for randomised trials. When you've got randomisation, it's always sensible to do meta-analysis. Some people treat meta-analysis of observational data as if it were randomised data, and they're very different.

The argument that we had in that book was that there are circumstances where observational data can be meta-analysed, but you have to be exceedingly cautious in your interpretation of it. I think we could have had more of that kind of argument in there, but it would have been argument that, to many of us, would be obvious. We'd know the history of that over the last 25 years. It would have perhaps been better had we had expansion of that.

Sonia Macleod: Can I just clarify, the book that you have there, that was written before the Expert Working Group?

Stephen Evans: Yes.

Sonia Macleod: So it was prior to that and it wasn't influenced by it?

Stephen Evans: Yes.

Sonia Macleod: Okay, thank you.

Ailsa Gebbie: Probably nothing would have changed our conclusions at the end. We could have probably agonised over this for a lot longer, but bearing in mind the very small numbers we were considering, the exposure of, potentially, over a million women to this hormone over 28 years, it was such a difficult task to try and pull out any relevant statistics, with the best of our ability, despite having some of the best experts on the group at the time.

Valerie Brasse: But in some extent, that's come back to bite, hasn't it? Because of course that has been now a meta-analysis done and, of course, there is a new expert working group...

[Over speaking]

Ailsa Gebbie: But we considered it and it's concluded in the report. Why we didn't do the meta-analysis is included in the report. We chose to do a re-analysis following the advice of our experts at the time. I think the findings still remain consistent and conclusive.

Stephen Evans: I've seen nothing that has made me change my mind. I'm ready to be wrong. I've been wrong in the past. One of the members of our Expert Working Group published a letter in *The Lancet* pointing out an error I'd made 40 - this was around 40 years ago when I worked with [REDACTED] on perinatal issues. It was on the safest place for birth. But I didn't see anything since we published that that caused me to say, there's something wrong in there. We included data that were not included in a Heneghan meta-analysis. We did not exclude anything that they included.

The only thing that was not included is a letter by some Belgians under the name MIRA. They wrote a letter pointing out that hormone pregnancy tests were going on being used in Belgium after they'd been withdrawn in the UK and other places. They remarked that the number of people who had it was so many and they noted that there - in them, there was one oesophageal atresia, I think it was. They don't make any remark about any control group. They don't attempt to do that, yet that has been used in the Heneghan meta-analysis as if it were a proper study. They have assumed that in the others there was zero congenital anomalies. In 450, that just is infeasible, really.

The other thing that we didn't probably make as clear as we might have done is that thalidomide had relative risk of at least 100. There are documented risks of 8000 for the relative risk and we're talking, in the Heneghan meta-analysis, of something that's 0.4. So thalidomide was just so, so different. It was easier to detect because of the enormous relative

risk. It was easier to detect because it had congenital characteristic defects. It probably affected nearly everybody who took thalidomide and it caused more than just the limb-reduction deficits. But nearly all of them were also symmetric deficits.

Most of the time with drugs, you don't find one arm affected and the other arm totally unaffected. They may have different degrees of being affected. Had we had that kind of thing, then we would have said hormone pregnancy tests are a cause of these problems. But we - the conclusions we had, I would support. We definitely did not say we excluded it. We made it very, very clear that you cannot exclude a risk unless you show it has a benefit. So for example, with MMR and autism, you can't exclude a risk unless you show that MMR prevents autism. We said that at least twice in the report, that we cannot exclude a risk. That's obvious from the start, that you just can't do that unless you show a benefit or you show convincing evidence of an actual risk.

Julia Cumberlege: Can you explain, then? Because you set out, very honestly, where you felt you could have been clearer. But certainly the prep patient groups and, indeed, the All-Party Parliamentary Group as well have said on many occasions that - why should they be the ones to have to prove the size? They clearly have not enough confidence in the working group to actually accept your recommendations. Now, you've said that you should have been clearer on two issues and so on. Do you think that that would have actually satisfied these people who feel that the report of the working group was actually - well, shouldn't - really did not stand up? That's what they think.

Ailsa Gebbie: I think we would all defend the scientific rigour of the process, probably to a man. Obviously the findings of the report were deeply disappointing for the individuals in this situation. No one can underestimate the heartbreak and misery they've experienced of bringing up children in this situation, but as others have said, the science has to stand and support an association.

Julia Cumberlege: So, going back to the actual working group, I understand your expertise and, together, it was quite a rounded, I suspect, committee. But in the course of your discussions and deliberations, did you find that there was excessive weighting in one particular part, one particular aspect of the science as opposed to another?

Ailsa Gebbie: Not - I would say not at all. I think it very fairly covered all the different strands of evidence that we considered, and the toxicology Zebrafish data that we looked at in detail. Having two clinical geneticists on the group

was extremely helpful in explaining baseline incidents of congenital anomalies. For example, when Stephen and I spoke to the members of parliament, they - there's a very poor understanding that congenital anomalies happen anyway. When anybody's having a pregnancy, you worry, is the baby going to have 10 fingers and 10 toes?

I think people find it hard to grasp that two to five - or two to four per cent of babies are born with a congenital anomaly just by nature alone. One in five pregnancies end in a miscarriage. So it's very, very hard to tease out an effect from the evidence that we were presented that there was any significant effect above that of nature alone.

Diana Wellesley:

We also looked at the type of anomalies. In other things, if you look at thalidomide - we've discussed that - you get phocomelia. If you look at warfarin, you get nasal hypoplasia and stippling. Often you can find a reason. Here, we looked at all the anomalies and compared them with anomalies that you might expect elsewhere. So we looked at the prevalence. There wasn't an increased rate. Obviously we didn't have a judgement, but there was no evidence there was an increased rate of it. We looked for clusters of anomalies, so we went through them all.

Even though the information we had on the anomalies that these people had was quite limited, I have - we saw there was no evidence of a cluster. There was no evidence of an unusual anomaly, unusual patterns. All the anomalies were ones that were commonly seen, had incidence of one in 4000 or one in 800 people. We looked at combinations of anomalies. Did we more often see a heart anomaly with missing limbs and that kind of thing? There were a couple of small ones that were - you would see in EUROCAT.

The only thing that possibly came up was there was a slight increase in multiple anomalies in the HPT group versus EUROCAT. But the EUROCAT group, multiple anomalies are - so that relies on more than one being - anomaly being written. So for EUROCAT, we get anomalies that come in from 43 registries round the country and then three of us curate them. Because if you have, for instance spina bifida, talipes, club feet and hydrocephalus, they're not three anomalies, they're one.

The spina bifida caused the talipes and the hydrocephalus. So that's not multiple anomalies, that's a single anomaly. If you have missing kidneys, your - you don't produce any urine, you don't have any fluid around the baby, that baby will then have small lungs, will have a small chin, may well have talipes. Again, that's one anomaly. That's not multiple.

So we do that incredibly rigorously for all the EUROCAT cases and so I would say that we cut it down by two-thirds. So probably the number suggested here of multiple anomalies is the same as we would get for EUROCAT before we curate them, but ours are very carefully curated so that we can compare the data from Belgium with the data from France, from Holland, wherever. So we do that and have done it for many years. We tried to do it with the data here, but because the information was so poor, we had to err on the assumption that it was a multiple rather than it wasn't so we absolutely could not be seen to be taking out any cases. Not that it mattered whether they were multiple or single, but we were looking for patterns. So we erred on the, well, if we don't know, we'll have to call it a multiple.

So I think that is probably evidence that - we gave the numbers we had, but in truth, if we were to analyse them, if we were to see each child or see all the medical reports on each person, we might be able to curate that better and give a better evaluation. But I think there wasn't anything that came out, from looking at the reports of individuals and what one would see on a day-to-day basis in prenatal practice. We - most of the people I see whose babies have anomalies do not have a family history of that. They occur as a one-off.

We don't know the reason for the majority of anomalies, still, particularly like diaphragmatic hernias, like exomphalos, gastroschisis. We still don't know the cause of those. We might one day, but we haven't yet found that. So the fact that there isn't an obvious other cause of the disease doesn't mean that it was due to HPT. It just means that we don't know, and we don't know for the majority of people, sadly, that I see. We are producing more genetic diagnoses quite a lot, but we're still - that's still the minority rather than the majority.

Julia Cumberlege: So just returning to Primodos, just to clarify for me and for the panel and for those who are going to look at the website to see what's being said, can you actually categorically say there is no causal relationship, no association, no possible association between Primodos and these children that have been born deformed?

Ailsa Gebbie: We cannot rule it out. That's why, within the report, we say because of the nature of the data we looked at, a weak association could not be either ruled out or proven with absolute certainty. We've been absolutely clear all along. We didn't find a causal association, but because of the nature of the data, it is possible either way. It could or it couldn't exist. If I may just - picking up on what Diana said, mention one thing, which I think is a good example of this. When the first signal that there might be an

issue with hormonal pregnancy tests happened it was to do with neural tube defects.

Actually, reviewing all the data, Stephen has - we found that actually there was not an association. Then the whole issue with folic acid and neural tube defects came to light, but that was the original trigger for thinking there was a problem with hormone pregnancy tests. In fact that now, from the data that we have, we can say we did not find an association. But it was the initial trigger for thinking there was an issue.

Julia Cumberlege: So you are ambivalent about there being no causal association?

Ailsa Gebbie: No, well, I...

Stephen Evans: Can we - can I just come in on that? Saying none is not necessarily terribly helpful. If you're saying there's a risk in one in 10 million, that could still be a causal association. We certainly can't eliminate that. We can be absolutely certain that this is nothing like thalidomide. That we can be absolutely certain about. We cannot exclude a very small risk. The level of risk actually that we can exclude is itself somewhat uncertain, but even a risk that is a tenth of, a hundredth of the thalidomide risk, I think we can exclude. But a 40 per cent increase we certainly can't exclude.

Epidemiology is at the limit there. You need randomised trial data to do that. These days, one of the key things we do assessing whether an observational study is reliable, is to envisage the randomised trial we would do if we could. It may be unethical, it may be impractical, but we try and think of the randomised trial. None of these studies - all of these studies, except one, did not approach it in that way. The only study that we found, and that Heneghan has found, that looked at that is one by Torfs. Torfs is the only one that compares different hormonal pregnancy tests. Because if you are doing a randomised trial, you would find somebody who wants to have a pregnancy test and you would randomise them to one test or another, generally. You might even randomise them to a test or no test, but you wouldn't generally do that. You would randomise them to different tests. The paper by Torfs has description of hormone, serum and urine tests. They tended to be available at slightly different times.

So one of the interesting things, in the peer review of the Heneghan report, Dr Olszynko-Gryn says this, more optionally, the authors - this is Heneghan and - et al. The authors might consider reflecting on the extent to which the association they identify implies a causal association. An association between the use of HPTs and birth defects has long been

recognised and was rarely in dispute. We don't dispute that. There is an association.

But that is like going to the Bristol Royal Infirmary Inquiry and saying that, among those children who had operations for congenital heart disease - there were deaths. There was an association between deaths and being operated on in Bristol, but that is not in dispute. The question was, were Bristol surgeons having a higher rate of mortality than the rest of the country, who were our comparators group?

So the whole object of these studies is to try and say, have we made a valid comparison? Now [inaudible] Bristol argued that Bristol saw more severe cases. We could not find any evidence that that is so. However, with hormonal pregnancy tests, there is evidence, particularly from the Torfs paper, that those who got tests were slightly different, not in all cases, but were slightly different to those who didn't get the tests. It doesn't mean that everybody is, and so somebody might have got it just at random. But some people got those tests because they were worried. Some people had it because they'd had previous problems in their pregnancies.

One of the things that you'll find in the Torf paper is a very interesting graph. I think I'll wave it to you here and you may be able to see it. I don't know whether you can. But there, this is gestational age and this is the probability of a death from conception. The solid line at the bottom is their general population and these wavy lines above them are all the different tests. It shows you that all of those getting tests had a higher risk. This is on a logarithmic scale. So some of it is enormously higher at different gestations. So those who get the tests, it isn't all of them, some of them get it randomly, but some get it at a different rate and they have reasons for doing that.

The other thing that is important is that that paper is the only one that I can find that, in discussing these issues, makes it very clear that there is a distinction between serious congenital anomalies and non-serious ones. So it's also important to say, when did I ascertain that there was a congenital anomaly? We talk about congenital anomalies as if you say yes/no. Dr Wellesley knows that that isn't so. But if we look at the serious ones, the cumulative incidents at birth was 1.1 per cent; at one year, 2.5 per cent; and at five years, 3.7 per cent. So it depends when you look.

You've got to be very careful. You've got to make sure you're looking at the same time. If you were doing a randomised trial, you would do that. If you look at non-serious ones, the rates for the same period, well, 1.8 per

cent, 6.2 per cent and 11.3 per cent at five years. I - there is data from Fiona Stanley's group in Perth that shows an enormous rise between five and six years, or around then, between four and six, because when children go to school, they get a head examination and you then find anomalies.

So you've got to be very careful in your definitions of these things. Most of these studies were pretty weak in doing that, to be honest. That's why taking the totality of the evidence, I listened. I'm not an expert in clinical genetics. I'm not an expert in the animal data. We listened to all of them, and the pattern from all of it was, we don't see a problem, but we certainly can't exclude a very small increased risk. [Unclear].

Ailsa Gebbie: Yeah. Just to pick up a little bit more on that, the wording of all this was very difficult. In our terms of reference the first sentence was to consider all available evidence and possible association. Again, we know there's a possible association. That was why we were doing the report. But then when the report came out, we were criticised because we hadn't actually picked up on saying was there a possible association or not. But there is a possible association. To have done all that work, we had to look at the evidence and then decide what we considered relevant and important, but we did not find a causal association. But everybody admits there is a possible association and that's why the report was carried out in the first place.

Shirley Price: Can I just...

Julia Cumberlege: Sorry, I was...

Shirley Price: I was just going to add, with the non-clinical data, the issue that we had there was that we looked at all the animal datasets, rodents, mice and rats, [unclear] rabbits and then the non-human primates. We took them on board. There was about 80 studies that we looked at. We took on board the dose, what dose was given. We looked at the abnormalities that had been reported and considered now looking at it on whether or not these were spontaneous or if they were within the controlled data.

We did talk to Professor Vargesson about the Zebrafish work. At the time that we produced the report, that was new, unpublished data. It was still considered that. Since then, there's been the paper by [Brown et al.] But because of all that and taking that into consideration, we didn't feel the non-clinical data supported a causal association. But that's the non-clinical data. Of course, there's a lot more than that you're taking forward with the clinical data.

So I think for that side of it, the non-clinical, we would say there was not a causal - we didn't feel the data supported a causal association with the malformation [unclear].

Julia Cumberlege: Why do you think the patient groups, then, are so certain in their own minds that there is an association?

Shirley Price: I think when you're looking at all of this, yes, it was very - it was traumatic for, obviously, the patients that came to talk to us and for us to listen to what was said. But I had to look at the - I looked at the science that was produced and looked at the scientific evidence. I can sit here and go through it again and say that I did not feel, looking at all the data that was produced at the time, actually produced a non-causal association, from the data that I have been able to analyse at the time.

Sonia Macleod: In terms of looking and saying that you considered all of the available evidence, one of the criticisms that we've heard is that not all of the available evidence was considered. That's the Vargesson paper, which you have said you looked at, although it wasn't published at that time. Then the Royal College of GPs' report by Norman Dean was another paper that's been mentioned. Also, one was the - there's a 1972 Isabel Gal paper in advances in teratology, which is a much more comprehensive description of her original earlier paper that I don't think you considered.

Shirley Price: So Professor Vargesson's was quite important because it's current work and it was looking at using Zebrafish, which is used as a screening tool. There's no dispute about that at all. I think when I looked at the data myself, I felt that there was some areas that I would like to have questioned, but of course at that point it wasn't correct for me to question it. But it did go to two other committees to question. It was around the actual levels to which the Zebrafish had been exposed to, for example.

The methodology, absolutely fine. They changed the membrane to allow for better exposure, quite common in that methodology. But again, I'd like to have understood a little more about the exposure to which the Zebrafish, and also how the Zebrafish were exposed over a period of organogenesis, similar to the two-day exposure that one has with the Primodos. So that's the sort of information I'd like to be able to understand.

At the time, quite rightly, Professor Vargesson hadn't published that data. He kindly provided it to the Expert Working Group so we could actually listen and understand what was being proposed. Since the publication,

we've been able to have a look further. We always said that anything that was to come out we would be very keen to review and to take that information forward and any other data would be - that was coming from that we'd be very keen to look at.

The other papers, no, but we did look at documentation that did come forward. There was one mouse study that did actually show some malformations, but that was 30 times of the daily dose of Primodos used every day in the period of foetal organ development. The lower doses in that study did not produce the same malformation. So again, as a scientist, I'm having to balance the two. I appreciate the - we heard from the association, but I'm looking at it from a science - I'm looking at the science that's being provided to be able to go through that. On top of that, I was very keen to look at what Professor Vargesson has now produced with his group in Aberdeen.

Ailsa Gebbie: We definitely considered Isobel Gal's work. I can't remember exactly - we'd have to check back - which papers we looked at, but we - her name came up frequently and the data was examined. Stephen, you would agree?

Stephen Evans: Yes. I think that there was some republication of data there. That was one of the problems.

Sonia Macleod: There was.

Stephen Evans: It's interesting that Heneghan only uses Gal 1972 there. But she was particularly interested in neural tube defects. At that time, in spite of what Smithills said - and he was a great hero in this field - it was not fully known that folic acid would prevent neural tube defects. It wasn't until Wald and Cakul did their randomised trial, which showed that giving folic acid to pregnant mothers prevents at least 80 per cent of neural tube defects. So an association with neural tube defects is, in some sense, inherently unlikely with hormonal pregnancy tests because we know that it is almost entirely due to absence of folic acid in a mother's diet.

It's very interesting, but as far as I can tell - and you may know more about this than I do - it's just in October 2018 that the UK's made a decision to add folic acid to flour, is it? Certainly - or other foodstuffs. Is that right?

Sonia Macleod: Yeah, that's right.

Stephen Evans: So it's taken a long time to realise that that is so. So I think that anything else that we have missed, I haven't seen anything, and I've looked at what

they have said. The problem is, one has to have enormous - we didn't just deal with the numbers. We were concerned for patients, but it is not the right thing to do to abrogate our responsibility to truth in sympathy with patients. Many, many parents were totally convinced that MMR cause autism. When I first led and funded the first studies, beyond what Andrew Wakefield had said, I didn't know the answer then. But we have subsequently done studies and shown that MMR does not cause autism, at least not at any noticeable rate.

But there are still people out there, probably President Trump and certainly Andrew Wakefield, who believe that MMR causes autism. There are lots who do. So changing the minds of people is terribly difficult. When you're involved in a tragedy and you have been convinced over a long period of time, it's very difficult. To be honest, I sent an email to Mrs Lyons following some things that were said in parliament, where there were people who said in parliament - as our Expert Working Group had begun, they had said that we were all corrupt, essentially. They had said that we were - they were utterly convinced, prior to our expert review, that there was a causal association. They didn't use that word.

Diana Wellesley: But the temporal time is also relevant, actually, because - like anencephaly occurs 23 to 26 days after conception. People took HPTs - people then did not, the minute their period was missed, go for a test.

[Over speaking]

Diana Wellesley: They actually tended to go after two missed periods. A few of them might have gone after one. But I've seen a few patients with this problem. Certainly more than one took - they said they took their pill after their second missed period. The anomalies would have well happened before that. So despite evidence, as Stephen says, because this has been a mind-set for a long time, it isn't something that's - it's - they want a reason. It's very hard to prove one, except for - the gestation is very relevant here.

We didn't go into that in great detail because most people, in truth, couldn't really remember what - when they took it. But in those days it was a tendency, after two missed periods, to test for pregnancy, or at least a few - a couple of weeks after one missed period, when a lot of the organogenesis would have happened. That's - we couldn't really consider that because people couldn't remember and it wasn't fair to imply something on them. But that is relevant.

In fact in one association and a few people I have met, who I asked when they took it and then we discussed development and they - the ones I've

met that do remember when they took it, one was very young. She remembered she'd had two missed periods and was worried and so she went for a pill and that kind of thing to find out her pregnancy. So I think there are situations like that that we weren't able to examine. We weren't able to assess those sorts of things because it's such a long time ago.

Ailsa Gebbie: So there are so many variables involved. The numbers of events, I think 253. Where maybe there were 8 million of these pregnancy tests issued in the UK, maybe 1.2 million women actually used them. So finding the denominators and trying to work out any effect is impossible.

Valerie Brasse: But isn't that just one of the problems, that we know that - how many may have taken it or we have an order of magnitude, but actually, the numbers that would have reported, that would have made the link, makes that - your job so much harder because in fact you have so few cases? It's one of the things you were saying that was making...

Ailsa Gebbie: So few cases to work on.

Valerie Brasse: So really, when you're looking at that clinical side of it, actually, you've got very little to work on.

Ailsa Gebbie: Absolutely. It's so...

Valerie Brasse: But the women concerned, who now, much later on, think, okay, this is what happened to us, they still don't have this grip that you had the sort of evidence you need to be able to come up with a conclusion other than there was a weak association. One of the things I wanted to pick up from you, Mr. Evans, you say you cannot exclude a risk unless there's a benefit. What was the benefit to taking HPT as a pregnancy test?

Stephen Evans: No, what I meant there was, if...

Diana Wellesley: Protecting...

[Over speaking]

Stephen Evans: ...there was a benefit in protecting from congenital anomalies, I was meaning that. Now, in terms of the benefit of taking it, my wife was pregnant with our oldest son in 1974 and I asked her about these things. She said one of the things was that the urine tests around at the time took a number of weeks to come back and so if you were a little bit instant - well, it's men who suffer from instant gratification, not women. But if you wanted an instant answer, then the hormonal pregnancy tests did that.

The other thing that I think Dr Olszynko-Gryn again points out, that it was something you could do privately. You didn't need to reveal it to anyone. You could go and take it yourself and you didn't have to have a test result that anyone was aware of.

Cyril Chantler: You couldn't get it privately, though, could you? It would have to be on prescription.

Stephen Evans: No, you took it privately.

Cyril Chantler: Oh, I see.

Stephen Evans: The result was private to you...

Cyril Chantler: Oh, I see.

Stephen Evans: ...the woman. You didn't have a lab test result coming back through your GP. You had to go and get the test from the GP...

Valerie Brasse: So we're talking about a convenience rather than any therapeutic or any other way?

Stephen Evans: So it's a convenience. There was certainly no - well, some people at the time probably thought that it was therapeutic. It might prevent the loss of the pregnancy. That was a belief at the time. Of course, they were giving things at even high doses than Primodos at the time to prevent...

Ailsa Gebbie: To prevent miscarriage.

Stephen Evans: ...recurrent miscarriage, and that was being done a great deal. A number of the papers grouped together hormones given for recurrent miscarriage or threatened abortion with hormonal pregnancy.

Cyril Chantler: So you didn't find any evidence of people discussing the benefit/risk ratio before prescribing this tablet, bearing in mind thalidomide had already occurred, so you'd imagine that people would be pretty cautious?

Ailsa Gebbie: No, there was nothing - people were literally given something from - often from the top drawer that the GPs had been given as a free sample.

Cyril Chantler: Do you have a view about that? Did you, as a working group, have a view about that?

Ailsa Gebbie: We all found it very hard to understand that that could happen, but it was of its time. The pill had just been launched. This was riding on the heyday of suddenly there was oral contraception to help women, but it's another matter how we practise nowadays.

Cyril Chantler: Do you think, looking back, that was right? Do you think - did you have a view as a working group as to whether women were properly warned about the risks?

Ailsa Gebbie: We - as a group, we had no remit to look at regulatory actions. So we had personal views, of course, that this sounded, now, to us, totally unacceptable. But if I may go back to your very first comment, would we have done anything differently? I think we might have done more to support the families. They came on a busy afternoon of work. We had a fleeting opportunity to speak to them. They were very upset. Then I think, inevitably, the conclusions of the report were very disappointing, so I think if - we could have spent more time speaking to them and helping them understand the language and the scientific methods.

But during the - one of our final meetings [inaudible] during the meeting, let's try to find something to make the families feel better. Let's say there is a slightly increased risk of congenital heart disease. We actually had to stop and take a breath and say, we cannot do this. This is a scientific group. We must adhere to scientific principles and produce the report that is absolutely accurate. That was difficult and one feels so sorry for the families involved who brought in their children, with multiple disabilities, who are now young adults. That was very upsetting for everybody.

Julia Cumberlege: Can I just ask you, you just said this was a free sample produced by the manufacturer. So was there any pressure from the manufacturers in terms of trying to ensure that this pill was taken?

Ailsa Gebbie: I don't think so. It didn't sound as though it was being marketed with a particular commercial benefit. I think the pill was the big thing at the time that everybody was pushing and millions of women were taking it in these early days that we know now...

Cyril Chantler: Do you mean the contraceptive pill?

Ailsa Gebbie: Contraceptive pill.

Cyril Chantler: Thank you.

Ailsa Gebbie: Many women who were older and were smoking were just prescribed this pill. Everybody thought it was the best possible thing. We're now much more aware of the risks and benefits and prescribe oral contraception very safely. But I think hormone pregnancy tests just came out a bit as an aside and people were given free samples. It was just thought to be a little added benefit that GPs could give their patients. It was also used for

treatment of menstrual disorders. Women who had absent periods could be given this to see if they had a...

[Over speaking]

Cyril Chantler: I don't understand why they'd give them out as free samples. What was the purpose?

Ailsa Gebbie: That was very common practice in my past, even when I was a junior doctor. We were showered with free samples from pharmaceutical companies.

Cyril Chantler: But why this to a GP? I don't understand what the reason for it was.

Diana Wellesley: There would have been other free samples.

Ailsa Gebbie: Others as well.

Diana Wellesley: This is the only one we're discussing. There would have been others.

Ailsa Gebbie: There might have been drug lunches to promote oral contraception and GPs were given this as free samples.

Cyril Chantler: But some were given out on prescription...

[Over speaking]

Ailsa Gebbie: Some were given on prescription, yes.

Cyril Chantler: Then the National Health Service would pay for it.

Stephen Evans: The same thing happened with non-steroidal anti-inflammatories. People were inundated with the latest new non-steroidal anti-inflammatory and they'd be given out as free things. Now, that happened a great deal more in the US so that, in fact, in the US, there were many women exposed to thalidomide through free samples prior to it being licensed in the US. Frances Kelsey, who got the congressional medal of honour from President Kennedy for stopping thalidomide in the US, didn't actually stop it. She stopped it being approved as a medicine, but people were given out free samples.

Another thing we were criticised on was in combining oral contraceptives and hormone pregnancy tests. We did not do this. We looked at both of them, but we didn't at any point pool the data between hormonal pregnancy tests and oral contraceptives. Some authors did and some didn't. Certainly, somebody like Bill Inman was enormously concerned

about having a pill scare by making too big a fuss about the possible effect of hormone pregnancy tests.

As you say and imply, there is no - that we know now, no therapeutic benefit to giving it. It was just convenience. When there are other things that you can now rapidly get a pregnancy test for, then there would be no reason to have it on the market and it would have been withdrawn as a precautionary principle.

Valerie Brasse: The - in fact the MHRA timeline suggests that the Predictor home pregnancy urine test was available from 1971.

Stephen Evans: Yeah.

Valerie Brasse: So in fact there were these other things on the - if you were just looking on the convenience scale, there was something else. So we're left with this still being prescribed or given out as a sample. It's also the case, interestingly, that it's exactly the same component and exactly the same dosage, taken exactly the same way as for the treatment of secondary amenorrhoea, for which Primodos was actually licensed. So in fact it could be prescribed and certainly the prescribing chemist or dispensing chemist would not have known for what it's being treated.

It carried on being used, potentially, and the only record you'd have of why it was being used was presumably on the GP's notes. So it's exactly the same dosage for the treatment.

Stephen Evans: It was - probably also went on being prescribed - and certainly there's a letter that says that it went on being prescribed even after it was officially withdrawn. One of the things, of course, is that medicines regulation regulates the industry and not practitioners. They're free to do as they wish, and one has to realise that. I think, probably - I don't know. My wife had trained in medicine by then. I think there was this belief that these pills were giving women a hormone that is absolutely vital for pregnancy.

Progesterone, as a natural hormone, is absolutely vital for a pregnancy to progress. You cannot have a pregnancy progress - the mother will reject the tissue that is implanted and the progesterone seems to be able to prevent that. So I think it was a general belief that these things were good.

Cyril Chantler: However, you did just say that nowadays it would be withdrawn as a precautionary principle. When would that have happened, bearing in mind what we know now? It wouldn't have happened in 1958 when it was introduced.

Stephen Evans: No. I think it would - and you could see, in different countries, on the similar precautionary principle, it was withdrawn at various times. Some withdrew it before the UK and some withdrew it after. The best, sensible thing would probably, given the availability of other things, would be to withdraw it for that purpose earlier. Certainly the suggestion was that. So I carry no flag for the pharmaceutical industry. I think they're giving these pills out to try and hope that once they've given out a few and had a good result, the GP will then write a prescription and they make money from that and not the others.

It's like free samples of Coca Cola given at Waterloo Station. They hope that you'll buy it next time, and that's part of the way the industry works. I don't - the industry has certainly behaved appallingly in regard to thalidomide. I don't think they were quite as bad in regard to this, but certainly I fought the industry over contraceptives and venous thromboembolism

Cyril Chantler: You talked earlier on about the lack of randomised controlled trials. You also mentioned that there are times when we'd all wish we could carry out a randomised controlled trial, but it's either impractical or would be unethical. If you were going back now to 1958 and you were introducing something like this, how would you - what would you recommend as a way of doing it? Because one of the concerns of our review is to learn from the past to try and secure a better future, if you see what I mean. So could you just perhaps instruct us how you would wish to introduce something like this?

Stephen Evans: I would want to have - if there was an alternative test, I would want to be interested in the efficacy of this test. The hormonal pregnancy test was not 100 per cent sensitive or specific. It gave false results in both directions in certain circumstances. So at - if I were doing...

Cyril Chantler: By efficacy you mean, does it work?

Stephen Evans: It doesn't work perfectly. Then...

Cyril Chantler: Nothing works.

Stephen Evans: ...nothing in medicine works perfectly.

Cyril Chantler: Yes, but you're asking the question, with efficacy, does it work?

Stephen Evans: So I - back - you're asking me to go back to 1958. I would design a trial comparing Primodos with an alternative pregnancy test that probably existed and I would randomise people from - to one test or the other. I

would then follow them up. At the time, I would probably not be terribly interested in their propensity to have a congenital anomaly. I'd be more interested in, did it predict pregnancy? Did it result in a live birth at a higher rate or a lower rate? That [might be]...

Cyril Chantler: After that? After that?

Stephen Evans: After that, I would want to follow them up to see whether they had congenital anomalies.

Cyril Chantler: But how would you want to do that? What are the methodologies that you would...

Stephen Evans: Well, we have methodologies now for following up people after randomised trials on occasions. The industry don't always do this, but on the whole, academics are a little bit better. We don't have really good tracking...

[Over speaking]

Cyril Chantler: You're not talking about the Yellow Card at this point?

Stephen Evans: No, definitely not.

Cyril Chantler: Something much more systematic?

Stephen Evans: No, something much more systematic than the Yellow Card.

Cyril Chantler: Yes, but we don't always do that, do we?

Stephen Evans: We don't always do that. Now, most medicines these days have a pregnancy register because it's regarded, generally, as unethical to give treatments that are not intended for pregnancy, for pregnant women. There is often a requirement - especially if Shirley has done some work and found a slight hint of a problem for a medicine. Then there will be a demand on the industry to have a pregnancy register to record all the women who were pregnant who got that. We had this for SSRIs. We've had it for a whole lot of other drugs.

Shirley Price: So just on that, one of the recommendations is to look at sharing of data across the stakeholders, be it the industry, be it CROs, be it the patient groups, so that we all understand, and the academics. Last week we had the first of a - series - hopefully a series of workshops, but our first workshop on predicting safety of medicines in pregnancy in the era. There was about 30-ish stakeholders from across the industry, both from the...

Cyril Chantler: When was that?

Shirley Price: That was - it was held in the MHRA offices...

[Over speaking]

Cyril Chantler: Yeah, when, though?

Shirley Price: Last - I think it was last - not last Thursday, the Thursday before. So we're - at the moment, because I'm working on that because that was one of the recommendations...

Cyril Chantler: So this is a new initiative?

Diana Wellesley: This is one of our recommendations.

Shirley Price: A new initiative, one of the recommendations. Now we're working on those recommendations. Actually, we had two sessions, a morning and an afternoon session. We brought speakers in from academia and the industry to talk about issues. One of the key areas that came about was sharing of data. That came up in the morning session and it came up in the afternoon session. We had some other people there. We had the MRC representative. We also had the NC3Rs' representative because they've done a lot of work in - through initiatives such as CRACK IT.

So that's something that we're looking at now. There are a number of recommendations that we're working through. They will be circulated to the stakeholders and we will put that together. It will come back to the CHM at some point. I'm hoping that wasn't the one-off workshop. There will be further workshops to then start to work through those recommendations.

Ailsa Gebbie: But it's incredibly difficult to assess the safety of medicines used in pregnancy. Most pregnant women are excluded from the standard trials of any new medicines, but yet we know women are having pregnancies who already have chronic diseases and may be continuing. Sometimes they're on very potent medication. Women become ill during pregnancy and need to take drugs. We're very poorly informed, that whole area. Again, picking up on our recommendations, we want to do better and study that area more.

Diana Wellesley: I think that's already happening. I've been asked to be on the evaluation of the congenital anomalies on two trials of drugs, so new ones - they're actually areas of drugs we've used before, but a new version of. So there's now - I think people are listening to that, not only to us. I'm sure it's coming from other areas. But they're starting to do trials in pregnant women. So women who need medication for whatever reason, we're

comparing this one to that one or this one possibly to nothing, but usually this one to that one.

I think that is really starting, and it's been just in the last couple of years, actually. I've suddenly been asked to join quite a few, evaluating infants after birth or the anomalies during pregnancy. That's never arisen before, so I think there is a new era of really taking pregnancy and medication seriously.

Simon Whale: Can I just...

Stephen Evans: There was a major initiative at the European Medicines Agency as well in the last 18 months. Certainly I can't - I was trying - sorry, I was looking as though I was being rude, on my phone. I was trying to find the date of when the Europe one - I'm sorry.

Simon Whale: Can I just go back to your report and the conclusion of no causal association? But you also say in the report, I think, that there's a known risk of genital abnormalities...

Diana Wellesley: Yes.

Simon Whale: ...such as virilisation.

Diana Wellesley: That's - yeah.

Simon Whale: So as a layperson, forgive me, but isn't virilisation a congenital malformation?

Diana Wellesley: It might be, but it wasn't present. It wasn't present - I don't think - there was one incidence of hypospadias, which is quite a common anomaly. But I looked through all the anomalies - within the last week - and there's actually a paucity of problems like that. So that really was not - and if you look at the - I don't know what page we're at here. Page 55. It's comparing data. You see, genitourinary doesn't even come up. So there was not - absolutely not an increase, which you might...

[Over speaking]

Simon Whale: So there's - so there is an association, but you found no evidence?

Diana Wellesley: No...

Ailsa Gebbie: Again, nobody...

Diana Wellesley: [Would maybe know].

Ailsa Gebbie: ...would understand the dose of that. Norethisterone is a progestogen, but it has a slightly androgenic effect, like testosterone. That's the effect you would get in a female foetus. But it's not come out in the data we looked at, but it's been documented in the past.

Diana Wellesley: Maybe for longer times...

Ailsa Gebbie: Yes, from the longer exposure.

Diana Wellesley: ...of taking it, because it was only two days. That's why it was good reason. It makes sense that it didn't have an effect, but we didn't find that. It's been documented where it's been taken for longer periods, but for the two days it did not seem to be relevant.

Ailsa Gebbie: So again - but it is a nice example of how there was effect, that shows effect on the genital tract, the sexual organs. Similarly with Stilbestrol, which was another teratogen identified previously. It affected the genital tract. Again, these are hormones, which, again, goes against the array of anomalies that appeared in the group that we looked at.

[Over speaking]

Simon Whale: It does tell you that the hormone can reach the developing foetus.

Ailsa Gebbie: Yeah. Oh, absolutely. We're not denying that, but they are hormones. With Stilbestrol and androgens, they cause effect on sexual organs and genitalia, which we know there are lots of receptors. That goes against the other data we looked at, which was limb abnormalities, congenital heart disease, neural tube defects, et cetera. It's quite different, but we're not disputing that these are hormones and in high doses, in particular circumstances, with long periods, they can have an effect.

Shirley Price: So it was picked up in the animal studies, you're quite right, but again, it was the dose that you have to look at. What's the level compared to what would be exposed to in humans? You've also got to always be careful how we translate data that we see in rats, mice, rabbits to humans. Obviously the closest is the non-human primate, but that, as we've said in the report and as we know now, it does have ethical considerations. Also, statistically, when you're looking at a non-human primate, like us, they will produce one, if not possibly two foetuses and there's a longer gestation time.

That's not to say we shouldn't be doing it. What we are looking at are alternative methods, one of which is a screening method using, for example, Zebrafish. But that is a screen...

[Over speaking]

Valerie Brasse: Can I just follow up the point on the non-clinical studies? Because if we're talking about what might be embryo lethal, so we will have lost a proportion before they ever - anyone gets to look at them and say, and was it the amalgamations that caused the death [unclear]? So that's an entire group that, presumably, you've got no information on.

Shirley Price: So it is very difficult, I agree; sometimes there will be some overlap between embryo lethality and malformations, but usually at very high doses. Often embryo - lethal doses to the embryo is often an issue that may be due to some maternal changes as well. Can we see that? No, you're quite right. It's very difficult because if you're looking at - what we're often looking at is day 19 in the rodents. Then the - when you take those foetuses and look at them, you can actually look at solid tissue malformations, skeletal malformations, by putting them into the various fixtures that you need to do.

You really need a very good eye to do that, and that comes with a lot of experience. But these are very tiny foetuses, very small, to actually be able to determine that. What you'd also look at - and I've done some multi-generation stuff. What you also look at is resorption science and you look at any discolouration. Does it tell me if there's any malformation? No, but then I'm looking at that and comparing dose levels and also our controls. I think, looking now, we have a lot more data on many, many compounds and [unclear] of compounds at both historical control data, so I can look back and look at, if I've got a wavy rib, is that because of the compound or is that because...

Valerie Brasse: But that's what you can do now. The fact is that those that were looking at them then presumably could not in the same way. So we've really got partial data...

Shirley Price: You couldn't, but I think...

Valerie Brasse: ...at best.

Shirley Price: ...it's very difficult. If you - you could, and if somebody wishes to take that forward and to present a method which you could look at foetuses at day 13, day - between days 13 and 15, but it would - I - to look at those malformations would take a lot of being able to understand and doing a lot of [unclear]. I think if we look at the data that we've currently got - I totally agree with you, it's then and now. But if we look at the data that we've currently got and analyse that, I think I would stand with the scientific output and results of the data I've taken from that.

Valerie Brasse: Can I come back to another question, if I may? That is about the governance processes around how your working group operated. What were they?

Ailsa Gebbie: The...

Valerie Brasse: Governance.

Ailsa Gebbie: ...governance?

Valerie Brasse: Mm.

Ailsa Gebbie: The group reported to the Commission on Human Medicines, and they are the top level independent group of experts advising the government. In terms of governance, the MHRA provided the secretariat and did that to an incredibly high standard. There was very careful scrutiny of - in terms of conflict of interest, particularly. Is that mainly what you're...

Valerie Brasse: Well, I was thinking, then, as you're coming towards the end, you are, of course, the experts and it's maybe almost impossible, but presumably your draft report was not peer reviewed, as such, by any other group of experts.

Ailsa Gebbie: Well, we were reporting to the CHM and, in essence, that's exactly what they did. We completed the report and submitted it to them. They totally agreed with all the findings. We clarified - they felt our wording was not clear enough, so we did reword some of the findings, but nothing was changed. So in terms of governance, we reported to CHM. They looked at it in great detail, fed back to us. The only thing that happened was that some wording was clarified.

Valerie Brasse: Is that all? Because, actually, what we hear from the patient groups is that there were quite substantial changes between the draft report and the final report.

Ailsa Gebbie: I would dispute that. They were done in a way that was on the basis of improving the evidence and the clarity. There was nothing more sinister or Machiavellian than that.

Simon Whale: Well, what we've been told is that the changes resulted in a report that was more definitive, more definite about the lack of a causal association than your previous draft.

Ailsa Gebbie: Well, at the patient meeting I did use the word strengthen, which maybe wasn't absolutely ideal. It was more clarifying the findings, but the findings - none of the findings were changed at all. But as you can

understand, it was a very scientific report, so if anything, they made it more understandable from the lay perspective.

Valerie Brasse: What about...

Ailsa Gebbie: That was the clarification.

Valerie Brasse: ...the Forest graphs? Because I gather that was in the draft and then came out of the final report.

Ailsa Gebbie: Well, maybe, Stephen, you'd like to respond.

Stephen Evans: What are these?

Valerie Brasse: The plots.

Stephen Evans: They're the Forest plots. They're there. The only thing that might be said is that in some of them, technically, some might have had a summary element that I would have insisted shouldn't be there because it is a spurious accuracy of the numbers that you have because most of them didn't adjust for confounding factors in regard to that. As I say, it was the only one. So I don't recall anything being extracted from there. All the Forest plots that I can recall are there, and not only that, we have made it clear what our view of the quality assessment was. You can see lots of red, which says, not very [clear].

Simon Whale: Well, can I just ask about that? So those seven criteria that you applied, who decided on which seven criteria to apply?

Stephen Evans: Well, we had discussion among ourselves and with epidemiologists in the MHRA and we decided on those that were specific to our needs rather than using the Newcastle Scale. The [ROBINS] scale was not fully developed then. I'm one of the collaborators on the new ROBINS scale that is to be used by Cochrane collaboration. I've been involved with Cochrane for many years.

Simon Whale: When each of the relevant studies was assessed against those seven criteria, was that done by one individual?

Stephen Evans: I think we didn't do it in a formal way of sitting down, and that perhaps you might criticise, but as a group, we looked at whether we agreed with those. It might have originally been done by one individual. We didn't look for concordance between those, but a number of us went through those and said, do we agree with them? That possibly wasn't ideal, but I don't think there was anything that says, this was a very high-quality study and somebody else says it's a really bad-quality study.

Sonia Macleod: Just so I'm absolutely clear, one person went through and ranked them and then you as a group sat and said, do we agree; do we disagree? So they weren't independently ranked by more than one person?

Stephen Evans: I don't think so. I can't be certain of that.

Diana Wellesley: But you all chose the criteria, in a big group.

Ailsa Gebbie: Yeah, it was all agreed.

Diana Wellesley: When the criteria were chosen, we had a big meeting discussing that, so they were agreed and then applied by...

Stephen Evans: Being honest, I can't remember the exact process there. It may be that, compared with an ideal thing of doing it double blind and all the rest of it - one of the problems is, of course, here, is that if you are doing proper protocol - proper systematic reviews, you should have a protocol beforehand. I imagine that Professor Heneghan had a protocol. He doesn't mention a protocol in there for his systematic review. There may be one, but the very best quality stuff these days will preregister a protocol. But we know people don't keep to protocols. When you know all the data, there's a very great danger of writing your protocol to get you the answer you want. That's - as I say, I think there are some things that we did, but I don't think they affect our conclusion.

Ailsa Gebbie: To go back to governance - every meeting was very carefully minuted. A question - if there were particular queries relating to that, you - we could easily go back to the minutes and to the discussion.

Valerie Brasse: It would be helpful to have - to know whether that was or was not done in terms of the independence, so perhaps you could come back to us on that.

Cyril Chantler: The National Academy of Medicine in America, they - when they set up a review they also invite, from their members, a peer review process to look at the review before it is accepted by the academy. This didn't happen here. Do you think it should have done?

Ailsa Gebbie: It's very difficult to answer that question. I don't think we'd have changed the conclusions, at the end of the day. This was agreed by others, with the Minister of Health and the MHRA, that this was the process to be undertaken. We reported to the CHM. That was how it was set up and that's - we fulfilled our remit to do that. It was - that was what was decided. Many people wanted a proper public inquiry and in fact

throughout the process kept referring to it as the inquiry and we had to rein it back in and say, no, this is a scientific review of the evidence.

Shirley Price: Can I just add...

Ailsa Gebbie: Yeah.

Shirley Price: Because I sit on the CHM when the report came, so I sat back, because I was asked questions by Professor Ralston. But actually, it was for clarity. That was - and that will be minuted. It was around, does this - is this clear? We have lay members on the CHM who also contributed to that.

Cyril Chantler: But on the CHM, you had people who are expert in the science that you'd evaluated.

Ailsa Gebbie: Yes.

Shirley Price: Yes.

Ailsa Gebbie: Absolutely.

Shirley Price: But it's something a lay member would have picked up, but that would be minuted. But it certainly was really good clarity, to go through that. Can I just come back on one other small point with the organogenesis? What we did through the course of the work is that we did also look at some experiments that had actually been taken over giving Primodos to animal studies in two days, but over the whole period of organogenesis. Although lethality was seen at the highest doses, what we didn't pick up on or what wasn't [unclear] rather was any malformations. So, if you like, that was the nearest we could get from the data at that point.

Julia Cumberlege: Yes, sorry, Professor?

Stephen Evans: I think, for example, had a different process been gone through, that the Academy of Medical Sciences was asked to review it, that would be a different question. They frequently do have peer review through that process, but if you go to a public inquiry you don't have peer review. When we dealt with the Bristol Royal Infirmary...

Cyril Chantler: I'm thinking more about the Academy of Medical Science because that's the equivalent of the National Academy of Medicine.

Stephen Evans: That's the equivalent. The guidance that the FDA have on meta-analysis, it's interesting that they say they don't offer any guidance on observational study meta-analysis because it's controversial. I was one of the panellists who provided guidance to the FDA on that, and they do

involve outsiders. I think that the UK is not always as good as it could be in doing that, but it's a process. If you go to the Bristol Royal Infirmary inquiry, we didn't have peer reviewers there in some senses.

Cyril Chantler: That was a very different review, if I may say so. This - your review is very much a science-based review. You're looking at scientific evidence because the role of an inquiry is...

Stephen Evans: Yes, on - from the statistical point of view, we were trying to look at it as a science thing. That was a key element, was the rate or mortality in Bristol higher than elsewhere? There was a lot of very clever science there from David Spiegelhalter, who's so much cleverer than I am. I think that we might have done something better on that, but that would have required creating a precedent for reviews of the Commission on Human Medicines that hasn't existed in the past. I think that there are reasons to say one might suggest doing that in the future, but it's a very different way of working.

Julia Cumberlege: Can I just ask a question? The Chairman of the All-Party Group for Primodos asked a question in the House of Commons. I don't know if it was written or whether it was oral, but the reply - she was asking if the Secretary of State would make an assessment of the merits in the conclusions of the 2018 report by Professor Carl Heneghan on oral hormone pregnancy tests and the risk of congenital malformations. Now, the minister replied that in line with the government's commitment to review any new evidence in relation to hormone pregnancy tests, the Commission on Human Medicines is convening a new expert group to conduct an independent scientific review of the publication by Professor Carl Heneghan.

She goes on to talk about the European Medicines Agency as well. Can I just ask you, on the Commission on Human Medicines that is now convening this new expert group, can I ask you what you think that group might achieve and whether you've got any knowledge of who's going to be on that group and how it's going to work? Do you know anything about it?

Ailsa Gebbie: I'm personally not involved. Shirley may be the best person to, as CHM.

Shirley Price: Yeah. So from CHM's point of view - and I don't know. I'd have to go back to the minutes, if indeed we have got anyone actually listed. So what normally happens is if working groups are set up, for example, this expert working group, CHM asked for us all to look at the remit of the group to consider what the working group's going to look at and then to consider

experts. Those expert names are taken forward and they go through a complete review of whether or not there are any conflicts, et cetera, et cetera.

For this group, I was - I didn't put my name forward at the time. I was recommended, I believe - It'll be minuted - by Professor [inaudible] to sit as the non-clinical expert and I was happy to do so. But that's the normal process. But again, the MHRA will be able to clarify that process and it will be minuted as to what the working group's remit will be and how that's then taken forward. We have a discussion at CHM about that very area and the CHM commissioners can put forward names to take forward as the experts.

Ailsa Gebbie: But a definite commitment was made to reviewing any new evidence. Our role, in a way, has been completing the publication of the report, but the MHRA will look at any new evidence and report back through an expert group, and with involving the European Medicines Agency as well when appropriate.

Julia Cumberlege: So an independent group...

Ailsa Gebbie: Independent.

Julia Cumberlege: ...from us, so entirely independent...

Ailsa Gebbie: Yes. Yeah.

Julia Cumberlege: ...and we have no influence?

Sonia Macleod: So like the ad-hoc Zebrafish working group?

Ailsa Gebbie: Yes, exactly.

Shirley Price: Absolutely independent.

Valerie Brasse: Can I just come back and ask a couple of questions on just some of the challenges that have been raised, just coming back to this report [unclear]? I believe I'm right in saying that the report says that the studies were updated. We all understand that [unclear]. But then it could be found that any association that they came up with was overstated, possibly. Is it just as likely that any association could have been understated?

Stephen Evans: That's a very good question. I wonder if I can just read something from Diana Pettiti, who said, 'in the group of non-experimental studies in which the results of some studies are positive and some are negative, it is always

possible that the positive ones are the result of bias or uncontrolled confounding and the negative ones are free of bias and confounding, or vice versa. Even when all of the studies are in the same direction, they might all suffer from the same bias or might all be uncontrolled for the same confounder.

Like Dr Shapiro, I believe that simply estimating the effect size from a group of studies does not shed much light on the truth', so we have to acknowledge the possibility and theory that the studies have had a bias that is downwards. Some elements of what we have would be likely to bias results downwards. If you have misclassified exposure, you tend to bias results downwards, but that is only really guaranteed to happen if you have a single exposure and you have a single outcome. If there are other factors that are at play, then misclassification can work in the other direction. So it is possible that it's been exaggerated.

Valerie Brasse: Was that said sufficiently well in your report?

Stephen Evans: No. That's one of the things we might - but on the other hand, what we could show, and there is evidence, that particularly in studies of drugs in pregnancy, that there is a bias towards the results that are positive, being published. Now, this isn't the same bias that you get with randomised trials. You can do tests with randomised trials because very big randomised trials will get published, but small randomised trials that don't show the - an interesting answer will not get published. I've got a letter, or at least I did have a letter from the editor of the *Journal for Quarterly Medicine*, where we'd done a trial and he said, we're very sorry, we won't publish your trials because they're - results because it isn't significant. That kind of approach, in theory, doesn't happen, but still happens.

So I think a lot of the explanation of this is that people have done studies and the interesting bits are published. The other thing that happens is they may study multiple anomalies and they don't report on the one that was reduced, they report on the one that was increased. That is a continual problem. It happens in randomised trials. It is always...

But you can understand, then, from the patients' group point of view that, frankly, you're left here with, was all the available evidence actually looked at? What is it that we're dealing with here? To come away after all of this work saying, you know what? I'm not quite sure we're so much better further forward.

Stephen Evans: Well, I'm - when I began this I thought there'd be very little evidence. I - having worked on perinatal epidemiology and published on all contraceptives and their effects, I thought there wouldn't be much evidence, but we ended up finding very large amounts of evidence out there. But nearly all the things that will encourage publication are towards the positive results. So while it is theoretically possible that some of those results could have been in the other direction, I don't think they are.

What we can say definitively is that in the Heneghan meta-analysis, results are not adjusted. We would recommend, when doing observational meta-analysis, that you take adjusted results from people. So, for example, in his presentation of the Torfs results, if you look upon page - sorry. If you look on page 12 of 27 on my printing off of that, the Torfs one, in figure 2, has 40 out of 203 events in the hormonal group - it's the last of the cohort studies there - and 2541 out of 17,057 in the supposed control group. But that was not their control group. That was the totality of others.

In the Torfs paper, they wanted to use the other test as their comparison group, and that, to me, is the right comparison group. If I do that and look at the serious congenital anomalies only and not at those that have accumulated up to five or six years, then I find that the relative risk, instead of being 1.4 is 1.12. So we have actually got a bias upwards there by not paying attention to the proper design of the study, and so that is likely to have happened in a number of the others.

They say in the paper that the important confounders have been taken into consideration, but they don't say what the important confounders are. Reproductive history for a woman who has had one pregnancy is a very important confounder, but most of the studies didn't have data on reproductive history. Only a few of them did. The other problem is that knowing that in your family there was a congenital anomaly might be something that isn't in the medical record and isn't down in your pregnancy. That might be part of the reason for having a test and that might not be there.

Valerie Brasse: But that's a might. The evidence as to whether that group who took the hormone pregnancy test were in fact different to the rest of the population, the evidence for that?

Stephen Evans: Well, the only study we have on that is, essentially, Torfs and that shows, unequivocally, that there is a difference. Their previous pregnancy loss has a relative risk that is about 1.4/5, is my recollection, with a P value of 0.401. So that is a highly significant effect. That graph I showed you shows

that even prior to that, because they're looking at things at birth, prior to, from conception up to the point of 40 weeks or so, the rate of loss is much higher in those who had the test.

Julia Cumberlege: I'm going to bring this session to a close because we are going to go into another session, another oral hearing. But before I do that, I'm just going to ask my colleagues if they've got anything else they want to ask or state, and likewise with you. So, Sonia, anything else?

Sonia Macleod: [Unclear].

Cyril Chantler: No, thank you.

Simon Whale: I've got one just very quick point. On the draft report, before you went back to the CHM, am I right in saying that the phraseology and the conclusion was something along the lines of it wasn't possible to reach a definite conclusion on association, whereas the final report says there is no causal association? That's quite a big change and quite a meaningful change at the very end of the process.

Ailsa Gebbie: Yes. Again, I think we'd need to go back to the minutes just to check exactly how that phraseology was changed. I don't think it changes the essence of our findings at all. It was, again, our way of trying to just make it clearer. Again, it's the words possible, causal, that everybody became very unhappy with that just right at the very end. It was done with the best of intentions to give greater clarity and I don't think it changes the conclusions of our report. I think we all stand by that, conclusively and unanimously.

Stephen Evans: I think the wording says, it does not support. That's subtly different from what you've said. It does not support. We didn't say, it doesn't support.

[Over speaking]

Ailsa Gebbie: Yeah, we're happy to go back and double check.

Stephen Evans: It supports no causal association. No, we didn't say that. It does not support causal association, and that's a scientific statement.

Julia Cumberlege: Valerie, anything else? Right. So if I could ask you, any final word you want to say?

Stephen Evans: I apologise for talking too much already.

Julia Cumberlege: It's been very interesting. Thank you.

Ailsa Gebbie: No, thank you.

Shirley Price: Can I just say that we'll send you the programme of our ...? I'll get that sent over to you. The only other thing, I just wanted to point out, in the slide from Professor Vargesson - and it was something that I remembered at the presentation, but of course it was presented - in fairness, presented - Professor Vargesson was presenting on published work. But again, from the science point of view, there is a slide that talks about partial recovery for 72 hours after being placed in fresh water following 24 hours' treatment. Again, this is looking at some partial recovery, not damage to eyes, ears or the fins, which is still evident at 96 hours.

It talks about dilution of the compound, but again, I'd like to understand a bit more about the mechanism behind all of that. That particular one, I think, is something that I would like to - if I have the opportunity, to investigate further.

Ailsa Gebbie: I would just like to say thank you very much for listening to us today. This was an enormous piece of work, I think done to the highest standards. I can't see it ever being replicated or redone. But we, as a group, totally felt for the suffering of the families who've been involved in this. Although we didn't find a causal association, we really hope the legacy of doing all this work will be that the recommendations are taken forward by health ministers and the government because we've tried to make this a forward-looking report. Anything we can do to improve the health of women and babies in this country is - will be very worthwhile.

Julia Cumberlege: Well, thank you very much indeed. I don't think we underestimate the amount of work you've done. Thank you very much indeed.

END OF TRANSCRIPT

Session 2: Association of British Neurologists (ABN) & Royal College Psychiatrists (RCPsych)

START OF TRANSCRIPT

Julia Cumberlege: So if I could introduce my colleagues here, and then you might like to say a bit about yourselves, and I'm not sure if you've got any statement, short statements you want to make, but it doesn't matter if you haven't. So if I could just say, I'm Julia Cumberlege. I was invited by the Secretary of State to chair this Review, with its three different aspects.

On my left is Sir Cyril Chantler, and he is the Vice Chairman of the panel, and on my right is Simon Whale, who is the third member of our panel. Next to Simon is Valerie Brasse, Dr Brasse, who is the Secretary to the Review. On Cyril's left is Dr Sonia Macleod, who is our Principal Researcher. So that's us.

So I understand that you've completed the COI that we asked you the statement on any issues you've got in terms of having any sort of connection with other organisations that might influence your views, and I think you don't have. I think the statements have been put forward, and also you've sent us evidence, and we're very grateful for that.

So if you'd like to start by introducing yourselves.

Heather Angus-Leppan: I'm Heather Angus-Leppan. I'm a neurologist and epilepsy lead at the Royal Free Hospital, so my interest is in general neurology, but particularly epilepsy and migraine. I'm here as the representative of the Association of British Neurologists on the Epilepsy Advisory Group.

Julia Cumberlege: Right, thank you very much. Yes.

David Baldwin: I'm David Baldwin. I'm a psychiatrist, Professor of Psychiatry, at the University of Southampton, and I'm here in my capacity as Chair of the Psychopharmacology Committee of the Royal College of Psychiatrists.

Julia Cumberlege: All right, well thank you very much indeed. Do you want to make any statements or anything, or should we just start with our questions?

Heather Angus-Leppan: Why don't you start with questions, and then we can...

Julia Cumberlege: So we've heard, because we've been right round the country talking to a lot of patient groups, and in this case certainly those that have been connected with valproate, and we know that they feel that on occasions, they've been misled by clinicians as to the risks associated with valproate.

We understand the practices related to informed consent, which is an issue that's come up time and time again, but they have changed since the 1970s, at that time.

But I just wonder if you could be kind enough to outline to your current practice and whether you feel the best practice provided actually gives enough adequate information for patients to understand the consequences of taking this particular drug.

Heather Angus-Leppan: That's obviously a central issue. I think that there is evidence from surveys that despite quite a lot of publicity, until recently, a lot of women didn't know about the risks of valproate. Epilepsy Action and surveys in other countries as well have suggested that, so it is something that needs to be addressed. For people who are going to epilepsy clinics, this is now I think very well covered. The risks of valproate are discussed, as well as the potential problems of alternatives, and I think that's something that needs to be emphasised as well, that sometimes valproate is the only medicine that will control a person's epilepsy, so it's quite a complex equation.

If there was an alternative that was as good as valproate, then we would always be able to use that instead, but it's not always the case, so people are facing sometimes very difficult decisions, having to weigh up a number of different factors. So I think that for those who are in a clinic, there is usually a good opportunity to discuss all of that. The concerns we have are really in terms of making sure that we have enough time and resources to make that discussion meaningful for the individual. That's an extremely individual decision-making process, and simply giving a lot of information without discussion is not adequate, so we need, we think, more resources to do that adequately.

Our other great concern is the people who are under the radar, who have been on, say, Valproate for a long time, who probably their symptoms are very well controlled, so they may not have contact with a specialist clinic. They may not even see their general practitioner very often and we need to identify those people and make sure they're given the information, because they're particularly vulnerable to not having the information.

Another group that obviously needs special time and attention and overlaps with David's area are people with intellectual disability, where often they won't be able to make a decision themselves, and that will have to be done in terms of best interest practice, which needs time and needs expertise.

Julia Cumberlege: So when you talk about the clinic, this is a clinic that is a specialist clinic in a hospital?

Heather Angus-Leppan: Yes, yes. Sometimes in a community, but usually in a hospital, so where someone would see either a specialist nurse or a specialist doctor who has expertise in epilepsy, in my case, or in other related areas.

Julia Cumberlege: So there is quite a danger that the GPs who are prescribing something like Epilim to control the problem that these women are suffering, they could easily just continue with the prescription, the woman continues to take the Epilim, and no question is put about the pregnancy and the result of...

Heather Angus-Leppan: I think that has definitely been a problem in the past. Because of the alerts that are now placed on prescribing, that's less of a problem, but it is still is potentially an issue, and it's difficult - we don't really have a clear idea of how - who is not getting the information. It's quite difficult to measure that.

Valerie Brasse: Can you say what proportion of the epilepsy population who might be taking valproate are not actually being seen regularly by a neurologist? They're stable, [clinician] stable, as you say, or they could be at a follow up through a GP. Do you have any idea how that proportion changes between those being seen regularly by a neurologist as opposed to those who go to a GP for their follow-up. Do you have anything?

Heather Angus-Leppan: It's difficult to give you - I can't give you precise figures. However, if I just give you some of the things we know about, first of all, people with epilepsy who are taking valproate are likely to be part of the one-quarter of people with generalised epilepsy, and of those, most will have had - it's unusual for general practitioners to commence prescribing of an epilepsy medication, so that's going to be extremely uncommon now.

So it will be people who may have been on it for a very long time, started a long time ago, before there was this awareness. It's going to be a small percentage, probably, but we don't know the exact figures.

Julia Cumberlege: So how do you - do you discuss with the patients about alternatives?

Heather Angus-Leppan: Yes, yes.

Julia Cumberlege: Alternatives that they can take when pregnant that will not have disastrous consequences.

Heather Angus-Leppan: Well, I think we discuss the whole range of those issues that you've highlighted. We discuss the alternatives. We discuss the risks and benefits of alternatives, because some of the alternatives also have a risk

of teratogenicity, and we also discuss the risk of not being on any medication at all in terms of the small risk of having a very major seizure, occasionally that people can sometimes die during a seizure and what the consequences would also be for their child if they had a major seizure. So we try and cover all those possibilities as relevant for the person, because obviously that will depend on whether they want to have children, when they're planning to have children, all those sort of factors.

Julia Cumberlege: So patients have told us in the past that they haven't been made aware of the risks, and in fact, we've heard from some patients when we've been around the country talking to them, listening, who have said, I would have preferred to take the risk of having a seizure...

Heather Angus-Leppan: Yes.

Julia Cumberlege: ...and clearly now, you're pretty convinced that women are actually told the risks and are made able to make the choices which might not agree entirely with your medical expertise, but you would respect those choices?

Heather Angus-Leppan: Absolutely. That is at the heart of the whole process. It's something that we have really championed, because we do think that we need to make sure we're not imposing our own view, our own worldview, on people, allowing them as much as possible to be given the information to make informed choices. Because there isn't one size that fits all, and people will - you mentioned there I have patients who have really severe epilepsy who have decided, as you've said, that they would rather take the risk of having severe seizures, perhaps, and being on a less efficacious medication than have the risks of teratogenicity. Others who say exactly the opposite, that they really - that they want to put their safety as the number one concern and that they will take the risk of teratogenicity, so there are a whole range of different views.

Julia Cumberlege: So do you in any way - I don't want to use the word train, but inform GPs, about the approach that you think should be taken?

Heather Angus-Leppan: We do. Whenever we write a letter, we try and summarise the discussion that we have, and we've all - we've been involved in publications discussing all of these issues, which GPs have access to, but in each letter, we try and summarise that so that it's something that is also hopefully educational for other discussions they may have.

Julia Cumberlege: All right. Thanks very much indeed.

Simon Whale: Yes, Professor Baldwin, could I just ask you - and obviously, some of these considerations, all of these considerations apply in the case of patients with bipolar disorder.

David Baldwin: Yes.

Simon Whale: But you're dealing with a very different cohort of people.

David Baldwin: Yes.

Simon Whale: So it'll be interesting to get your reflection on that.

David Baldwin: Yes, thank you. Yes, that's right, it's a very different area of medical practice, and the balance of risk and benefit obviously differs from one subject area to another. We know that about 24 per cent of women under the age of 50 who are receiving inpatient or outpatient psychiatric are exposed to valproate-containing medicines. A survey from the College - the Prescribing Observatory in Mental Health showed that there was evidence that those women had been warned of risks in only half of the cases...

Simon Whale: Sorry to interrupt, but do you know...

David Baldwin: Yes.

Simon Whale: What are the absolute numbers? Twenty-four per cent equals how many women?

David Baldwin: In the survey that was published, it was across 55 mental health - it's probably a few thousand if it was across 55 mental health trusts. I can get that information to you by sending the publication, but the point I wish to make, really, was that that's in the case of women. Valproate's mainly used in bipolar disorder in psychiatry, but it's also used in other areas as well, and I suspect those figures are similar for the other areas, such as schizoaffective disorder or schizophrenia.

When I became aware of the concerns relating to valproate and was in a position of being able to do something about it within the Psychopharmacology Committee, it struck me that the first step is really to review the evidence for where valproate is used and to look at all the possible alternatives. So obviously, you start off with acute mania, the treatment of women with acute manic episodes and then prophylaxis, the long-term treatment and prevention of new episodes and so on, which the committee did. In summary, there are always alternatives to valproate that have similar effectiveness and roughly similar tolerability.

- Valerie Brasse: So that's a big difference in psychiatry as opposed to...
- David Baldwin: Yes, completely. It's a different area of practice, and this is what then led to the writing of our guidance. I don't know if you've been - because we wanted to summarise the evidence and then remind people of the alternatives and then give guidance on how to change from valproate-containing medicines to other medicines. Obviously, we had to think about essentially a two-by-two table where you have the woman who is currently psychiatrically well or psychiatrically unwell and then is pregnant or not pregnant and we have to provide guidance on each of those four areas.
- But this guidance came out just before Christmas and has been circulated to all members of the College. It was also contributed to by members of the British Association of Psychopharmacology, and it's been distributed to all of their members as well. So the guidance has been distributed to all psychiatrists in the UK and another 900 people on top of that, and the College is trying to have a series of awareness-raising further publications through we have something called *Insight* magazine, which is very well read by the psychiatrists. We'll be having an article in that and discussing it with our International Congress and our divisional meetings and be [inaudible] to include questions about valproate and the [inaudible] next generation will be keenly aware of potential hazards.
- Simon Whale: How do you make sure the guidance of this importance is adhered to by those in practice? Or if it's not your role to do it, which it may not be, whose role is it?
- David Baldwin: Yes, well I think when the MHRA statements were published, my own Trust almost immediately was able to produce a list of patients, anonymised but with NHS numbers, that were sent to the individual psychiatrists within that Trust saying, these women under the age of 50 may well currently be taking sodium valproate. We urge an urgent review of these women, and I know that that system worked in our local Trust.
- I think that's probably what you have to do. You have to devolve it down to not the lowest level, but the most immediate level to the consultants who are working.
- Simon Whale: Has that happened in other Trusts, as far as you're aware?
- David Baldwin: As far as I'm aware, it has. I don't know when it's happened in all Trusts, but I know other colleagues where a similar approach has been used.
- Simon Whale: So it's the employer who should...

[Over speaking]

David Baldwin: Yes, I think so, and I think it would be a very careful liaison between Trusts, medicines management committees and the pharmacies, including the community pharmacists.

Cyril Chantler: Can I ask you, in the appraisal and revalidation process...

David Baldwin: Yes.

Cyril Chantler: Your Royal College, the colleges have a relationship with the General Medical Council to authenticate.

David Baldwin: Yes.

Cyril Chantler: Could you explain what that is and how the College of Psychiatrists might take the advice you've given and check it through the appraisal process?

David Baldwin: Well, the appraisal process is obviously based to a certain degree on the continuous professional development needs of individual clinicians, together with mandatory training and various other educational activities. At the moment, the College doesn't have any input into that, so that would have to be a new system to be...

Cyril Chantler: But it does set the standards which the GMC relies on you to determine what those standards are and compliance with good practice advice and keeping up to date I assume is part of that standard.

David Baldwin: Yes.

Cyril Chantler: If there was evidence in the appraisal process of somebody not doing that, I would imagine that would be then the person appointed in your Trust as the person who validates on behalf of the GMC would be informed of that, presumably.

David Baldwin: Yes.

Cyril Chantler: I don't want to put words in your mouth.

David Baldwin: No, but it could be made a requirement, couldn't it, as part of the annual appraisal process, that the clinician provides evidence that they have read recent documents relating to the safety of medicines in their particular area?

Cyril Chantler: Yes. Now, is it?

David Baldwin: No.

Cyril Chantler: Would that be a good idea?

David Baldwin: Personally, I think it would be a good idea.

Cyril Chantler: How can you make that happen?

David Baldwin: Well, as Chair of the Psychopharmacology Committee, I suppose all I can do is have discussions with the College Council and the Registrar and the President. I imagine, having had strong support from the Registrar and the President for the development of this document, that they would be minded to agree, but obviously that's a discussion that I would need to have.

Cyril Chantler: All right.

Valerie Brasse: I'm assuming the other groups would be little there that those who deal with like the CQC would provide a unit itself to say that if you are looking at the Division of Psychiatry Services...

David Baldwin: Yes.

Valerie Brasse: ...you would expect to have seen evidence that this is being followed.

David Baldwin: Yes, yes, that's right.

Valerie Brasse: But again, it's making that connection and then whether that's going to happen.

David Baldwin: Yes, yes. That's a very good idea.

Simon Whale: Can I just come back to the 24 per cent figure that you mentioned earlier?

David Baldwin: I'm sorry?

Simon Whale: The 24 per cent of women of childbearing age.

David Baldwin: Yes, yes.

Simon Whale: So half of those were not aware...

David Baldwin: Well, there's no documented evidence that they were warned, and that's a slightly different matter. You have to assume that if it's not documented, then it didn't happen.

Valerie Brasse: Didn't happen.

David Baldwin: Didn't happen. You have to assume that.

Simon Whale: So my question is whether since the introduction of the Pregnancy Prevention Programme...

David Baldwin: Yes.

Simon Whale: ...you think or you know that that statistic has improved?

David Baldwin: I don't know whether that's the case. The Prescribing Observatory on Mental Health is led by Professor Thomas Barnes. He is a member of the Psychopharmacology Committee. He has talked about how we could conduct another audit of the 55 Trusts. I'm pretty sure the College would be very keen to do that.

Heather Angus-Leppan: May I make a suggestion? The risk acknowledgement form, which all of us have to fill out if we're prescribing valproate could be made an online form, which would allow us to gather information about the outcome of these women too in an anonymised way, and to see - firstly, to check, to look at the rate of information, correlate that with the number of prescriptions to females and see how those people are doing as well. So we gather information about their safety as well, which is not being done at the moment. We're missing a golden opportunity.

Cyril Chantler: There is a registry. There is a registry in Ireland.

Heather Angus-Leppan: Yes, but that only - that is only 25 per cent of all people.

Cyril Chantler: I know it is, but it's likely the women would give permission to go on the registry, which you have to seek through GDPR.

Heather Angus-Leppan: Yes.

Cyril Chantler: But would it logically follow what you just said, that that could then link to such a registry.

Heather Angus-Leppan: That could as well. Yeah, that could link in, but if you had those forms online, then you could - we've got the technology to do that in a very clever way and gather the information.

Simon Whale: Why hasn't what you're suggesting, which sounds very sensible, happened already?

Heather Angus-Leppan: Because it costs money.

Valerie Brasse: At the moment, we're right in thinking we don't know how many are on the PPP?

Heather Angus-Leppan: We're right in - we have a piece of paper, which we give a copy to the patient. We give a copy to the GP. A copy's meant to go in the notes. You can imagine that the capacity for one of those forms to be lost, not to get in the right place, is immense, and then to try and gather back the information from each person's notes, it's cumbersome, so I really think we should do this. I've made that suggestion.

Sonia Macleod: Why was the PPP made as a paper system, when there's clear evidence, certainly international evidence, that you can run similar pregnancy prevention programmes as online systems?

Heather Angus-Leppan: I think it would be a good idea to make it that way and to take a leaf out of other countries who do this a lot better than us, such as Scandinavia.

David Baldwin: A paper-based system wouldn't really work in psychiatry, because half of the Trusts use exclusively electronic medical records. It has to be on...

Cyril Chantler: Can I just ask Professor Baldwin about off-label prescribing.

David Baldwin: Yes.

Cyril Chantler: So in the case of some psychiatric disorders, valproate is used off label.

David Baldwin: Yes.

Cyril Chantler: Can you explain why and how that works, and whether you've got any concerns about that?

David Baldwin: Yes, so off-label use would be in patients with schizophrenia or schizoaffective disorder, which is very similar to bipolar disorder - recurrent depression, and in people with various forms of personality disorder, I suppose. The College has produced guidance on off-label prescribing, which came out in December 2017, and it starts off with I think 10 key points for practice, and for a start, becoming very aware with all the potential benefits and potential risks of the proposed intervention, and weighing up in the balance against other forms of treatment and then talking about discussing it with a colleague if needs be, making sure you've had a full discussion with the patient, and if needs be, with a relative and so on.

I wrote it, and we know that that's been quite widely adopted in Trusts across the UK. That guidance, as I say, came out in December 2017. It probably will need to be looked at again towards the end of this year. Most College documents, we look at them after two years, but I don't imagine that it would change. It's about principles of practice, but we'll obviously have an open mind about that.

Simon Whale: So when it's - if valproate is, or when, it's used off label, and if the woman then goes on to have a child, which is affected by valproate spectrum disorder...

David Baldwin: Yes.

Simon Whale: Where does the responsibility lie in that situation?

David Baldwin: Well, I suppose it depends on the degree of the conversation that the clinician had with the patient at the start of the pregnancy or even prior to pregnancy, and you need to make sure that the clinician follows the body of opinion regarding what constitutes good practice. That's why I was concerned a year and a half ago to make sure that there was very clear guidance as to what constitutes good practice when considering the prescription of medicine outside the terms of its product licence. The College initially produced its guidance in 2007 on this, and we revised it in 2017, and we looked at it periodically to make sure it was still okay.

But we revised it in 2017, because the GMC guidance relating to this aspect of medical practice, the wording of that had changed, and we wanted to make sure that our wording accorded with that in the GMC statement.

Valerie Brasse: Because in fact when you talk about sodium valproate not needing to be the first line of treatment...

David Baldwin: Yes.

Valerie Brasse: Some of the things you're suggesting would be off-label prescribing, when you [unclear] certain psychiatrics [physicians] comply with their [unclear].

David Baldwin: Where it's mainly used is in acute treatment of manic episodes, and there are always other treatments, which are possible, which...

Valerie Brasse: But those too would be off-label?

David Baldwin: Yes. Yes, and that's the case usually isn't it, with a pregnant woman?

Valerie Brasse: So when it comes to something like adverse event reporting, does that fall out with the off-label usage?

David Baldwin: I'm sorry, I just - an antipsychotic would not be off-label for an acute manic episode, because in the BNF, some of the antipsychotics are described as anti-manic drugs, so it's not off label.

Valerie Brasse: So I may have read it wrong, but I thought you were saying that for some of these where you're suggesting not using sodium valproate, the use of the drug in those circumstances in a given range might be off-label.

David Baldwin: It would be off-label in patients with schizophrenia and in recurrent unipolar depression, but in mania, bipolar disorder, it is within label.

Valerie Brasse: Okay, so we have a situation now where we are suggesting there are some areas or concerns psychiatry will be using them off-label. Adverse event reporting...

David Baldwin: Yes.

Valerie Brasse: When you're using an off-label drug...

David Baldwin: Yes.

Valerie Brasse: The same sort of rules apply, or is it no one actually taking any notice about it because it was never meant to be prescribed for it in the first place?

David Baldwin: Well, our guidance to our members is very clear that in that situation where you are prescribing a medicine outside of the terms of its licence, particular vigilance is needed, and adverse events should be sought and documented and reported as necessary.

Valerie Brasse: Okay, and do you know that that's what happens?

David Baldwin: No.

Simon Whale: Do you know - sorry I keep asking about numbers. Do you know how many women are receiving valproate for off-label use, or how many patients in total?

David Baldwin: I wouldn't want to guess that. I could very easily provide that information on the basis of the POMH survey. As I said, it was 24 per cent of women across 55 trusts, women under the age of 50. I could get the number for you and then we could look at that as a proportion of all trusts across the UK. It would be easy to do that, but I'm conscious that I'm being recorded. I don't want to give the wrong number.

Simon Whale: No, that's fine.

Sonia Macleod: That would be lovely, if we could have a follow up afterwards.

Simon Whale: But that would provide us with both licenced and off-label use?

David Baldwin: Yes, that would. Yes, it would.

Simon Whale: Yeah, that would be very helpful.

Julia Cumberlege: Sonia?

Sonia Macleod: What I was just going to say is in terms of thinking also in terms of women who are epileptic, if they are - if valproate for example is going to be used outside of the terms of its label, so the terms of its label are quite clear. There must be a PPP in place, and if people...

Heather Angus-Leppan: Sorry, I didn't hear the last bit.

Sonia Macleod: In terms of using valproate outside the terms of its label, which says there must be a PPP in place...

Heather Angus-Leppan: Yes.

Sonia Macleod: ...if women choose not to use contraception and are still on valproate, and that is a choice that is taken...

Heather Angus-Leppan: Yes.

Sonia Macleod: ...what are the responsibilities of a doctor in terms of follow-up in terms of presumably that then becomes an off-label prescription, if you are aware of that?

Heather Angus-Leppan: We - at the moment, that obviously needs to be incredibly carefully documented. The PPP form - what our practice would be, would be to annotate that in a lot of detail and then also in the notes as well. We're also - we've made the point that there are times when the PPP is not appropriate, for example, because of someone's religious beliefs which preclude them from using certain forms of contraception, some major health-related problem with using the forms of contraception suggested, or if they have significant intellectual disability to the point where they can't make informed choice, then they would also not be able to make informed choice about having a sexual relationship.

So the only way in which they could become pregnant is if they were abused, so their family and their carers may think that it's not a fair burden to place them on regular injections, for example. So we're annotating that form very carefully, but we have made a plea that the form be given - that there are exceptional circumstances where it's not appropriate, and that needs to be taken into account.

I think in medicine, it's important not to be too rigid and too dogmatic, because there are going to be exceptions certainly for epilepsy, and I think maybe even in psychiatry. There may be times although you go through all of the standard treatments, someone is still resistant or has a problem, that you may end up thinking valproate is the right choice for them if they are agreeable and they understand. They may decide that that's the best choice for them, so I think we need to have some flexibility.

Cyril Chantler: We live in an age of increasing specialisation compared with when I qualified it was a long time ago.

Heather Angus-Leppan: Yes.

Cyril Chantler: We think there are maybe as many as 20,000 people who have been affected by valproate in England, and the suggestion has been made that to meet their needs, both medical and social, that it would be useful if there were a limited number of centres that acted as hubs in different parts of the country, where they could go to get very special expertise and could also help around their regions in making sure services are adequate. For instance, in clinical genetics, it's been pointed out that there is a - this is a very special sort of genetics that is interested in valproate and genetics.

The same thing might apply to neurologists, it seems to me. There are some neurologists who specialise in epilepsy and so forth. The point is, do you think from your point of view and your point of view that such centres would be useful?

Heather Angus-Leppan: If there are enough and if they have enough resources, then yes.

Cyril Chantler: Well, you did mention - I made a note you want more resources. This might be a way of providing them...

Heather Angus-Leppan: Yes. I'm sure I'm not the first person to have asked for that. But I think we also have to obviously take into account the practicality that a lot of people with epilepsy can't drive, so getting to a centre that's not close to them is particularly burdensome. Also, they may have developed a wonderful relationship with a general neurologist who's looked after their epilepsy for a long time, and they may not really want to go to a super-specialist.

Cyril Chantler: That's why I said it's a hub, so if you were in the hub or wherever that was, you would not only - you'd have a register, but you'd have a relationship not only with the patient but with the neurologist.

Heather Angus-Leppan: Yes. Yeah, that...

Cyril Chantler: As a paediatrician, I used to have a relationship with general paediatricians around the southeast, for children with kidney disease.

Heather Angus-Leppan: Yes, that could work very well. Yes.

David Baldwin: Yes. I think it could work well, too, actually, if it were done on a regional basis with close liaison between neurology and psychiatry and the other disciplines. I suppose we know quite a lot about what happens to babies that have been affected, but undoubtedly, more could be understood about their development and course into adult life, so I think it would be a useful clinical service, but also an opportunity to actually characterise the problems that people have in more detail. That should lead to greater understanding of the problem.

Cyril Chantler: Thank you.

Valerie Brasse: Can I ask, giving the right contraceptive advice is obviously so terribly important in both of your fields and talking about prescribing valproate. Are neurologists and psychiatrists comfortable doing that?

Heather Angus-Leppan: No. We can't give specialist contraceptive advice, and we have to obviously liaise with the general practitioner or with - sometimes with a specialist gynaecologist, and that's not within our expertise. We can only give very general signposting about that.

Valerie Brasse: So they come to you, and valproate is the desired choice...

Heather Angus-Leppan: Yes.

Valerie Brasse: ...in terms of treating your epilepsy, realising there is a problem, because this is a woman of childbearing age, so the first thing you do is refer them somewhere else [unclear] their contraception.

Heather Angus-Leppan: Well, sometimes it's already quite clear. For example, if someone had an intrauterine device which they were happy with, then that's quite straightforward.

Valerie Brasse: On the basis they told you that.

Heather Angus-Leppan: Yes, yeah, so we have to make inquiries. We have to have an understanding of what their contraception is, and then if it's not - if it's not within that guidance, then we have to liaise if they need more specialised advice about it.

Valerie Brasse: So that would be a specialist gynae or a GP.

Heather Angus-Leppan: Or - yeah, it depends. Some GPs are very skilful at that and that's well within their...

Valerie Brasse: Some are clearly not, because they told us last time. They refer back to the neurologists.

Heather Angus-Leppan: Yes.

Valerie Brasse: In psychiatry?

David Baldwin: Well, I think it's timely in a way. In our guidance, we talk about an increased role for the perinatal psychiatry teams, and of course, recently announced an expansion in perinatal psychiatry services, and I know many psychiatrists who are currently working in the area of general adult psychiatry are actually going to be moved into perinatal psychiatry. So I think there's an opportunity for raising awareness, increasing people's confidence in discussing contraceptive matters, and perinatal psychiatry now tends to deal with women in the late stages of pregnancy and the early weeks after delivery. But actually, there is an opportunity for it to go back in time.

Valerie Brasse: Yes.

Julia Cumberlege: Can I ask you a much more general question, and we're obviously looking at these three different areas, but what has united them – a), of course, they're women's problems, and we understand that. But secondly, they are areas where the patients themselves have been so concerned that so little has been done to help them with these different conditions, and with valproate we've got some patient groups who are terribly well informed. I'm sure they come across your desk, as they do ours.

They've done a lot of research, but actually it has been Parliament in the end - it has been the Secretary of State, who has brought this to the attention of the population generally and certainly to the medical profession and others. Can you think of any ways that actually we should listen much more carefully to what people are saying? I'm talking about patients who have been affected in these areas or indeed in other areas?

How do we bring that to fruition in terms that actually action takes place? This Review was stimulated by the patient groups. That shouldn't really happen. One should have mechanisms that it brings this to the fore without having to involve people putting in so much effort, so much of their lives in order to ensure that attention is given.

Heather Angus-Leppan: In terms of making sure that healthcare professionals are doing a better job of this, I think that there's a need for not only sticks, because there are sticks, there are punishments if you don't do the right thing, but also a change in the focus and the way we're thinking of patients. It has happened a lot over the last decades. Even when I started medicine, we thought that you gave information to people, you told them what to do, and that was thought to be the way that you treated patients. That was the model, and it has reversed, and it is all about patient empowerment, and that is - to make that more than just an empty phrase, then I think we need - that has to start with education of doctors and nurses and everyone who's involved in looking after patients.

That is about respecting their rights for full information, which is what recent rulings have stressed, and which again is not just - it's going away from the paternalistic attitude that you just tell people what you think they should know and you make a decision you think is in their best interests. I think a lot of us are aware of that and doing our best. It's always - it needs to be continuously promoted from when people are starting to do nursing and medicine.

Julia Cumberlege: Because collectively they can make an impact, and they have through the parliamentary system...

Heather Angus-Leppan; Yes.

Julia Cumberlege: ...and other methods. But as individual patients, it is quite difficult to feel empowered.

Heather Angus-Leppan: Yes, well, I think that needs a lot of on-going work. I think we also have to remember the patients you're not hearing from, who want to stay on valproate and want their rights respected as well, not just the more vocal members. It's very important.

Julia Cumberlege: Thank you.

Simon Whale: Can I just ask about issues around consent, as Baroness Cumberlege mentioned at the beginning. We've heard from many, people about how they didn't feel that they were properly informed and couldn't make them the kind of choice you would want them to be able to make, based on what you just said.

I guess in psychiatry, there's a cohort of people who it's quite difficult to provide informed consent to, or for them to provide informed consent to you. How do you tackle that situation, and is it a significant problem?

David Baldwin: In relation to valproate, I suppose the area that might cause greatest concern is in women with acute manic episodes, who may well have significantly impaired insight. In the other areas, I think there's always time to prescribe alternatives and to have lengthy discussions, if you are thinking about valproate. But in acute mania, I personally don't see the need for valproate to be prescribed, and this is what we say in our guidance, because there are alternatives that are safer in pregnancy. The antipsychotic drugs are.

Now, of course, you may still be prescribing at a time when a woman is not able to provide full consent, but at least you're using a medicine that is potentially less hazardous. So I hope that the guidance is clear, that in that situation, it makes sense to use a tried and tested and safer medicine. I can't see a reason for someone to prescribe sodium valproate in a lady experiencing an acute manic episode.

Sonia Macleod: Would you prescribe valproate in a man having an acute...

David Baldwin: Yes, you could. Yes, you could.

Sonia Macleod: But would you?

David Baldwin: Personally, I don't. I very rarely prescribe valproate, because I don't find it a useful drug. We know that there are men who are prescribed valproate...

Sonia Macleod: I guess what I'm trying to get at is it's not that women with acute mania are being offered a slightly less efficacious drug because of the risk they'll get pregnant. It is that it isn't a drug that you will necessarily use.

David Baldwin: I think obviously the balance of risk and benefit, you get into that in women, but usually in acute mania, you're wanting to get the patient settled very quickly, and valproate is not as good as the antipsychotic drugs in doing that, and that's particularly important in a robust young man, actually, that you get them settled quickly.

Sonia Macleod: Yes, I can see that. Yeah, okay.

Valerie Brasse: Can I ask, just about looking back and about looking forward, valproate's had about a 45-year history. One of the things that is really at the heart of the patient concerns is who knew what, when? The manufacturers are very clear that they've always known about its teratogenicity, and that's been put out in the data sheet, the data sheets that went to doctors, not from a patient information booklet. You're both here as the representatives of your associations or colleges. To what extent should

doctors have been much more upfront, knowing what they should have read in the data sheet but not actually saying to patients back a number of years, this is a risk that you're taking?

Heather Angus-Leppan: I think that clearly we have a duty to inform about all of the risks of any medication we try and about the benefits as well of the medication. All of the - so I think that most of us have been or certainly within specialist care, have been informing about teratogenicity of valproate for a long time.

Valerie Brasse: Way back, at the point at which you would have received the information on...

Heather Angus-Leppan: Well, I wasn't - way back, I wasn't actually working...

Valerie Brasse: I realise I'm asking you, but some responsibility.

Heather Angus-Leppan: Yes, I think people have been trying for some time. However, I think that the degree of teratogenicity has become more highlighted recently, definitely, and it's more - it's put in more stark terms now, definitely. But we - in epilepsy care, you have to - you have a number of other factors like the teratogenicity of other medications, the benefits of other medications in terms of seizure control versus valproate, so it is a complex equation.

Valerie Brasse: I know it is. I suppose the issue for me is that whatever, that there was information in those data sheets, and there were studies happening alongside that, and the extent to which the colleges are taking cognizance of those studies, what they're saying, is raising concerns, and are they - should they be saying to doctors, look, you've got these patients coming in. You should be saying something to them, and I'm not sure where that responsibility...

David Baldwin: I was looking back into the history a couple of weeks ago, actually, comparing some talks, and it struck me that the first case report was around about 1980.

Valerie Brasse: A long time ago.

David Baldwin: Yes, and the case series, just a couple of years after that, and then I was thinking about when does evidence become reliable, and I thought, well certainly at the time of pharmaco-epidemiological studies, where you can look at potential confounding factors, and then at the time of meta-analysis of those pharmaco-epidemiological studies, which seem to be coming through around about the mid-1990s.

Valerie Brasse: So...

David Baldwin: Yes.

Valerie Brasse: A lot of babies were born...

[Over speaking]

David Baldwin: But you want a time when the evidence is reliable and unequivocal.

Valerie Brasse: But the question is, did it happen soon enough?

David Baldwin: Yes, yes.

Valerie Brasse: I think that's a big question that remains thus far unanswered.

David Baldwin: Indeed, but from that point onwards, then it's clear that people should be warning people.

Valerie Brasse: They probably are. Going forward, we have a new generation of anti-epileptic drugs, like Keppra.

Heather Angus-Leppan: Yes.

Valerie Brasse: Are you convinced now that we could not have a repeat of the valproate story for a new drug like Keppra?

Heather Angus-Leppan: No. We can't be convinced of that at all. We - there are...

Valerie Brasse: Are studies being done, the adverse events reports flowing? Are we doing it better?

Heather Angus-Leppan: I think we are doing it in - we've got pregnancy registries. We've got reporting. It's ad hoc. I think we should be doing it in a much more rigorous way than we are. We should be gathering information about all pregnancies, and some countries do that. I think we're doing it pretty sloppily, quite honestly.

Sonia Macleod: So what would we need to do to make it better going forward?

Heather Angus-Leppan: We need to have a registry of all women who have epilepsy who become pregnant without and with medication, so that we're monitoring all of the registries. The UK is the best one. It has about a quarter of people who sign up to it, and some of the others...

[Over speaking]

Valerie Brasse: Follows every month until the baby is three months old.

Heather Angus-Leppan: Yes. So I think that we could - that should be incorporated, and I think from people I speak to, most women would be quite prepared to do that anonymously and would be pleased to do it.

Sonia Macleod: How long should the follow up be?

Heather Angus-Leppan: Well, we need to follow up for quite a few years, until at least school age, at least until the five or six, when you...

Sonia Macleod: It's the long-term...

Julia Cumberlege: Because it's often at school age that things really become apparent.

Heather Angus-Leppan: Yes.

David Baldwin: Yeah.

Cyril Chantler: Would they want to be anonymous? Most people I've spoken into in the registries are delighted to be on a registry, because they know then that the research is being done which will benefit them. So patient-identifiable information may be useful to them, and so it is true that under the confidentiality rules, you've got to do it anonymously, but if you want patient identifiable information, you've got to ask the patient.

Heather Angus-Leppan: Yes.

Cyril Chantler: But I would have thought they would probably say yes, wouldn't they?

Heather Angus-Leppan: Yes. I think a lot of people would opt in to being un-anonymous, whatever the word is. Identifiable, I think, it's probably...

[Over speaking]

Cyril Chantler: ...security.

Heather Angus-Leppan: Yes.

Simon Whale: Who should run such a registry?

Heather Angus-Leppan: The government. It should be a centralised initiative funded by the government, so that it's really impartial.

Cyril Chantler: That's not the same as who might run in. Who funds it?

Heather Angus-Leppan: Yes. Well, I think you'd need to have a consortium of people from different areas, neurology, psychiatry, epidemiology, pharmacology, who can make sure that the data is well analysed, and statisticians, of course, various entities.

David Baldwin: In psychiatry, we have a monitoring system for the drug clozapine, an antipsychotic drug, and when the drug became available again, having been withdrawn, the requirement was that all patients exposed to clozapine would be part of a monitoring service. That was very important, because you need to monitor the blood count every week initially and then less frequently, and then generic drugs became available. But for those manufacturers to get a licence, as it were, for their product, they also had to agree to offer this monitoring service, and patients with schizophrenia who generally don't like being monitored and are often quite worried about being monitored actually seem to take part in this without difficulty.

There are people who are in sight less and don't want to have treatment, but the concern isn't about being on a monitoring service. It's for other reasons, usually. But the system has been running since 1992 for clozapine, and it works well.

Sonia Macleod: But it's a fairly low level of usage, isn't it?

David Baldwin: Yes, and it probably should be used more, actually. Clozapine should be used when people have not responded to two antipsychotic drugs, if possible, and so it should be used more, but it's been running a long time, and so very large numbers of patients have actually gone through this process, and it might be that if you look at the clozapine monitoring service, it will provide some suggestions of how this can be done in another area.

Julia Cumberlege: I'm going to draw this to a close, if that's all right with you, and I'm going to ask my colleagues if they've got any final questions they'd like to put to you, and likewise, if you want to ask us anything in particular. So, Cyril...

Simon Whale: No.

Julia Cumberlege: Right, so...

Heather Angus-Leppan: Would you like us to send some more information that we think might be related, some facts and...

Sonia Macleod: Yes, please.

Heather Angus-Leppan: ...things that are related to what we discussed.

Sion Whale: Yes, please.

Heather Angus-Leppan: We send that to Donna?

Julia Cumberlege: We are great Hoovers. We like to...

Heather Angus-Leppan: You like to stay up all night reading documents.

David Baldwin: I hope to send you a quick summary of what we're intending to do to raise awareness relating to this document.

Julia Cumberlege: Right, well thank you so much.

Cyril Chantler: Thank you very much.

Heather Angus-Leppan: Thank you.

Julia Cumberlege: It's been a really interesting session, and I do want to thank you for coming. It's been really, really helpful.

David Baldwin: Thank you very much. Thank you.

Heather Angus-Leppan: Thank you.

END OF TRANSCRIPT

Session 3: Royal Pharmaceutical Society (RPS)

START OF TRANSCRIPT

Julia Cumberlege: Would you like to introduce yourself?

Sandra Gidley: Right, yes. My name is Sandra Gidley. I chair the English Pharmacy Board at the Royal Pharmaceutical Society, which is a bit of a convoluted title, but we are where we are. The English Board basically deals with health policy in England and because we have a devolved structure, so there are also boards in Wales and Scotland. But on GB-wide policy issues we would try and have a joined-up approach which can be sometimes a bit weighty. I'm a community pharmacist by background, and I've chaired the board for four years.

I don't know if it's a declaration of interest, Simon Whale's company Luther Pendragon provides a secretariat up to the All-Party Pharmacy Group of which the Royal Pharmaceutical Society is a sponsor, I think is the correct term. So that's probably about it really. I've taken an active interest in the valproate issue in the last four years, and I also sit on various bodies on the MHRA which now deals with this. So I've probably had a fairly close interest for that length of time. So do you want me to just say a little bit more about the organisation just to clarify for the record who we are and what we do.?

Julia Cumberlege: [Unclear]

Sandra Gidley: The Royal Pharmaceutical Society is the professional leadership body for pharmacists. Up until the year 2010, there was a joint regulator and leadership body and the government of the day decided, in my view quite rightly, that the regulatory function should be separated from the professional leadership function. So we're a fairly new organisation, and the regulation side is now in the province of the General Pharmaceutical Council. So we probably won't be able to answer any historic questions about governance and from a regulator's perspective. Also, just to clarify, the word pharmaceutical can be a bit misleading, it implies links with the pharmaceutical industry which we don't really have.

We are occasionally sponsored by a company for a piece of work that is generally open and transparent. We represent pharmacists from all aspects of the profession, from hospital, community, also those in academia and the emerging roles such as pharmacists who are based in GP's surgeries. We also have a section of the membership which represents pharmaceutical scientists. Now they are not on the register,

but they generally have a medicine's related degree in some shape or form and generally work in the pharmaceutical industry. So that's generally who we try and represent. Right, do you need to know any more about us?

[Laughter]

Julia Cumberlege: I think we've got the gist of it.

Sandra Gidley: Right okay.

Julia Cumberlege: Thank you.

Sandra Gidley: So do you want a history of how I know that the organisation has been involved in the valproate issue because that's been our main focus? We haven't really had any dealings with the pelvic meshes and actually very little with Primodos.

Julia Cumberlege: Just on Primodos, and it's only one question I've got on Primodos. But I just wondered, and you probably know about the way that it was dispensed by doctors as a free sample that was given to women to test whether they were pregnant or not?

Sandra Gidley: Yes.

Julia Cumberlege: Since that time, presumably practices and things have changed, and perhaps you'd like to tell us a bit about that?

Sandra Gidley: A bit about what, the practice of free medicines. I mean generally well going back to when I was first on the register there was a rather unhealthy practice. It's fair to say that the pharmaceutical industry wasn't very well regulated. This is anecdotal, but I saw it all the time in practice; the pharma companies would often give doctors free samples of various drugs and so that they tried them out. They were far less regulated than they are today with regard to what incentives might be given for prescribing, should we say.

So, 40 years ago when I first came on the register we were in a very, very different position to where we are today. So, all of that has now been tightening up, free samples are not generally allowed. I don't think any GP who was doing things by the book today would give out anything like that to test, particularly for a pregnant woman. It's almost unthinkable.

Julia Cumberlege: Right, well that's very comforting I must say. So, can I just ask you then about pharmacists and their role in protecting patient safety? We've heard from patient groups that the Pregnancy Prevention Programme for

valproate hasn't been implemented consistently across the country. Can you tell us a little bit about how that compliance should be ensured?

Sandra Gidley:

Well, from a pharmacy perspective, the pharmacists obviously don't implement the Pregnancy Prevention Programme. But if a woman is having a sodium valproate prescription dispensed at her community pharmacy, there are certain procedures that should be followed. So, most important is that we check whether the woman has a plan in place. Obviously that has to be done yearly, and it's fairly new so getting the message across to everybody has been quite a challenge. But what should happen is the pharmacist or member of the pharmacy team were to have a conversation to ask whether the woman was aware of the risks of valproate and whether she was on a Pregnancy Prevention Plan.

There is a booklet that should be given out, and there is a card. The booklet only has to be given out once, but the card should be given out at every dispensing, and it's an aide-memoire. Also, the packs that are given out should have the pictogram on it which depicts a heavily pregnant lady with a cross, which - it could look as though you should say don't get pregnant, but I think the message is don't take during pregnancy. Now those conversations should be recorded, and most pharmacists do. I work as a locum so I've been spot-checking this, it's my little hobby horse when I go in. I think the record keeping is happening.

What is sometimes not happening, if I'm brutally honest, is occasionally the card isn't given out a second time, or the packs aren't dispensed in the packs with the pictogram on. They may be re-dispensed into a white pack. There are stickers available from the manufacturers, and these should be affixed. But I think the differential is in talking to the people that I've queried why they're not doing it, is staff say well they've had the card, they've had the leaflet so surely, they know? We've made a record.

Talking to the patient groups, they are very clear that the message needs to be given every time because they say that sometimes part of the condition is short-term memory problems and memory loss. But that little part of the story does not seem to be communicated to the pharmacy teams in its entirety. It's quite a difficult message to get across because actually, some women who are living with epilepsy might be quite offended at the idea that they might not remember from one month to the next. So it's quite a delicate area.

But generally there is a good awareness of this in pharmacies, and there've also been a couple of audits to audit the women coming in and check that they've had a plan. Now we've produced a flow sheet - you've

probably seen this of valproate [unclear] pathway. That's quite clear that if the woman is not on a plan, she should be referred back, but the medicine should be dispensed because there are dangers to a woman living with epilepsy in not taking the medicine.

Julia Cumberlege: Can I just ask then two things arise in my mind. First of all, I think you've got pharmacists who are prescribers.

Sandra Gidley: Yes.

Julia Cumberlege: So, from the point of view of those people, and I imagine it's a small minority of the workforce, do they have the patient record? Do they have information about the patient?

Sandra Gidley: Right, so there are pharmacist prescribers, and they are in many settings. There are relatively few in community pharmacy, and most would only work within their sphere of competence. So, usually when a pharmacist becomes a prescriber, it's in a particular area of medicine. It's only when they can demonstrate competency in other areas that they would extend that in any shape or form. So it is extremely unlikely that - there may be one somewhere so I'm not saying never, but it's extremely unlikely that there would be a community pharmacist in the role of prescribing sodium valproate.

If they were based in the community, it's just unlikely that they would have access to the medical notes. There are a small handful of pharmacies around the country that do. It's possible that a pharmacist in a hospital setting who is a specialist in this area would prescribe, but they would access to the notes in that case.

Julia Cumberlege: Right, because I was involved in the committee that were looking at specialists in pharmacy and with pharmacists, and I remember it was on PD, Parkinson's Disease, we were looking at specialist pharmacists for that. But I take your point that they're likely to be in a hospital setting...

Sandra Gidley: Yes.

Julia Cumberlege: ...as opposed to in the community. We've heard from the patient groups that what you have described in terms of the leaflet going out and the packs. Some of them are just white, and they haven't got the warnings on them. So, we've heard from them, and they've done a survey, and it shows really that there are - and they've videoed it so we can see exactly what's been happening or hasn't been happening. I'm just wondering from the point of view of your organisation, and I do understand you're

not a regulator, but what can you do to ensure that the pharmacists are fully aware of what should be happening from women with epilepsy...

Sandra Gidley: [Unclear]

Julia Cumberlege: ...and who are taking sodium valproate?

Sandra Gidley: Well we have done quite a lot over the years. Before even there was ministerial interest in this subject, we had produced a briefing note on valproate because we'd noticed that the advice about the risks had changed and felt that was appropriate. That would have been communicated to pharmacists generally via email. Not all pharmacists are members of the professional body, sadly, we have over half the register, but not everybody would necessarily see that. But we did also - we regularly meet with the superintendent pharmacists.

At one of the meetings in 2015, I actually highlighted this issue, and they referred it to the Community Pharmacy Patient Safety Group headed by Janice Perkins and looked at what was possible. I have to say some companies responded very enthusiastically to try and do something; not all did, but there was actually with the patient safety group an opportunity to have another part of the system, looking at it if you like. That group has representatives on it from a lot of large multiples, so they've done some work to try and disseminate.

The problem I think is in practical terms that sometimes this information only goes out once or twice and it's the usual - it's not an excuse, it's just a reality these days, the paper overload in a busy community pharmacy plus a lot of electronic materials that come your way. Sometimes, trying to work out which actually is the most important and the most relevant.

But we also worked with the pharmacy media to run a number of articles around this issue, around one of the epilepsy awareness days. So, there was quite a lot of information going out at the time, and there have been reminders since.

I'm also aware that the General Pharmaceutical Council wrote to all the pharmacists and the pharmacy technicians reminding them of the change in dispensing of valproate. I think that had an impact because people generally read things from the General Pharmaceutical Council because if you don't adhere to what they say, then you may lose your livelihood. The Chief Pharmaceutical Officer has also contacted all pharmacists in various ways. So there has been quite a lot of effort to raise awareness of this.

Julia Cumberlege: Thank you very much for that. I think one of the great strengths of community pharmacy is that they can double check the prescription that

has come from the doctor. If they are well known in that community one can understand a lot aren't...

Sandra Gidley: Yeah.

Julia Cumberlege: ...because if they're working for a big company they may move around with different pharmacies within the company. But is there an alert system that the pharmacist will have if the woman is within the age of being pregnant, 16 whatever it is to 50, do they get any sort of alert like that?

Sandra Gidley: I'm not seeing an alert that links - it's quite difficult to link the age to the sex and the drug. You'd think it would be quite straightforward, but the warning that generally comes up is warning attached to valproate. Is this woman of childbearing age? Again, there are two problems with that, potentially. So, in some locations the pharmacist might not even see the warning, because I've seen practice where the person dispensing it will see the warning, and you get so many flagged up that the people typing in the information into the system and generating the labels, don't put it into context.

Some practices they will actually - some systems allow you to print off the more severe warning labels and the pharmacist can then make a decision. So, it's an imperfect system and even the GP systems, until recently one of them only had the valproate as a level two warning, not a level one warning. I was surprised to hear that it's about two years to change a GP system, and 18 months to change something on a pharmacy system. So, it was very slow to change. So the awareness really had to be through the professional channels, pharmacy media and such as that.

Julia Cumberlege: So my final question then is about the pregnancy protection programme.

Sandra Gidley: Yeah.

Julia Cumberlege: Have you seen, do you know through the community pharmacists and other pharmacies whether there's been prescribing habits changed as a consequence of this PPP?

Sandra Gidley: It's hard to say really, I'm aware of only a very small number of women who have changed their medication. The problem is that I think a lot of women who are on the medicine don't want to risk losing their driving licence. It has a real lifestyle impact if you change your medicine and it doesn't suit you. If you're a busy mother you already have children, you might be working. The thought of not being able to drive and have your car I think is very, very difficult for some.

So I haven't noticed a lot, certainly locally, but I know in some areas of the country they've been better than others at a concerted effort to try and reduce it. But that's been more a whole system approach with the COP leading from the hospitals and quite a lot of engagement activity. But that is not universal throughout the country.

Julia Cumberlege: Right, thank you. Sonia?

Sonia Macleod: One of the things when you said that sometimes some pharmacy systems allow you to print a warning label.

Sandra Gidley: Yep.

Sonia Macleod: What happens to that label, does it go in the box...

Sandra Gidley: No. So there are warning labels that go on the box. So the labels on the sodium valproate I think now say don't take in pregnancy anyway. But it's kind of the small print at the bottom. These are labels that are printed off. They look like dispensing labels, but they are printed off for our information. So the pharmacist would look at them and assess whether there was anything that needed to be done. Because occasionally you can get warnings coming up which say, you've got two medicines for hypertension. Is this right? Actually you know it is, because they're not controlled, but if it was about sodium valproate and a woman of childbearing age, then that would act as a prompt to have that conversation.

Sonia Macleod: Okay so they're for internal pharmacy use they're not external...

Sandra Gidley: It's internal pharmacy use, yep.

Simon Whale: Can I just ask if the pharmacist is concerned that the woman in front of him or her in the pharmacy is not on a form of contraception, is compliant with PPP. What you'd want is for the pharmacist to be able to raise that quickly...

Sandra Gidley: Yes.

Simon Whale: ...to the prescriber so something can be done very...

Sandra Gidley: Yes.

Simon Whale: ...very quickly in the women's interests. How does that work in practice?

Sandra Gidley: Well it works in a number of ways, if I'm honest. Because people work in different ways. Ideally, you've got a good relationship with the GP. You should be able to flag that up straight away, and the GP can do that. There

has been an increase in recent years, sadly, of, and I can understand this, that the GP is not wanting to be disturbed. Again, this goes back to changes in practice, 40 years ago when I rang the GP I was always put straight through. Now the norm seems to be that unless something is flagged up as urgent and even then, it just goes on their computer system. So they get a computer warning, and they decide whether to take it or wait to the end of the surgery.

Now if you've got a woman who, particularly if the pharmacy is near the surgery, it helps if they can go straight back. But again, the conversation is quite a delicate one because the women might - she might already have a child. The child might be unaffected, she might not be aware that the risk is so high. There has been, not in pharmacy circles but certainly in some of the medical circles, a discussion about whether or not a woman actually has a right to be pregnant knowing the risks. Which I find a rather strange human rights issue, but nevertheless those conversations have taken place.

So ideally, you would be able to get through to the doctor's surgery, but sometimes if there's just a lot going on, on the day, making that phone call might be really difficult, and the patient might just be told to go back to the doctor. But the advice is that you should contact the GP and inform the patient and refer them back.

Simon Whale: Because if you can't do an immediate referral back then, the woman has not got her epilepsy treatment, presumably she's run out, and she's there for the repeat prescription or is about to run out?

Sandra Gidley: Well she would – no, because the advice is to dispense.

Simon Whale: So you would dispense anyway?

Sandra Gidley: You would dispense because the advice is to dispense because there is a risk to the woman...

Simon Whale: Exactly, okay.

Sandra Gidley: ...in her not having her epilepsy medicine. It's not an ideal situation; sometimes they haven't got a plan, but they are on some sort of contraception. They might not be on a long-acting form of contraception. They may not want to do that, so there are a number of different scenarios that might take place.

Simon Whale: Does anyone keep any records centrally of how many incidents of that nature happen?

Sandra Gidley: Of what nature -those conversations?

Simon Whale: Where the woman - yes. Where the woman is not on a PPP approved form of contraception but gets the medication anyway?

Sandra Gidley: There was a pharmacy audit that looked at all of this, but that audit only took place over a period of a few weeks. I believe it was part of the quality payments scheme as well. So there is a snapshot in time, but the only way that information would be routinely captured would be potentially on the pharmacy patient medication record. That is unique to that particular pharmacy, and one of the larger chains shares information between their pharmacies, but nobody else would be able to access it. It would be very useful if there was some way of writing to the patient record so that the pharmacist could actually record that conversation.

Ideally – well some pharmacies have referral forms and there's a copy for the GP, a copy for the patient and a copy for the pharmacy which highlights the issue. Because sometimes people say I'm not really sure what's going on, what's all this about? So if you write it out in that form and then you can make sure a copy goes to the GP, and the patient's got a copy as well. But not all GPs are aware of the importance of this either, because the - well the GP's can speak for themselves but in meetings at the MHRA it's been quite clear that some GPs have had a woman go to their surgery. They've been called because part of the system works and then the GP hasn't known why they are there.

Simon Whale: Right.

Sandra Gidley: Because they are not up - they weren't up-to-date. I would hope that is a bit better now, but certainly, this is less than a year ago.

Simon Whale: But this scenario in pharmacies as you've described it could result in different things happening...

Sandra Gidley: Yes.

Simon Whale: ...because you've got - there's no coordination of approach or systems or records. So different pharmacies, different places will end up - may end up doing slightly different things?

Sandra Gidley: They will probably have protocols in place which they follow for referral to GP, and each company have a slightly different system. There will be a system, but they will be slightly different.

Valerie Brasse: Is whatever the outcome or whether knowing that the person is on a PPP or not, they were planning a family or not, it will always be here is the

prescription the pharmacist will dispense it. Then take whatever follow-up action if you can't do it immediately [unclear]

Sandra Gidley: Yes, yes.

Sonia Macleod: So there's never a situation where you say 'sorry this is far too risky, not giving you this prescription at this point'...

Sandra Gidley: I would hope not because the protocol is quite clear, I'm going to say that the flow diagram...

[Over speaking]

Valerie Brasse: Whatever the [route]

Sandra Gidley: Yeah. I think the green is, you know, I probably wouldn't have chosen those colours personally...

Valerie Brasse: It's a go [unclear]

Sandra Gidley: Well, it is a go, but I think maybe green and amber might have been prudent. These things as you know are designed by committee.

Simon Whale: Can I ask a slightly different question? Medicine shortages have been in the...

Sandra Gidley: Right.

Simon Whale: ...news quite a bit recently. Are there actual concerns about the availability of valproate now, and have you got concerns about supply in the future?

Sandra Gidley: There have been problems with a huge variety of medicines. I'm not aware of any long-standing problem with valproate. If we have a hard Brexit we would be in uncharted territory with regard to medicines supply. I am aware that there is an intense amount of time, effort and probably money being devoted to making sure that supplies continue and that medicines will be made a priority. But I can understand that people are concerned. There has been some publicity about the - I can never remember the name of it, sorry, the serious medicines', the shortage protocol. There was particular concern from people with epilepsy.

Now the way this protocol is supposed to happen, emergency legislation is being passed that so that in the case - if there is a severe shortage, and it has to be deemed a severe shortage by the government. Then in that case they will be discussion between consultants, pharmacists, GPs, so that everybody is clear what the alternative supply route is - what drug

will be given, and if there are any occasions where the replacement can't be drug B but will have to be drug C. This will actually help patients because instead of being chucked back to the doctor, which is not a very technical term, but they are very often referred back to the surgery, it will take that loop out. The GP will know what has been prescribed instead, so everybody will know.

Simon Whale: So, in theory, it should work?

Sandra Gidley: In theory it should work, but with epilepsy drugs it's unlikely that they will form part of this because of there's often quite a fine balance in getting somebody stabilised on the right medicine. I think the Secretary of State, Matt Hancock, has already said that this medicine switch of the dosage is quite critical, such as that in epilepsy drugs and drugs for transplants they won't be covered.

Sonia Macleod: So there's no chance of, say, people on one antiepileptic being switched on to valproate because obviously that would have implications in terms of [unclear] coming on?

Sandra Gidley: I'd be extremely surprised if that happened (I wouldn't say) never, but certainly at the moment I think those drugs would be made the priority of priorities because the government has already said that they don't plan to use the protocol for those sort of medicines. But I can see where you're coming from because if a woman was suddenly put on valproate instead of something else, that could be really quite frightening, but I'm pretty sure that won't happen.

Julia Cumberlege: And the reverse, if she's put onto something else that isn't valproate...

Sandra Gidley: Yeah.

Julia Cumberlege: Does she have to give her consent? Does she have to know the consequences of this change in her medication?

Sandra Gidley: Well, any woman been prescribed valproate would have to know the consequences of valproate and those conversations would have to take place, but given the publicity there has been over valproate the whole move is to try to reduce the prescribing. So we are seeing few a younger woman coming through on sodium valproate. That's the change that has been noticeable, because they are being swapped over before they are driving and what have you, so they won't have the problems of changing drugs later on.

They are sometimes difficult conversations to have because the criteria is childbearing age. So if you're talking about a 14-year-old, parents are often uncomfortable with their daughters being thought of as childbearing, but the reality and practicality of modern life is that early teens is probably a good time to start thinking about changing people over. So, hopefully, there will be relatively few women on sodium valproate and already the Royal College of Psychiatrists has taken a view about the use of valproate in certain conditions and said it's just not acceptable at all.

The difference with epilepsy is that is actually life-threatening and for some women there just doesn't seem to be an alternative. So I think there will always be a very small number, but that number should decrease with time.

Julia Cumberlege: Right, thank you.

Simon Whale: Just thinking about medicine use reviews and valproate, what happens at the moment? Is valproate one of the medicines where pharmacists can...

Sandra Gidley: No, sadly. This is something the Community Pharmacy Safety Group were quite keen on. In fact, Howard Duff, when he was Director for England did raise this with Deborah James who was in charge of commissioning pharmacy services at the time, but it didn't really get any traction because I think we were probably slightly ahead of it being as much of a government priority as it is. But it would certainly make sense for women to have that review if they are on valproate. If that was targeted, then the women would be much more likely to have a review.

Some do, because you have to do a proportion of targeted to untargeted, so it could form part of you're a targeted practice. But the reality is people have little pet subjects quite often that they might like doing medicine use reviews on, and that would be it. There is a concern about - there are some women who have their medicines delivered, or might access via an internet pharmacy, and we are not sure what happens and whether those conversations take place on those occasions. So that is a potentially weak area of the system.

Julia Cumberlege: Right, thank you. Cyril?

Cyril Chantler: I gather you give advice about the off-label use of medicines in the National Formulary. Is that monitored in any way?

Sandra Gidley: Oh, you have me there. It might be by the business statistic [unclear] probably not, actually. No, because when prescription numbers are

analysed, you wouldn't have the diagnosis data. So unless somebody potentially it could be because you could use the NHS number, but you would have to be doing some very clever computer...

Cyril Chantler: But it isn't monitored at the moment?

Sandra Gidley: No, not that I'm aware of.

Cyril Chantler: You say that your members read your journal, therefore - my mother was a pharmacist and I can remember it arriving every so often, yes. But is there any other way that you can actually monitor the compliance of pharmacists with the advice that you give them?

Sandra Gidley: It's very difficult. I gather the GPhC inspections teams are now actively looking at this, but they are...

Cyril Chantler: GPhC?

Sandra Gidley: General Pharmaceutical Council, which is the regulator, so they are actually the best placed to look at that.

Cyril Chantler: So as a society it's the regulator who deals with compliance; you give the advice?

Sandra Gidley: Yes, yes. We provide standards advice information.

Cyril Chantler: Yes. How do you connect? One of the problems of my profession is how the Royal Colleges connect to the General Medical Council...

Sandra Gidley: Yeah.

Cyril Chantler: ...to make sure that people are practising safely. So how does that work for you in the new arrangements you've got?

Sandra Gidley: We have regular meetings with the General Pharmaceutical Council. I've got one in a couple of weeks' time, so we generally share items of concern...

Cyril Chantler: That would be at the policy level, but not at individual member level?

Sandra Gidley: No, no. The two organisations are separate with regards to their communications to pharmacists.

Cyril Chantler: Okay. That brings me to my last question, is partly because of the other part of your line. This review has come to pass because patients have suffered, and it's taken groups of patients dedicated to bring this to the attention of society, and politicians forming associated parliamentary

health groups has led to this review being set up. So as a doctor I feel surprised but also concerned that it took the activity of patients and politicians to draw the professions notice to something which is going seriously wrong or has gone wrong in these areas.

Sandra Gidley: Yeah.

Cyril Chantler: What could we do better as a system? I don't want to blame anybody but what can we do better?

Sandra Gidley: Well, I've spent quite a lot of time thinking about this and I wish I knew the answer, because in the early days we thought that just greater awareness would solve the problem. So there was quite a lot of effort devoted to trying to get the message across. Sanofi produced materials, they didn't even arrive in half the pharmacies. Quite frankly the results were really disappointing, and I say that as a pharmacist seeing the take-up from pharmacy and also the awareness of GPs. The whole system failed these women in effect. Even the consultants weren't all admitting the risks were as high as they are, and the more that this is being looked at more evidence seems to emerge of the problems.

So, one thing I have noticed is I used to regularly receive Committee of Safety of Medicines briefings to my home address, and I no longer receive those for some reason. Because I'm a registered pharmacist I can only assume they're not sending anything out. Those had the advantage if there was something of particular concern it was probably the one thing you really, really, really make sure you read if you were to do your job properly. Because it has the emerging concerns, things you could look out for, things you should be giving certain advice with. The most important problems, and I'm not convinced that those are going out anymore.

I tried to remember when I've last received one, and it must have been a few years ago, so certainly before the interest in valproate. I think the message for all health professionals, if I am absolutely honest, is listen to the patients because very often there is an attitude of - I won't say doctor knows best, but pharmacist knows best as well. So to professionals, some paediatricians said well we noticed there was something going on, but nobody believed us. The parts of the system just didn't join up and put two and two together.

Cyril Chantler: Where can patients go when they have these concerns? I mean they can go sort of everywhere, but wherever they go nobody seems to have listened?

Sandra Gidley: No and very few patients report an adverse drug reaction because we now have a system where the patients can report that, but I think very few do. I don't know what the figures are. Sometimes it's only when something happens a second time that you think oh that's odd and start to put two and two together. Because obviously there are a lot of factors in an individual pregnancy, so you wouldn't immediately associate it with sodium valproate. But somewhere along the line, somebody should have noticed that a lot of children were being affected.

I can't quite understand how that wasn't picked up earlier, and it seems to have been some of our colleagues in France particularly seem to have been ahead of us there. I wish I had an answer, but it's not just about more information because we all suffer from information overload, so it's how do you get emerging queries, key information out so that they are noticed and it's this is your must-read.

Cyril Chantler: But you know in your position as a politician who's sat on a health committee and a practising pharmacist, you do have an important perspective of these issues.

Sandra Gidley: Yeah.

Cyril Chantler: So if any ideas occur to you will you...

Sandra Gidley: I will. I have thought about it and I really wish I knew because quite a lot of - so what was evident in one of the MHRA stakeholder events - I'm not trying to apportion blame but the CCGs all had to have a plan in place, and they had to communicate the importance of valproate to the GPs. Well, a lot of the GPs - the letters had gone out but not every GP in every practice had seen it, because sometimes there is a lead GP and they may not have felt fit to inform the other GPs. So, you look at the number of medications we have, medicines we have these days compared to a few years ago. I mean my first BNF was one of those little pocket-sized ones, and now it's quite...

Cyril Chantler: [Unclear]...

Sandra Gidley: Well, now it's quite chunky. So again with all the new medicines it increases the opportunity for something to do well, but you ask all the CCGs and they're very smug and they tick the box and say, we've done our bit. But if it has no impact then there's no point in just creating a paper trail for the sake of it. So I don't know how you can make people individually accountable to this. I suppose one way, if there was something deemed of sufficient importance would be to make it part of the annual declaration. I don't know if it's the same for doctors, but

certainly when I renew my pharmacy registration every year, it's a number of questions we have to ask. Most of them are about whether I've had a speeding ticket or I'm not well, but that could be used to say 'are you aware of XYZ?'

Cyril Chantler: Do you have a personal appraisal system like they have introduced into medicine where you sit down with a colleague, a peer who and you have to produce evidence and so on?

Sandra Gidley: Yes, well, the system is changing. So peer review is coming in this year along with I think a reflective essay. How much that could be used for that I don't know, but I think almost any solution has to have a regulatory element otherwise I don't think it'll happen, is my - I'm reluctant to say that, but that's the conclusion I've come to after following this issue for a few years.

Cyril Chantler: Okay. Thank you.

Valerie Brasse: Can I ask a question? You were talking about the manufacturers not getting the materials into the pharmacies in relation to sodium valproate, and one of the issues I know was about the pack size.

Sandra Gidley: Yes.

Valerie Brasse: So if the pack size was larger then the pharmacist would be breaking open these packs...

Sandra Gidley: Yeah.

Valerie Brasse: ..., putting them in the white box, then the patient information leaflet was not going in. We have been told that that is all resolved now, and as of October that should be the case. Is that your experience?

Sandra Gidley: Well, I haven't seen so many of the smaller packs actually, there are still quite a lot of large ones in the system, but all pharmacies are being sent a bright purple folder so that it stands out a mile, and in that are supplies of stickers and things. But that is the bit that will sometimes, in all honesty, be missed. The conversation I have very often is, it needs they need X, and the automatic response particularly if it's a pharmacy where they know the patient well is 'oh they've had it before'

Valerie Brasse: So I was told...

Sandra Gidley: Yeah.

Valerie Brasse: ...the pack size itself, the original manufacturer...

Sandra Gidley: Yeah.

Valerie Brasse: ...has gone down from 100 down to 30, so that should be every pack will come with its own PIL?

Sandra Gidley: It will, but well there should be a PIL in any way...

Valerie Brasse: It should be, but we know that they're not put in the white boxes always.

Sandra Gidley: ...but there's still a lot more packs in the system.

Valerie Brasse: Right, so we are not there yet?

Sandra Gidley: We are not there yet, but it's only a matter of time because that's what should happen, yeah.

Sonia Macleod: When the box is broken down and put into white boxes...

Sandra Gidley: Yep.

Sonia Macleod: ...there are stickers?

Sandra Gidley: There are stickers and most people...

Sonia Macleod: Do all pharmacies have them?

Sandra Gidley: Yeah, they're part of this purple folder.

Sonia Macleod: Yep. Do they use them?

Sandra Gidley: Hm, evidence would suggest not in all cases because I've seen photos of where they haven't been used.

Valerie Brasse: I have another question which really goes back to where we started, when we started talking about Primodos and linked to that there is, I suppose, a modern day concern about it. The prescription reimbursement scheme as such, we learnt that Primodos was no longer to be reimbursed after 1970 I believe after the McGregor committee had reported. That the indication to use it as a pregnancy test was removed. But I also know from looking at the past historic records that the secondary amenorrhoea, the treatment for which Primodos did have a licence, was in fact exactly the same dosage. Same composition of ingredients, same number of times to be taken as the test for pregnancy.

When a doctor writes on the prescription what it is he wants prescribed, he doesn't as now presumably then, what he wanted it prescribed for? So he writes the prescription in terms of this issue of what could be

reimbursed, how did the prescription person of authority know what the drug was actually being issued for?

Sandra Gidley: They wouldn't in that case.

Valerie Brasse: So, in fact, that was a lever that really had no control?

Sandra Gidley: Well, historically - a lot of it is computer checks these days anyway because they're all scanned. But the '70s were in the days of handwritten prescriptions, and with handwritten prescriptions you're less likely to get any indication on the prescription than you are now. Some practices will often put an indication for a drug but it's by no means universal. It's more common for the pharmacists just to be presented with the prescription with no indication as to what it is for.

So it would be exceedingly helpful if pharmacists could have access to the medical - the clinical records. If there was a compunction then to check, double check. Baroness Cumberlege mentioned that one of the strengths was checking but at the moment with the Summary Care Record - I don't think even that would be the major - if there was a major diagnosis that's there but not everything [unclear].

Valerie Brasse: So in the past, the notion that those pregnancy tests would not be reimbursed were sort of an irrelevance because no one would know whether it was given for secondary amenorrhea or a pregnancy test.

Sandra Gidley: I would have to double, and it's hard to check back in the '70s but for some medicines, so for example, there are some oral contraceptives that can be prescribed for acne and not for contraception. The GP has to mark that as for contraceptive purposes if it's for contraception. That is only because the woman then doesn't pay but if she has acne she has to pay. So there are mechanisms that could be brought in to flag up whether something needs to be done or what the indication is, but there would have to be a - there is usually a financial reason. It doesn't happen...

Sonia Macleod: Historically, going back to the 1970s, were diagnostic tests put on the same forms of prescriptions?

Sandra Gidley: I can't really answer that I'm afraid because I only qualified in 1979 [laughs]...

[Over speaking]

Sandra Gidley: But I can't recall seeing it. Well, you say diagnostic tests but there have always been things like testing, urine testing strips.

Sonia Macleod: But were they put on prescriptions?

Sandra Gidley: They're on prescriptions yes.

Sonia Macleod: Okay.

Sandra Gidley: There is a list of what is allowed but obviously if the diagnostic test is also allowed as a drug for another indication then it wouldn't be much help.

Julia Cumberlege: Well, Sandra thank you so much.

Sandra Gidley: Thank you.

Julia Cumberlege: It's been really, really useful. I'm just going to ask my colleagues if there are any final questions they would like to ask, or points they want to make. So?

Sonia Macleod: No, thank you.

Cyril Chantler: No, thank you.

Simon Whale: No.

Sandra Gidley: Okay, if you think of anything that you need more information on then, such as the early '70s which I don't think happened but if you contact us we might be able to find out, get our library onto it.

[Over speaking]

Julia Cumberlege: Very knowledgeable...

END OF TRANSCRIPT

Session 4: Professor Shakila Thangaratinam

START OF TRANSCRIPT

Julia Cumberlege: Just for the record, because we're filming now, I'd be grateful if you could just say who you are and how you're working and [so on].

Shakila Thangaratinam: I'm Shakila Thangaratinam. I'm a Professor at Queen Mary University of London. I'm also a Consultant Obstetrician who's working at the Barts Health NHS Trust. I led the development of the Royal College of Obstetricians and Gynaecologists' Green-top guidelines on management of epilepsy in pregnancy. I was also the project lead of NHR (HTA) funded EMPIRE trial looking at antiepileptic drugs in pregnancy but not valproate, other drugs apart from valproate.

Julia Cumberlege: Right thank you, that's very clear. I think you didn't actually provide us with any written evidence because we've already met you and had a - and I'm not sure if you provided any COI, conflicts of interest, did you?

Shakila Thangaratinam: Ah no.

Julia Cumberlege: No, well...

Shakila Thangaratinam: I do not have any conflict of interest.

Julia Cumberlege: Oh right, all right. So that's...

Shakila Thangaratinam: I was not aware of a form - I haven't - I don't recall any form being requested for signature.

Valerie Brasse: No, we just asked individuals whether they would give a statement as to whether they had any conflicts of interest...

Shakila Thangaratinam: No, I do not have any conflicts.

Valerie Brasse: ... with the industry or any other body, regulatory body.

Shakila Thangaratinam: No.

Valerie Brasse: Thank you.

Julia Cumberlege: All right, thank you very much indeed. So, if I could just start then and ask you, we obviously have the pregnancy prevention

plan now in place and that's a step forward. But, do you think that women really are aware of that? Are you seeing that actually taking place in your practice? Do women - aware of the PPP and since 2016, when you were involved, have you seen a change in practice?

Shakila Thangaratinam:

So, I - my involvement in care of epilepsy is primarily from a research aspect rather than from a direct one as a clinician because the clinical management of women in my Trust are seen by my colleagues, not by myself. If you ask me, based on my discussions with my colleagues, both general practitioners as well as my consultant colleagues, yes, there is an awareness amongst the healthcare professionals. Pretty much almost everybody who's involved in the care of women with epilepsy but clearly the reproductive age group are aware because we've all received emails, the mandatory emails on the change.

I think it's a bit early to comment on has it trickled into a change in increased awareness amongst pregnant women or women of reproductive age group unless there is a specific exercise that's being ongoing either a survey or some sort of communication. So, I think I'll find it difficult to say if it's resulted in an increase in awareness amongst the pregnant women.

Julia Cumberlege:

Right.

Valerie Brasse:

What about numbers of unplanned pregnancy?

Shakila Thangaratinam: Since last year?

Valerie Brasse:

Since 2016 when it was a voluntary programme?

Shakila Thangaratinam: I don't have the figures with me no, I don't know.

Valerie Brasse:

A sense of that?

Shakila Thangaratinam:

No. I think if you look at the other services like the sexual health services, it might be helpful to look at the number of mothers who are going for terminations with an indication that they are on valproate. I think that might be one way to find out or if there's any change in the numbers who are coming through who'd like to - who are requesting to end the pregnancy.

Julia Cumberlege:

So just thinking about your clinical practice and also your wider remit, can I ask you that - we've heard about women who actually switch from valproate when they find that they're

pregnant. So, they go onto another medication and I wonder if you could tell us a little bit about that and the impact that might have taken place in terms of the management of their epilepsy and their general health and wellbeing? Also, the impact that might have had on the development of the foetus?

Shakila Thangaratinam:

So, there are three ways in which women end up being on valproate when they're pregnant. (1) They've already been started on valproate as a child for epilepsy and at some point in time they get transferred for their care from the paediatric services to the adult services. That is one way in which there could be a mismatch or miscommunication. The only person who is the [strand through] is the general practitioner. So, I think they fall - women - the [unclear] through the gaps because we need to switch them when they move from being a child to being a person who is now in the reproductive age group. That information needs to be contacted, needs to be provided to the secondary care epileptic specialist. So that's one there. They've been on it as a child but then they've never been switched as an adult.

The second one is they have been started on valproate for the first time while they are of reproductive age group. That happens when they have some other indication - we don't know that they are actually planning pregnancy in the immediate or the long term. For those women, there needs to be an ongoing discussion with the general practitioner or hopefully with a yearly discussion they're now going to have. Are they going to have a contraception? Are they going to continue the pregnancy? So again, it's the general practitioner who is the first person - first point of call to alert us in second care, look, this is the plan, this woman has now changed her mind, she wants to get pregnant, can we change the drugs?

The third - the third scenario is they started on valproate for the first time when they're pregnant. I think that's a very, very rare scenario that somebody who's never been on valproate, has now been started to control the epilepsy. I can only think if the epilepsy cannot be controlled with any medication or any number of drugs and this is the only option. But it's extremely rare for such a scenario to take place.

So, if you look at each one of them, when you switch them to other antiepileptic drugs - and I'm only talking in the context of

epilepsy, not other indications for valproate - the main thing to look for is how effective are the other drugs. Often neurologists, and I'm not a neurologist, I'm not fully qualified to explain that, but often neurologists would want to switch them to a drug that's got an equal effectiveness in preventing the seizure. Sometimes one drug might not be enough, they might need to have them on more than one non-valproate drug.

Again, that's a decision that neurologists have to take because high doses of other drugs are not necessarily always safe. Do we need to keep them on a lower dose of valproate with a five milligram of folic acid to prevent any neurotome defects or are we going to put them on multiple drugs on high doses which also could potentially be dangerous. I think that that's a discussion can only be held between the neurologist and the woman, taking into account how well the epilepsy is controlled with other drugs.

Julia Cumberlege:

So, for some women, probably the easiest access for advice is their GP. I just wonder - you talked about the annual review of their medication and their health generally and that sort of - what evidence do you have that that annual review does take place?

Shakila Thangaratinam:

I think it has been mandated more now, pregnancy prevention programme. I'm not aware that this has been mandated for the general practitioners to do it on a yearly basis with - but clearly the specific details of [unclear] contraception. Since it is mandate, I'm hopeful that we will be able to have this discussion with the mums. Of course, it depends on the woman actually turning up to the clinic and having the discussion.

I think it would be good to have a further plan of what happens if someone says 'I actually don't want to go on a pregnancy prevention programme'. Then the next discussion is, okay, if you're planning pregnancy, let's start you on five milligram of folic acid. That's a higher dose of folic acid than what is routinely provided because that has a potential to prevent neural tube defects, one of the known abnormalities associated with valproate as well as minimise [long-term] neural development problems these babies may have in the future.

If the woman says, 'okay I'm not so sure if I want to get pregnant but neither do, I want to have a contraceptive', then

again, there needs to be mechanism in place for them to then talk to their neurologist taking into account this is where we are, what do you want to do? So, I think the PPP, the pregnancy prevention programme is the first step but there needs to be some additional information for general practitioners on what to do in somebody who doesn't want to enter the PPP. Are they going to get pregnant? How long are they going to wait? I think it would be helpful to have some more details on that.

- Julia Cumberlege: Would a general practitioner seeking more information, would they go to your Green-top guideline? Would you be circulating that?
- Shakila Thangaratinam: It is available, the Green-top guidance, but it's mainly to do with pregnancy or it's to do with management of epilepsy in pregnancy. So, for pre-conception counselling, it would be guidance just the NICE which covers the general population. I also think MHRA has now given out a lot of information on the discussions to be had with women on valproate who are considering contraception or to try to get pregnant. I mean that has been part of the communication which all general practitioners have received.
- Julia Cumberlege: So, I'm just thinking of the general population for a GP. If he has 2000 patients, what percentage of women who have epilepsy and of a child-bearing age, would he have in his practice?
- Shakila Thangaratinam: I think nationally we have around 27,000 women who are taking valproate.
- Julia Cumberlege: Sorry I have missed the first...
- Shakila Thangaratinam: Twenty seven - 27 to 33,000 take valproate of the reproductive age group. I think we estimate around 350 to 400 might be getting pregnant on valproate every year.
- Julia Cumberlege: Thank you, and is there a follow-up on those women other than - I suppose it relies on the annual review with a GP?
- Shakila Thangaratinam: If their epilepsy is well controlled, then - I'm not a primary care practitioner so it's a bit hard for me to understand what happens in primary care. So, the only time I get in contact with them is when they get pregnant and then they enter my speciality. However, we do inform GPs and that's through GP - regular GP updates. So, we have these annual or bi-annual

training programmes depending on the area - region they're in, on the need to refer these women, mothers, to us early as soon as they get pregnant. That's number one.

Also, to start them on, again, the folic acid, even before they're planning pregnancy, three months pre-conception. So that's also very important. So, these are things that are slightly outside our control, the pre-conceptual one. But a good pre-conceptual advice would prepare these women to start the - either change or if they can't change at least to start them on five milligram of folic acid.

Julia Cumberlege:

Thank you very much.

Simon Whale:

So those 400 or so women who do fall pregnant whilst taking valproate, do we - do you know anything about the reasons why they fell pregnant? Is it because no one warned them or is it because people did warn them, but they took their own decision to continue with valproate anyway? Do we have any information about...

Shakila Thangaratinam:

Yeah, I mean - [not] [be surprised say] less than half of the pregnancies are planned and that's looking at the general population. So, it's very hard for us to - so all we can say is around 45 to 50 per cent or even more of pregnancies can be unplanned. It's not that that's a conscious decision to say, okay, I'm - over the next six months, let me start thinking about falling pregnant.

Simon Whale:

It would suggest that they weren't using contraceptives.

Shakila Thangaratinam:

Yes, so that's [the] thing. So that's - so why - that's the reason why when they come and see the GPs and they say I'm not going to be on the PPP, the pregnancy prevention programme, then there really needs to be a good discussion, okay, what are your alternatives? Also talk about not all contraceptives are the same effectiveness. Also give advice on the contraceptives that are more effective and some that may not be as effective in preventing the pregnancy.

So, one reason why women could become pregnant on valproate is unintended pregnancy, just didn't expect it. So never took any contraceptive and therefore became pregnant. Two is, despite being on contraceptive, maybe something happened, they had vomiting, they were throwing up, they

forgot their pill. So, there could be other reasons that - and certainly the failure of a contraceptive. So, these are women who didn't want to get pregnant but unfortunately did fall - become pregnant, despite being on contraceptives.

There could be a third group who consciously did make a decision fully knowing they are on valproate. Maybe they had a discussion with their neurologist who weighed the risks and benefits and decided that their control of epilepsy can only be achieved with valproate, and whilst there's a risk to their baby and still made a decision to become pregnant.

The last group did not have pre-conception counselling with a neurologist whilst on valproate, knew about the risks but still decided to get pregnant. I think that would be a very small number.

Simon Whale: But is there any - is anyone capturing data on how many women fall into each of those different categories?

Shakila Thangaratinam: I'm not aware of - for those who are on valproate - the reasons why they become pregnant.

Simon Whale: Do we know anything about how many of them have the baby and keep the baby as opposed to terminate?

Shakila Thangaratinam: I don't have the [unclear] but what we do know is in women who are on antiepileptic drugs, up to 15 per cent who is wanting [unclear] - there is data on that. The data shows that 15 per cent will just stop the drug themselves without having a discussion with a healthcare professional because they are very worried about their baby. They don't necessarily - they may not necessarily always tell their healthcare provider for fear of being judged that they're not taking whatever they've been advised.

I think that is one thing we need to be aware of as clinicians. Yes, we tell mums about all of the risks of valproate, but we also don't want them to stop it because it could be the only thing that's actually preventing them from having seizures. In fact, I think two of the nine mothers who died in the last Confidential Enquiries, they did stop the valproate. I think [unclear] about [8] - for a very small minority, this could be the most effective way and I think these discussions should be coming up in the pre-conception counselling.

- Sonia Macleod: When people - I mean when women do stop their medication, do they usually stop it pre-conception? Do they stop it when they find out they're pregnant? Do we have any feel for that?
- Shakila Thangaratinam: No, based on my own experience in the joint epilepsy clinic that I used to do, it's usually when they find that they're pregnant that they end up stopping because it was just not something that they thought about earlier. But then once they get pregnant, realise oh my god, I'm on a drug that's going to harm my baby and your first inclination is to stop whatever you think is harming your [unborn] child.
- Sonia Macleod: I was just trying to work out it's not a pre-conception planning thing unnecessarily, it's...
- Shakila Thangaratinam: I think if they are usually thinking that much through then they usually are the ones that have spoken to healthcare professional. It's usually, I'm pregnant, okay, let me just stop the medications I'm on.
- Simon Whale: Can I just ask about the Green-top guidance? So, when that came out in 2016, was there any formal guidance around before 2016?
- Shakila Thangaratinam: There has not been any dedicated guideline targeting only pregnant women with epilepsy before that, or in fact there has not been any guidelines before or since, apart from UK's own guideline. There have been guidelines such as NICE and SIGN, the Scottish guidelines which target all individuals with epilepsy. So there are sections for pregnant women, pre-conception, children, but not something dedicated on how we manage someone with epilepsy in pregnancy, during labour, post - and postnatally, so that's the first one that we did.
- Simon Whale: Has awareness of the risks associated with taking valproate while pregnant amongst obstetricians and gynaecologists - has awareness amongst the professionals increased or do we not know?
- Shakila Thangaratinam: I would expect it to be increased, particularly among the - so every time a new guidance comes, all of us in the profession are aware of it. So, it is just by the fact that a Green-top guideline is something - is an important one that's going to have implications on our management. So, the fact it's a Green-top guideline itself does impact on our practice. Again, trainees are

very aware of these Green-top guidelines. It becomes part of their curriculum. In fact, it's part of their exam as well. If they're asked for [unclear] clinical management issue, they study for their - definitely for their exams.

I don't know how many hospitals now have epilepsy management as part of their routine guidelines. So, we have guidelines on management of diabetes, induction of labour and things. The last time when we did the EMPIRE trial, not all hospitals - not even half of them - had guidelines for managing women with epilepsy and that could be because no such guidelines with the Green-top existed. So, I don't know if it's translated into local guidelines but definitely the national guidelines are applicable throughout.

Simon Whale: What about the appraisal processes. Should it be [easy] or should it be incorporated in the present processes?

Shakila Thangaratinam: It should be part of their appraisal but clearly if they're managing pregnant women with epilepsy, yes it will be.

Simon Whale: It will be.

Shakila Thangaratinam: It will be yeah.

Valerie Brasse: Do you find it extraordinary there was nothing prior to 2016 on the management of epilepsy in pregnancy? Epilepsy is not a rare disease and the issues around sodium valproate have been with us for decades. So, it is quite extraordinary to think that there has been nothing...

Shakila Thangaratinam: Yeah, I think one - I mean I was also equally surprised and I think it could be because obstetricians see women with epilepsy or possibly have looked at it as if it's something in the realm of what neurologists [unclear] because it's all medical condition and then neurologists when somebody get pregnant it's seen as a mainly an obstetric one. Then the midwives think this is - this is not a low-risk but it's a high-risk condition. Definitely this is something what we observe in - when we set up the EMPIRE trial was in some hospitals, we had to actually introduce the teams to each other, the neurologists, obstetricians to set up the trial. I think that could be one of the reasons.

There are other conditions like diabetes in pregnancy for example where we have a really good working relationship

between the diabetologists and obstetricians. But epilepsy is slightly rarer compared to diabetes, so I think awareness is - has been a bit slow.

Sonia Macleod: So how do you build the relationships? How do you get it to a position more like diabetes where there is a joined up [unclear]?

Shakila Thangaratinam: So, we made - one of the recommendations is that in the Green-top guidance, it said we recommend a joint obstetric neurology clinic to be in every unit that's looking after pregnant women with epilepsy. I think it also does need support from NHS England and the bodies to promote this joint obstetric epilepsy clinic. Also, neurologist - and also the general practitioners to refer the women much earlier. You often find that they first come around 20 weeks or later. So, we need earlier reference for us to have these discussions, do scans early, talk to women on what they want to do with a pregnancy.

Simon Whale: Is there capacity within the system to have this kind of multidisciplinary approach?

Shakila Thangaratinam: I think it depends on the hospitals. So, if they are in a tertiary unit such as the Royal London Hospital where I work, yes you already have a joint clinic. In a district general hospital, it may be a different circumstance. But even there, there are neurologists and there are obstetricians. I think it's to have a mechanism to have them both bring together - bring them both together.

Simone Whale: Do you need this multidisciplinary approach everywhere or should there be centres that focus on this rather than trying to make it happen everywhere?

Shakila Thangaratinam: In the last Confidential Enquiries, more women died from epilepsy in pregnancy than pre-eclampsia for which we are very good at managing. So, I think the more efforts we make to bring together the neurologists, midwives, epilepsy specialist nurses and obstetricians, I think the better we will be in improving outcomes for these women. I think there definitely - yes, it's the place or if they don't have the capacity at least have a system in which they can actually refer to a closest tertiary unit for care of these women in pregnancy.

Simon Whale: Just taking a step back for a minute from the guidance, this review is looking at three different elements as Baroness Cumberlege mentioned at the beginning. One of the themes that runs across all three is the - it's about women, women who've raised concerns about what's happened to them and to their children. What we've often been told as we've travelled around the country and met many hundreds of people affected, is that they've been ignored or worse, actually dismissed, by the medical profession. Does that surprise you?

Shakila Thangaratinam: I think we as a medical profession from my interactions with the neurologists and obstetricians have been aware of the risks that valproate poses. I wouldn't necessarily say the medical profession would be dismissive if somebody says I have got concerns about valproate intake, or the dose because it has been recognised to be a drug that has or the potential to cause harm to the - a high potential in fact to cause harm.

So, I can't really comment that the concerns would be dismissed because that's not been my experience working with clinical colleagues, either neurologists, epilepsy specialists or obstetricians.

Simon Whale: I think in the case of valproate, it's concerns expressed after the birth of the child as opposed to concerns about taking valproate. It's the woman noticing or family noticing that there might be something wrong and then trying - battling to get support and treatment and diagnosis in the first place for what's wrong. They've really struggled to do that.

Shakila Thangaratinam: I think it will be the neonatologist with whom they'll be having these conversations with because they have concerns about the baby, the first port of call is talking to the neurologist - the neonatologists and then coming backwards and asking the obstetricians.

Simon Whale: I just wondered whether it's symptomatic of a general problem within medicine that there's a tendency not to believe the patient.

Shakila Thangaratinam: Oh, my own practice has been to address any concerns that the mum has, so much so they even bring them afterwards for a six week detailed chat about delivery of the baby. So, I think it's

very hard for me to overall say that it has been - I'm - I really - it's difficult that some of them do feel that way. Without the individual - details of individual case, I think it would be very hard for me to actually comment on that.

Simon Whale: Okay thank you. Cyril.

Cyril Chantler: You're a Professor in maternal and perinatal health?

Shakila Thangaratinam: Yes.

Cyril Chantler: Do you see mothers and babies who are affected by other teratogenic genetic agents, foetal alcohol, warfarin, immunosuppressants?

Shakila Thangaratinam: Many of them will be diagnosed if - in trying to be done through the foetal medicine unit who deals with malformations in the foetus. If they are also coming to the epilepsy clinic, then, yes, their babies with [unclear]...

Cyril Chantler: Have you done any work or research on other teratogenic agents other than valproate?

Shakila Thangaratinam: No. My focus has also been in epilepsy. My research has been on epilepsy and antiepileptic drugs. Not specifically on valproate or malformations, it's only in the context of my overall work.

Cyril Chantler: Thank you.

Valerie Brasse: What about the new generation of antiepileptic drugs? So, something like Keppra. We have women who have now moved on to Keppra and actually some who've said we think we've got problems with that too in babies who are new-born.

Shakila Thangaratinam: Absolutely. I think that's - it's very important we actually know the effects of these drugs. So that's - so two things. (1) You want to know the immediate effect of these drugs, physical manifestations and that's why we need every single mum who is on antiepileptic drugs to register themselves in the UK...

Valerie Brasse: I was going to ask you about the...

Shakila Thangaratinam: UK pregnancy registry. Then the next one is the long-term effects of these agents like Keppra for example, we are planning to follow-up the babies who are born in the EMPIRE trial. So,

these babies are now five years of age and they have been exposed to newer antiepileptic drugs like Keppra and offers a good opportunity for us to study and actually compare. These are randomly allocated so there's a group who are exposed to possibly higher dose of Keppra whereas others are the smaller doses.

Valerie Brasse: So, have you got any earlier results of findings from this?

Shakila Thangaratinam: We need to get the funding to follow-up. But we have got consent from mums to follow their babies up, because it's better to wait - I've been told by the neuropsychologist it's better to wait a bit longer to have some definitive answers on the effects of the neurodevelopment and they can't do it at an earlier age. But that's something that frankly - that's something that needs to be done. Not necessarily in trial context but even in - as part of routine practice, we need long-term safety data.

Valerie Brasse: Well, because we don't want a repeat of the sodium valproate story.

Shakila Thangaratinam: Yeah definitely.

Valerie Brasse: Can I just ask you about the register because at the moment the way it's set up, I think is it only follows through until the babies are - reach a three-month stage, the UK Epilepsy and Pregnancy Register?

Shakila Thangaratinam: I don't - I'm not involved in that follow up of the registry.

Valerie Brasse: So, you haven't used it? You've not...

Shakila Thangaratinam: No, I have not used it, no. But I ask mums to go on and enter their details. I think the team that's involved in it might be able to give you better answers on [unclear] [they're following up].

Valerie Brasse: I'm just wondering about its usefulness if that is indeed one of the parameters that it stops at three months. It doesn't sound like it's giving the sort of follow through data that you want.

Shakila Thangaratinam: They may be able to contact mothers for a long-term follow up.

Valerie Brasse: Yeah, they can do that, thank you.

Julia Cumberlege: Yes, we heard this morning from another witness that really, we should follow up to at least they go to school these children go

to school because then other things you can decipher that [unclear]. Is there anything else you want to tell us?

Shakila Thangaratinam: No, I think we've covered everything but please let me know if you need any information that I may not be able to provide you today and I can provide you by email if needed.

Cyril Chantler: Thank you very much.

Julia Cumberlege: I'm just going to ask my team; do you have any further questions?

Sonia Macleod: I just wanted to - in your evidence, you said that going forward it would be useful to have a qualitative study on women's views of epilepsy in pregnancy and their risk [unclear], is that in progress or is that...

Shakila Thangaratinam: As part of the EMPIRE trial, Professor Elaine Denny, she's from Birmingham - the group has done qualitative work on the groups of mothers with epilepsy in pregnancy and on taking antiepileptic drugs. So that's actually out as an HTA report. It's published on their concerns about taking the antiepileptic drugs, but these are not women who are on valproate. I can provide you with a copy of that report.

Sonia Macleod: Oh, so that - so that pre-dates this though doesn't it? I wondered if things had changed since...

Shakila Thangaratinam: No, they haven't done any qualitative work since.

Sonia Macleod: Okay.

Julia Cumberlege: Well, thank you so much for coming. I just want to say at the very beginning you were talking about less than half of pregnancies are planned. I just want to say I was extremely surprised to find when I was pregnant but actually delighted. But you're quite right. Thank you for all the information you've given us but thank you particularly for all the work that you do for women and I'm sure they and certainly we are very grateful to you, thank you.

Shakila Thangaratinam: Thank you for giving me the opportunity to come here today and if it has been helpful.

Multiple speakers: Thanks.

END OF TRANSCRIPT

7th February 2019

Session 1: British Pain Society

START OF TRANSCRIPT

Julia Cumberlege: Perhaps if we could just start by introducing ourselves and for the purpose of when this goes up on the website, if after I've introduced us, perhaps you could introduce yourself for me and say who you are, et cetera, so that we've got a proper record. Just one of the things that we've been asking people is whether they've got conflicts of interest and I don't think we've actually had anything from you on that particular subject yet. So, I don't know if you want to say anything right now, or whether you would send us something later.

Andrew Baranowski: I have no conflicts of interest, financial or otherwise, but obviously I've been involved in a range of guidelines committees over the years and that will bear relevance on my perspective of...

Julia Cumberlege: Right, that's good, thank you very much. So, I'm Julia Cumberlege and I was invited by the Secretary of State to chair this review. I just felt it was very important that I got the people I could around me, so we've achieved that. On my left is Sir Cyril Chantler, who probably you know, but is hugely respected throughout the land.

On my right is Simon Whale and Simon is particularly looking at communications and things, but he's part of the three panel that we've got. But of course we need very high level support and so on Simon's right is Dr Valerie Brasse, who is our secretary. On Cyril's left is Sonia Macleod, who is our principal researcher. Then we've got other people in the room who are just here to help us make sure we run this correctly. So just for the camera, if you could just say who you are and what your position is, that would be helpful.

Andrew Baranowski: My name's Andrew Baranowski, I'm a consultant in pelvic pain medicine and neuromodulation. I'm based at the National Hospital for Neurology and Neurosurgery, Queen Square, which is part of UCLH NHS Foundation Trust. I've been involved in the management of those living with chronic pelvic pain for 25 years. I've been running a dedicated pelvic pain clinic, using the multidisciplinary team model, for over 20 years. I've been running joint clinics with urogynaecologists, neurosurgeons, radiologists and rheumatologists for much of that time.

I've been involved, as I suggested earlier, in guidelines as a panel member of the European Association on chronic pelvic pain guidelines, which is highly respected as an education and training tool in the United Kingdom for chronic pelvic pain since 2004. I led the British Pain Society's maps for pain, including and surpassing the map for care of pelvic pain. I've written widely on the subject, lectured on the subject and I was the immediate past chair of NHS England's clinical reference group for highly specialised pain services and am currently president of the British Pain Society.

Julia Cumberlege: Wow, very interesting career, thank you very much. Can I just say that we listen a lot to the patient groups and we have heard a huge amount from them. We've had complaints from women that there really doesn't seem to be any formalised pathways and it's almost a matter of luck whether they get referred to the correct services. I just wondered if you could say whether you feel that these pathways are clear and whether women are given enough information to know how to access them.

Andrew Baranowski: I think the guidelines for the pathways are quite clear. I think that the service specification for highly specialised pain services, that I drew up which is the D08 specification, made it quite clear as to how it should fit together. I think it's still in draft format, but the latest version, the D07, quite clearly talks about pathways of care in terms of providing appropriate expertise, local to where the patient lives, but then referral onwards to more highly specialised services as appropriate to seeing the right specialist at the right time, local where possible and at a more regional and national centre where necessary.

The problem with the pathways then is whereas the professionals have defined them, I would say the problem is a lack of resources to actually provide them clinically, rather than actually they're not defined.

Julia Cumberlege: So obviously this is seen very much through the specialist, through the people who are providing pain clinics and things like that, but how does that information get to women? Because at the moment they're saying that it's purely by luck whenever they get to a really very good specialist who's going to address their problems.

Andrew Baranowski: If you're talking about pain specifically, there are only four or five centres in the United Kingdom that can provide highly specialised pelvic pain services. Therefore, it's done basically by word of mouth amongst the clinicians. So most, if not all, of my pain management colleagues would know about the services that patients can access. There is obviously interaction between pain speciality and other specialities in terms of

education by lectures and so on, but that is informal. So the patients are quite correct in saying that it is very easy for them to go round in circles.

One of the issues that I'm dealing with at the moment, I'm sorry to say this is particularly a problem in the private sector, is where patients go around in circles from one person to the other locally, as opposed to having an umbrella opinion. So I believe that one suggestion is that there should be localised mesh centres, the number of which is not for me to determine, all of those services should have a consultant with an interest in pelvic pain associated with it and any highly specialised pain services should then have highly specialised clinicians involved with it who have got the experience and the knowledge.

So it's only by having the clinical pathways, I think, that the patients will access them. Obviously, there's information on the British Pain Society website and there are patient forums through the Twitter campaign, this, that and the other. They know about the different systems there are, but that's all informal.

Julia Cumberlege: Yes, please.

Cyril Chantler: If I understand it correctly, you're saying that there are five specialised centres recognised by the British Pain Society dealing with pelvic pain. Are they recognised by NHS England? Because you've mentioned that they weren't appropriately resourced.

Andrew Baranowski: There is then this issue about the role of the professional societies in recognising different departments and that's probably not an appropriate thing for me to discuss. So the British Pain Society purposely does not recognise centres; it provides education, training...

Cyril Chantler: Then who does recognise them?

Andrew Baranowski: NHS England certain specification clearly states what those services are and then the NHS England commissioner of the specialised services commission body would recognise them.

Cyril Chantler: So are you specialised - you're supported by specialist commissions?

Andrew Baranowski: Yes and it's those commissioners that recognise the services, not the British Pain Society.

Cyril Chantler: Right, well there is the plan, which is now being developed as par for the course, for specialised mesh removal centres to be also supported with specialised commissioning and accredited appropriately. Would there be

a coterminosity then between the pelvic pain centres and those mesh removal centres?

Andrew Baranowski: When I was chair of NHS England's clinical reference group for highly specialised adult pain services, pain was acknowledged as being a cornerstone for any other highly specialised service. The problem has always been that pain management is considered a Cinderella speciality. Then when I talk about lack of investment, you will find that a lot of clinicians are working on their own without appropriate support from trained pain management physiotherapists, psychologists, nurses, and that they're struggling. As far as I'm concerned, there should not be a highly specialised mesh removal service without involvement of a highly specialised pain management team, which does not mean just a doctor; it means a team of doctors helping the patients.

So the model at University College London is a model where I've been supported and I started off with myself, my nurse who still works for me 25 years on, a psychologist who works around the corner, a physio who works with me 25 years on, and a consultant whose retirement do I go to after this meeting. Now we have a team of 90 people because the hospital has supported us and we can provide psychology, physiotherapy and dedicated nursing on drug reductions, drug manipulations, neuromodulation and all those things. Therefore, that is what I would advocate, personal view obviously, that's what should be available at those highly specialised services.

My understanding is that there will be some services who will be removing mesh on the grounds - well we probably need to discuss that, removal of mesh is a separate issue, but if the decision is to remove mesh, there will be some services that remove it based on the grounds that there's an infection, there's an alteration, there's an erosion and that would be one group of services. Plus looking at the numbers of people involved in this, six services would never be able to do that.

Then there will be, as I understand it - and you probably know more than me - a number of highly specialised services. So first set should have pain clinics attached to them, the highly specialised should have high specialised pain services attached and that should be something that NHS England should lead on.

Julia Cumberlege: Can I just ask you, it's very interesting, clearly yours is a model and you would like to see it replicated in these other centres. But you're talking about four or five centres and I'm just thinking about these women who are in excruciating pain and actually they're finding it extremely hard to

travel at all. Accessibility is actually very, very difficult for them, so they obviously go to places where there isn't quite the same specialism, there isn't quite the same setup that you've got, which is clearly resource intensive.

So how about those women? What do you do with those who are not in your profession, in the area that you work in, that are not specialists? What do you do with those people giving some advice to women, but clearly for some women it has been a waste of time?

Andrew Baranowski: As I was saying or trying to make the point that actually there should be pathways of care; no pathways of care exist. So the problem is, to some extent, you're talking about this in terms of lack of resources in those areas.

Valerie Brasse: How big is the resource gap?

Andrew Baranowski: I can't give you an actual figure, but if you look at the map of England where they say what clinic it is, it's really quite bad. There are big gaps where there aren't pain services and one of the problems when you look at the - I can't remember the name of the map of distribution of services, but when you look at that, I think there are 600 pain doctors in the country and a lot of them are working independently.

Sonia Macleod So they're not part of the team. So in terms of...

Andrew Baranowski: So they're hardly supported, yes.

Sonia Macleod: I mean in terms of the capacity within the system to enable the patients to access specialist services, are you saying that...

Andrew Baranowski: So we talk about speciality and specialised services, it's the speciality services we're talking about where many of those doctors are working independently and under pressure. If we look at the impact of pelvic pain on the quality of life, pain in its own right in the more severe end has a greater impact on quality of life than most serious conditions. If you then throw into that pelvic pain, where you've got the patients who can't sit down, they get debilitated and then you get all the comorbidities. So in the pain service we have to look at things like it's not just the mesh; there is the result of having chronic pelvic pain and not just localised, it becomes regionalised.

Therefore, these patients will possibly have primary bladder conditions as a result of what got them to where they are at the moment, but we know that this group of patients will also then have secondary phenomena

related to the chronic pain mechanisms. So, the World Health Authority now acknowledges that pain is a primary condition in its own right, ICD-11. That means that you can have pain without an obvious pathology, so an infection, an erosion or whatever. Those mechanisms are of the central nervous system and that results in a centralised process which affects other organs.

One of the problems, I understand, is that patients are not being listened to because they've got a small piece of mesh and they're complaining of bowel, bladder, sexual dysfunction and then they're complaining about systemic disorders. There is good evidence that in the bladder pain syndromes that the systemic disorders are modulated or mediated by the central nervous system. So in non-mesh patients with bladder pain disorders we see a higher instance of chronic muscular pain syndrome, fibromyalgia and long-term chronic fatigue, but you also see a higher instance of autoimmune disorders such as Sjogren's disease, dry eye syndrome and you see a higher instance of endocrine abnormalities such as hyperthyroidism.

So the phenomena these ladies are describing have a scientific background and basis, which can be substantiated. So when we're looking at these people, there are going to be major issues on the ground that cannot be dealt with by lone consultants; they need to be working as part of a team. They need to be working with appropriately trained pain management psychologists, appropriately trained pain management physiotherapists, where the approach is different to hands-on physiotherapy. But it is that interaction and of course, clinical nurse specialists. My nurses are running the show whilst I'm here.

Julia Cumberlege: So how successful are your treatments? How many women actually go to these specialist centres and then actually find that it's been pretty ineffective?

Andrew Baranowski: I think it depends what you're looking for and I was thinking about this in terms of mesh removal earlier. I think it comes down to patient expectations and what they're looking for. What we have to acknowledge is that pain is (multidimensional) and it's associated with a huge impact on quality of life, so emotional distress, depression, anxieties, fears, social breakdown, marital breakdown, sexual relations falling apart and all of those things. So pain is multidimensional. If you're looking for purely a reduction in pain, then the outcome of the procedures is limited, but there are certain things that, if it's appropriate, neuromodulation, electrical stimulation of the nerves and so on.

In that you may see a 30 to 50 per cent reduction in the pain. The problem is part of the reason why I emphasise the MDT is that actually any treatment is doomed to fail unless you take on board the concerns of the patients, the psychological and behavioural ability to do things, behavioural impact of the pain, all physical treatments are going to be a problem. I'm thinking of patients I've seen recently whereby the issue has then been about tape removal. As a non-surgeon there are clear indications when you might want to remove the tape.

We're going to get into problems when we have these issues where the patient wants the tape removed and there's a question about actually what is going to be the outcome of that. So it's not only about the outcome of the pain management intervention; it's about the outcome of any intervention for pain if you're not addressing supporting patients in terms of understanding what the outcome is going to be. That could be an accusation of the meshes in the first place, is that they didn't have informed consent.

When you've got a distressed patient who's suffering, how can they give informed consent unless you're addressing that? So unless you're looking at pain management strategies in terms of medications, possibly drugs and various things like that and injections, but then we need to combine into that the psychologist support and the physical support so that you have a stable position to work on. Complicated answer for a complicated question. That's why you need the team and that's why people working on their own will struggle.

Julia Cumberlege: Thank you very much. Simon, did you want to...

Simon Whale: Can I ask whether you know how many women suffering mesh complications get referred to pain clinics?

Andrew Baranowski: A small proportion. It's a small proportion, I think, which is what you're saying, that's the patient experience.

Simon Whale: Does the British Pain Society collect any data on that?

Andrew Baranowski: No, no one's collected that data. We've just started collecting that data in our departments, to look at the number of patients that we see. In January we referred 12 patients and we think that's an increase in number. Now, 12 patients may not sound much, it isn't in the scheme of things, but actually that is the work for a team in a sense in a month, to see 12 patients.

Simon Whale: Are they all mesh-related?

Andrew Baranowski: Those are the mesh-related patients. I don't know what the - I'd be guessing if I said we get hundreds of referrals. I would easily imagine it's going to increase from five to 10 per cent up.

Simon Whale: So it's around five to 10 per cent?

Andrew Baranowski: I'm guessing.

Simon Whale: If you think, I don't know, over the last five years...

Andrew Baranowski: It's gone up, it's the last few months, last six months.

Simon Whale: Why do you think that is?

Andrew Baranowski: Greater awareness by the surgeons around the implications probably of not working with a pain team and the management of the patient. I think patients have anxieties and concerns about coming to pain clinics, because they feel that they're actually going to have their pain managed and not have the underlying condition managed.

Valerie Brasse: Would they be right?

Andrew Baranowski: No, I don't think so. It depends on the clinician. A lot of these patients I see in joint clinics and I've restructured the service recently to make sure that these patients have a proper pathway of care when in hospital, whereby they're triaged as appropriate. If we look at something like endometriosis associated pain, nurses are quite capable of taking a look at that population on board, triaging them and managing a lot of their fears and concerns. Doctors then become involved in others, and those more complicated patients I will do in the clinic with my urogynaecologist, my urologist and so on.

I've just set up another service parallel to that, with another consultant like me who is in the clinic with a urogynaecologist and nurses and we have access to psychology and physio. Even in my hospital, management is saying well where's the money coming from for this? Because we're taking on board new work in theory by restructuring, so it's going to be a knock-on effect. So no, we are taking on board, we are the most holistic group and we've done over 25 - well since pain medicine started, we're one of the oldest professions obviously.

Valerie Brasse: So it's not a question of if you get the pain management right you can actually avoid some of the bigger complications of removals around mesh.

Andrew Baranowski: You can, yes.

Valerie Brasse: That's what I'm trying to get at, in a way linking in your specialist centres sort of suggests you need the specialist centres earlier, lower down, but it's a way of dealing with this so that they don't end up having to have complicated mesh removal surgery.

Andrew Baranowski: The model that we're working on at the moment is that group which people often will say is a surgical decision to remove mesh, or joint with the patients obviously. Then there's that group where the mesh is not causing an anatomical abnormality or pathological process and that will fall into two groups, as I understand it. One is where the mesh is not quite right, in that it's too high or too low and does anyone really know what that means? Then there's the group where it's perfect but they've got all these symptoms.

So, in terms of the future, it's really imperative that we collect data on the mesh removal, because in 10 years' time there's going to be people saying 'why were you doing that?' That group of patients where it's much more difficult to make a decision, the pain doctor and the pain team should be involved much earlier, in my personal opinion, to try and stop that. The issue comes when you have a patient who is so traumatised by what they've been through - and I do a lot of work with veterans, I do a lot with post-traumatic stress disorder and the relationship between PTSD and chronic pain like this, PTSD goes up with the chronic pains.

So in those patients who've been traumatised by their experiences of the complications from the mesh, for what was a minor procedure, then who have been going through a process where they've not been believed and listened to, then have been traumatised by painful investigations and so on and so forth, you need to be managing that before you make a decision about removing the mesh. The problem is in that group of patients, sometimes they can be determined that the next thing they want is the surgical removal, so we may not be able to stop them, because we have to listen to our patients as well. It's just making sure that they have been given the information they need.

Simon Whale: I guess the question is how frequently and how commonly surgeons would see pain management as one of the early line, first line or second line, options prior to removal, as Valerie says, not just in your own clinic but elsewhere.

Andrew Baranowski: It's a major problem, when we have been saying for 25 years and publications go back that all surgeries associated with chronic pain, 10 per cent incidence. That's a figure that we would say that if you're consenting for any operation, it's over 10 per cent. If it's a thoracotomy it may be

higher, if it's a vasectomy maybe five per cent, but even simple things [unclear]. So surgeons, we would say, should not operate on a patient for pain reasons. The outcome of operating on the patients because they're complaining of pain can be very poor, if that was your first approach and that applies to everything.

Simon Whale: How confident are you that surgeons understand what you've just said?

Andrew Baranowski: I'm not confident. Recently through some of the work that we've been doing, partly through the British Pain Society and partly by trying to interact with our surgical colleagues and there is the mesh meeting that is scheduled, we're getting the message across to the highly specialised groups. I'm hoping that NHS England will support that there are those services set up that actually pain management would be a cornerstone and it will not be a total cornerstone; it will be a proper service.

Julia Cumberlege: Can I ask you, clearly what you're doing here is a model, intensive in terms of resource and not just money but obviously expertise. How about the women though who just are in such agony, in such pain that they go to their local area and there's somebody there who's saying 'yes, I can deal with the pain for you?' What do you as an organisation, as a society, what do you do in those circumstances? Do you do any further training of those people? How do you...

Andrew Baranowski: Our society, as I said, does not recognise - well it is based on education and training and it is primarily to support our members, who are pain doctors, psychologists, nurses and physiotherapists, to actually support them in their work locally. So, to a certain extent, it's about teaching teachers. So I would expect the members to be actually going to the local hospitals because of the resource implications; all of our conferences are open to anybody with an interest in the field, whatever their specialism in the interested field. All of our resources, our publications, so we recently published publications on things like education around pain in medical schools, where if you're a vet you get more hours on pain education than you do in a medical school.

So now the work we're doing with [unclear] the work that we're doing at the moment, joint work with the faculty of the Royal College, which obviously has more of an official role, as it were, is around medical schools beginning to actually take on board basic pain management strategies and training. That's how bad it is, that we're only there now.

Simon Whale: Is one of the symptoms of that a cultural problem within the service?

Andrew Baranowski: Yes.

Simon Whale: So how would you describe typically the relationship between surgeons and pain management teams?

Andrew Baranowski: It's a Cinderella speciality isn't it, then I guess it's not for me to - there is I guess an element that if you give a surgeon a patient that needs a surgical possible approach, he will go down a surgical line. You might say that if you gave the patient a pain management approach, they'll go down the pain management line. I think pain consultants have had to work across the disciplines, because we work with sickle cell disease, we work with cancer and all that. We have to work as a team and therefore, I think you're talking to people who are going to be much more open and prepared to work in that way.

A surgical MDT quite often consists of a group of surgeons with similar ideas in the same room. An MDT in my department, we've got a lot of people there, I would expect 30 or 40 people in that room every week for one hour; major resources, talking about the patients with complex drug dependency problems which usually started elsewhere. Complex issues, psychologically, psychiatrically and socially, and in that room we will have input from psychologists, physiotherapists and nurses and doctors. The doctors will have different interests [unclear] to patient care recently.

So obviously yes, an elite area, but there's no reason why an MDT in a DGH hospital cannot take place with other people. We should include, if not a psychologist, a psychiatrist, though there are differences in their approach. It should include a pain management person, it shouldn't be a roomful of surgeons. Now we've started doing a bit of that at UCLH. You're probably aware there are differences of opinion in the teams I work with, both teams, I've already made it quite clear that the services we provide will be equitable for all services. I was recently at an MDT meeting full of surgeons, I was the only pain doctor there and it made a difference, I think.

They asked me would I see the patient, I said 'no, this is a surgical issue'. They asked me would I see a patient, I said 'yes, I think this is an issue where pain management could take part'. Unless you actually do that, interact, you're going to have the problem of it's one modality, one speciality making the decisions and that's not correct.

Cyril Chantler: It used to be the case in my day, if I could put it this way, that most specialists in pain management came from a background in anaesthetics. Is that still the case?

Andrew Baranowski: That is still the case. It's interesting because anaesthetists are sort of like this, aren't they, in terms of keeping people alive, this, that and the other. The background to that was that - and there is still an element of pain doctors going to it because they enjoy doing interventions. So I enjoy the neuromodulation of spinal implants and so on, but there are clear guidelines as to when that should happen, NICE guidelines are perhaps some of the strongest guidelines out there [unclear].

So there is that element and then it is interesting that actually you have anaesthetists with that psychological sort of background, who are involved in supporting these sorts of patients. Most of the anaesthetists I talk to actually embrace the MDT approach, but what they'll say is that in the smaller hospitals they don't have the same opportunities.

Cyril Chantler: Can we talk about outcomes?

Andrew Baranowski: Yes.

Cyril Chantler: I think many people, myself included, believe that when you look at outcomes, (a) that it's very important for clinical research and audit to concentrate on outcomes. But particularly look at outcomes in terms of what are the clinical outcomes, but what are the patient-related outcome measures that the PROMs have been applied and the patient experience. Then you have to integrate the COMs, the PROMs and the PREMs.

If you can actually look at the overall resource cost of that intervention, you get a notion of value which is the way of actually trying to make sure that the multidisciplinary team approach, where the outcomes are positive in terms of value, gets properly resourced. So could you tell me about the outcomes measured in those terms that you get from your involvement in the multidisciplinary team and also point us to any publications?

Andrew Baranowski: Yes, so the British Pain Society, I commissioned a document on outcome measures last year as a joint piece of work with the faculty for pain medicine, Royal College of Anaesthetists, on outcome measures. That is available on our website, I think it was eventually published after a bit of delay a few weeks ago. That document reviews all the outcome measures and those measures are around quality of life measures as well. So they look at psychological, emotional side of things, physical disability, as well as pain scores which are actually only a part of the issue.

If you're looking at outcome measures in terms of procedures and input by the teams and so on, it becomes difficult because of what I'm saying, we're looking at a team approach. I sometimes will be using a procedure

not to purely get rid of the pain, but actually to be able to work with the patient. We're looking at maybe reducing some of the stress, some [unclear] minimally invasive types of injections or whatever will help us be able to work with the patient more from the psychology of the pain management, the behavioural approach. So it becomes a package that we're talking about.

The evidence base around pain management programmes and so on, so there are [unclear] and I think this document I gave you, there may be something in there, but there are lots of publications by the King's group, by our group and so on, looking at the evidence base for pain management programmes.

Cyril Chantler: Have you published a series of your own team's involvement in pelvic pain?

Andrew Baranowski: Pelvic pain, I've been mainly involved as a clinician with the guidelines, I've struggled to publish because I haven't got the resources, so it's about what you do. My team has actually collected all the data that we publish in terms of posters looking at the amount of distress that patients have, and that information shows quite clearly that the patients with pelvic pain are of the highest distress group. That the patients with more systemic elements are of the even greatest widespread pain as well, instead of just local. So we've got that sort of data in publication.

Cyril Chantler: You've got follow-up data?

Andrew Baranowski: The problem with follow-up data in pain patients is actually how do you make sense of it, because of the fact that it's a team approach. So each patient has a personalised treatment plan, rather than this being...

Cyril Chantler: I understand that, I'm not really seeking an answer to the question of process, what works, what's efficacious, if you like. I'm just - what is effective in terms of outcomes, but if you've got 100 patients who are referred to you with pelvic pain, going forward one, two, three, five years, have you been able to make their lives more tolerable?

Andrew Baranowski: The simple answer is yes, and you can look at it from the perspective of actually looking at the individual patient that comes in on a gram of morphine and you can reduce it down to a sensible dose, then that is a direct clinical effect. So in that sort of way - and obviously looking at medication usage is a reasonable way - we can look at things like casualty attendance, we can look at things like attendance at GPs and we've shown...

Cyril Chantler: But is this data published, that's what I'm seeking?

Andrew Baranowski: Some of the data's published, but not specifically around pelvic pain.

Cyril Chantler: Are there any reviews, any papers on outcomes on pelvic pain specifically?

Andrew Baranowski: There are papers by Curtis and Nichol and so on in Canada, which would show that if you have specific programmes and specific groups of patients with pelvic pain, but they're not necessarily women...

Cyril Chantler: Because we've heard that there are some women who are suffering terribly, but where mesh removal is probably not possible in its totality. So where do we offer them hope, is what I'm seeking.

Andrew Baranowski: It's very difficult to give you the outcome data that you're talking about. On an individual basis, if you look at things like the responses that the patients give us internally about their journeys and so on, then you'll say that actually they're getting an improvement, they're seeing benefit. What you will find though is there will be always some patients who are very distressed, and it is a three or four year journey to try and actually resolve that. So to monitor that in terms of providing outcome data becomes very difficult.

Cyril Chantler: One of the recommendations which is part of the pause is that all interventions should be registered, national database and then a more complicated register working with it. But my experience of working on other areas, that's hugely valuable because you can then look at outcome data of one, two, three, which is comprehensive, nobody excluded. You can then work out what is effective and what is less effective. I would think that the responsibility of specialised centres should be absolutely to engage in that sort of research.

Andrew Baranowski: There are certain aspects of the data that has been collected and that has been published, but we have to remember that actually we're talking about a large service which has different components and therefore there are different aspects that have been published. So as a service it is committed to publications and research.

As a Cinderella service, we have struggled to keep academics, so I stopped doing research 15 years ago, primary research [unclear] type of research because of the lack of resources and lack of support. It's become more and more difficult to be a jobbing clinician as well as to publish that research. We have collected the data on a range of things such as [unclear] modulation and so on and getting that published as a part-time

researcher is really difficult. So that comes down to having appropriate resources.

Valerie Brasse: You're not actually following that through, you're not recording those interventions on a database, so the pain management side of following a patient who's got pelvic mesh problems...

Andrew Baranowski: We've only just got to the stage of there being a national registry for neuromodulation and even that's not been followed through by all of the centres. So there isn't a system for doing that.

Sonia Macleod: Presumably when you're talking of pelvic pain, you are not talking just mesh pain; you're talking the full range.

Andrew Baranowski: I'm talking about the full range, yes, so that's why we've separated out the mesh patients, to try and deliver what you are talking about. The initial stage of looking at the mesh patients has been to look at how they compare in terms of distress to the other pelvic pain patients. The outcome of that is suggesting that they are worse off than the pelvic pain patients, which are worse than general pain patients. So pelvic pain in general and patient pain are amongst the most severely compromised individuals and the mesh is worse than that.

Julia Cumberlege: Do you think with the introduction now of modern technologies in terms of communications and things like that, would that help you?

Andrew Baranowski: Is this going back to the communication of patients...

Julia Cumberlege: Well it's the database, because it's having to collect the information, you said, as a jobbing surgeon, sorry, pain specialist, you would find it difficult. But we've just been in another field altogether looking at how - it's in maternity services - how that actually when you can introduce new electronic methods...

Andrew Baranowski: Yes, so we tried to do that three years ago with the iPad outcome measures and so on, which would answer your question and there was an issue of lack of resources to provide that type of technology. I don't know what the throughput of patients is within our service and you'd then have to look at patients who are presenting for individual care, but we also have group programmes. The group programmes are where most of the data is collected, because that is an intervention that is well defined. That outcome information is positive, it actually shows that you improve quality of life of individuals living with pain.

We run dedicated services for head and neck pain, in terms of pain management programmes, head and neck pain, pelvic pain, nerve pain, facial pain and so on. So we have dedicated pelvic pain management programmes. We have that data and that data is published. But individual data, the journeys of patients, is more difficult. What you're suggesting would be helpful, it comes down to resources.

Cyril Chantler: Can I move on, because I'm conscious of the time. NICE guidelines, are there NICE guidelines on managing pelvic pain?

Andrew Baranowski: Are there NICE guidelines on pain? So at this point in time, they're drawing up NICE guidelines on pain and my understanding is that's going to become primary pain specifically. We then have the argument of what is primary and what is secondary in terms of things like mesh. So there is an element of - and this is part of the problem, the WHO guidelines which several of us have pointed out to you, is when does something become primary and something become secondary.

So at the moment they're looking at primary guidelines and as with NICE, it has to be all evidence-based and well indicated. There is a problem in that there also needs to be common sense. So, this is like the mesh removal, I can see there's a common-sense approach to certain things and some of it you're not going to have the evidence for. It's the same for pain, some things are common sense and other things that will be evidence-based. I think those guidelines that are due to be published in the next 18 months or two years are probably not going to be helpful in this situation. So the answer's no.

Cyril Chantler: Thank you.

Sonia Macleod: So what would be helpful in terms of guidelines? In the executive summary to the APPG you said that specific guidelines on the management of complex issues secondary to mesh are needed. So how would they be useful? Where would they come from?

Andrew Baranowski: Sorry, can you ask...

Sonia Macleod: Sorry, in your executive summary to the APPG you said that there should be specific guidelines for the management of complex issues secondary to mesh and such. Could you please tell us a little bit more about...

Andrew Baranowski: This comes back to then, I think - there are several pathways for this. There's the pathways of care that we've alluded to, making sure that you're seeing the right person at the right time. The NHS England service specification DO7 quite clearly sets that out and as we've identified,

there's a gap in the speciality secondary care services compared to the highly specialised. So that guideline exists, it's a matter then of implementation. The guidelines in terms of pain management exist by [unclear] the British Pain Society.

So what we then have got to do is look at the relationship between - again it comes back to the question [unclear] about the relationship of pain specialists, including the team, with the surgeons and there needs to be guidance from, I think, NHS England on that as to yes, these links should be approved and should be happening. I think that comes down to a common-sense approach. It's much more difficult to actually prove it in terms of evidence-based and that's where I'm concerned about the evidence base.

To me it makes sense that actually you don't have a meeting with just the surgeon, but we have a meeting whereby actually you get representation from other people. That may include rheumatologists, if we're thinking about a widespread pain network, that may include radiologists as well. So that's the sort of guideline which probably needs to be drawn up as to how it all fits together, so it's a pathway that meets the needs of the patients.

Sonia Macleod: So more integrated?

Andrew Baranowski: More integrated.

Julia Cumberlege: Did you want to come in?

Sonia Macleod: No.

Julia Cumberlege: Dr Baranowski, this has been so useful, I can tell you. What I'm going to do is to ask my team if they've got any further questions. Then if there's anything further you want to tell us. So Sonia, [unclear].

Simon Whale: No.

Valerie Brasse: Just one other one and maybe you might want to [unclear] this afterwards, can you discern from the patients who come to you a difference in terms of pain between those that have had pelvic mesh and those that have been treated with [unclear] procedures like colposuspension?

Andrew Baranowski: I think there's a common-sense answer to that in that those patients who have pelvic mesh are going to present being more traumatised than if they had pain for other reasons. I guess there is an issue that if you didn't have pain for procedure - and the problem with this simple procedure can

be colposcopy looking inside the cervix (I had a lady recently like that) or a cystoscopy or something like that. You go in with a relatively minor problem and you come out and you end up in chronic pain. Then it causes distress and that may be childbirth, or it may be something very simple.

Valerie Brasse: Colposuspension of course is not a minor procedure.

Andrew Baranowski: Precisely, so then if you look - this is my inclination. So if you're going in - so my concerns are that I'm not in a position to comment on whether or not mesh should or should not have been used, that's not my skill.

Valerie Brasse: I'm not asking you...

Andrew Baranowski: No, no. So my concerns are around the consent process and the previous investigations that certain patients have undergone prior to having mesh. It's not my responsibility to say exactly what they are, but having worked in joint clinics with urogynaecologists for quite a significant period of time, I consider myself being at a district general hospital level in terms of understanding what I think should happen before the mesh removal.

If you then have someone who's been through a process where they've had minor symptoms, some incontinence or something, they've had minor symptoms, which can be distressing, but they've not had properly informed consent, then they're going to be even more distressed again. So if you're having a more major surgical operation, then the complications, you're going to have them explained to you a bit more. Can you take that on board? No.

Valerie Brasse: It's just the difference, obviously there are people now saying we really need to revert back and it's a skill base about who can do pelvic [unclear]; from your perspective of patients who deal with pain, just try to give them an understanding there's a differential between those that respond with the mesh and those...

Andrew Baranowski: I could not give you that data because we haven't got enough information, but there is a common-sense viewpoint as well.

Julia Cumberlege: Can I just clarify one thing? I think you said that when you're working here you've got 90 different clinicians involved.

Andrew Baranowski: Yes.

Julia Cumberlege: Yes, that's very interesting.

Andrew Baranowski: That started from half a dozen of us, but they're not all involved in pelvic pain.

Julia Cumberlege: No, I appreciate that.

Andrew Baranowski: So we have a patient [unclear] complex neuropathy. So it is one of the largest [unclear] in the world and it is one of the, if not the largest in the UK. So we're very spoiled, but then we've been supported.

Julia Cumberlege: Yes, well you have to win support, so congratulations on that. Anything finally you want to tell us?

Andrew Baranowski: No.

Julia Cumberlege: You can always write to us.

Andrew Baranowski: I'm just advocating that actually pain management services do have a role in the assessment and support of these patients. It's difficult to prove it, but to me the common sense is there. The figures and percentages of pain can be variable, but in the self-reported questionnaire it was 100 per cent so...

Julia Cumberlege: Right, well, thank you so much. If there are any other further thoughts you have, we're very open to communications and do write to us or send an email or whatever. Thank you.

END OF TRANSCRIPT

Session 2: Chartered Society of Physiotherapy

START OF TRANSCRIPT

Julia Cumberlege: So if you'd like to just start off by saying who you are and what you do, and then we'll record that.

Natalie Beswetherick: Thank you. My name is Natalie Beswetherick. I'm the Director of Practice and Development of the Chartered Society of Physiotherapy. I am a physiotherapist and a registered practitioner, but that's my day job. So thank you very much for the opportunity for us to actually provide some detail about what physiotherapists do in the field of pelvic floor disorders. So I've prepared a briefing which I'd like to read, which has been gathered from researchers in the field and from experts of our professional network that focus on delivering on pelvic floor [new] muscle training to women with either stress urinary incontinence or pelvic organ prolapse. So if I may, I'll just read that through.

Julia Cumberlege: Yes.

Natalie Beswetherick: I have got a copy here that I can obviously send and forward a copy electronically to you, subsequent to this hearing. So we're aware that up to 30 per cent of women experience a problem with their pelvic floor muscles at some time during their lives, and pelvic organ prolapse is estimated to affect between 41 and 50 per cent of women aged over 40. The most common problems that we are aware of experienced by women with pelvic floor disorders are obviously unwanted leakage associated with physical activity, sneezing or coughing, which we know as stress urinary incontinence. As well as we know that this reduces - and can do - women's activity levels, these disorders can cause secondary health conditions as people age, commonly, urinary tract infections, skin ulceration and as well as depression. We know for many women, having a problem with urinary incontinence means that they are less willing to leave the house and they actually frequently stop doing regular exercise. So that's why we get engaged with it.

We know that pelvic floor muscle training are proven treatments to improve urinary continence, reduce symptoms of prolapse and improve women's quality of life and should be the first line of treatment for this condition. We are aware that a third of women suffer from a pelvic floor condition normally after childbirth, including stress urinary incontinence and pelvic organ prolapse, and while childbirth is the biggest cause of pelvic disorders, they can be quite common following a hysterectomy, and they can be seen as menopause symptoms.

We are aware since the early 2000s many women with pelvic floor disorders were offered transvaginal mesh implants. However, we are also aware there's growing evidence there's a risk of some complications for some women with pelvic organ prolapse, and we're aware that perhaps up to one in 15 women have later had to have their implants surgically removed. Whether or not mesh implants should continue, the actual - the raising of this issue has put a spotlight on the fact that many women asking for help from the NHS are not offered conservative treatments first and are directed to surgery.

Physiotherapists who have experience in dealing with women with these problems - so they're specialised in this field - or have experience of treating women with pelvic floor disorders, what they do is provide assessment and conservative - which I mean by nonsurgical management. This comprises a training and strengthening of the pelvic floor muscles, and physiotherapists also provide advice to women with stress urinary incontinence and pelvic organ prolapse on key public health messages which will help them, including weight loss, a reduction in caffeine consumption and fluid intake, smoking cessation, and of course, trying to reinstate regular physical exercise.

The specialist women's health workforce in the UK is not large. We are aware that there's about 800 physiotherapists in the UK that have specialist knowledge of women's health and expertise in assessment of these disorders. We know that the size of the workforce, the specialist workforce, is insufficient to provide pelvic floor muscle training in all those who require it, so current service provision is limited. We're aware of that - and variable across the NHS in the UK.

There's very strong evidence for pelvic floor muscle training to be used. The Cochrane Database Systematic Review of 2014, which is the most recent one, demonstrates that pelvic floor muscle training can cure or improve symptoms of both stress urinary incontinence and other types of urinary continence. It may also reduce the number of leakage episodes and the quantity of leakage. I'm aware that NICE are currently reviewing its guideline on urinary incontinence and pelvic organ prolapse in women, , and the publication of that updated guidance is due, I understand, in about April of this year.

I know the guideline will update the guidelines of the previous ones, including 2006 and 2013, and previous NICE guidelines for urinary incontinence advocates strongly, and this has not changed with subsequent advice, a trial of supervised pelvic floor muscle training of at least three months' duration as first line treatment to women with stress

or mixed urinary incontinence and a continuation of an exercise programme if pelvic floor muscle training is beneficial. There is also growing evidence that pelvic floor muscle training can at least slow progression of pelvic organ prolapse, and in some instances, improve symptoms.

I'm aware of the PROPEL study, which is a 2018 study funded by the National Institute for Health Research, NIHR, evaluated different models of delivering pelvic floor muscle training for pelvic organ prolapse, and this was to increase access for women to conservative management.

The service models that they looked at included some that trained different healthcare professionals at various levels to increase capacity to provide this much-needed exercise for some women. We - the CSP realises that there will never be enough specialist physios to see every single woman in the UK. That's totally unreasonable, but we do believe that more attention should be paid to the workforce - a wider healthcare workforce. That might be health visitors, midwives, and it could be exercise instructors, that could be taught a range of simple exercises to get women started, particularly at the six-week postpartum exam.

We do recommend that women who do have prolapse or stress urinary incontinence are referred for pelvic floor muscle training, ideally with a physiotherapist or specialist as a first-line treatment, but if we get a wider workforce, they should be encouraged to see somebody. We do need to see an increase in the specialist physiotherapy workforce and the wider workforce that can actually help women have conservative management first.

Julia Cumberlege: Thank you very much indeed. Thank you for that statement. Can I just pick up something that you were saying that in your experience in light of your Society, women are not offered physiotherapy as a first form of treatment. I'm just wondering why that is. Is there something to do with the dynamics of the professions that are looking after the women in terms that maybe the surgeons don't really rate physiotherapy?

I don't know specifically. We know it does happen. It seems to - the variation seems to occur where maybe physiotherapists are not part of that wider team, so in centres where you have specialist physiotherapists working alongside gynaecologists, there seems to be a much more openness to actually trying conservative management first, and then if that is unsuccessful, a surgical route may be offered.

But because there is such a shortfall in that specialist number of, I think, physiotherapists working in this area, there may not be access to people that can actually help them.

Sonia Macleod: Why is there that shortfall? Is it that people don't want to go into it as a sub-specialism?

Natalie Beswetherick: It is quite popular, because it has such a massive impact, a positive impact, on women's lives, so the people who are actually into it, who actually are specialised in this area, that's certainly the case. But often, it's not seen as a priority. When you're looking at funding in NHS for a whole range of different population groups, this one has never been at the top of a list that I've ever seen. So, it may be in part because it's not seen, but you'd argue that increasingly, this should be seen as available in primary care, and I think there is very little physiotherapy in primary care available. We normally find the specialists associated with secondary care provision across the UK and normally working alongside the gynaecologists where they are there.

Sonia Macleod: So when you were saying, for example, with a postpartum check...

Natalie Beswetherick: Yeah.

Sonia Macleod: Would that be an example of where you would think you could integrate?

Natalie Beswetherick: Because of the work done by - particularly on that PROPEL study, and I know that [REDACTED] who is a specialist physio researcher in that field is one of the team that has been looking at that, they're actually doing a dissemination event in fact next week, one in actually London and one in Glasgow. But I think that's a time to start to look at how we can actually get more people trained in a different way to increase the capacity of people that are available and I think in primary care, as a first point of call.

There has been work done in Scotland that within the information given to every new mum, they - it is included something around their pelvic floor muscle exercises and if they need to see a physiotherapist. So I think that's really encouraging, but that's not - I'm not aware of that anywhere else.

[Over speaking]

Sonia Macleod: But certainly, in the literature we've read that they have said that although there are instructions given to people to do pelvic floor exercises...

Natalie Beswetherick: Yes.

Sonia Macleod: ...people don't necessarily do them the right way...

Natalie Beswetherick: That's - yes. So I think there is - the discussion I've had with experts and then researchers are saying we need to find a workforce that can do first line, and if it's not working, then you can actually ensure that the people that need to see a specialist do then see a specialist. Because what the specialist would do is in turn exam and to do a much more detailed understanding and actually help the woman to exercise correctly.

Sonia Macleod: Are there any devices or anything like that that could fulfil that role? Because I'm just thinking if you're lacking specialists, is there a way to...

Natalie Beswetherick: We've not - not necessarily. If people have got into a bad habit of exercising badly, you need to actually break that down. So it's like exercising anything badly. The pelvic floor's no different, but we do use - part of that, some services will use what you call biofeedback, which actually helps people understand that that's the muscle they need to contract. Some people do need that specialist intervention, because they really can't get it, and it's not them not wanting to. It's just really hard...

Sonia Macleod: Working out which muscle.

Natalie Beswetherick: Which muscle you need to contract and how you need to contract it, and then you can actually then start practising it.

Julia Cumberlege: So if people are exercising incorrectly...

Natalie Beswetherick: Yeah.

Julia Cumberlege: ...is that actually damaging?

Natalie Beswetherick: It's just not effective on the symptoms. No.

Julia Cumberlege: So it isn't that it's damaging.

Natalie Beswetherick: No, no.

Julia Cumberlege: It's just not effective.

Natalie Beswetherick: No.

Julia Cumberlege: Then of course they get disillusioned.

Natalie Beswetherick: It's like I suppose human nature, if you've had any injury and you're exercising but actually you're cheating, it's not doing any harm because you're exercising, but you're actually not exercising in the right way to maximize the muscle strength, and that's what you want to get, maximize

the muscles that are required to hold that pelvic floor up. So it just means you're wasting a lot of effort on something that's not going to actually help your symptoms. That's all. It doesn't do any harm, though.

Julia Cumberlege: I'm afraid I don't know the ins and outs of the Chartered Society, so I don't know what sort of research you do, but clearly, you're committed to physiotherapy, because that's your clinical work. Do we have any evidence that it really is effective?

Natalie Beswetherick: The NICE Review and the Cochrane Review...

Julia Cumberlege: You go with the NICE, right.

Natalie Beswetherick: ...is absolutely adamant this is grade A level evidence that pelvic floor muscle training works. No doubt about that.

Julia Cumberlege: Yes, that's fine.

Sonia Macleod: Being the case, and this may not be your area, but given physiotherapy has an evidence base that says it's effective, how did we end in a position where so many people were having surgery? Is it availability of services?

Natalie Beswetherick: I think it's about the availability. We have done some previous work, very positively, with the Royal College of Midwives, because we have known for some time that there isn't a big enough workforce out there. So we have worked with the Royal College of Midwives, because they have an important role in terms of postnatal checks, and I think that's a really - we have actually tried that. So there has been exercise formats and things that have been shared through RCM out to their midwife population. But I think it's just the sheer volume of workload for the whole workforce that makes this really difficult to actually add on to everything else you're doing.

Cyril Chantler: What about health visitors - do you...

Natalie Beswetherick: Yeah, we haven't - we have not done that.

Cyril Chantler: You should do that, because they take over at six weeks.

Natalie Beswetherick: Yes, they do, and so that's something we think with the widening of the workforce, we need to actually look at much more carefully, because I think midwives could play a really important part here.

Cyril Chantler: Health visitors.

Natalie Beswetherick: Sorry, health visitors, as you're right, at the six-week post check.

Simon Whale: If you take a step back from that, isn't there something missing in terms of education for girls and young women?

Natalie Beswetherick: Yes.

Simon Whale: What needs to happen?

Natalie Beswetherick: Well, ideally, women - well, young girls need to be taught, probably at the age of 13 and 14. We know that if you've got good public health through your lifespan, it's going to help enormously, but it's never mentioned, but I would argue that, yes, it can make a difference if you actually have a really strong pelvic floor.

Simon Whale: Has the Chartered Society made attempts to engage with the education system?

Natalie Beswetherick: Some of our members who are experts in this area do this at a local level, but it's...

Simon Whale: There's no coordinated...

Natalie Beswetherick: ...not been something that we've done at a national level.

Simon Whale: So there's no coordination.

Natalie Beswetherick: There isn't at the moment, no. It's not been seen as a priority I think, in terms of public health, so where we'd need to go to would be the Public Health England in terms of is it a priority for young people to actually be aware of this early on.

Simon Whale: Can I just ask about the 800 specialists that you mentioned...

Natalie Beswetherick: Yeah.

Simon Whale: You're saying that that's simply not adequate. Do you have any sense of the number that would be adequate?

Natalie Beswetherick: My view, I haven't looked at that, to be honest, but my view is you'd never have enough for the entire population you've got in the UK, if you think about how many live births we have per year, just on that level alone, and then if you added other prevention agenda, it's massive. So we've got to think about doing this in a different way, so I think it needs to be probably looked at it's everybody's business rather than just seen as a few people's business. So, looking forward, you could argue that it's - it needs to be part of the physical activity agenda, but specifically, about raising people's awareness of good pelvic health earlier on. Because then that would actually translate.

Some of our members have made very good links with Mumsnet and other organisations to try and pass these messages out. NCT do a great job as well, so it's all of it together helps, but it's still not actually reaching enough women.

Sonia Macleod: Plus, that only reaches women who are having children, essentially.

Natalie Beswetherick: Yes, yes.

[Over speaking]

It's a big proportion, but it won't reach those that don't.

Valerie Brasse: We understand that in France, there's a mandatory programme is there not? For women who've given birth...

Sonia Macleod: Postpartum.

Valerie Brasse: Postpartum or eight weeks' training that they're expected to do, and whether they actually comply and do it, I don't know, but it is part of better women's health going forward, and it seems...

[Over speaking]

Natalie Beswetherick: That sounds fantastic.

Valerie Brasse: The other question I was going to ask you is the route to accessing these specialist physios is presumably always via the specialist surgeon that a woman has been referred to. I'm trying to get at here the primary care - are women being pointed in the direction of specialist physio before making an appointment to see a specialist consultant about problems with the pelvic floor?

Natalie Beswetherick: I think it would - I think that that there is massive variation. I think where primary care are aware that there is a specialist service they can refer to direct from primary care, they will refer. But the GP knowledge base is normally not brilliant when it comes to knowing every area.

Valerie Brasse: It seems like an obvious one, because if this is always recommended as the front-line, first-line, well, conservative treatment, wasting time to put a woman on a waiting list to see a consultant when...

Natalie Beswetherick: Absolutely.

Valerie Brasse: ...frankly when we could divert from that and go straight to the physio, because that's presumably what they would offer in the first place, because it's the obvious thing to do, so it seems to me that every GP

should be thinking that this is potentially a problem. We should be able to access that service direct.

Julia Cumberlege: I don't think in my area...

Natalie Beswetherick: In some areas, you may...

Julia Cumberlege: You do have direct access. In my area, it doesn't have to go through a GP.

Natalie Beswetherick: In my area, it...

[Over speaking]

Julia Cumberlege: Women can approach a physio.

Simon Whale: But how often...

Natalie Beswetherick: But that's not universal at all, and I know - so for example, Hertfordshire area, everything has to go through a GP, everything. You can't see a physio. You can't see anybody unless you go to see the GP, and the GP has to be absolutely explicit about what they're asking for. Otherwise, they get sent back to the GP, and - it's a real variation, so where I live, I live in Gloucestershire, and I've got full direct access. I can refer myself wherever I want, and that's because I've got knowledge as well. A lot of areas are like that, and where you've got self-referral, people do, but that's far from being universal, and that's to do with the contracting mechanism that's there.

Simon Whale: But how many GPs - I don't mean an exact number, but in your view, is there a problem in that GPs wouldn't necessarily see it as the first line of treatment, or do you think that they do? There's a separate question about whether they can find the treatment for the woman, but if a woman presents with mild stress urinary incontinence, in your experience, is the GP that she goes to, because that's the most likely person she'll go to in the first instance, going to say we need to get you on some physiotherapy, some specialist physiotherapy? Or is he or she likely to say, I'll put you in to see a gynaecologist.

Natalie Beswetherick: I think there would be probably an absolute mix of people that have no idea there's a conservative option and people that refer direct to a gynaecologist, but they may have a specialist on their team, and there will be others that say, you need to be referred to conservative management first. I think we would see that massive variation across NHS.

Simon Whale: That would suggest quite poor knowledge base [amongst] GPs.

Julia Cumberlege: I would think it's not - it's not in the top 10 of their areas that they would be thinking of.

Julia Cumberlege: Do you think part of it is to do with commissioning?

Natalie Beswetherick: Yes.

Julia Cumberlege: So probably in Hertfordshire, this is what the commissioners are asking the GPs to do.

Natalie Beswetherick: It is, yeah.

Julia Cumberlege: So how are we going to break that down, because certainly self-referral really is in the women's interest.

Natalie Beswetherick: It is. I completely concur.

Julia Cumberlege: How can we try and promote this? How can we ensure that it happens in more places? I suppose you have to talk to the commissioners.

Natalie Beswetherick: Well, I think for England in particular, the recent announcement of the GP contract and the long-term plan would give me personally hope that they're seeing that we need to have a change in direction, where more services are provided for within the primary care team, rather than the first port of call being the local hospital. There is - within both of those, there's obviously a strong indication that government wants to see a strengthening of access to services and seeing the right person first time at the right time is central to that. So, I think there is a shift for NHS England, specifically recently, as in January and last week, that we're going to see this sea change.

So I think it is an opportune moment for the primary care networks to actually effect that, because that's where the power will be. But you are correct that it's the commissioning at that higher level, and I presume that will be at the moment at the STP or still can be the old...

Julia Cumberlege: CCGs?

Natalie Beswetherick: CCG level where the barriers are. I don't believe that the work that's been done by RightCare, which was part of the NHSI arm's length body, looking at pathways of care, I'm not sure that one has been looked at women's health issues. There is a commitment to long-term plan about maternity services, so as an organisation, CSP will be driving a campaign to say, you've said this, so we need to see this. So I think that's an opportunity for us as a profession to exert some influence in that.

But the RightCare pathways which have been established for frailty and for - I'm aware that they're looking at one for community-based rehabilitation, and others, where they've been put into place, that puts pressure on the commissioners to commission the evidenced pathway for that population group. But I'm - I don't believe there's one for women's health issues. There'd be a whole range, but that might be an area that can be considered in the future.

Julia Cumberlege: I wonder if you'd be kind enough to write to us on this, because I think the detail is very important.

Natalie Beswetherick: I'd be happy to...

[Over speaking]

Julia Cumberlege: It's something that some of us feel very strongly about, and that would be helpful.

Simon Whale: Can I just ask about data, and in particular, when there's a pelvic floor physio intervention as part of treatment for SUI, how is that recorded, and by whom and who's it shared with?

Natalie Beswetherick: That would be done at a local level, so at provider level, that data would be collected at that level.

Simon Whale: Is there any national data that would show us a national picture of...

Natalie Beswetherick: Not to my knowledge. Not to my knowledge.

Simon Whale: Would that be useful or would that not be?

Natalie Beswetherick: What I am aware that is going to be developed across community services is called the community data set, and a new way of capturing interventions for different groups. I think it's been a bit delayed. It was supposed to be part of like now, but it has been delayed with probably other things that are going on. But they were going to develop these what you call community currencies, which they were around like children and young people. I'm sure there was one for maternity or a big part of maternity services, frailty and short-term conditions, et cetera. So it would be interesting to see if that's a way that you would get aggregate data about what's happening, because that would be the first time a community data set would actually be collected across the whole of England.

To my knowledge, at the moment, data that is collected, and it will be because of the tariffs and payment systems, would be limited to just that.

Simon Whale: No data about outcomes presumably?

Natalie Beswetherick: It would be done at a local level, but there's no way of aggregating that, because there's no system in place to aggregate the data that is collected locally. Clinicians will do that routinely because they want to see if their interventions are working.

Simon Whale: In terms of women presenting with mesh-related pelvic floor issues or pelvic pain issues and the use of physio in management of pelvic pain, have you got any data or trend data on that?

Natalie Beswetherick: I have not. I can certainly ask one of the specialists that I've been dealing with for this hearing today to see if she's aware. I'm not aware. I'm aware that there are specialist physios that do deal with pelvic pain, but there may be a range of reasons why there's pelvic pain, which may include mesh, but could also be for other reasons. But I don't know how much work has been done on that or research in the extent of people presenting with pelvic pain. But I'm happy to come back if I can find any evidence from the experts and the researchers in this field.

Simon Whale: Yeah, please. Thank you.

Cyril Chantler: Have you done any work with the Royal College of Obstetricians and Gynaecologists? You mentioned the Royal College of Midwives, and they are working much more closely together now around the whole issue of women's health and a life course approach to it. Do you participate in those kind of approaches?

Natalie Beswetherick: The CSP hasn't itself, but our professional network, which covers pelvic, obstetric and gynaecological problems do work with the Royal College, normally through their national conferences and so there is an interchange there.

Cyril Chantler: Yes, so this is a subgroup of the Chartered Society?

Natalie Beswetherick: Yes, absolutely. We've got a number of professional networks that comprise the whole of the Chartered body, and one of them is about 800 physios who actually work in the specialist field of women's health.

Cyril Chantler: Will there be any advantage to a conversation at your level with the President of the RCOG and the head of the RCM about working together?

Natalie Beswetherick: I would never say no, so I'm sure every opportunity - we wouldn't want to miss it.

Cyril Chantler: I'm trying to find out whether you would be one to initiate such a conversation.

Natalie Beswetherick: I'd be happy to, honestly, because we've got enough specialists in the area who are really, really keen on this. This is - for some people, it's like a life work of actually really ensuring that women get the best deal and the conservative management, it's not invasive. It's simple, it's easy and it works, so we know - we're doing work with a number of our specialists to try and get messages out to women in very, very different ways. We've seen some fantastic work done by a physiotherapy who happens to be a comedienne, and she's called Elaine Miller, so if you're ever at Edinburgh Fringe and you see her, her entire work is actually around women's health issues and about not avoiding - terrible use of a word, voiding, isn't it? In terms of the importance of pelvic floor.

But for some people, actually, making it - translating it into a different way has opened up ways in to whole communities, and another specialist is looking at particularly hard-to-reach communities where this topic would never be even discussed. So where you've got populations of particularly Asians where this is a real - can be hidden for years.

So we're looking at different ways to access groups with key information, and it's not just the usual ways. We need to be aware that actually sometimes social media and other things can actually work in a very positive way and can help signpost people.

Cyril Chantler: That links me into - first I was going to ask you, is we've been told that a 10 per cent reduction in bodyweight, which I agree is quite a significant reduction in bodyweight, leads to a 40 per cent increase in continence. Is that part of your approach, to encourage that?

Natalie Beswetherick: Yes, we know that that's one of the public health messages that we would normally deliver to women as part of our assessment that the less you weigh, the better. It is almost actually for anything, any muscle, actually.

Cyril Chantler: Yes, including the heart.

Natalie Beswetherick: So if you've got a dodgy knee or your heart or whatever, if you lose weight, actually, the less weight on the muscle, the better it is, as well as actually the strengthening. So we do know that helping people to lose weight, as I said also about caffeine reduction and some of that fluid intake...

Cyril Chantler: So in the guidance that you give...

Natalie Beswetherick: Yes, that is all part of it.

Cyril Chantler: ...that you publish, that is there?

Natalie Beswetherick: Yes, it is. There's - I can leave that one, but there's a really good one that's been done by our professional network all about that that's been written for people in...

Cyril Chantler: It says you should lose weight.

Natalie Beswetherick: Yes, and it's got loads of other things that you can think about as well. So little tips about how you can actually do your exercise and make sure you actually stick to them.

Cyril Chantler: Thank you.

Julia Cumberlege: Yes, you - at the very beginning, when you were giving us your very interesting little talk at the beginning, you talked about using instructors, the introduction of instructors.

Natalie Beswetherick: Yes.

Julia Cumberlege: I think there was something else you were saying, a middle way between a physiotherapist and an instructor, and I think it was somewhere in the middle you were saying. But I just wondered about these instructors, because when you're so short of the workforce, it seems you're trying to be really creative in thinking of other ways of spreading the very good systems that you want women to adopt in terms of strengthening their pelvic muscles and things.

So could you tell me a bit about that? Would they be qualified people? Would they - would you have some sort of examination, some sort of test of competency?

Natalie Beswetherick: Yes, so...

Julia Cumberlege: If you were to introduce them.

Natalie Beswetherick: So my understanding, particularly from this PROPEL trial, which is just completed and is about to be disseminated, they looked at a whole range of models of training different healthcare professionals, as well as people that are exercise professionals. My understanding is that that would be an assessed - the training that was then consequently assessed and people were determined they could actually teach that particular set of exercises.

So I don't know any more about that, because it's actually just pre-publication. I want to go to the event next week and find out more myself, but I think it's really quite exciting that we do need to be creative about looking at the wider workforce and the people who are trained in a whole range of exercise techniques that may be really useful. Because we have a number of them, and they are trained to different levels. So it's looking at where would pelvic floor muscle training fit with, and what are the lines which should say, actually, this person needs to see a specialist? This is not - this is actually - this is not working or this lady needs some more help, that actually it's outside what I can do to teach.

So I think there are some really exciting models that have been tested. I think once we see those results, I think it's about looking at how we can advocate ways of people using those models locally and certainly having that discussion with commissioners of services, particularly in England.

Julia Cumberlege: I think I might have missed out, which I should have done at the very beginning, to ask you if you've got any conflicts of interest?

Natalie Beswetherick: You asked me at the very beginning.

Julia Cumberlege: I did, all right. Okay, short-term memory loss.

Natalie Beswetherick: I have that, too.

Julia Cumberlege: All right, so I'm just going to ask my team if they want to ask anything, and anything further you want to tell us? Simon?

Cyril Chantler: Are you organising the PROPEL meeting?

Natalie Beswetherick: I'm not organising it. It's being done by the researchers who led the actual Review.

Cyril Chantler: Okay, where are they based?

Natalie Beswetherick: Glasgow, the main research.

Cyril Chantler: But there's going to be one in London/

Natalie Beswetherick: Yes.

Cyril Chantler: Is it possible to get a ticket?

Natalie Beswetherick: I can forward you the link that I got.

Sonia Macleod: Thank you very much.

Cyril Chantler: Can you send it to Dr Macleod?

Sonia Macleod: I'll send you an email.

Natalie Beswetherick: If you send me an email, I'll send it, because I'm thinking of trying to get there as well.

[Over speaking]

Because I think it was so exciting when I actually saw the - I think it's got real potential to help a lot more people.

Sonia Macleod: I think one of the other things that we've heard about is apps and things like that.

Natalie Beswetherick; Yeah.

Sonia Macleod: So another mechanism of just communicating and reminding people, because this does require effort on the part of the person doing it. So I think that you do have to say, okay, what can we do to make life easier, and certainly, I don't know what your position will be on things like that.

Natalie Beswetherick: Apps certainly play a role. For people who like prompts and people that think that somebody's just prompted them saying, have you done your exercises yet today. It makes you think, right, okay. I better go do those. So we've - a lot of physios encourage patients to use any device, including apps, if it helps them remain compliant with an exercise regime. The Public Health England's Active 10 and stuff like that, and it doesn't matter what it is. It can actually - any app that helps people. It could be - I've seen them included in Fitbits and stuff like that. The technology these days is going to be really helpful for the future to actually help us with this.

Julia Cumberlege: Right, anything else?

Sonia Macleod: No.

Julia Cumberlege: No. So have you anything further you'd like to tell us?

Natalie Beswetherick: No, that's fine. Thank you.

Julia Cumberlege: So you're just going to send us a bit more material that we've asked for.

Natalie Beswetherick: Yeah.

Julia Cumberlege; That document looks really good. Thank you very much indeed. So thank you for all you're doing for women and for the professionals.

Natalie Beswetherick: Thank you very much. Thank you for inviting me today.

END OF TRANSCRIPT

Session 3: British Association of Urological Surgeons (BAUS), British Society of Urogynaecology (BSUG), Pelvic Floor Society (PFS)

START OF TRANSCRIPT

- Julia Cumberlege: If you would like to introduce yourself.
- Chris Harding: My name is Chris Harding. I'm a urology consultant from Newcastle and I'm the current chair of the BAUS section that covers female urology.
- Roland Morley: I'm Roland Morley, previous chair of the section consultant urologist, Imperial London and I was involved with the NHS England mesh review and also seconded to the Scottish mesh review.
- Jonathan Duckett: I'm Jonathan Duckett. I'm a consultant urogynaecologist from Kent. I'm currently the chair of the British Society of Urogynaecology. I've had a similar experience as Roland with the NHS England mesh review and the things that have followed on from that.
- Swati Jha: I'm Swati Jha. I'm a consultant urogynaecologist at Sheffield Teaching Hospitals and I'm current vice chair of the British Society of Urogynaecology.
- Andy Williams: Andy Williams. I'm a colorectal surgeon at Guy's and St Thomas's and the present chair of the Pelvic Floor Society.
- Shahab Siddiqi: I'm Shahab Siddiqi. I'm a colorectal surgeon in Essex and I'm the treasurer of the Pelvic Floor Society.
- Julia Cumberlege: Thank you very much indeed.
- Andy Williams: Can I ask who the observers are, not that you're not welcome in any way but just so that we know what your background is because it might be useful perhaps.
- Observer: So, we're in the communications team. I was in communications at the Royal College of Obstetricians and [unclear] Specialist Society and we're independent of the Royal College [unclear].
- Andy Williams: Fantastic. That's very helpful, thank you.
- Julia Cumberlege: If I could just start by asking you, and it's really up to you who wants to answer the questions. So, I'm not going to particularly mention one of you to answer it but I'd just like to ask you first of all, in your opinion, how safe is the use of mesh in the procedures that you're going to be talking about today? I don't know who'd like to field that.

Jonathan Duckett: We've learned quite a lot about the safety of mesh that has been researched recently within the NHS. So, we've relied previously on past, on randomised controlled trials which may be of short term and may not give us all the answers for the longer term. But more recently, we've been using large data sets, so NHS England data sets, which give us, we think, fairly accurate and good levels of risk associated with TVT type mesh procedures, more so than the prolapse mesh procedures so we can understand fairly, we hope fairly accurately of the risk associated and also from randomised control trials the benefits of the various mesh procedures.

The NHS data suggests that 3.3% of patients will have a mesh removed by nine years having had one inserted for stress incontinence. Other data possibly suggests a complication rate of up to 10% although those may be minor complications. So, we have a figure somewhere in the region of what the risk of a TVT or a synthetic sub-urethral mesh procedure is.

In terms of success which we always like to think about as well, and it's important in counselling our patients of both the risks and the dangers, a study of 40,000 tapes from the British Society of Urogynaecology database suggested that 94% of our patients were complication free and had a good outcome with synthetic mesh operations.

Julia Cumberlege: Right. Anybody else want...

Chris Harding: I think the data that we draw on is as good as we've got at the moment but there are obviously inherent flaws in all [unclear]. We're talking about high level evidence and as consultants, we're trained to give that the highest priority so things like Cochrane reviews, big meta- analyses and a lot of those outcomes have been centred around treatment and cure of stress incontinence rather than complications that have been reported. So actually, the move across to using large data sets which is HES and NHS digital data has been, I think, a positive one and enabled us to get some real-life data within there.

I still think the issue is, you know, we can talk about percentages and rates and things like that but actually, the nature of complications, we still don't know. So, we've got a HES data set of over 90,000 which talks about a 10% complication rate but if you actually drill down and look at the appendices to that paper, 50% of the complications are classified as complications not classified elsewhere. So that really doesn't give you any specifics with regards to the nature of the complications so that is the evidence gap at the moment and I think that remains.

Julia Cumberlege: Can I pick up on that? Can you just say to me, tell us, the panel here, what are the complications and were they unexpected? Because one of the things that has come to our mind is the paucity of research when this was first introduced and the way that it really took off, these particular operations. So, really concerned about understanding, as you see it, the complications, what they are and the percentages et cetera.

Chris Harding: I think that the complications that are listed in the current RCTs that are available, things like mesh erosions, failure, chronic pain and they're all fairly reasonably detailed in the reports that have gone previously such as the MHRA Report, the York Report, the European Union Review, they've looked at those. But a lot of the RCTs were powered to look at success only i.e. cure of stress incontinence. So, therefore it's very difficult to assign any level of accuracy to the ascertainment of complications.

What a lot of the patients are saying is that many of these complications are not occurring for a significant way down the line following their surgery and a lot of the studies are just short to medium term and the ones that are long term, there's drop-out rates and things like that. So, they are [unclear]. There is in my mind still an evidence gap in terms of us being able to fully counsel patients with regards to the risks of mesh surgery.

But then the real-life data has advanced us a little bit in that regard so we've got the HES data which goes out I think to eight or nine years and then the recent JAMA paper which goes out to nine years. That's looking at reparations and removals and I think that gives you a broad idea, but it still doesn't answer specifically and accurately the question that we need to answer which is the nature of the complications and the variety of them.

Julia Cumberlege: Because there are some reservations about using HES data which I'm sure you're well aware of. So, thinking about the insertion of mesh, how is that - how does that compare with other procedures that could be used instead, in terms of safety, in terms of complications, in terms of removals?

Jonathan Duckett: We probably need to make a distinction here as well because we have mesh inserted for vaginal wall prolapse which has been graded by NICE as only usable for research purposes. I think when most of us are talking about mesh, most of us are referring to retropubic synthetic sub-urethral slings which is the only operation that urologists would do. So, when we're talking, most of those things relate to synthetic sub-urethral slings.

Andy Williams: I think that's quite an important point because, from the bowel point of view, the world is slightly different and really mesh has been used in three indications broadly. So, we've got urinary incontinence as you say with sub-urethral slings. We have vaginal support for vaginal prolapse and the word prolapse is taken in under a guidance because it means different things depending on whether you're a urologist, a gynaecologist or a colorectal surgeon. Colorectal surgeons would call prolapse when the bowel comes out of the anus and hangs out of the anus either transiently as a result of strain in defecation or permanently.

So, in the bowel world, the third indication for using mesh is for either obstructed emptying of the bowel, so someone who has constipation, has to strain because of mobility in the bowel causing it to infold and therefore block out the exit. So, the mesh is used to support it in place to enable a smooth passage of faeces through the bowel during emptying. The second indication is for full thickness prolapse of the bowel out of the anus.

Our data set is probably not as mature as the urogynae and urology data set. We do have the advantage of the largest systematic review of all of the evidence that we do have, which admittedly is from some randomised trials but mainly large case series from around the world, predominately Europe because it's much more common in Europe than it is in the States and the northern continent

We know that our complication rate related to mesh is in the region of 2%. Of those, probably 1%, so half of that 2% relates to mesh pain, mesh erosion, some fistula formation with the other half being detachment of the mesh leading to failure of the surgery but not debilitating morbid complications. Just to put things in – it's a much lower magnitude than one might see for the other indications.

Julia Cumberlege: So, the failure of the surgery, is that about competence? Is that about training? Is that about education? Is that about skills?

Andy Williams: Inevitably, potentially it can involve all of those factors. The surgical community is very aware of training, competency, mentorship, learning curves, and so nowadays, I'm fairly confident in saying that surgeons are not embarking on procedures that they've not done before without seeking out training and the support and the mentorship. A lot of what we've done is to provide a form of platform so, if you wish to start doing this, you can go through your workout. Most importantly, the indications and in whom to do it and when but then we have animal models, we have cadaveric models, we have training schemes and we're in the process of

setting up mentorships so that your first few will be done with direct supervision of someone who's an accomplished experienced surgeon.

Julia Cumberlege: Because prior to the pause, and we'll be going on to the pause in a minute, but prior to the pause, we heard the expression 'they'll have a go' and that deeply worried us because we felt these were people who felt that they were competent to do it and they would have a go. We weren't at all comforted by the fact that we didn't feel that necessarily things that you've been talking about were actually in place.

Andy Williams: Rest assured, I don't think any of us sat here are comfortable with those phrases either. Certainly, from the Pelvic Floor Society, and I'm convinced that urogynae and urology societies are exactly the same. Prior to the pause, we'd detected the public feeling and the sort of resolution that we see more and more problems and so we could see the problem arising. So actually, prior to the pause, certainly the Pelvic Floor Society has pre-empted it by putting in place the bits to really sort of oversee professional conduct, both with training, with MDT working, with supervision and starting the database and registries which luckily, we started about a year and a half, two years before the pause and so hopefully we were hitting the ground running.

But totally agree with you and I don't think any of us would agree that 'have a go' is appropriate. It's never been appropriate but now...

Jonathan Duckett: I would be appalled to hear those words coming out from any surgeon. As a professional society we would find that completely unacceptable. We have developed a stronger or an updated emphasis to allow training to take place which Swati has been leading on.

Swati Jha: One of the things that we recognised when the pause came into place is how well-equipped we were or how poorly equipped we were to deal with or offer a service to women with incontinence when the mesh was taken away as an option. That made us stop, pause and think about how we were going to address that. Now there are two cohorts of people. They include the future NHS consultants, they include the doctors in training who will be the consultants of tomorrow, but then we had a huge cohort of consultants in practice who were either not trained at any point in their careers to perform the non-mesh continence procedures or who had been trained but had just become deskilled.

In response to the pause, what the BSUG have done in the past six months is set up a mentorship scheme for non-mesh continence procedures. We launched this in November so within six months, we've

written the entire log book with - it goes hand in hand with supervised training where a senior clinician provides proctorship to a junior consultant or a consultant wishing to either retrain or learn for the first time one of these non-mesh continence procedures. But it also encompasses other aspects which go hand in hand with training, such as cadaver dissection, learning on models, because you can't just have a go on the patient. That isn't the way to learn any form of surgery.

What we have done through the mentorship scheme, we already have about 10 units registered, 10 consultants registered for this throughout the country. They identify consultants wishing to learn these non-mesh continence procedures. They identify a mentor. They then register with the BSUG. The BSUG then sends them a log book which they then complete and this log book is then returned to BSUG and then we issue the certificate to say they have had the appropriate training.

This mentorship scheme has been approved by the RCOG, the education quality assurance committee of the RCOG. So, we have the RCOG support and backing with this as well. But we see this as one of the positives that have come out from the pause because it's made us stop, think, assess and make things better.

Valerie Brasse: How many of them go through this?

Swati Jha: So, it's going to be very much at the discretion of the consultants but we, as a consultant body, the one thing that we've all been hearing, and I'm sure I echo the views of all three Pelvic Floor societies, is that consultants will not just do a procedure. The days of see one, do one, you know, see one...

Andy Williams: Teach one.

Swati Jha: ...teach one, yes, are gone. We are now in a situation where, until we've done several cases, multiple cases, until we're feeling totally confident that we can do it in isolation, we won't just go on and do them. So, we've had expressions of interest from over 20 and you have to remember the email regarding this only went out under two weeks ago and 20 people have already contacted us to be sent the details. It just shows the new wave within NHS consultants and the recognition that, if we're going to do a procedure, we need to be adequately trained and we need to be able to demonstrate that we have had that training.

Valerie Brasse: What's your estimate of how many are needed to be trained?

Swati Jha: That's a good question and that comes back to what the caseload is going to be and that's not a - I wouldn't want to pluck a figure out of a hat for that. I think that's work that we would have to do in collaboration with HES in terms of the total number of cases because you have to remember, this is very fluid. This is not a fixed number. So, if we go back five years ago, virtually the only continence procedure being done was the midurethral tape. So, you would need hundreds of clinicians to do that.

If you look at the HES data from five - the same timing, the number of colposuspensions done in that same time was under 70. The number of autologous slings done was even less. But if we look at today, the number of colposuspensions being done is well into the hundreds and two hundreds. The number of autologous slings similarly. So, the number of clinicians required to carry out or offer a service will be very much dependent on the number of cases.

So, I don't think that we can answer that question in isolation. I think it has to be in collaboration with the commissioning bodies, such as NHS England, which are working on just that. They are working on the caseload and then determining how many clinicians we need and how many units should then be offering those services based on that caseload. That's fluid.

Jonathan Duckett: I think what will happen is...

Julia Cumberlege: Can I say, I think that's encouraging – what you've been doing. But haven't you come to this rather late? Because what the women have been telling us is that they felt that they were guinea pigs in a sort of mesh trial and that all this was happening and there really wasn't the sort of, well, the things that you're promoting now suggesting will happen. Don't we owe something to these women who feel they have been really, really badly treated, lives turned upside down, huge suffering. Terrible impact on family and all the rest of it. Do you not think that they deserve an apology and more than that? What can we do to help them now?

Chris Harding: I think that's a slightly separate issue from your original question which was looking at safety of alternative procedures. Again, we go back to the level of evidence we have and probably the best out there was the *Lancet* publication from the Scottish group in 2017 which looked at adverse events after mesh surgery and non-mesh procedures for stress incontinence and found that the mesh procedures were actually associated with a low risk of immediate complications and a low risk of subsequent prolapse surgery.

They had a similar rate of longer-term complications and a similar need for further incontinence surgery. So as surgeons, we're trained to look at the highest level of evidence that's there and that's what we did. So, I don't think women were guinea pigs in terms of primary mesh surgery. I think as surgeons, and certainly in my practice, I was looking at what's out there. I had Cochrane reviews, I had European Union reviews, I had RCTs, *Lancet* papers.

That's a strong evidence base and if you look at one of the statements in the Cochrane review, mesh surgery is one of the most highly researched surgical procedures there is. We were relying on what was out there. I think what we're coming around to now is the realisation is perhaps our outcomes weren't right and definitely that our length of time we looked at these women wasn't right. Most studies closed at a year or two years. What we need, according to the patient groups are five-year, 10-year data.

So, I think yes, we do owe women an apology without a doubt and I would give that unreservedly on behalf of BAUS. But I think you've got to put yourself in the position of the surgeon at the time who looked at the evidence available to him or her and it's only more recently that it's come out that these complications can firstly occur anything up to 10 to 15 years after the primary surgery, and secondly, at just how numerous they can be and how devastating.

Simon Whale: But it's also about the type of complication, isn't it? I mean, you're right about duration and long-term complications and we've certainly been told that by many women. Some women experience immediate complications, some experience complications 10 years later. There are many in between. But it's also about the type of complication and whether the data that's existed up until now has adequately captured the real meaning of complication.

Chris Harding: Absolutely. That's why I say I don't think the outcomes in the original trials were correct. We didn't capture chronic pain. We didn't capture loss of mobility. We didn't ask about loss of sexual function. All of these things are massive domains in the overall quality of life of an individual but the trials looked at [unclear] rates and overall patient outcomes. We could have done better of course.

Roland Morley: But if I can give you a partial answer to the question that you've had, don't patients need an apology, because I was involved in the NHS England and Scottish review. One of the things that actually came out of that, and I was chair of the information consent, chair of that review, and

one of the things that actually came out of that of course was are patients getting adequate informed consent. So, you may have a trained surgeon who could do a TVT, a TOT or prolapse mesh repair, but were patients being offered all the alternatives and being informed properly? It was quite evident at that time not all patients were.

One of the recommendations that came out of both the English and Scottish reviews is that every patient had the right to a properly informed consent, that they had to have access to all the treatments. Now that doesn't mean that that individual surgeon has to be able to offer all the treatments, but the patient has to have access to it.

That recommendation was put in by NHS England and what is happening with both the British Association of Urological Surgeons and [unclear] the RCOG, is ensuring that all patients have access to that. One of the things that has happened as a result of the cancer drive towards multi-disciplinary meetings, exactly the same thing is happening within urology and urogynaecology is such now that all patients, whether they're having primary or recurrent surgery, will go through an MDT, will have an outcome that shows them that these are the options they have. Then those options are taken to the patient for information and consent at that time.

If that surgeon cannot offer that procedure, then they should have access to all the others. But what we've got to ensure is that NHS England and the other devolved nations ensure that that is carried through to all patients.

Andy Williams: I think that last point is crucial in that I was going to follow up on what Swati said, in that what has changed over the last certainly five years, and probably longer than that, is the fact that the MDT process has formed the cornerstone of delivery of care for any patient with pelvic floor pathology.

Valerie Brasse: But it's not 100%, is it? And your own survey shows it's not 100%. I think it was 85% of procedures went through an MDT. So, we've got 15% that are not.

Andy Williams: One of the difficulties that we have as the professional organisations, is that we do everything we can to ensure that we recommend what should happen. We make it as user-friendly as possible. We give every resource to make it almost harder not to do it than to do it. But it still is down to the individual trust and the individual consultant, his or her self, as to how

they conduct their practice without any other regulation. We have no authority over - we can only advise.

Roland Morley: Therein lies the problem. We're advisers, not regulators.

Valerie Brasse: Where do we go?

Roland Morley: What came out of the review is every trust was written to, every medical director and every chief executive were informed of the recommendations to ensure the governance process came about. But one thing that we had done via Professor Keith Willett was also suggested that ideally, there should be a key performance indicator. Now if you have a key performance indicator for these outcomes, then the trust has to deliver on it. It's not an option. They have to deliver.

Chris Harding: There has to be a mandate though, doesn't there? I mean, if you take the BAUS registry for example, we have regularly captured between 70% and 75% of the stress incontinence procedures undertaken by urologists year on year. But that leaves one in four that we don't capture. So, we've taken quite a lot of steps to try and ensure that that is increased.

One of the things we did as BAUS is we wrote to the medical directors of the trusts who we identified by HES data weren't putting their data in. We got very little engagement but that's because BAUS is toothless as a regulatory organisation. Therefore, we need a stronger mandate from somebody or an organisation perhaps like NHS England and that's one of the things we're talking about at the moment, setting up the registry. So, we've had engagement with NHS England and HQIP, and one of the things that we said at the very outset is this has to be mandatory.

There's several other factors we've got to look at with regards to registries but the key thing is that it has to be mandated. We have to get a capture of all data for all stress incontinence surgeries because we need to be able to say well, if you choose procedure A, the likelihood of success is X and the likelihood of complications is Y and the same thing for all of the different formats. So, that would only - that represents proper consents and at the moment there are just so many blind spots in the evidence that we have to be able to do that. Although what BAUS did do is produce an options leaflet to try and encourage the sort of general discussion with the patient of all the options that are on the table.

What I'm seeing at the moment is that women with stress incontinence actually don't want to come through for surgery and you can see that in NHS digital figures. 48% decrease in stress incontinence surgery operations and that's because we've lost their trust and we need to regain

that. The only way of doing that is to show a robust pathway from start to finish and beyond.

Julia Cumberlege: Well, thank you very much for saying that because this is the other thing that's really struck us. We know that there are good surgeons in this country, highly respected, doing a very good job. But we've heard a lot from the women who have been harmed that they have really lost trust in surgeons and these are of course the surgeons they've met. We've heard a lot about denial, surgeons who have actually denied that mesh is the problem et cetera instead of working with the women and other organisations. So, you quite rightly said that you've got to ensure that you regain the trust you've lost and you're thinking that you do that through data, through evidence, through - but I think it's more than that.

Swati Jha: May I just pick up on the question you asked initially about did we not owe women an apology, and again, I think I speak on behalf of all of us when I say that some women have suffered devastating consequences from mesh and that really isn't good enough. But I would like to assure the women who have had these problems that as organisations, as professional bodies, we have been trying for so many years, but again it comes back to the fact that we cannot mandate anything.

So, in response to the fact that we had concerns about some clinicians possibly having a go, we set up the process of accreditation so that we could make sure that, if a woman was asking for continence services in Aberdeenshire, it was exactly the same and standardised as it would be if she was having the same services in Plymouth. In response to the fact that meshes were resulting in complications, we set up a database. Again, we have encouraged and asked all members to database their cases but again, it's not something that we can mandate.

With regards to patient consent, even before the pause and for over a year now, BSUG have been working in collaboration with RCOG and we were due to publish our patient decision aids which involves every procedure that is incorporated by the pause so that women can make informed decisions. They can make decisions based on their values because again, as surgeons, we know there is no surgery that is with no risks or complications. All of them have risks and that is why it comes down to what is important to an individual patient. It is their right to choose and we want to empower women and by developing these decision aids, that is what we hope to achieve.

Following on from the pause, we've now amalgamated the decision aids that we worked on with NICE and these are now due to be published with

the NICE guidelines in the first week of April. So, this has again been a huge body of work that we have been working on in collaboration with other organisations, but it's all aimed at empowering women. Giving them the choice, allowing them to make the decisions based on what's important to them and their values. So, I do think we've tried our best.

Julia Cumberlege: Can I say, I have actually read all the stuff that you already put out for patients in terms of ensuring that they do have proper choices, they know what's involved and all the risks, and your consent form and everything. I do think that's a huge step forward. So, I will look with great interest to what's coming out in April.

Cyril Chantler: You mentioned accreditation which is a big issue and we are seeing presently the Royal College of Surgeons and the Royal College of Obstetricians and Gynaecologists later today and that's one of the issues that we will want to explore with them. Should there be a register of the, or an accreditation for surgeons on particular procedures? This is not a new idea, I know, but what is your view of that and would that be held by the specialist groups or by the Royal Colleges and [unclear] interact with the appraisal system, revalidation of the General Medical Council? I'll be interested in all your views about that please.

Swati Jha: I think accreditation is part of the appraisal process. So, within the appraisal process for a consultant, we have to demonstrate that if we are doing a procedure, we have been...

Cyril Chantler: But I'm thinking about - I've interrupted, sorry - is that this would then be publicly available. So, that I, as a patient, could check a database that tells me that the surgeon who's operating on me is actually accredited to do that operation.

Swati Jha: I think that would be a huge step in the right direction. I think we would all be very supportive of that.

[Over speaking]

Roland Morley: One of my other hats is I'm chair of urological training within the UK, but across the board, they're not too dissimilar. So, a trainee, be they a urologist or a urogynaecologist or a pelvic floor surgeon, will go through a training programme within their chosen specialist area. So, from a urogynaecological point of view, they will get to a point that they have to develop and deliver a certain level of competency. That will apply for colorectal surgeons and it will apply for urological surgeons who've developed an interest in that area.

If they are developing techniques beyond that area, then they go and get fellowships. You will hear from the Royal College of Surgeons and O&G later on. Some of those are accredited and some of them are not accredited.

A group you may or not have heard from are the GMC because the big move now is towards prevention. So, say for instance you have a consultant that comes out of urological or gynaecological training now and has learned a technique, but like everything, we are consultants, a new technique comes around. What is likely to happen under the umbrella of the GMC is the credentialing in that procedure. That's something that we've been calling for, for a register.

Cyril Chantler: And that would be on a register?

Roland Morley: That would be on a register. Credential will be on the register.

Cyril Chantler: Which could be accessed by the public.

Roland Morley: Yes. So, you have the specialist trainees, you have the fellowship trainees and then you have credentialing which will occur post training.

Cyril Chantler: Yes, because we go on learning all our careers.

Roland Morley: As we go on learning through our careers.

Chris Harding: I lead probably the only Royal College accredited fellowship in female function urology in the UK. There are many other fellowships which are equally good but the one in Newcastle is the only one that's badged by the Royal College of Surgeons. We agree with the college, prior to even being granted the fellowship, the numbers of procedures and what we're doing. Obviously, that's been a bit of a change in [unclear] lately with the mesh pause, but we do have that agreement in place. So, anyone who is awarded the fellowship from my unit will have done a minimum number of procedures to a minimum level of competency.

But I think what's probably coming with specialised commissioning is the, perhaps accreditation is not the right word, but designation and quality standards will be issued by NHS England by which units will be commissioned and that will come with complex incontinence and it will also come...

Cyril Chantler: Well, that is actually part of the pause, that the specialised units should be a standard for mesh removal and then they themselves will have to be accredited.

Chris Harding: I think that's work that's well, well underway. I think Jonathan and I and others in the room have liaised very closely with NHS England to try and assign these quality standards and look at what's needed. When we started out, we were thinking of very small numbers of mesh removal centres in the UK but the demand is so high. If you look at NHS digital data, and I think I worked out that the median number of mesh removal procedures of any kind was 60 per month from those figures. So, four centres probably can't do this. We probably need double or even more with regards to that.

One thing we're working on with the specialised commissioning groups is to assign, not just the competence of the surgeons, but the infrastructure in the unit because it's pathways that hold these patients up as well access to surgery. It's an access to investigations, to scans, to urodynamics, to things like that. I think we have to - any units that are going to tender for this, they're going to have to demonstrate that they've got the infrastructure in place so that the pathways are as streamlined as it can be.

Jonathan Duckett: So, the service specification for specialist commissioning has been agreed and gone out for consultation and come back in. It's due to go to the Women and Children's Health Board on 28 February for the specifications to be signed. So, there will then be specifications for the mesh removal centres and specialist centres. So, when you talk about numbers, there'll be 40 to 50 specialist centres and it's not then dependent on individuals, but those centres will have to provide a number of different surgeons who may concentrate on different operations.

So, there will be the specialist centres providing all of the surgical procedures that patients may wish to choose from within the continence sphere of having their treatment if they failed a conservative therapy. So that's all moving on very quickly and also the mesh centres will be commissioned. Whether we have four to eight, 10 to 12 or whatever, that will hopefully - sorry, the process is in full force now and going through quite quickly to have those commissioned.

Valerie Brasse: Can I just clarify, the four to eight specialist centres that you've been talking about, that will be mesh complications and mesh removals?

Chris Harding: Yes, mesh salvage surgery.

Valerie Brasse: Mesh salvage. So the 40 to 50, you're talking about would be insertions.

Chris Harding: Complex incontinence - well, complex incontinence...

[Over speaking]

Jonathan Duckett: So, they would be able to offer their breadth of continence surgery that a patient would be counselled from and may choose any of the four current procedures that are recommended by NICE.

Cyril Chantler: Can I just finish the credentialing question? Pelvic Floor Society [unclear].

Andy Williams: Absolutely. We thought long and hard about this as well as to whether to try to instigate a certificate of competency, for want of a better term, about any particular operation. Bearing in mind none of that exists for any of the other operations that we've ever done, to my knowledge. We went further - if you look at where the problems occur with any particular individual, often they relate to the decision making, not necessarily the operation that's been performed, but the decision whether it's the most appropriate operation and indeed is it indicated.

A lot of it comes down to the consents and whether all of the other options and the potential complications were included. Without doubt, some of it will come down to technical competency of performing the operation itself, which goes back to how I answered your original question. And the majority, and I'd say 70%, were the [unclear] points. All of those - the responsibility for patient protection and care come under the umbrella of the multi-disciplinary team service. So, we would argue, and the way that we've gone about it in the Pelvic Floor Society, is to accredit units rather than individuals, which encompasses the whole process, the pathway.

Into that, governance is written because it's not an individual. Many of the cases where problems have occurred, you may well have had an individual who clearly knows better than anyone else, who has dictated what the operation may or may not be, and therein lies the path of sorrow. If you have an MDT process, you will have rehearsed all of the other options, you will have ensured that non-surgical treatment options have been maximised to avoid surgery altogether.

Within that is also, to be accredited you have to demonstrate adequate review, entry of data into the database, audit of the outcome of the unit and adequate training and mentorship of each individual within that unit.

So, I would suggest that we aim for unit accreditation which can all be publicised and we've set that up with the Pelvic Floor Society. There are now two units that are accredited in the country. I'm pleased to sit here and say that mine is one of them but clearly, if it wasn't, you'd have to ask why I'm sat here in the first place. But again, that is voluntary. There's

nothing in it for anybody, there's no incentive other than pride of one's service and maybe that needs to change. But for that to change, we can't do that. We need the weight of the NHS or the government to say...

Cyril Chantler: We recognised this when we recommended the pause and I guess that's also part of our responsibility to make recommendations which is why we're all here today.

Chris Harding: So I suppose it comes back to resource again. So, as a professional organisation, BAUS would struggle to set up an accreditation process and roll it out. It's amazing that we've sort of done that. But I think if you look at a logical comparator which is the cancer MDT In my hospital, the cancer MDT has an MDT coordinator, they have administrative support, they have radiology time, you know, the consultant's time is job planned and that doesn't occur for functional urological problems and we have MDTs just the same as they do. You almost need that driving force behind to make the trusts say well, right, this is a necessary component of a service delivery and therefore, we'll resource it.

Cyril Chantler: That's a good point.

Andy Williams: If we look at the [unclear] data for cancer for colorectal, and one of the pre-requisites is has the case been discussed in an MDT? What was the outcome? What is the management strategy? You'd be the first to go to the wall if you said 'oh, I'm just doing the odd cancer here and there. I've done some, it's quite straightforward. I don't need to talk to anyone else'. I mean, I'm being completely facetious because we're all laughing internally because it seems ludicrous. And yet, we've got benign work where the stakes are so much higher because it's about quality of life.

As we've already heard, the complications, certainly from a colorectal point of view, is maybe one in 100 who has a major complication. But when it occurs, it is life destroying potentially. We're fully aware of that. The difficulty comes is that the other 99 won't have had their lives destroyed and at least 60 or 70 will have had their lives transformed for the better so they get on with their life as a result of the surgery. It's getting the protection of the balance right.

Valerie Brasse: But a service that is a service for all, means that even this 5%, 3%, 2%, 1% for whom it goes wrong, the service has to be able to provide the right pathways. What we hear from the women is that they do not know where to go, they are going around and around, they're chasing themselves because they aren't getting the help they need. So, I hear

what you're saying but none of them can be left on a heap somewhere without a care pathway. So that's what they're suffering from.

Andy Williams: We totally agree with you. None of us would disagree with that. It actually pre-empted this, we're already making moves a) to get more clarity with who to go and where to go for help, number one. Number two, having more of a structured pathway so that we know what that help will look like in a structured way. Number three, trying to avoid the situation in the first place by trying to get regulation or consistency in the process that's led them to have the operation in the first place.

Valerie Brasse: It's taking a long time to get to this place.

Andy Williams: Because we're doing it with, just because we feel it really needs to be done.

Roland Morley: The one thing I want to say is that we've lost three years because again, going back to the NHS England and Scottish reviews, two big things came out of that was that every patient had to go through the MDT process, but we needed the resources for it. Secondly from a GP advice point of view, that all patients had to have access to GP advice. That wasn't resourced in Scotland. Thirdly, and more importantly, is the recommendations of the complex failures.

At the time of 2016, when the Mesh Review came out, neither BAUS nor the Royal College of Surgeons are regulatory bodies, so we came up with self-regulation in terms of nominated mesh centres that we felt could offer the facilities. Not necessarily be able to treat everybody but allow a patient into a pathway that then lent them onto treatment. So, you had a port of entry and that port of entry then allowed you to access amongst your colleagues, because some of these complications are very severe complications. You may not be able to deal with it but your colleague may. That colleague may be in a different institution.

Chris Harding: I think that's a really important point. One of the things we did to try and help the patients as a first port of call was point them in the direction of the BAUS website where mesh advisory/removal centres were located. I think there were 20-something of them on the BAUS website. Not all of them were doing high volumes of mesh removal and certainly, perhaps only half of them were doing the complex removal but it was a first port of call. Because what we were hearing is the patients were going to their GP with pelvic pain say eight years after a mesh and they were going for a hip x-ray or a back x-ray and the pathway was so meandering that we thought right, this is where - and it spanned the whole of the England,

Scotland and Wales - to give people a point to where to go first. Not necessarily to see a surgeon who would end up ultimately treating them, but at least to get you on that path to avoid this meandering before we actually get to 'oh well, it could be the mesh'.

Jonathan Duckett: We've had our first national meeting of mesh centres in December last year where all the mesh centres came together to discuss how patients were imaged and treated and to actually produce some guidelines about how patients should be treated and managed in the future. So, we have understood that problem and within the context of a small charity which is what we are, we've tried to address that informally or without any additional assistance from any wider bodies. So, we've driven through patient care and safety or we've tried to, where we can, within the limitations of what we can do.

Simon Whale: Can I just ask - sorry, just a quick one. All the things that you've been describing, the efforts you're making to address the problems that you, I think, all recognise exist, have they not all come about because of the efforts of patients organising themselves into groups?

Swati Jha: I would say we started way before that. The accreditation of units that was set up by BSUG is now six years old. It goes back to what Sir Cyril Chantler was asking about credentialing of clinicians. The whole aim of the BSUG accreditation process was to make sure that the people performing the continence and prolapse procedures had the certificate, had the knowledge, had the skills to do so. That's what the accreditation system did.

It made sure that certain standards were being met and though we were accrediting units, it was the clinicians within those units that had to demonstrate that they met all the criteria, which is a form of credentialing. This is now, you know, we've had several units now reaccredit because they have to be reaccredited after five years. So, this is going back a fair few years.

Simon Whale: But until the pause came into effect, women were at the hands of 'have a go' surgeons. Right up until that point, they were lacking the ability to give informed consent. When complications did arise, there was and still is no clear pathway for them to go to. The pressure that you're responding to seems to me is largely from those patients and the politicians who have taken an interest in their cause. It wouldn't be happening if...

Chris Harding: I think that's fair. I think that's a fair point. I think that they've raised awareness and they should be congratulated for that. Certainly, the patients getting themselves together in groups. I'll take you back to what I said at the start, we believed what we saw in the level one evidence we read which was these procedures were quick, straightforward, largely successful and free of significant complications. Of course, only the patients alerted us to the fact that they were getting them but we were also starting to see more and more come through in our practice.

Andy Williams: I think both are true. Clearly, movement was made prior to the massive public interest and we knew that there were certain problems, certainly from a bowel point of view, okay, our incidents were far lower but it's not zero. When it happens, it can be catastrophic and so we take that very seriously. There's no doubt that the public concern the pause has driven this at a pace, which actually personally speaking from the Pelvic Floor Society, we welcome because it's given us a platform and it's given us some momentum to actually make some change and make some difference.

Because otherwise, as we said, we can advise and we can suggest and we can say well, we would do this, but the root of the problem, this has come up time and time again, but none of us have said is that the surgeons for whom you're not worried about are the ones who are engaged, they're interested in communication, consent, they're members of our societies and active members and they are proactive.

That's great. You don't have to convince them about MDT work and everything else. The difficulty comes is, as you say, up until the pause, you will have people who say well, that doesn't seem too hard, I'll have a go at that. Clearly, I'm being blasé about something that's never quite hopefully that blasé, but those are the surgeons that we need to be watching and we need to bring into the fold to work as part of a team. We have no power of doing that.

Julia Cumberlege: Can I just say, I mean, I was really interested, Mr Morley, in what you were saying that we'd lost three years. In those three years, a lot of operations have taken place. I am sure some are successful, some I'm sure have caused terrible complications and difficulties. So, I absolutely sense your frustration because you are not executive, you are membership organisations and all the rest of it. But what I just want to pick up is that you're saying you want things mandated. What does that mean? Who does the mandating? How do you ensure it holds? Where are other examples? Could you just tell me a bit more about mandating?

- Jonathan Duckett: Can I answer that? That's always been the difficult problem and that's been the problem right from the start and it's the main problem today. So, if we came away from this meeting and you could mandate compulsory use of the registry and a variety of other things, I would be...
- Julia Cumberlege: We can't do anything. We can only recommend and actually, that's why we had to work very hard to get the pause to happen. Because we couldn't do it. We had to work with NHS England and the Department of Health.
- Jonathan Duckett: I would be the happiest man, and probably with the whole group here if we could mandate the things that we've been trying to achieve as societies for many years and mandating registry would be the way forward. The problem comes when we've had these discussions with NHS England is they say they can't mandate care because they buy or purchase services.
- Julia Cumberlege: Yes, they're commissioners.
- Jonathan Duckett: They're commissioners. So, we fall within this area where there is no one to mandate the care. We try it through the government system and the appraisal system but actually, this is the crux of the problem. We can't mandate these things and we would love them.
- [Over speaking]
- Julia Cumberlege: Sorry. Who can? Who can mandate?
- Andy Williams: I think the commissioners can because if you say that the commissioners will only pay for a procedure, if you can fill in the - I hate to say fill in the form - but you can prove that they've gone through an MDT process, you can prove that they've come from a pelvic floor unit, you could add into that initially a [sequin] benefit for an accredited unit. I think if you make it only accredited units that are able to be commissioned, you would stall the whole of pelvic floor services nationally because there won't be enough units that can do anything. But you could start by saying right, we recommend a [sequin] target for accredited units and if you are going to be paid, because it all comes down to money whether we like it or not, you only get paid for a procedure if you can prove that it's gone through an MDT and you have the correct governance.
- Roland Morley: So, the classical example of that where it works well, where there has been a [sequin] and key performance indicator is cancer. If you use the cancer pathway model for this, you would get those outcomes because people that are not trained basically give up and are not accredited. So,

they fall by the wayside. You only get those people that are doing them properly, in high volume, going through the whole MDT process that do the surgery.

Julia Cumberlege: Right, thank you. I think a lot of people wanted to come in and, Cyril, do you want to...

Cyril Chantler: I'd like to just deal with consent. One of the recurring themes as we've gone around the country, and we've met hundreds of people now, personally met them within the team as well as met them online and in correspondence. We've observed people that were terribly suffering. One of the complaints has been 'I never was told what was going to happen'. Now I accept the point you can't know what you don't know. I mean, it's the unknown and we didn't have the outcome measures to do that. But the process sometimes seems to have been quite extraordinarily trivial and unprofessional. If explained in the - if it actually happened as it's been explained to us. So, the question is how can we actually prove that?

In my practice, I would always sort of try and write a letter after we've done that and send it a copy to the patient as well as [unclear]. But maybe in this day and age, and particularly with Montgomery and the things that go with that, we should have a more formal consent process because it's a process and it's not an event. Can you think of any ways that could be improved? Do you think people should keep an audio record of it on both sides? Can you think of anything that we can do because we get back to this issue of trust at this point?

Jonathan Duckett: The patient...

Cyril Chantler: Let me finish - which is an important part to me of being a doctor. You've got to be trusted for medicine to work. So, what do we need as a profession to do to improve that? Jonathan, I interrupted you.

Jonathan Duckett: The patient decision aid is one of the cornerstones of making sure that patients have full choice and informed consent. Yes, I think the consenting in the past was not as good as it could be and I think we've learned from that within this process. So, within the new patient decision aid, they will have all the risks and complications that we are aware of at this moment explained to the patient. Then it's the patient's choice to decide which operation they would want surgically. I think that's a great step forward and I think it does cover Montgomery and, within as good as we can, allows the patient to be fully informed.

We've done some work with the - some qualitative work looking at consent, in fact, and with the London School of Tropical Medicine and Hygiene with an NIHR grant. It involved interviewing patients before they'd had surgery. So, they were naïve to the treatment options and it is very interesting to determine what makes patients choose surgery and which operation they actually want.

There were many other things which other than the surgical success and the complications that the drivers are actually for patients choosing surgery are where they are in their life. They take advice from the woman down the road who's had an operation. So there were many different drivers that we're starting to understand about the consent process. But it's not - what we're doing at the moment is we will hopefully give them the risks and complications and allow them to choose, but that isn't what makes them make their decisions. It's other life factors that are really important to them.

Julia Cumberlege: Can I just say, I have already paid a tribute to your decision aids. That is the presumption that people can read, that they'll take it home and all the rest of it. What patients really want is the quality of the consultation that they have with the surgeon or whoever is going to be advising them and the operation involved and so on.

Now when I chaired a trust, at that time the surgeons then, because it was old world, used tape recorders. They'd put it on and they recorded everything that was said in that consultation. The patient then took that home with them, they discussed it with their family and really it brought out all sorts of other issues because their family were just as concerned. Then they went back to the surgeon and said look, these are the questions that now we want to ask you.

The decision aids are telling people, no, we are saying that actually, it is the patient's choice. It is up to the patient that has to be well informed and that takes place, apart from anything else, of the quality of the consultation that's taking place. Now Sir Cyril has said that with the modern world of course we've got iPhones, we can record stuff. Now, don't you think it would be a good idea if we moved forward and, in this case, then actually ensured that the patient had a record of the consultation that took place, discuss it with their family and others and then come back with their questions?

Chris Harding: We've got the options leaflet from BAUS and it's designed to be filled in in the consultation and actually, I write down where it says I would want this option because, or I would not. I fill it in with the patient and that, to me,

is a proper consultation with fully informed consent because we take every option, I give them the facts, we talk about whether or not it would be for them and write down what they've said to me about why they perhaps would or wouldn't choose...

Cyril Chantler: Do you give them a copy of the form?

Chris Harding: They get it, yeah. They get it and they bring it back and then it goes in the medical notes when they have their surgery. So, they get that and that's why I think the options leaflet from BAUS is a very good idea because it - it's no good as a leaflet you give to a patient to take away. It's about a recording of the conversation between the doctor and the patient.

Julia Cumberlege: Yes, but what you're telling them is often not what they're hearing. So we've actually been given in some of our sessions we've had patients coming with their patient notes and they're very full and the area where they had mesh inserted has been Snopaked out. So that has gone from the record. Now I'm not suggesting any of you do anything like that at all. But I'm just saying that I think that what you fill in, it's your view and I'm sure it's full of integrity and professional and everything else, but the patient may not be hearing that.

Chris Harding: No, but it's not my view. I write down what the patient tells me is their opinion when they're first given the information. Because it says 'I would like this operation because.' and that 'I' refers to the patient. Not me, I can do all of them. But I record what the patient says. Oh, perhaps I wouldn't want injectables because it really only works 50% to 60% of the time or I wouldn't want an autologous sling because it means two incisions.

I write those things down and then I say, go away and have a think about that and that's why the decision aid, the options leaflet from BAUS is such a good tool because actually, all you're recording is not necessarily what you're telling the patient because that information is printed. It's what they then tell you about their initial thoughts and it gives you a sort of window into the thought processes of them.

As Jonathan says, it's so variable. I've got patients in Newcastle who are waiting for a mesh pause to be lifted so they can have a tape. These are people who've weighed up all of the evidence. But individuals will vary and then I've got other patients who will say 'I'm never having any of that mesh. I've seen it on Victoria Derbyshire'. It's so different across the board and that's why you need all the options to be outlined and you

need some record of the conversation that you've had and what the patient said to you.

Roland Morley: If I can make a comment about the record and you're opening up a whole big can of worms in terms of informed consent because it's not peculiar just to match this across the whole...

Julia Cumberlege: That's why we're doing this review.

Roland Morley: ...across the whole of service.

Cyril Chantler: This is modern medicine.

Roland Morley: But if you actually just go to the GMC website and Good Medical Practice, there is a whole ream sitting there on informed consent. In any consultation, you need to discuss the procedures, the alternatives to the procedure you're recommending, what the risks of that are and what questions the patients have got for you and that should all be recorded. Certainly, when I do my letter that goes out to the patient, that whole letter with all that discussion goes in the letter.

Now that doesn't happen with everybody but it happens with good practitioners. They will do all that. But you're talking about changing the face of what we record, and going back to recording now, with the latest changes in GDPR, you actually can't do that. They actually can't record, go back and come back with it because that may have gone viral on the internet, tweet or whatever. So, we've got big problems with the data protection.

Cyril Chantler: I do know a bit about that but I'm not sure you're right. But it's not the subject to discuss.

Roland Morley: But, I mean, we are opening up a whole [unclear] discussion.

Cyril Chantler: As somebody who did once chair the committee on the [sundry] care record, you get permission from the patients. Then you can do pretty well everything in that way. But you have an absolute requirement, unless it's a legal opt out from GDPR, to restrict the information to the medical team and not beyond it. But patients thankfully can still do what they want to do but you can't do what - well, you wouldn't do, but people can't do what they might want to do with patient data without asking them. But I don't think that's a defence but there are other issues here.

Simon Whale: I think the BAUS decision aids include recognition of unknown territory, as it were. So, what happens if a woman falls pregnant after the insertion of mesh and how that reacts and so on. How often do you get women

saying to you, any of you, in the case of SUI or prolapse as was, what can you tell me about the risks of having polypropylene in my body for the rest of my life?

Chris Harding: It's not common.

Jonathan Duckett: No.

Chris Harding: It's not common.

Simon Whale: Do you think it's a good question?

Chris Harding: Yeah. [Unclear] question but I don't know what the answer is in terms of long-term effects. I mean, my engagement with the patient groups has shown me that there's quite a lot of patients coming forward with autoimmune disorders that they relate to mesh and there is some [unclear] supportive evidence with regards to that. So, I don't know what the answer is, I have to say, but...

Jonathan Duckett: There's an MHI position statement on polypropylene mesh that was published in the International Urogynaecology Journal a couple of years ago. But yeah, I think as Chris said, we're not 100% certain what the long-term risks and complications are and hence why we do need to study these procedures longer term.

I've just written a paper for the, another paper for the International Urogynaecology Journal looking at the reaction in the body to mesh and things and we understand there may be inflammatory markers which are listed or caused to develop by mesh in some patients. But our understanding the science behind that and how it relates to systemic disease is quite rudimentary at the moment.

Simon Whale: So, when women tell us, as they have done on many, many occasions that they feel like guinea pigs, you still think they're wrong?

Andy Williams: I think history will give us the answer to that. If in 100 years' time there's a clear development pathway between having polypropylene mesh and developing a condition, then clearly, we've been ill advised. The trouble is we're only seeing one side of the argument in that, supposing your risk of an autoimmune mesh related complication is 0.1%, do you then leave the other percentage wet, prolapsing, incontinent? It's a balanced argument. Nobody in this room will underestimate how devastating a bad mesh complication can be. We all are in agreement with that.

We're all advocating a responsible structured MDT robust process to counsel, consult, consent and deliver surgery in the safest way possible.

Follow patients up for as long as we think is necessary and we don't know how long that is. But equally, to say yes, it could cause an autoimmune, therefore we will ban all mesh, mesh will be used in hernia repairs, it's used all over the body and if we stop using mesh, you will put surgery back by about 50 years. You'll be back to a 20% recurrence rate, 30% for a simple groin hernia, whereas at the moment it's less than 1%, probably 0.1%.

So, we have to put everything into perspective. Which is why I say we can't answer that question and this is what I tell women and men when they say I'm not having that mesh put in my body. I say well, I totally respect that. This is what else I can offer. These are the pros and cons of that, this is the evidence as far as we know it at the moment, but clearly, things can change. You tell me what you would like.

It comes down to the Montgomery flaws where the checklist and Shahab will tell us that we've produced a similar checklist for consent. Maybe as an aide-memoire and a discussion point because it is no longer adequate for me to say the chance of mesh erosion is 1% in this big systematic review. Your chance of pain is 0.5% in this review, your chance of this - because we will say these are the published literature but I will then say I have done 120 of these operations and I have had two mesh erosions. One was treated very simply, the other one it destroyed that woman's life. She then had to have this section of her bowel out, she had this operation and I spell it out.

Because if you say to a woman, she may have a total understanding, you say mesh erosion, she knows what that means. But I say 'do you understand what that means?' and they say, 'well, yeah', and I say, 'it means you could be passing faeces and gas through your vagina without your control, such that you become burnt and excoriated and ulcerated around the vagina. You live in daily pain which cannot be controlled, and even if we take the mesh out, it will still be in agony and it may be incurable'. So, spelling it out in those words is now what the majority of the responsible consultants, and I think we're all nodding, will say.

Chris Harding:

But then you have the other variable which is the variable patient views. I have, as I said before, women who are waiting to have sub-urethral tapes because they've looked at the literature and decided that actually, the odds are in their favour. The likelihood is they will get a good response which is complication free. The HES data tells us 94% of patients don't have a readmission or a reoperation and similar from Jonathan's group's work, whereas I - and those patients, they don't want the alternative

because they know about the complications from colposuspensions autologous slings, which are significant.

Whereas on the other hand, I have people who won't want mesh at all, won't entertain the thought of it, but it's about empowering patient choice. They've got to make the decision. I can't make it for them. The worst question I dread is 'what would you do if it was your wife?' Well, they don't want that. They need to make the decision so what's important to them by way of the facts because there is no operation that is complication free.

At the meeting in Sheffield, we had the chair of the British Pain Society standing up and telling us that up to 10% of patients under any major abdominal surgery got chronic pain. So there's nothing we do that's risk free. Nothing.

Swati Jha:

But on the issue of consent, I think we would all agree that we haven't done justice previously. We haven't done as well as we should have done. The consent process did fall below a reasonable standard. I think Montgomery changed that. Montgomery made us aware that we needed to talk about all the options and that's one of the things that the patient decision aids are very much designed to address.

So, the patients have to write down why they're choosing something. They have to write down what's important to them. It may be that the fact, as Chris was alluding to, it may be that the fact that they don't want mesh is the single most important factor, in which case, a mesh procedure is just not an option. But it may be that actually what is most important to them is a very short hospital stay, in which case it might be that in that patient, the mid-urethral sling is the most appropriate procedure. But that's for them to decide, not for us.

The other component we've incorporated into the decision aids is actually a page for the MDT to write so that it demonstrates that not only has the patient made the decision, but that has then subsequently been discussed within an MDT context to, in some ways, confirm that that decision is appropriate. Because, for example, a patient with a BMI of 45 may decide that they want a laparoscopic colposuspension but they would be hard pressed to find a surgeon who would be willing to do that.

So, it comes back to the appropriateness of the patient for a particular procedure but the first thing that we have to bear in mind is their choice and their decision before we can then percolate that through to the MDT.

Julia Cumberlege: Well, thank you. We're absolutely at one with you on that. Thank you very much. I'm sorry, I'm going to have to draw this to a close because we've got other meetings, I'm afraid, this afternoon. I'm trying to keep to time and we have overrun already. But can I thank you so much for coming. I'm really, really grateful. It's been a very, very interesting and informed discussion as far as I'm concerned. So, thank you all very much.

END OF TRANSCRIPT

Session 4: Royal College of Surgeons (RCS)

START OF TRANSCRIPT

Julia Cumberlege: So, if we could start and if you could just say who you are and why you're here.

Derek Alderson: Yes.

Julia Cumberlege: That'd be nice.

Derek Alderson: I'm Derek Alderson. I'm currently the president of the Royal College of Surgeons of England. I still hold an emeritus chair in surgery at the University of Birmingham, where I was the head of the academic department for ten years. Before that, I was professor of surgery in Bristol. I worked there for seventeen years. My own area of clinical interest was in oesophageal and gastric surgery, mainly oesophageal and gastric cancer, although I did do a lot of hernia surgery in my earlier years and certainly in my training, and was involved in some types of mesh-related, minimally invasive laparoscopic surgery in the later part of my career.

Julia Cumberlege: Right. Well, thank you very much for that. I just wondered if you could say a little bit about your colleagues in the profession and how you think these operations have been performed, and really whether you feel there's been in the past enough skills, enough education, enough knowledge on how to insert the mesh into the areas that we're looking, which is the pelvis.

Derek Alderson: It's difficult for me to comment, of course, on behalf of the community of gynaecological surgeons because they are a separate college and they have a separate training pathway from surgery in general. There has been a separate college for some time, and obviously many of the meshes that have given rise to concern are related to gynaecological practice and uterine prolapse. The urological surgeons, of course, have inserted tapes and meshes for urinary incontinence, and they of course are members of our college. I've spoken to the urologist about this.

Clearly, there has been training of urological surgeons for a substantial length of time. Whether or not we believe that the methods by which we train surgeons in new technologies is fit for purpose in the future, I think is something that definitely needs to be visited and examined very carefully. What happened in the past of course reflects the way in which surgery was being taught, let's say, in the 1990s, and things have evolved since then. So it may have been acceptable in its time, but I would say

that that methodology is no longer acceptable for the introduction of a new technique, a new technology, or whatever it happens to be, now, in the 21st Century.

Julia Cumberlege: Yes, well thank you. I mean we know how medicine, how surgery and all of the related professions and things keep changing because, I believe, that the Royal College, your college, has produced a very interesting paper on the future and how you see robotics, and various other things are being introduced. So obviously we are going to go forward, but we also have to look back a bit about what's happened, why it happened, could it have been avoided? Should it have been avoided, and so on. But you wrote a very interesting article, Innovation and Enthusiasm, and there is a very charming photograph of you.

Derek Alderson: [Laughter]. I was a lot younger.

[Laughter].

Julia Cumberlege: You also say that new developments obviously need to be designed to improve patient outcomes, and to need better research, innovation, and quality improvements as a continuum. I'm just wondering where you feel in the past this sort of thing was not addressed.

Derek Alderson: Okay, so I would say that whether we're talking about implants, mesh; whether we're talking about the use of new technologies, robotic surgery or keyhole surgery; or whether or not we're talking about the use of novel devices in the context of that new type of surgery - so implants, devices, and new technologies. The big mistake, I believe, is that we did not have compulsory registration of devices and technologies by the time they reached the clinical workplace and started to be used in patients, let's say beyond preliminary trials, etcetera.

Even now, I think that I mean obviously they might be done in the context of research studies, so there is a type of registration that might be there, but discarding that very small number of patients at the beginning of it, I think that we definitely have failed patients by not having compulsory registration for these devices.

Julia Cumberlege: Perhaps we do want to come back to that.

Cyril Chantler: If we can just explore that now, can we? Since we've raised it. My experience with registries was with the European Dialysis and Transplant Association Registry, and every child who, in Europe, had a kidney transplant was automatically registered there and then that it had taken place. The Registry was more complicated, because then you went back

and asked very specific questions about outcomes, the whole range of outcomes, not just clinical, but effect on the family and so forth. That required an input of resource to do that.

Derek Alderson:

Yes.

Cyril Chantler:

It wasn't something I could fill in, any more than you could fill in if you'd done an operation. So we've been interested in the notion that the first thing that needs to happen, picking up your point and what you said in *The Future of Surgery* - which I think is first-rate, if I may say so - is you need to register the fact this operation has taken place...

Derek Alderson:

Correct.

Cyril Chantler:

...and it has been done by Professor Alderson. He's done it on Cyril Chantler, and he was suffering from this, and this is just the operation date and this is what you did.

Derek Alderson:

Yes.

Cyril Chantler:

You bar code what you did to me...

Derek Alderson:

Yes.

Cyril Chantler:

...and it goes on a national, central database, and it could be done at the same time as you fill in the operation date.

Derek Alderson:

Absolutely. Yes, I agree 100 percent with that. Of course, it's the next step that's the critical one. I'm sorry, you'll have heard this 1,000 times, I'm sure, and I'm not trying to oversimplify. The registry, of its own right, does not create patient safety. It's just a list. The registry must contain information that can be audited. So the next bit of the puzzle is the bit that costs a lot of time and a fair bit of money. The registration process, I agree, should be relatively simple. You should be able to do it at the time that you put the implant in or use the new technology during the operation. Correct. Held by a responsible body; it could be a professional association, but the registry simply allows you to carry out a high-quality audit.

Of course you might say the items that you want to collect in the registry should be items that you are reasonably confident would be worthwhile auditing down the line. If it's a new implant, I want to know were there any short-term complications related to its implantation. Of course, in turn, high quality, well-conducted audits lead you to be able to ask sensible research questions that bring the thing full circle, and you're set

up to do the proper research study to answer the next thing which has been highlighted by the audit.

So, if we were to take just any imaginary mesh, we would register the use of those meshes in whatever group of patients it is. We collect information. We say whether or not there are certain complications that we perhaps did not anticipate, and we then think okay, how do I now devise a research study to tell me how do I get rid of these complications, or how do I minimise the risk of these complications?

Cyril Chantler: The second stage there...

Derek Alderson: I'm sorry for elaborating in such a slow way.

Cyril Chantler: No, no, that's fine, because it's a very important part of that (rapport), so it's absolutely topical to talk about it. So the second path of the procedure is then to set up a register, which would often be sponsored by the appropriate professional body, say the Pelvic Floor Society, for example.

Derek Alderson: Yes.

Cyril Chantler: Now, that requires the patient's consent. You cannot set up a registry without the patient's consent under GDPR.

Derek Alderson: Yes.

Cyril Chantler: But that is usually relatively forthcoming because why wouldn't they want to cooperate? But then there's also the problem, how to pay for it, and that's an issue. But if it is part of the introduction of a new technique, then it is sensible to make sure that takes place in places where they know what they're doing by people who know what they're doing...

Derek Alderson: Yes.

Cyril Chantler: ...and that they are resourced to run the registry which then is a dynamic inquiry that goes on year-in, year-out...

Derek Alderson: Yeah.

Julia Cumberlege: ...and which will pick up both short-term and long-term problems, and can also, because it's linked through the NHS number - with the patient's permission - it can link to MHRA or any other body. Does that make sense?

Derek Alderson: Yes. Yes, and I think that the funding in that particular set of examples, you can think of ways in which that could be, I think, quite readily achieved because we already have some examples of that. The National Joint Registry, that adds a small surcharge to every implant that is placed. So if it's a device or an implant that's being used, there would be a small surcharge. I think if it's a new technology, then I think you're right, new technologies, if we were to take robotic surgery, which we do believe is likely to become more prevalent and more widely used, I do not think that it's appropriate that every hospital, every Tom, Dick, and Harry should be, as it were, experimenting and learning how to do robotic surgery.

There needs to be a commitment made by Trusts with sufficient expertise and infrastructure to introduce the technology reasonably, and perhaps there could be some type of funding that would be allocated to the designated centres, and the centres could compete. They could interview to see who should be awarded contracts to try and develop a certain type of technology. So I think each bit of the puzzle can be addressed. I'm not saying those are the only possible solutions either, but I mean I couldn't think they'd be beyond the wit of man.

Cyril Chantler: The principal strategy, you would support.

Derek Alderson: I would.

Cyril Chantler Thank you.

Julia Cumberlege: Can I just ask you, Professor, when we've been going around the country listening to patients and the problems that they've had with the insertion of mesh, and it's been horrendous, really horrendous; can I just ask you though, because there is a suspicion that in some cases there's been a very active medical device industry that has actually had an influence on some of your colleagues to insert the mesh. Now, this has been put to us by patients. We don't have evidence of this, but I just wondered if that's an issue that ever comes across your desk or anything that you feel should be done about it?

Derek Alderson: Well, I think it's a common issue that's raised. I mean, we see it in the press, we see it on TV, and I can't believe that it's entirely fictitious. I do believe that the majority of people who insert meshes do so with the patient's best intentions, etcetera, but we do know from recent history of the behaviour of some surgeons in other spheres that not everyone behaves honestly, and if there are financial inducements from independent companies and people who practise independently, then of course some people are tempted and will do things that are perhaps

inappropriate. But we don't have any data on that either. We only know about the few people in the surgical profession who have been significant outliers in terms of their behaviour and the harm that they have done to patients, Paterson being the most obvious example in recent years.

Julia Cumberlege: So, do you think something that should be done when we establish, and we hope we'd be able to with these registries, that the conflicts of interest should be declared by the surgeons who are doing the operations?

Derek Alderson: Most certainly.

Julia Cumberlege: So that the patients can see it on the web or whatever, and they can see what support the surgeons are getting from the industry.

Derek Alderson: I think that that is absolutely essential. The tragedy is that we have to do that in the first place.

Julia Cumberlege: Yeah. Can I just say it happens to Parliamentarians, so we all have to declare our interests and it's reviewed every year.

Derek Alderson: Yes, yes. No, I...

Julia Cumberlege: People know exactly...

Derek Alderson: I think that the culture of transparency within the profession as a whole in surgery still has some way to go. I think surgeons are doing better than many other branches. We publish all our results from our NHS practice at least. Nowadays you can go on the internet and find out what a surgeon's results are like. So we do do that, and I think the culture of openness is there in the profession as a whole. But of course there's a difference between what people do voluntarily in their NHS practice, and what people will do compulsorily.

Julia Cumberlege: Thinking about mesh implants, what has certainly come to our notice, again through the patients and patient groups, is that initially it might have worked very well, but over the years we've heard about how the mesh disintegrates. Sometimes it stretches. Sometimes it contracts. Sometimes it certainly moves around the body, the mesh then encompasses other organs so that actually to take the mesh out is as dangerous as it possibly could be.

Derek Alderson: Yes.

Julia Cumberlege: I'm just wondering what we do. How do we ensure that the longer-term outcomes are notified and that we learn from all that?

Derek Alderson: I think there's two things here because the reason that you have to have compulsory registry at the start is so that you get an accurate denominator of the number of people who have meshes put in, and when you set the registry up and you decide on the information that you want to collect, you have to think very carefully not just about, let's say, technical issues related to placement. So that's, you might say, intra-operative or peri-operative things that might work and not work. You then have to think about short-term complications.

You might believe in the context of, say, a mesh implant that knowing what happens within 30 days is not really worthwhile, but knowing what happens, say, after 90 days might be a better short-term outcome and I'm sure the experts could tell you what they feel would be best. Then of course, you're right. You have to think okay, are there possible long-term risks related to this device? Does the device last? Does it leach ions of a certain metal into the bloodstream, as we saw, for instance, with the metal-on-metal hip replacements? People have to think very carefully about the types of information that could potentially be worthwhile, and of course people will make mistakes. Something totally unexpected will happen.

No one is trying to suggest perfection, but we have to get the best minds to create the best registries that last for an appropriate length of time, the audits last for an appropriate length of time, so that the problems can be spotted before you have thousands of people affected by significant complications.

Julia Cumberlege: Well, thank you, and then my last question for the moment is really about how sometimes patients have said to us that they felt that the surgeons have been very dismissive of the worries that they've put to the surgeon. They haven't recognised, really, what has happened, as the woman feels certainly has happened to her body. How can we change some of that culture?

Derek Alderson: This is a very difficult question and I'm not going to try and duck it in its entirety, but I think that the problem begins right at the initial consultation and the rapport that has to then exist between a surgeon and the patient. And understanding on your part that you are going to allow me to do something very invasive to you. I will forget who you are when we meet in Waitrose in ten years' time, but you will certainly not forget who I am because I did this to you. So I think we must move away right at the outset from that old-fashioned concept of you simply consent to what I tell you to do, and we enter into a more shared decision-making

process in which I explain to you just about everything. In fact, everything that you decide that you want to know.

So there's a bit of patient education here. Patients have to learn that that's how things should be in the future. The surgeon has to understand that two minute consultation, I'll put you a mesh and you'll be fine, is not acceptable anymore. I think there has to be far greater rapport at the outset between the surgeon and the patient. Only in that way I think will the surgical community, who perhaps as you say, a small number of people may be dismissive of patients, only by having a bigger involvement at the outset I think will the surgeon then be more cognisant of what it is that is bothering the patient afterwards.

So I don't think it's simply a case of saying to surgeons, you have to be a bit more responsive to the patient's complaints. That's fine, I can say that until the cows come home. I think you've got to start right at the beginning of the journey and get the patient and the surgeon to have a much better understanding.

Julia Cumberlege: Thank you very much. We had quite a robust discussion earlier on this subject, so I'm not going to go into it again. Simon?

Simon Whale: Yeah, I mean what you just said touched on something I was going to raise about informed consent. Many of the women that we've spoken to, met, feel that they weren't adequately warned about the incidence or the severity of mesh complications prior to the procedure being done.

Derek Alderson: Yeah.

Simon Whale: This raises issues around the risk-benefit balance. It's not specifically on mesh, you may wish to comment more generally, but as far as mesh is concerned, how do you think the risk-benefit balance should be assessed when complications can be life changing?

Derek Alderson: Well, there's lots of different things I would say are important here. Of course there is a real need to have a very full understanding of what it is that patients really want out of a certain type of intervention, and what type of outcomes are meaningful for that patient related to that intervention. I'm sure you've heard all day about patient reported outcome measures and things that measure truly the health-related quality of life of that patient in relation to that specific type of intervention. If you don't have such a measure at the outset, you will make the mistake that surgeons did for many years in many areas, there's what I believe, as the surgeon, that's important, which is usually the

physical result of my intervention on you: you look great; and your feeling about what constitutes a reasonably quality of life.

I didn't want you to make me live forever in this miserable state, I wanted to go down to the pub with my mates and enjoy a drink, but I can't do that anymore. So I think that we have to work really hard on the development of high quality specific patient-related outcome measures, things that properly measure the outcomes that the patients are interested in, not what the doctors think the patients might be interested in, which is the old-fashioned way of doing it. Of course, that's really what gets you into the shared decision-making process, as opposed to what we used to call informed consent.

Even the law, I think, is very clear on this. Montgomery is absolutely explicit. You must tell the patient about every material risk that that patient might be concerned about. Well, you can only know what the patient is concerned about if you have a good measure of what it is that concerns the patients.

Sonia Macleod: But even so, sorry, with new interventions, part of the issue is that you aren't necessarily aware of risks. They may come out as these are put into practice. So how do we ensure that surgeons are as aware as they can be and up to date with the latest risk information and are adequately conveying this?

Derek Alderson: It goes into a bit of a \$64,000 question: you can't predict every unknown risk, if you know what I mean. Even experimental evidence may not disclose a significant risk when something goes into clinical practice...

Sonia Macleod: Particularly with crisis.

Derek Alderson: Yes. But I think that's the reason why when you set registries up at the very outset, you have to have appropriate expertise there in order to, as best as you humanly can, think of all the things that are reasonably likely potential risks, particularly, I mean this is, just to get back to your point, you can have something that's a very common risk or common complication, but it's relatively trivial, or it may be short-lived, and it's not of any great long-standing importance and it doesn't have a longstanding effect of quality of life. Or you can have a very rare but very severe complication, and many operations carry with them rare complications, but which are devastating should they occur.

So if I take one of the things I used to do is gall bladder surgery, the risk of the surgeon damaging the bowel duct may be one in 4 or 500 patients, but of course if you do it, it is absolutely life-changing for that patient. A

rare complication, if it's a severe enough one, should be discussed with patients. Some patients will say well, if the risk is really small I don't really, I don't mind. I'm happy to undergo that procedure on that basis. Another patient, the next patient in the door will say oh, I'm scared; now I don't want the operation. They're not right or wrong that's just the difference in people.

Simon Whale: Do you think it's important that surgeons are honest about what they do not know?

Derek Alderson: Yes.

Simon Whale: So, in the case of mesh, for example, there's a lack of clarity over the long-term effects of having mesh inside the human body.

Derek Alderson: Yes.

Simon Whale: Polypropylene inside the human body.

Derek Alderson: Yes.

Simon Whale: For a lifetime, because it's designed to be there for a lifetime. Surgeons, presumably you'd agree, but tell me, surgeons should be very clear that they just don't know what the lifetime impact might be.

Derek Alderson: Yes, I think that's absolutely correct. If patients, at the outset when these meshes and tapes were first put in, they said what are the results like after 20 years, people should've said we don't know what the results are like after 20 years because no one's had one in for 20 years. Sometimes of course you can make, let's say, educated guesses based on analogies from other bits of the body with similar things, but you have to be very careful about doing that. I mean, there is a difference between implanting a piece of polypropylene, for instance, in the inside of someone where there are organs and things, and putting polypropylene in the body wall, for, say, an inguinal hernia repair.

We've been doing all of them for 30 years and by and large we know about the long-term results too, and we know what happens to mesh over a long period of time in the body wall. We shouldn't make the assumption that mesh inside your abdomen functions and acts in exactly the same way, and that its fate is identical, because that's not the case.

Simon Whale: I recognise urology and urogynaecology are not your own personal specialties, but, well, I'll ask you this question anyway. TVT and TOT, the tapes that we're talking about for SUI, as we understand it, are inserted

completely blind. There's no use of a camera or any other imaging technology. Is there any other form of surgery where that happens?

Derek Alderson: Blimey. That's a bit of a - that's a difficult one to answer off the top of my head. I feel as if I ought to be saying here, of course, but now that you've put me on the spot and asked me to think of a one...

Cyril Chantler: I've been thinking about it for a week and I can't find the answer

Derek Alderson: Have you Cyril? No help?

Cyril Chantler: No, no.

Derek Alderson: Well, there are we are.

Simon Whale: Does that raise any concerns in your mind?

Derek Alderson: Not necessarily. You see, there are things that we do that you would call blind in certain situations where things are sort of acceptable. But, I'm thinking off the top, I'm trying to think on my feet here of some appropriate examples. We do occasionally, for instance, in cancer patients, if we're trying to open up a blocked tube, you can't see the way through to the other end, but we do use image guidance to be sure that we've ended up where we think where we've ended up. There are risks in doing that. I'm sort of out of my depth here. It's not my area of expertise. I've never, ever seen a gynaecologist insert one of these tapes or meshes, or a urologist do it. I haven't actually personally witnessed it.

Simon Whale: Would it be a sensible conclusion to draw that the people who do do a procedure such as this blind should be people who are very well experienced and know what they're doing and not just have-a-go-types?

Derek Alderson: There's no place for have-a-go types anywhere anymore. We'll park that one. I don't think that that's acceptable at all to modern society or to surgical profession. I think that people should have the opportunity to practise. I think of course in the very near future the ability to simulate and carry out a simulation beforehand will be viewed as essential. I do not think the surgeon, in ten years' time - I've written about this - will carry out their first operation on a human being, albeit under very careful instruction from a senior and experienced surgeon who you've watched do it, or you've done bits of things and then he says okay, now it's your turn. That's how I was trained. That's how we had to train.

I don't believe in ten years' time that that will be the case. I don't think society will accept that, and I don't think that the training group of surgeons will accept that. I think that you will have to have practised on

some type of simulation system, some high- fidelity model, and shown that you can do the procedure competently. The thing in the operating theatre is to learn the issues around judgement when things are slightly different, etcetera. I think people will be expected to have undergone team training, rehearsal, with the other people who will be there because there'll be lots of technologies, robotics engineers, etcetera. So I think in ten years' time the way in which we train surgeons will be different.

So the scenario that you imply, I think if it's still happening, and I hope it isn't, I don't think that it has any realistic chance of still being the norm in any way, shape, or form ten years from now.

Cyril Chantler: That leads me to ask the question, which I think I may have spoken to you before about, and that is should surgeons be credentialed to do certain procedures and should a register be kept which the public can access?

Derek Alderson: I think that it's very difficult to credential broad areas of practice because there's so much to do and the risk of variation becomes so great. I think that credentialing should take place in very restricted niche parts of surgery. Let me give you an example. Say, in the world of urology, where we're here, yes? You might say well, should we have a credential in urology? Well, there's so much diversity, no surgeon actually does everything across that spectrum of disease any longer. So you could say okay, well, should we credential in uro-oncology? But then I would say well, all well and good, but there are some areas there that are highly complex.

I do not think that every urological oncologist should be removing, doing retroperitoneal lymph node dissections for young men with advanced testicular cancer, and I do not think that every uro-oncologist should be dealing with kidney cancer that's invading your vena cava when you have tumour all the way into your heart. These are very complex operations. We need a trivial number of centres in the United Kingdom to deliver these very complex services. I think we should credential the centres and the surgeons who work there. So let's just return to this specific issue: mesh removal. You might credential that small number of centres and surgeons who should be doing this particular complex surgery.

Cyril Chantler: Then you could, maybe, make sure that you incorporate the quality control through the annual appraisal?

Derek Alderson: Absolutely. Absolutely.

Cyril Chantler: That's very helpful, thank you.

Julia Cumberlege: Any questions? Anybody? Any questions?

Valerie Brasse: Yes, I have one question if I may. HES coding.

Derek Alderson: Yes.

Valerie Brasse: We talked earlier about new techniques, new procedures. It seems to me that HES coding is always catching up after new procedures, and certainly in the area that we've been looking at.

[Over speaking]

Derek Alderson: Yes.

Valerie Brasse: ...but also trying to separate the partial removals from the full removals. The coding isn't right, we're getting it wrong, we don't have an overview therefore of what's actually going on. How do we do this better, this catch-up? Which seems to lead people to knowing really what the overview of activity is?

Derek Alderson: We could be here in this time next year to talk about HES coding. I mean, the principle of HES coding is fine. I think the problem is that, you know, and the coders by and large do a great job, but it's just another part of our NHS that is creaking and it's a struggle to try and do it. I would say at the outset of course you've got to try and create a series of quite specific codes that fit for the types of intervention that are being proposed, and you should create those codes obviously at the time that you think of creating your registry.

You have to, as Sir Cyril says, one of the things that culturally we need to do, of course, is to get surgeons to understand that documentation of what you've done with a new device implant, new procedure, is a fundamental part of the conduct of that procedure. It's not an optional extra that you can choose to do or not do. That includes accurate coding. So I think that this onus falls on the individuals who are carrying out the intervention.

Valerie Brasse: That's about getting the coding right, because I'm saying it's a new procedure that hasn't got a code. It's the catch-up bit. HES coding takes a long time to get a code for that procedure. So in some senses for a while, procedures are happening with no overview of the activity because no one's coded it and I just don't know how that process should work better.

Derek Alderson: I don't have a specific answer for you. I think one of the things that I would say, though, is that whatever coding you have, even if it's a temporary form of coding, it has to apply across all sectors of healthcare,

at least in this country. That's every bit as important. So, you know, many new procedures and new devices and new technologies are offered in independent hospitals before they are offered in the NHS for financial reasons. It's unacceptable for there to be two different systems of, let's call it healthcare accountancy, and by that I mean everything that we've talked about so far.

Cyril Chantler: May I just say that my question and suggestion in relation to the operation note would have to apply in the private sector just as it does... It wouldn't be an optional extra, and indeed, at the moment I should declare the interest of a non-executive director of the Private Health Information Network as set up by the markets, organisational authority or whatever, does actually require the linking of private and NHS data. Can I just ask you something else to end with?

Derek Alderson: Yes.

Cyril Chantler: One of the concerns that I felt as a doctor on this Review is that it has taken the activities of individual patients forming into groups, and then lobbying into Parliament, and then being taken up by Parliamentarians to actually bring to our attention the problems that they have experienced through both Primodos, sodium valproate and the insertion of surgical mesh. And I say to myself why has that actually happened that way? Why have I, as a doctor, not got there before them? Do you have any observation of that?

Derek Alderson: I think it's very sad. I'm sure you and I share the same sentiment there. I think one of the things is when I talk to my colleagues about events in the past that perhaps have not worked all that well; if I were to take breast implants as an example, my breast surgical colleagues tell me that they wished to have a registry, that they made approaches to parts of government about setting up registries in order that they should be able to carry out effective audits, and their overtures came to nothing. So I don't want to go backwards and blame people for things that didn't happen in the past. I'd far rather that we just cast those aside. But they do tell me that, as a profession, many professionals actually sought to have registries and audits in order to prove safety and efficacy for patients, and that financial constraints inhibited them from doing it.

Sonia Macleod: Sorry, did you look, if you go right back to '94, SERNIP, the Safety and Efficacy of New, Register...

Derek Alderson: Yes.

Sonia Macleod: ...of New Intervention and Procedures. Now, that sounds like it should've, you know, been exactly what everyone needed. But it didn't happen.

Derek Alderson: Correct. Why didn't it happen?

Sonia Macleod: Yeah.

Derek Alderson: Yeah. Well, I mean, again, I think we can go back into a myriad of causes about why it didn't happen at that time, and as I say, you can have a fairly futile witch-hunt to try and determine who do you think is largely to blame for this, and I don't think you will get anywhere.

Cyril Chantler: But we could do better in the future.

Derek Alderson: But we could certainly do better in the future, and compulsion, I'm afraid, is the only way forward for registries and audits. I might say at the end of the day, an organisation that will act as a regulator. That would certainly not - be absolutely clear about this, that would not be a Royal College. We might hold a registry. I would be very happy as a college to set standards for the level of performance of surgeons, but I do not believe that the same organisation can be the regulator, and there would have to be a separate, funded regulatory body.

Julia Cumberlege: Yes, I can understand the reasons behind that. Can I thank you so much Professor Alderson for coming, and for giving us such an interesting session. Really appreciate it.

Derek Alderson: My pleasure.

Julia Cumberlege: Thank you very much.

Simon Whale: Thank you.

[Over speaking].

END OF TRANSCRIPT

Session 5: Royal College of Obstetricians and Gynaecologists (RCOG)

START OF TRANSCRIPT

- Julia Cumberlege: Would you like to say who you are and why you're here?
- Lesley Regan: Well thank you very much for inviting us. I'm delighted to be here and hope I can help. My name's Lesley Regan and I'm President of the Royal College of Obstetricians and Gynaecologists which, as you know, is a membership society. We have 16,000 fellows and members, half of whom are working overseas. I'm also the head of department of obstetrics and gynaecology at Imperial College based on the Mary's campus.
- Julia Cumberlege: Thank you.
- Linda Burke: I'm Linda Burke. I'm the Executive Director for Education and Quality at the Royal College of Obstetricians and Gynaecologists, and the guidelines work and the education work, sits under my directorate.
- Julia Cumberlege: Thanks very much indeed. As I was just saying, you actually have put in very full evidence to us, written evidence, and thank you for that. Also, your conflicts of interest and [unclear].
- Simon Whale: I was just going to ask, if I may, about the conflicts of interest statement. As Julia said it's a very fulsome and a comprehensive one for which we're grateful. Obviously, it indicates that you receive funding from device manufacturers. I was wondering if you could outline for us what you think are the right rules of engagement as it were around receiving funding from industry. I've got a quick follow-up question after that, if I may, as well.
- Linda Burke: Do you mean as a college?
- Simon Whale: Mm.
- Linda Burke: We have historically actually been quite conservative, I suppose is the right word, about receiving funding from industry et cetera. We consider - in terms of the rules, what we aim to do is to make sure that if we do receive funds, that the organisation that's giving us funds is very, very clear about, if you like, the rules of engagement. We are absolutely clear that we are independent, and that any funds will not influence any decision-making or any guidance in any way, shape or form. That's made very clear to any organisation if they give us any funding.

Simon Whale: I suppose it's challenging when you - if you come to the situation where you're reliant on funds for certain activities to maintain that balance I presume. I don't know...

Linda Burke: Do you want me to come back?

Lesley Regan: For example, we have we do receive some bursaries for student prizes and competition prizes from Ethicon. They have no influence on the judging of these. They basically put the money into a pot and this supports activities, for example, at a congress.

Simon Whale: Right.

Linda Burke: But as a general principle, we haven't been in the position, certainly recently, where we have been reliant on funding. Again, just to emphasise, because largely we're a membership organisation, and in terms of exams et cetera, et cetera, that will always be the bulk of our funding. That is actually the core funding that keeps the college going, so I suppose in some senses we don't have to rely on that kind of funding. If ever there was a compromise, we would be in the fortunate position of being able to say no.

Simon Whale: Okay, thank you. My follow-up question relates to your members and clinicians. Do you think there should be a mandatory register of Sunshine payments, that type of arrangement, for clinicians in this country?

Lesley Regan: A mandatory...

Simon Whale: Register of interest.

Lesley Regan: My personal view is yes. I think that we would support that as a college as well. You will have seen all over our submission to this review on this topic that we've been calling for a mandatory register of procedures that I think we're going to talk about for some time now.

One of the limitations that we have is we are effectively an advisory body. We are responsible for the training, the education, and the continuing professional development of these 16,000 fellows and members, but we don't have any regulatory powers. I can advise individual clinicians, or groups of clinicians, or one of the four sub-specialties in obstetrics and gynaecology - of which urogynaecology is one - what we think they should do.

We can provide them with outlines of best practice in terms of clinical guidelines. We can provide them with all sorts of other tools to help them achieve best practice locally, but I don't have the clout to go in and

mandate that it carries on with their individual healthcare provider. For that I have to rely on going to the medical director, or chief executive of trust, or whoever is in charge of - or whoever's the senior responsible officer for that healthcare provision.

Julia Cumberlege: From the view of patients who we've met going round the country, it's really helpful for them - it would be - if they knew what the conflicts of interests were for the different surgeons who are actually treating them. There's good precedence for that. For instance, parliamentarians, we all have to put in our conflicts of interest and it's updated every year so everybody knows where we're coming from, how we're being supported and so on.

Lesley Regan: For example, there are certain groups. Anybody who joins a committee - of which there are many at the college - fills in a declaration of interests. I don't think necessarily a declaration of an interest is necessarily a conflict. Certainly, all of the council members are quizzed on this not just once, but every year. The board of trustees which I chaired this morning, it just happens to be that we've gone round and I'm asking them all to fill in a declaration of interest once again.

I think for the vast majority of individuals that we're working with, and being an advisory body for, I don't think they would have a problem with that. I have to fill it in for Imperial, for the university. I have to fill it in for St Mary's Hospital Trust, I have to fill it in for an international organisation for women's health which I have become secretary general of, so I don't think that would be a problem.

Julia Cumberlege: What needs to happen to make it happen?

Lesley Regan: It has to be mandated.

Valerie Brasse: Mandated by...

Lesley Regan: Well, a regulator because I haven't got a regulatory function.

Valerie Brasse: I think what I'm getting is would your membership be resistant? If you propose this, do you think that they would actually all say no you're doing that, or that you could voluntarily ask them could they do this, and have they been asked?

Linda Burke: We asked them in the sense of - as Lesley's alluded to - in terms of college business which is where we hold power...

[Over speaking]

Oh, we do ask them to do that. I would also emphasise that in terms of the curriculum, for example, we very much make it part of the curriculum about transparency, and being completely ethical in terms of how people behave which would include this. But as Lesley's alluded to, we don't have the power. It's their employer that has the power, or a regulator that has the power, to make that. We could certainly propose it as a voluntary system, but whether they would – I mean ultimately that's...

Julia Cumberlege: Shall we just leave it there.

Lesley Regan: But in the same way that the GMC in so mandating that you have to state your sub-specialty training interest - I have beside my name obstetrician and gynaecologist in reproductive medicine. They could do the same, and I think that most people would be comfortable with doing that.

Julia Cumberlege: Okay. Perhaps we could get on to the real subject for today. I just want to ask - and I know Lesley, that you haven't ever inserted mesh, it's not part of your expertise.

Lesley Regan: That's my claim to fame.

[Laughter]

Julia Cumberlege: But certainly your college colleagues, many of them would. Can I just ask you from the research and things that the college has done, is mesh actually safe? Do we know how safe it is? Do we have any sort of evidence of that?

Lesley Regan: I think the evidence is accumulating now and we're, like you, very concerned about those patients who are telling us the problems that they've had. That's one of the reasons why obviously you're holding this review, and I think we are at one with the sub-specialty society of ESOG and others in wanting to insist that training is mandated, very carefully regulated, and just for the use of mesh if it's appropriate.

Also that we ensure that we provide really good informed consent, and the decision-making tools that we've been working on for some time now - well before this review was convened - are an important tool as well. Now that there is a call for some patients wanting to have a removal, I think it's important that the accreditation for removal centres becomes a mandate as well.

I thought it might be useful - this is just a - Linda very kindly printed it out large. This is the run-through training programme in our specialty. This is FY1 and 2. That's your, if you like, your houseman year as it used to be

known. Then you get a national training number and we have a seven-year run-through training programme. The core curriculum is delivered in those first five years, during which the trainee's expected to pick up their Part 1s, their Part 2 and then finally their Part 3 MRCOG, usually aiming to get there by ST5 at the latest.

At that point, at the end of this core training, of which there isn't a guideline - well there isn't an inclusion of mesh in that, so at no point would a trainee be involved in this. At the end of the fifth year of core training you would differentiate into becoming a consultant gynaecologist after you've got ST7 with a special interest in, or you would go and apply competitively, nationally, for a place to be a sub-specialty trainee. In our specialty, in obs and gynae, there are four sub-specialty areas of which urogynaecology is one.

If you go in at the end of ST5 to go into a generalist job with a special interest in, then you would be expected to take an ATSM - I think it's all in our submission, but I can happily send you a list of the acronyms - advanced training skills module. There would be one for some urogynaecology procedures. You usually need to have two ATSMs before you can collect your CCST and go on to the GMC register as a registered consultant.

If you go into sub-specialty training here at the beginning of year six, then you're involved in a much more intensive, and much more carefully regulated training programme. The first sub-specialty training programmes started in 1991 I think I'm right in saying, at St George's. That was Stuart Stanton's big push there. There are now 13 sub-specialty training programmes in urogynaecology throughout the country.

The training programme takes a minimum of three years. They will do two years of clinical. If all goes to plan, they're visited by the college sub-specialty training panels on site and their competence is assessed in terms of numbers of procedures, and skills levels attained at the end of each year. They do two years of clinical minimum - some of them have to do more - and they will also do a year of research in urogynaecology. It's a very detailed programme.

I think it's just useful to know that in those 13 centres - the first of which was in '91, there are now 13 - you're churning out, well not churning out, but you're developing urogynaecologists in a minimum of three years who will do the sub-speciality or specialist work of which this may be one aspect of it. In total we have 75 accredited sub-specialists in urogynaecology now in the UK. There are a lot of - my point is I think

making - I hope I'm making it clear, there will be a lot of other individuals who have done general training and developed an interest in you're not going to have that same skill - degree of skills.

Julia Cumberlege: That's very impressive. Thank you. Thinking about those who do insert mesh and the gynaecology, urologists and others, are you quite surprised that really we do feel that we get more complications than with other procedures? Has that come across your desk? Are you aware of that?

Lesley Regan: You started your introduction to me saying I haven't put in a tape and I haven't but I was - I did generalist training and when I became a consultant and then specialised in reproductive medicine, the week before I'd rung operating lists in Cambridge where I did umpteen colposuspensions. I did a lot of open surgery for surgical, or for stress incontinence. Although informed consent wasn't as robust as it was then, I remember consenting women that there was a 10 per cent complication risk with open surgical procedures. I'm not sure that that is something that people remember quite so robustly. There is a significant complication rate with open surgical urinary procedures as well.

Julia Cumberlege: Do you think that operation now - I think we have a difficulty that a lot of people don't know how to do the suspension. I'm just wondering, do you think that really is an alternative to mesh? Is that something we should be exploring as a...

[Over speaking]

Lesley Regan: Going back to this - which is why I still use it. If you're doing core training, you would only perhaps be trained or shown how to use mesh, open surgery is - it's very rare nowadays. I think there's the concern and one of the reasons why I wanted to take - why we've not wanted to support an outright ban, but wanted to support the pause, the investigation and review, is that I worry about those women who are unsuitable for procedures, having nowhere else to go. The colposuspension's a major surgical assault.

I also am concerned, in an advisory and training capacity, that we've got a real gap in the training skills of these surgeons now. They just don't know how to do it. Although I don't do urogynaecology anymore - you'll be relieved to hear - none of the trainees that I see on a regular basis have done colposuspension, or even seen one. They've become vanishingly rare. I'm worried that we will have a cohort of women for whom there is no relief from their quite debilitating urinary incontinence. This panel will know very well how common that problem is.

- Linda Burke: We have obviously reinforced - we very recently reviewed, and had approved by the GMC, a revised ATSM. We're looking at our sub-speciality training to actually try and build up that expertise again. Obviously, that does rely on there being people out there to be able to supervise and sign off. It will take time in terms of that expertise growing out there in the community.
- Julia Cumberlege: A lot of you have expressed that because mesh really got underway at quite some speed, you just saw the figures mounting, that alternatives then - well it could have become better, could have had keyhole surgery as opposed to open operations as you've described. It was described as colposuspension, as being in a cul-de-sac because it really wasn't - they had begun to develop it differently but because of mesh that really took over, that all stopped. I just wondered if there was an opportunity to regenerate that.
- Lesley Regan: I think there is. Indeed, there's mentorship programme starting for open and laparoscopic versions of the old procedures. As Linda's alluded to, it's going to take time to build up because always when you're training you need a cohort of mentors for the learning curve and potential complications. At the moment what we haven't got are those mentors, except possibly in the sub-specialty accredited centres of which - as I've said - there are 13.
- Linda Burke: As Lesley's alluded to, in terms of the training, it's about mentorship, but it's also actually about a very strict sign off procedure that people are actually competent to do this. You need to be able to have observed and then carried out quite a number of these to be deemed to be competent at them. We do have to make sure that we actually make sure that happens before creating a whole new cohort of people out there carrying out these procedures.
- Julia Cumberlege: Apart from the hierarchy that the NICE guidelines and things produced, a lot of women have said to us well, where is the alternative? It's quite difficult that at the moment but I appreciate what you're saying about having to build a cohort that has the expertise.
- Lesley Regan: If that is the recommendation from the review panel, then that, if you like, gives us a bit of armour to actually go and drive those mentorship programmes and training programmes.
- Julia Cumberlege: I'd like to tell you what's in the review, but we haven't written it yet. We're still collecting all our evidence. Simon.

Simon Whale: Just to pick up on that point, we heard from BSUG earlier and BSUG talked about a retraining programme for surgeons already in practice to refresh, as it were, skills around colposuspension and [unclear] but that's - I think they described it as being at the discretion of the surgeons so in other words, people could either take it or leave it.

Linda Burke: I think that goes back to - sorry to keep saying this but we're not the regulator or the employer. We as a college have been responsive about other issues, and are willing to be responsive in terms of training programmes and I've worked very well with societies et cetera to develop those programmes very quickly in other areas. I think in terms of what's within our power we're very willing to do that and to facilitate it, but in terms of the regulatory side of it, that isn't within our power.

Simon Whale: Would you be open to a greater impetus perhaps from us or from [unclear]?

Lesley Regan: Very much so. We've been calling for a mandatory registry, and for mandatory accreditation of all procedures. Now, as has obviously become necessary, accrediting centres for removal.

Linda Burke: Of course, revalidation gives us a great vehicle. We have a very good continuing professional development framework that we can use and is, without going into detail, extremely flexible in terms of how we can develop programmes much more quickly than we could have done in the past.

Simon Whale: Thank you. Can I ask a question - a slightly different question - about the procedure, one of the key procedures here that we're looking at which is TVT, TOT procedure for SUI? Our understanding - but it would be interesting to see what you think - is that it's conducted entirely blind as in there's no camera, and there's no imaging technology involved. Does that make it unusual in medicine, in surgery?

Lesley Regan: I don't like really to pontificate about things that I haven't got first-hand experience of, and I haven't put in a tape. I think a lot of procedures historically have been blind. It's only very recently that we managed to get Ds and Cs taken off the list of advisory procedures, and that was always done blind. When I say blind, I don't mean that you had a blindfold on but you didn't have a camera to go in. Now I wouldn't dream of taking a biopsy from a woman's endometrium i.e. her womb cavity, womb lining, without using a camera and fiberoptic instruments.

Yes, I think possibly I would say it is unusual in this day and age that the vast majority of minimally invasive procedures are undertaken with the

help of optics particularly and cameras and recordings of course. When I did my list on Monday morning at St Mary's I record everything that I'm doing so if there is a problem or a complication you can go back into [unclear] and you've either got hard copy photographs. In some cases, if you're anticipating potential complications, I would video what I was doing.

Simon Whale: Is that quite commonplace in surgery?

Lesley Regan: I don't think it's commonplace. I think you find it relatively available in the majority of teaching hospitals.

Simon Whale: So it depends on the availability of the technology, but also the discretion of the surgeon or not?

Lesley Regan: It's usually about the availability of expensive kit. In talking about how you can mandate these things, it's going to have to be chief executives and medical directors or SROs that understand that if they don't impose certain modes of practice or criteria in practising, that they will be responsible. I suppose one of the ways you could do that would be that if a surgeon doesn't do things in a certain way, then if that trust isn't then reimbursed by whoever's funding them, then we can - so then we get into all sorts of complexities about who's funding what and where the contracts are. I think there are ways of mandating it.

Simon Whale: One of the things that many women who we've met - and as Julia has said we've met many hundreds of women who've been adversely affected by mesh in many horrible ways - one of the things they often talk about is the lack of informed consent. That they didn't feel that the risks were properly explained to them, in some cases not explained at all. It raises questions around the risk and benefit of this procedure. I just wondered if you had any thoughts on how to convey risk benefit, and how to ensure that the patient has a proper understanding of the risk and the benefit.

Lesley Regan: Well I think explaining risk to an individual woman in my clinic is one of the most challenging things I do. I think as I've got more experienced, I recognise that the challenges get bigger. It's one of these things the more insight you have the bigger you recognise the issue is. Linda's appreciation of the risk of one in a hundred of her having a baby with Downs Syndrome, or having a complication as a result of a surgical procedure, is very different to Victoria's appreciation of what one in a hundred is. For some women the risk of one in a hundred is small, and for others it's absolutely unthinkable. For some they dwell on 'oh it's 99% fine, only one gets it'. Others think it's absolutely anathema.

I think risk is very difficult, but there can be no doubt that informed consent - some of the decision aids that we've been trying to develop, not just for urogynaecology but for all sorts of other aspects of our specialty - which remember is probably the most contentious field in medicine, obstetrics and gynaecology. We deal with almost every issue that's contentious apart from assisted dying. I think it's really important that we are leaders in that field and that we push for this.

We will get pushed back though from our administrative and our managerial stance. Because if I was to take your female partner and give her - spend time with her explaining what procedure I was going to do, ideally I would ask her to take away this paperwork, go and do her homework and come back again for another visit. She might possibly need a third visit to finalise her decision. Most of our directors are pushing us to get a one-to-one follow-up ratio from new patients to old. There're wide areas of the system that are then going to have to be brought on board to improve things like informed and decision-making if it's done properly in different stages.

Linda Burke: I think the other thing to say though is one of things that we have become aware of as a college is it's not just about the process and the paperwork however good. It's about how the information is given. That's some of the work we've really been pushing through the curriculum and through the training of doctors not just ourselves but through the other colleges as well.

It's actually making sure that doctors as they're coming through, and through their CPD, actually know how to give that information, and giving people the opportunity in all sorts of ways to ask the questions to do the thinking time, and to feel they can ask a question and they can challenge. That's something we have built in much, much more into training programmes generally is that whole how you give information and how you present the opportunity for people to actually think about risk in a different way.

Simon Whale: One of the other aspects of informed consent is being clear with the patient, the woman, that there are things you don't know.

Linda Burke: Absolutely.

Simon Whale: Do you think that - in the case of mesh - one of those issues would be not really knowing the long-term lifetime impact of having polypropylene inside your body. Should that be part of an informed consent conversation?

Linda Burke: Yes.

Simon Whale: Has it been, in your experience, up until the pause what people are doing now?

Lesley Regan: If that was an individual, it was dependent on the individual and their standards of what they would consider best practice in standards of care.

Linda Burke: We absolutely encourage, and I'd go as far as to say prescribe through the curriculum, that that is how it should be done. We have a number of working groups around different issues where we're actually saying that it's about being very clear about what you know, what you don't know, the risks that we have evidence for, and the risks that we have yet to have evidence for. Medicine is changing very quickly. There are a number of those that we don't have [unclear].

Julia Cumberlege: We had a little debate with your colleagues earlier on about consent and about the quality of the clinical appointment that you have with your surgeon, or your gynaecologist, or whatever.

One of the things that's come across very strongly from the patients to us is that they are convinced things weren't told to them which may well have been told to them. It's because you're so concerned about this particular event in your life, that you're going to meet this person who perhaps has inserted the mesh or whatever. We were just wondering with new technologies and things like that whether in fact you could have an oral type recording. We've most of us got iPhones and things, and you would actually be able to take away that recording to your family or friends or whatever so that you could discuss it.

Because one of the colleagues here today - who actually is involved in cancer in this particular area - he was saying to me that actually they don't take it in. All they want to know is have I got cancer or have I not got cancer. They don't hear the bit you haven't got cancer, but what you have got is so and so.

We're just wondering whether, with the new world that we're going to embrace very shortly with new technologies and things, whether actually that's something that you might consider that would enhance the consultation that you have.

Lesley Regan: Certainly. That thing about bring a friend when you're going to a difficult consultation is put in there for a very good reason. Like you say, you have selective hearing and you don't always digest things. Certainly, when I run my stillbirth clinic, I always encourage people to bring someone along

with them. Often on a second or a subsequent visit, I'll say do you remember I was saying, they'll say no and then the family member will say oh yes she did. Do you remember you said that because [unclear]?

I think it's very valuable so whatever way there is of being able - it's another way of conveying and explaining risk and that's why I think it would be helpful if recommendations for staged informed consent were adopted widely. That really does mean that the patient has to be prepared to do a bit of homework too. That you actually go along, you have your consultation. I could say go and see, for instance, Mr Cyril Chantler. You have a consultation and he gives me documents for me to look at, to read, or it could be a video recording or whatever you felt was most appropriate for that patient. They have to come back and almost demonstrate they've digested it all and understand what the risks are.

These are for [unclear]. I don't need to tell you on the panel they're incredibly time-consuming which is fine for me, but I think we will have to find ways of persuading our masters, particularly the contracts people, about how we're going to factor that in. But it's not a reason to shy away from it.

Linda Burke: Increasingly, people who are coming through the systems will be used to that in training. We use that role play-cum- recording all the time. The other advantage of course is it improves your own practice because you can hear yourself giving information. There's a lot of learning to be gained from doing that.

Sonia Macleod: We have certainly heard stories from women where they've gone into consultations and they've felt very - as though their symptoms were not being listened to. They were being very, very strongly dismissed, including one where a very eminent QC, who spends his life asking questions in very different circumstances - that is his profession, accompanied his partner and didn't feel he could ask questions of a consultant. If someone who's a professional, whose whole professional identity is that, that surely is very concerning.

Linda Burke: I think there's another angle to this.

Lesley Regan: Sorry what question are you asking?

Sonia Macleod: What I'm saying is if the person - as you say take someone along to accompany you. If you are taking someone to accompany you who is a QC, whose absolute job it is to ask difficult questions in difficult circumstances, feels he cannot question a consultant because the

consultant had been giving the impression that this is my area of expertise. That surely is quite concerning isn't it?

Lesley Regan: Well I'd be horrified by it, yes.

Linda Burke: I think there's something as well about the consent tools where - we've got a very good women's network I'm sure we've talked about that in the evidence, but it's really about also working with patient groups and that's something as a college I think we're seen as very pro-active in doing, and want to continue to do. In terms of how we really try to empower patients to feel, and women to feel that they can ask.

Valerie Brasse: Certainly, that's a critical point isn't it. It's a power imbalance.

Linda Burke: Exactly.

Valerie Brasse: That's what they're feeling and they just don't feel they can challenge that and certainly feels very vulnerable as I say the example that Sonia just mentioned is somebody should not have felt that and did. The question of these other women who are saying this to us we now quite understand they obviously felt they could not say or question and they weren't being listened to.

Linda Burke: Again as I say - I'm repeating myself now. We are really trying to get that across to trainees and through CPD with the doctors, but also in our role as a college working with the public and working with women in terms of helping to make them feel they can ask those questions.

Lesley Regan: I mentioned the MRCG has now got a Part 3, and the Part 3 is effectively how you respond and interact with patients. It's not really a knowledge-based thing. It's purely constructed around your interactions and that's done with role playing. There are members - lay members - from the women's network sitting in all these OSCI interactive stations.

One of the things that's been piloted is videoing people giving information, playing it back to them and demonstrating to them how they have thought that they were listening and it was a two-way thing, but actually they were talking for nine tenths of the consultation. It's a very useful way, and as Linda was just saying you can get people - often you show them how they performed their opinion of what they did suddenly changes and they realise that actually they weren't listening.

Julia Cumberlege: Cyril?

Cyril Chantler: I'm conscious of the time and I've got one question I'm burning to ask you, and Sonia has a question which she wants to ask you, which is

related to your expertise not as president, but in relation to hormone tests in pregnancy. That's to give you a warning what's coming.

[Laughter]

Lesley Regan: Oh dear, should I be frightened?

[Laughter]

Cyril Chantler: No, you shouldn't be. I don't want this to end before we got these two questions answered.

Lesley Regan: All right, yes.

Cyril Chantler: The first one relates to what the President of the Royal College Surgeons has been writing about a database for introducing new technology. I have to say I strongly support its views, and the notion is that you need to think of two things. One is a database which is one hundred per cent accurate. The other is the construction of a registry which requires patient consent – creating the database doesn't under GDPR. The registry would then interrogate the database which is a much more complicated procedure. It has extra cost and it would take place in centres where they're introducing technology which will be funded to do that.

The question relates to the database. The suggestion is that when the surgeon - and I'm not a surgeon, wasn't a surgeon - carries out an operation they always fill in an operation note [unclear] always. Even I did for those interventions I did. The notion is that that is not time consuming, but it has to - it would certainly have to have certain items filled in. One would be the name of the surgeon, the name of the patient, their NHS number, date of the operation, what was wrong with the patient, what the operation was. If a device was inserted, it would probably be registered on that with the barcode. That's it. That would be done centrally probably by NHS Digital, though we haven't spoken to them about that yet. That would then be the foundation of knowing unlike [unclear] you've got one hundred per cent accuracy and collection. Would you favour that?

Lesley Regan: Very much so. We've been supporting mandatory registration and a database for a long time now. The problem is the funding.

Cyril Chantler: Yes but it's a very particular way of doing it. It involves saying to surgeons please will you make sure you complete that accurately and in all cases.

Lesley Regan: I don't think it's going to be - I think that if your review says that's what's got to happen, then the communication has to be with chief executives and medical directors.

Cyril Chantler: I accept all that but...

Lesley Regan: I think it's possible to do. I always tell the story about how I'd written several letters to a chief executive at St Mary's about a problem - a patient safety issue - and couldn't get them to do anything about it. Then I was telephoned one morning as I was driving to work, about half past seven. I saw chief executive and I thought oh right this is great they're going answer, and they're going to sort this out. She said to me 'Lesley, I'm really sorry to bother you but you've come up on red on the trust thing because you haven't done your mandatory handwashing. I have to tell you that if you haven't done it by lunchtime you won't be able to operate'. It's quite possible to do these things.

Cyril Chantler: I don't know what to say now. This is a remark attributed to Charles I...

Lesley Regan: Which I didn't say oh I'll have the day off then. I said oh God I better get and do my mandatory handwashing.

Cyril Chantler: Well there's a remark attributed to Charles I - there's more to doing the doing than bidding it be done. There's more to the doing than mandating to be done. If we were to suggest something and the president of the Royal College of Surgeons, or RCOG, said well that's nonsense, that's not a good start so that's why I...

Lesley Regan: No, no. We'd be very happy to help support it and spread the word.

Cyril Chantler: That's all I want to ask. Thank you.

Sonia Macleod: Hormones and hormone pregnancy. As you know, one of the things we're looking at is hormone pregnancy tests. Primodos was the most commonly used. It contained 10mg of Norethisterone acetate, and 0.2 mgs of Ethinylestradiol. One tablet taken, another tablet taken 24 hours later. I was reading the PROMISE trial result which you were an author on. That demonstrated there were no harmful effects of progesterone for mothers or their babies when used to prevent an early miscarriage. Is there any sort of read across from that trial to the hormone pregnancy tests? Was there anything we could infer from it?

Lesley Regan: I think the hormone pregnancy test that you're referring to, Primodos, was pretty archaic. Remember what they did is they gave women - this was before HCG - human chorionic gonadotropin assays were freely

available. They would give a woman, effectively, the contraceptive pill ingredients. If she wasn't pregnant then her womb lining would have a burst of hormone and then it would effectively shed and disintegrate. If she had a bleed X many days later, they knew she wasn't pregnant. If she didn't, then they assumed that she was. It was incredibly primitive.

The progestogen that was used in the PROMISE trial is a different generation of progestogens but I think it was - we recruited a thousand women to that trial over seven different centres. It was a pretty extensive - pretty expansive cohort. I think if there had been meaningful abnormalities because of progestogen challenge to the foetus we would have seen it. It's interesting of course that there's no reason - and my biggest problem with that trial is persuading doctors to stop prescribing progesterone because it showed unequivocally that it doesn't improve recurrent early miscarriage so it's...

Sonia Macleod: But progesterone therapy is still being used to prevent [unclear].

Lesley Regan: Because if you go - most doctors who see women with miscarriages and repeated miscarriages feel that they need to do something. It's a bit of a double-edged sword. The messaging around that trial should be it's a complete waste of time and money, and we must move on to other things. We've been using it for nearly 70 years, progestogens in early pregnancy. It's been proven unequivocally it doesn't improve outcome. However, the message I think the selective listener had is, well it doesn't do any harm, so I can hand it out anyway.

Valerie Brasse: Was there ever the science to support that it improved [unclear]?

Lesley Regan: No, no. It was based on the hypothesis that when it was first discovered that you needed a corpus luteum i.e. what was left in the ovary after the egg came out, to produce this hormone progesterone to keep the pregnancy ongoing until the baby placenta had got established and could make its own production. That was known about in 1953 it was found that was the progesterone with the early pregnancy maintenance it was assumed that if you miscarried that you gave them extra progesterone, that it would sort the problem out.

So the hypothesis was completely flawed because if you're not producing enough progesterone it's because the messaging between embryo and placenta is wrong, usually because there's a genetic abnormality in the embryo. If you give progesterone it's effectively shutting the stable door after the horse has bolted. It may keep the levels up for a bit longer and prolong a pregnancy which was destined to fail.

Sonia Macleod: Would there ever have been a belief back in 1950s, '60s, that something like a hormonal pregnancy test with quite a large dose of progesterone could be beneficial?

Lesley Regan: I don't know because I wasn't practising then but...

Sonia Macleod: No, no - sorry Lesley I wasn't inferring that at all.

[Laughter]

Lesley Regan: I wasn't offended.

Julia Cumberlege: I think it was before you were born.

Lesley Regan: Well, Julia you know my birthday. It could have been, it could have been. It just seems such an extraordinary blunt instrument doesn't it.

Sonia Macleod: Yeah.

Lesley Regan: That you challenge a woman's womb lining and if she bleeds then she hasn't got longer in pregnancy than if she doesn't. Of course it was hopelessly inaccurate as well.

Sonia Macleod: Absolutely.

Julia Cumberlege: I'm going to draw this to a close if that's all right. I'll just ask my team, anything else you want to ask?

Valerie Brasse: No.

Julia Cumberlege: Anything finally you want to tell us.

Lesley Regan: Just thank you for conducting the review and thank you for inviting us.

Julia Cumberlege: Thank you so much for coming.

END OF TRANSCRIPT

14th February 2019

Session 1: Association for Children Damaged by Hormone Pregnancy Tests (ACDHPT)*

START OF TRANSCRIPT

Julia Cumberlege: I just actually want to say that we're very, very grateful for all the information you've given us. Terribly impressed by all the research that you do and the way that you run your patient group. Although we're looking at three elements in this Review, Primodos only has one patient group and that is yours. It's hugely effective. You are greatly admired by the way that you run it. We've had the opportunity of meeting some of your members and that's been really useful to us.

We've also met some of the young people now who have been affected by Primodos, and that was hugely, hugely important when you came last time. We saw Daniel Mason and Nicky Gubbin and had great insight from them as to what their lives are like. Really admired their courage and the way that they manage their lives, which were obviously very tricky

Marie Lyon: Very impressive.

Julia Cumberlege: Thank you for your evidence. We know last time you were very rushed and you didn't really have the opportunity you hoped you

Marie Lyon: No. I would actually like to say though that this is the first review team that's ever actually looked at the people, not just at the statistics, not at scientific evidence but actually taken the time to speak with people. Which is so important. Quite honestly has made such a great difference to the way that they feel, both about themselves and about the fact that they're being listened to. That's been hugely important and on behalf of them all I would say thank you very much.

Julia Cumberlege: Thank you. I have to say we couldn't have done this Review without them. They have been amazing. We have learned so much. As we're going to start screening now, perhaps you could just say who you are and your organisation so that when it goes up on screen, people will know who you are and why you're here.

Marie Lyon: Absolutely.

Julia Cumberlege: Okay, so it's over to you.

Marie Lyon: Okay.

Julia Cumberlege: I'll just say, we're now filming.

Cyril Chantler: Yes.

Marie Lyon: My name is Marie Lyon, I'm the Chair of the Association of Children we believe have been Damaged by Hormone Pregnancy Tests. I'm very grateful for the opportunity again today to speak about the ongoing issues surrounding the oral hormone pregnancy tests. It was actually my original intention to highlight the serious failings of our regulatory authorities and particular the MHRA and CHM - Commission for Human Medicines and Medical Healthcare Regulatory Agency.

But, after viewing the oral evidence presented by members of the Expert Working Group who were responsible for the scientific publication in 2017, it seems I already have a perfect example of the denial and protection culture endemic in our regulators. Denial when problems occur and protection, not for the patient but for the manufacturer. I refer to statements made in the oral evidence, presented by members of the EWG who were responsible for that scientific report. They conclude - the report concluded that there was no association between HPTs and adverse effects. That was quite equivocal.

I need to make it clear that in the conclusions of the report the group did not state there was a possible association or if there was an association, it was a weak one. The conclusion was absolutely unequivocal. No association. Also, the statement I would challenge is that

no group member had a conflict of interest. It's disingenuous at best. I did challenge the involvement of two members of the panel virtually immediately that that review started. One had produced a scoping study on HPTs which concluded there was no association between HPTs and adverse effects in pregnancy and women should be reassured by this evidence.

This was posted - this conclusion was posted on a 'Bumps' website which is for pregnant women. This was posted before the completion of the Expert Working Group, yet that person was allowed to stay within that group. Another member of the Expert Working Group was a German professor who had produced a study on HPTs included, again, in the expert working group evidence and referenced many times by the MHRA presenter as credible and robust. This professor personally gave evidence during a legal challenge on Duogynon which is the same as Primodos in Germany, stating there was no association between HPTs and adverse effects. He was also - believe it or not - remunerated by Bayer for work he produced for them in 2012. He later admitted at a public scientific conference last year he had manipulated figures in his study. That man again was allowed to attend. A third member of the group was a German scientist who studied at the same university as a prominent Schering scientist who was instrumental in producing studies repudiating the link to adverse effects for Schering.

I actually had a personal verbal attack from this person during one of the meetings, relating to the Landesarchiv documents which he did not believe existed. This actually prompted me to ask him had he ever worked with this scientist, and he said he didn't even know his name. He denied any knowledge of him, and he then abruptly left the meeting, didn't return and did not return for any further meetings. I have no evidence of why this happened, but it did happen.

The statement again from the Expert Working Group from Dr Gebbie was that I was invited to comment after every Expert Working Group meeting. This is absolutely untrue. I

was publicly admonished by the Chair at the first - at the very first meeting, when I attempted to question a statement from the MHRA. I was told I should not have attempted to speak as I had observer status only and would not be allowed to contribute unless invited by the Chair. I challenged this restriction which was not as was originally agreed and I sent that challenge to the MHRA in writing. I did not receive a response.

It was only with the assistance of some of the group members that I was able to challenge statements I knew were inaccurate and actually a barrister acting on behalf of the CHM and MHRA attended subsequent meetings. My request for the same facility - for one of our barristers to attend - was rejected. Towards the end of the review I was so concerned by the absence of clarity on the information provided and inaccuracies contained in the presentations to the group, I advised the Chair I will be withdrawing from the review. The response I received was exactly this. You will be shooting yourself in the foot if you withdraw now. I considered this remark a positive statement and agreed to continue to attend the meetings.

After the publication of the report I wrote to the Chair to challenge the statement she had made about shooting myself in the foot, but again I did not receive a response to that challenge. I would also like to highlight a remark from Professor Evans, where he said we included data not included in the meta-analysis produced by Professor Heneghan. The reason this data was not included for Professor Heneghan is because the data was not made available to him. A prime example of protection but not on behalf of the patients - on behalf of the government regulatory bodies.

The APPG supporting our members - the cross-party group - submitted a Freedom of Information request to ask for this raw data to be released. I have also written to the MHRA to request this information twice. I would question why this data was not included on the MHRA website in accordance with its pledge to provide full and transparent disclosure of all evidence. To date we have still not

received this data. Full and transparent disclosure apparently is only at the discretion of the MHRA and Commission on Human Medicines.

To ensure that we do have sight of this I would request please from yourselves assistance in obtaining full transcripts of all minutes relating to the expert working group meetings, which took place between the decision-making panel of the Expert Working Group, the MHRA and the Commission on Human Medicines. In addition, the minutes of the meeting prior to my presentation to the Commission on Human Medicines on the 6 October and the minutes immediate after my presentation on the same date. I believe this information is in the public interest and must be made available

.I must also challenge the statement made by the group in their oral interview, which was astounding. We cannot rule out with any certainty and - there is an association. Everybody admits there is an association and we never said there was a possible link. reasons for doing so and were different from women who did not

take them. [REDACTED]
[REDACTED] Jesse spoke personally

with members of the group to ensure they understood that any woman who visited her doctor to find out if she was pregnant either took a urine test, had a physical examination or was given a hormone pregnancy test. All of which are pregnancy tests. So not only were patients not protected by the regulator, but they were also being blamed for taking the medicines advised by their doctor.

This again is not based on fact, it is an opinion. The assertion by Professor Evans is an insult to our members and compounds the guilt we already feel because we did not question our GP. His view was challenged robustly by Jesse during his presentation to the group in 2017. Our members were not informed they had a choice of pregnancy tests or advised of the risks associated with HPTs. Therefore they were not provided with the information to make the informed choice Professor Evans accuses them of making.

There have been repeated comments by the group on the lack of credible evidence and historical scientific studies, yet evidence of the effects on women who actually took HPTs is discarded. Genetic testing on our members currently shows no genetic fault was responsible. There was no history of miscarriage or abnormalities in prior pregnancies in the majority of our members who were first-time mothers. There is no justification or evidence to support this claim by Professor Evans, but this is another example of denial to protect the regulator.

I really don't want to waste any more time responding to those issues with the oral evidence of the group but would prefer to address the more important issues concerning historical and current regulatory failures. During my previous oral submission I presented indisputable evidence about the historic failures of the government regulatory agencies and the deliberate suppression of evidence by both the drug company and the authorities.

Today I would like to address the continuing failures of the government health regulators - in particular the lack of transparency, lack of informed choice, lack of credible independent data on testing results of drugs and devices, and imposed confidentiality agreements, which are designed to withhold information from the public. The incidence of adverse effects will continue to increase unless information is made available to patients immediately as suspicion is raised. Risks and benefits must be re-

evaluated after reports of adverse effects, and information relayed to patients at the very first opportunity.

The delay by the regulatory authorities in sharing information about ADRs is due to an entrenched reluctance to acknowledge possible harm from a drug or device until protracted investigations have taken place. This is denial and protection at its worst, and leaves many patients still at risk, which is evidenced by sodium valproate and surgical mesh. By withholding this vital information from patients, adverse effects are allowed to continue. Warnings are not issued and there is no system to implement the withdrawal of products until this rigorous re-testing has been completed.

Failure to inform the patients of the risks impedes the patients' right to make an informed choice, as regulators continue to withhold information on suspected adverse effects. This choice is negated by the actions of the regulator, whose paternalistic -I would actually call it arrogant - approach has no place in medicines today. Patients must be allowed to determine their own powerful choices. The absence of transparency and openness in the current regulatory process is ill-advised and dangerous and requires a radical change in regulations which will ensure patients' safety is the first priority and not the protection of the manufacturer or the regulator.

The regulator needs to change focus, needs to provide funding for independent studies and for rigorous independent testing before accepting a drug or device for patient use. There needs to be an increase in research into the cause of ill-health instead of focussing on new expensive drugs to treat the symptoms and not the cause. To compound these failures, the MHRA and CHM impose stringent confidentiality agreements on participants involved in discussions relating to adverse effects.

Reviews are conducted in secret, which ensures information and evidence made available during these discussions are not subject to public scrutiny. The patient is once again deemed unfit to take full informed decisions on their own health. The regulatory process has got to change. We need a proactive process which keeps patients informed and engaged and ensures patients receive all the information necessary to make the right choices for themselves. We need a top-down independent review of the links between the regulator and the manufacturer.

We need to look at the lobbying that goes on, [REDACTED]

[REDACTED] - which is available to the

medical profession from the manufacturer. But this campaign is not constrained to the UK. There is also a campaign group in Germany, who had 615 members. BfArM at that time had actually received 450 instances of adverse effects. The German group follow our campaign closely, and on the 13 March I will be meeting with the two main political parties in Berlin, the Green Party, and health ministers to discuss our progress in the UK.

This will include presentations by Professor Vargesson on the zebrafish research and Professor Ralston on the meta-analysis he produced with Professor Heneghan. The meeting is intended to mobilise the German campaign group and raise awareness of HPTs within the political parties. This scandal is not going to go away. You asked me previously whether the Association intended to initiate legal action, and my answer was yes, we do. This legal action is now imminent. SPG Law is a unique law firm whose mission is to achieve justice for claimants around the world against some of the biggest companies in the world.

SPG combines the talent of some of the leading solicitors and barristers in the UK with the financial resources and expertise of American class action lawyers. Their statement is: 'no one intimidates us. No company is too big for us to hold them to account for their wrongdoings'. A partner from SPG is flying from America to the UK tomorrow and I will be meeting with them in the afternoon to discuss plans to initiate legal action on behalf of our association members.

It has been a long and difficult fight to bring this issue to the position we're in today and it is the ultimate example of denial by the regulatory authorities and protection of the manufacturers at all costs. However, in our case it's a human cost. The heavy responsibility placed on campaigners to provide evidence of harm is another example of the failure by the government health regulators to protect the patient. By continuing to insist we provide scientific evidence, they continue to protect themselves and the manufacturer while refusing to take responsibility for their own failures.

That was basically what I wanted to say today, but one thing that I will bring up if you don't mind - because it was actually mentioned during I think Jason Farrell's interview. There was a question - in fact it wasn't, I think it was at our last meeting. Sonia mentioned about 32 times the stronger dose that Neil used in his ad-hoc zebrafish study. Neil actually still does not know where that figure came from. He said, I'm at a loss to know where it came from. However, he did say it is acknowledged that doses need to be increased. He mentioned the receptors that are not known. He also said these large doses were used in the science for sodium valproate.

That science was accepted, but obviously Primodos science is not. You also asked at that meeting, have

there been regulatory failures? Well, I think we can say yes. When did the regulators and drug companies become aware? They became aware in 1968, '67, sometimes as early as '66. Were women deprived of information to make an informed choice? Yes, we were. You did also say you're not here to judge the science, and I'm quite heartened by that. Again, I know that you attended, Sonia, the zebrafish review and will be attending the meta-analysis so I'm assuming that is just in an advisory capacity?

Sonia Macleod: That's as observer status.

Marie Lyon: Observer status, that's fine. Another question that was asked that didn't seem to have clarity was when did the public and the doctors know? I think that was in Jason's interview as well. They actually didn't know. In February 1970 - I have a copy of a letter which I hope I've sent to you - the standing joint committee contacted Scherings to demand the removal of the indication for pregnancy on Primodos or they would remove the drug altogether from the market.

There's a letter quoting Dr Inman from Scherings, where it says, with the approbation of Dr Inman representing the UK health government authority, the indication was quietly withdrawn without informing anyone in the medical profession including doctors. The first information came in 1975 when the first warning was actually printed. Until then it had quietly [been in the letter] which had - the only thing is I am really sorry if I haven't sent you all the information you need. My assumption has been - which I should have clarified - that you would have access to all the documents I sent to the Expert Working Group. If that's - you don't?

Sonia Macleod: No. Well, I don't know if we do. If they are on their annexes and they're displayed on the website, then yes. If they're publicly available, we have.

Marie Lyon: They should be.

Sonia Macleod: If they are not on - publicly on the website then we wouldn't have

Marie Lyon: Maybe I need to look at these things and make sure that you have full clarity when it comes to...

Sonia Macleod: That would be helpful.

Marie Lyon: ...these important issues, because it is important. Doctors did not know. I actually take exception to doctors being blamed, ██████ to say well, they were responsible because the indication had been withdrawn. They were never informed. My feeling is the doctors were incentivised ██████ but in good faith I feel that those doctors believed when ██████ told them that the drug would not cause them any harm.

Sonia Macleod: My understanding - I want to check whether this is the understanding you have - is that the indication was changed and PROP List was changed. The PROP List was then sent to all prescribing doctors.

Marie Lyon: I would like to see evidence of that.

Sonia Macleod: That was where the PROP List was sent. It was sent to GPs, prescribing doctors and hospitals.

Marie Lyon: Have you seen - it says quite clearly in the letter from Scherings in Scherings own words, 'quietly withdrawn without informing any of the medical profession'. So that would indicate to me...

Sonia Macleod: That's something we need to clarify.

Marie Lyon: That is in a Scherings letter. So I would be very surprised if that's right.

Cyril Chantler: Is that the McGregor committee?

Marie Lyon: I think it is. It's called the Standing Joint Committee.

Sonia Macleod: Joint Standing Committee.

Marie Lyon: Which was also - they're responsible for MIMs as far as I know, for the indications that were actually printed.

Sonia Macleod: They were responsible for the PROP List, I think. They weren't responsible for MIMs as far as I'm aware.

Marie Lyon: Right. No, possibly you're right. I think I've mixed the two up or thought they were the same. But that is quite an explicit letter that they - and it is actually said those words are, 'with the approbation of'. So, he actually said yes you can do that.

Cyril Chantler: They said it wouldn't be reimbursed, is that it?

Marie Lyon: That's right. The original thing came...

Cyril Chantler: It wasn't withdrawn, it was just said we will not reimburse you for using it for that purpose?

Marie Lyon: No, the indication was - the indication was withdrawn at that time in February 1970.

Cyril Chantler: Okay.

Marie Lyon: They actually withdrew the indication and that's clarified in a letter from Scherings that we have on file.

Sonia Macleod: That would be hugely helpful.

Marie Lyon: I'm really sorry - I'm afraid that was a really bad assumption on my part that you would have been given all the information.

Julia Cumberlege: That would be really very helpful. Thank you. Can I just pick up one or two of the things you've said?

Marie Lyon: Of course.

Julia Cumberlege: Thank you for that very clear exposition. It was extremely good. Thank you for that. Can I just say that you did have an ask of us that we should get the minutes of these meetings between the MHRA and the EWG and certainly we will try and do that...

Marie Lyon: That would be wonderful.

Julia Cumberlege: ... for you and we'll try and ensure that we can do that, and also the minutes of the meetings that you were concerned about and we will follow that up as well.

Marie Lyon: Thank you.

Sonia Macleod: Can I just ask - the EWG meeting minutes are available on their website.

Marie Lyon: Not all of them.

Sonia Macleod: Right, that's what I was about to - there are some that aren't.

Marie Lyon: As far as I know, the minutes taken during the secret meetings that we were excluded from - there was only the core group allowed into those meetings - have never been made public.

Valerie Brasse: How many of those were there?

Marie Lyon:

I think there were about three in total. I'd need to look - because I did lots of notes at the time, which - maybe I should have sent those as well, because a lot of the assumptions shall we say that were made by the Expert Working Group have no basis in fact. A lot of the information - and particularly the scientist who worked for Bayer I had to write twice to ask him to be removed and yet that process was supposed to be rigorous. They were supposed to have made sure that there was no conflict of interest.

The other thing that I did question was why BfArM were there. That's the German regulatory agency. If this was a UK investigation, that also was quite an inexplicable decision to make. So my feeling at those meetings was that there was a definite bias towards making sure that they did not find any kind of link. The fact that they can now say in hindsight, 'we always said there was a possible link' -I would like you to look at the interview with Jason Farrell where he actually asked many times Dr Gebbie why had it been changed to a causal? There was no time at all that she actually said, 'ah well because we knew that there was a possible link'.

Again, this is very easy to say now. They're obviously going to defend their position, which is - again, another instance of protectionism.

Julia Cumberlege:

Can I reassure you that certainly we are trying to work with Bayer, and secondly we do have another oral hearing with the MHRA. We've had them once but that was just about information that was given. Now we want to look at the regulatory system and how it works and all that, so thank you for your testimony on that today. The other thing I just want to raise is the point you made about women feeling guilty about having taken this medication.

We've heard that often when we've been round meeting people who have taken Primodos and I just want to reassure them that really there is no reason to feel that guilt. You can only be guilty if you really know the consequences of what you're doing. Certainly they were not told the consequences. And if in any way we can reassure people, but I know it's deep, deep down and that they do feel guilty. But really, certainly we don't agree with that at all. We don't think that they should feel guilty in any way.

Marie Lyon:

I think they received that reassurance from the patient meetings that you held, and at the time my feedback to you all was that the empathy that you actually displayed to our members went a huge, huge way to making them feel less guilty. I don't think that will ever go away because it's just there, it's ingrained now. But it certainly helped and I think the fact now that they can see that really we didn't have a choice, we didn't dare to question our doctors so many years back because you were god, you know, that was it. The doctor knew what was best.

But, I suppose initially it was always going to be - why didn't I question? With this evidence, with the discussions with yourselves, I think now we can actually start to see that we actually were in a position that we wouldn't have been able to question anyway. Because the answer would have always been, don't worry about it, it won't do you any harm.

Julia Cumberlege:

Yes, absolutely. Right, well thank you for that. I think the real tragedy is that this meeting of patients and all the rest of it has taken this Review to do. It is the patient groups who have actually been determined that somebody should listen to them. We have listened. Clearly we can't tell you our findings yet and that will come out in our report when it's published.

But one of the things I just want to ask you. We were very careful on our terms of reference and we had to get agreed - those agreed by the Secretary of State which he did agree, and it was the previous Secretary of State, of course, Jeremy Hunt. In those terms of reference, we actually said that we couldn't re-examine the science in terms of us as individuals scientists. That really hasn't been possible for us to do but clearly we've listened to certainly witnesses and others - experts in the field - and have been to your sessions in parliament and heard - and the way that you've

been working with your party group and Yasmin Qureshi and all that. So, thank you for all of that.

I just do want to ask you - you have been so thorough. You have gone into so much of the history of this, what's happened and all the rest of it. I'm just wondering about - we've had reviews, the Expert Working Group, the ad hoc group on zebrafish and the MHRA and that. Just thinking about this Review, what are the things that you think we really should come out with? With what - what would reassure your group but also be fair to all those involved? If you could say a little bit about that. What are your expectations of our findings?

Marie Lyon: I absolutely agree that the science cannot be revisited by this group. That requires people like Professor Heneghan, Professor Vargesson - people with a huge background in research and looking at these kinds of cases. However, I would like to think that you'd take into consideration the reviews that they have conducted, look at the expertise that they possess and then measure that against some of the reviews that will actually be reviewing their conclusions to see if the same level of expertise actually exists in the people who are actually chosen to do these reviews. I don't believe it is.

Professor Heneghan in particular is actually Head of Evidence- based Medicines and the clue is in the title. That's his living. That's what he does all the time. So my wish would be that you actually look at the background of the people who are being included in both the ad hoc zebrafish review and also in the new reviews for the meta-analysis. I think that's really important. I feel that you already have an understanding of the failures with the regulatory authorities, particularly the historical failings. They are there, they are quite clear to see. I would also like to think that you have some influence on current regulatory failings, which are absolutely endemic

They need to be reviewed independently. That needs to be a top down review. We need to look at what kind of lobbying still occurs, and as I said before - it's not lobbying, it's bribery. They're going in and offering some sort of incentive to push these tablets. Sometimes these drugs are on the market when there's already a perfectly good drug available. I feel that the ties between the drug companies and the authorities need to be researched. One of the Expert Working Group/MHRA personnel on the group when the review was taking place actually left to work for one of the drug companies involved in the review.

That's the kind of thing that happens all the time. There's an incestuous link between drug companies, between regulators, that needs to be assessed. It needs to be looked at and I think the only way to do this is to actually start to get all this information into the public domain. To have truly independent people - which I actually think this team is, for the very first time - truly independent with no pre-conceived ideas, but actually putting the patient first. Let's have a look at what we need as opposed to what would make a profit, what would actually look really good in print. Let's get something that's needed as opposed to wanted.

Julia Cumberlege: Can I just say that one of the things that we are determined to do in the Review is to not only examine the past, because history is very important, but we really are concerned with the future. We think the future is just so important from the point of view of everybody involved - the medical profession and patients and citizens and everyone. I'm going to pass on now to Simon.

Simon Whale: Marie, thank you again for everything you've said today and previously. It has been - and is - extremely valuable to this. One of the things I was just going to pick up on - the point you made about the three meetings of the EWG that were closed or which you weren't involved in. Did they ever explain to you or anyone else why those meetings happened in that manner?

Marie Lyon: Because it was the decision-making process, which they felt we should not be involved in. That included other scientists within the group, it wasn't just the observers. It was the other scientists as

well. This was basically more of a closed group. What those discussions were, we never found out. We just saw the recommendations at the end of each of those sessions. To try to query them was impossible because we didn't actually know what had been said.

I did challenge - obviously - for a change - some of the decisions that had been made because I'd been in the discussions prior to those meetings where the other scientists had actually said, 'this information isn't good enough. Where did you get this information from?' The responses were, 'well, it's the best we could get'. One of the presenters actually said, 'I can't remember'. Which I found astonishing, and yet that was taken as evidence - not as 'well this is the best we've got' or 'oh I'm sorry, I thought that's what it meant'. I've got all those comments - I wrote those comments as those meetings were going on.

How they could then form a conclusion - one of the scientists actually said, 'can I ask why, when you ask a question it's always in the negative? Why do you always want to say 'we have not found - we do not agree?' That again didn't go in the minutes. A lot didn't go in those minutes, but they're in mine. Sorry, go on. Did that answer your question?

Simon Whale: Yes, it does, it does, it's helpful. As Julia has said, we'll do our best to get hold of transcripts and meetings - minutes of meetings that haven't yet been disclosed to us or elsewhere.

Marie Lyon: The raw data as well, please.

Simon Whale: Yes.

Marie Lyon: If you could.

Simon Whale: The other thing I was going to just quickly ask about is the issue of causal associations - of those two possible associations. As you will have seen, when the EWG members came in and spoke to us here, they said that whilst there are certain things they might have done differently and said and written differently, that it wouldn't have altered their conclusion.

Marie Lyon: They certainly did.

Simon Whale: Do you have a view on - what is it about the evidence - is it that the evidence of causal association is not strong enough, or is it that the methodology they used to interpret that evidence was wrong?

Marie Lyon: It's virtually impossible to find a causal association. Unless you actually use these tablets on a human being, there will always be doubt. This is something that they are aware of. This is why they've changed it to causal. I did actually bring you a copy - and I hope I've actually put it in here - that shows the difference between causal and possible. There are certain degrees which I think we mentioned last time. I did bring it with me, and I hope to goodness I have it - there it is. There is an actual criteria from the Uppsala Monitoring Centre - yes, so you have this?

Simon Whale: Yes.

Marie Lyon: Again, one thing I need to say is, one of the people I didn't reference last time was Tobias Arnt who has been an invaluable member of the team. He has been working exclusively as well for thalidomide. What he says: it's importance to reference the thalidomide case. Thalidomide is widely believed to be the medicine where the association to malformations are proven with a degree of causality. The latest research presented at a conference at the WHO in Geneva in 2014 says this is not correct, even for thalidomide.

'It is difficult to specify exact diagnosis parameters of thalidomide embryopathy. Thalidomide embryopathy can phenocopy genetic defects.' That's the scientific term, but you'll probably understand that. One would have to accept that there may be other effects of thalidomide which are not being diagnosed and there may be effects not due to thalidomide that overlap with the thalidomide effect. We find it astounding that the conclusions of the report did not take into consideration those factors which were available in 2014. Twelve months before the Review started.

Again, it is difficult to understand when the clear majority of epidemiological studies which demonstrate an association and were contained in the report were obviously not accepted as credible evidence of an association. Yes, to answer your question.

Actual 100 per cent causality is virtually impossible without physically giving the drug and looking at the effects. They knew this. That's why it was changed.

Simon Whale: Thank you.

Julia Cumberlege: Cyril?

Cyril Chantler: Carrying on a little bit further, then, how important is this understanding of causality in your view to legal redress?

Marie Lyon: I would say at the time of the original trial it was the focus. Causality was the focus, absolutely. Again, in the documents - what the legal advice is to Scherings is we must try to disprove the causality because we are guilty in every other area. We are guilty of not doing enough. We are guilty of basically suppressing the evidence. We are guilty that we didn't take the product off the market. The only way that we can actually look to mitigate the actions that we failed to take is to cast doubt on causality.

That was always a benchmark, if you like, in legal cases. That position has now changed, now that the legal profession are aware that causality is not something that can be absolutely proved. You've got to look at the degrees. The degrees mean our legal team feel that we have absolute cause to reopen the case, which is what we intend to do. Again, I'm really sorry - I've obviously not sent - you must not have seen those documents either.

Sonia Macleod: No, but actually if they are to do with ongoing legal proceedings that - we are better not seeing them, because they're covered by legal privilege.

Marie Lyon: Okay.

Sonia Macleod: I would not send us those unless you've cleared it with your lawyers first.

Marie Lyon: I will - I will ask tomorrow. Yes.

Simon Whale: Thank you very much.

Marie Lyon: That's okay.

Valerie Brasse: Yes. You've already mentioned the meta-study - Heneghan - and the fact that that's going to go before an ad hoc working group again. I just wanted to ask you really about your confidence in that process that's forthcoming, that will happen I think in March, I think? April? The date that we've got. How confident are you about the process...

Marie Lyon: I'm not.

Valerie Brasse: .. .and what would you be saying to them that would increase your confidence? What would they need to do to make you feel more confident?

Marie Lyon: The Expert Working Group and the EMA - I would like it to be that scientists are actually not chosen by the MHRA, the Commission for Human Medicines or the European Medicines Agency. Again, it's another pool of experts who are inclined to agree with whatever it is they're being asked to look at.

Valerie Brasse: Who do you think should choose them?

Marie Lyon: This is where the difficulty is. I think it should be independent scientists who actually put forward names of people that they believe are credible. I know with Ian - sorry, Neil's review, there were two scientists that he knew and he had confidence in. I know - I was only available for the initial discussions but I know in those discussions, they were impressed by that study. They agreed with Professor Vargesson that no, it wasn't conclusive - which he never said it was - but they agreed that the work that he had done was extremely promising. That there were indications in there, and the Chair actually said that - that there were indications that there were evidences of harm, but it isn't conclusive. We know that. Again, the conclusive evidence is really going to be extremely difficult. But there are ongoing studies with Professor Vargesson and most certainly Professor Heneghan is absolutely going to refute any discussion that actually negates his conclusions. He is actually again redoing some of his studies, but he wants to include this raw data. That is essential.

Valerie Brasse: Right, thank you.

Julia Cumberlege: Anything else that - sorry, Sonia? I'm just going to ask my team - we're happy?

Simon Whale: No.

Julia Cumberlege: Marie, thank you so much for coming for a second time.

Marie Lyon: It's a pleasure actually.

Julia Cumberlege: Very, very helpful, it's been so clear. The conversation and the discussion has been really helpful to us. We hope that we can help you with some of the requirements that you need in order to take this further forward.

Marie Lyon: That really would be so useful. I think - you've got to actually look at - you've got two independent scientists there. You've got Neil Vargesson. He actually became involved in this through thalidomide. He was one of the ones that found the link to the thalidomide adverse reactions, and he became interested because he's interested in any drugs that are to do with women. He made it clear again at the very beginning - this is research I'm doing. I'm not doing it for you, however I will share any results.

Carl Heneghan was exactly the same when I contacted him. His response again was quite blunt. 'I shall look at it but I will decide whether there's anything there or not. If there isn't anything that supports you, I will still publish'. I accepted those conditions. That is all that we want. Actually I felt quite disgusted by the remark by one of the Expert Working Group who said, you know, 'the poor things, we even kind of looked at whether we should do something for them'. We don't want that. We want the truth. We don't want to be patronised. We don't want someone to say 'wow, you know, should we just do something and then they can feel a little bit better?'

It won't make us feel better. The only thing that will make us feel better is the truth. That's all. A decent regulatory authority that looks after people in this country.

Julia Cumberlege: I think your message...

Marie Lyon: Sorry, I just feel so personally.

Julia Cumberlege: I think your message is very clear. Thank you so much.

Marie Lyon: Please don't take it - any of that.

Julia Cumberlege: Just before we part, because we've got another group just about to come...

Marie Lyon: I appreciate that.

Julia Cumberlege: Don't worry, don't worry. That's fine. I just want to pay a tribute to Mike, because I think Mike - who has been your observer - but we know he is not just an observer and that he puts a huge amount of effort into ensuring that you achieve what you want to achieve.

Marie Lyon: He does.

Julia Cumberlege: I just want to thank him for all the work that he does.

Marie Lyon: Thank you. That is appreciated because you're perfectly right.

Male off screen : Thank you.

Marie Lyon: Thank you all. Thank you for the opportunity again. I really appreciate it. I really appreciate - the other thing I must say is that you've agreed to see five more members of the Association, which I feel again will be so useful to you to see the disparity in the anomalies that we are all unfortunately suffering from. Thank you.

Julia Cumberlege: I must say Daniel and Nicky were fantastic last time.

Marie Lyon: They were wonderful.

Julia Cumberlege: Their courage.

Marie Lyon: That is what I - that's what keeps me motivated. The courage of those two people every single day to get up, get dressed, go out, work - it's just.

Julia Cumberlege: It's amazing.

Marie Lyon: They put me to shame, that's all...

END OF TRANSCRIPT

Session 2: National Institute for Health and Care Excellence (NICE)

START OF TRANSCRIPT

- Julia Cumberlege: Gillian, perhaps you'd like to start.
- Gillian Leng: Yeah, I'm happy to start. I'm Gillian Leng. I've got a medical background. At NICE, I'm the Deputy Chief Executive, so I'm here today wearing a corporate hat to give a wider perspective and some history of the work that we've done to get our guidance implemented across the system.
- Paul Chrisp: Hello. I'm Paul Chrisp. I'm the director of the Centre for Guidelines. I trained as a pharmacist. I've been with NICE for just under 10 years. Prior to that, I worked in medical publishing and medical communications.
- Julia Cumberlege: Thank you very much.
- Kevin Harris: Yes, I'm Kevin Harris. I'm the director of the Interventional Procedures Programme at NICE and a consultant clinical advisor to NICE. I also have a medical background and I was, until a couple of years ago, a nephrologist.
- Cyril Chantler: A what, sorry?
- Kevin Harris: A nephrologist.
- Cyril Chantler: Yes, I thought you were.
- Kevin Harris: Kidney problems.
- Julia Cumberlege: You have something in common. Can I say that clearly, we're all aware of NICE? I remember it being set up and it has been lauded across the globe as being a very good organisation. One of the difficulties that we've encountered with patient groups - and certainly for my benefit as well, could you just explain to us, with the processes and the policies that you have, the differences between guidance and guidelines? Because there seems to be a bit of confusion and the two words are used interchangeably. People aren't quite sure, when you're talking about guidance, what that actually means and what guidelines are. Gillian, I don't know if you'd like to start.
- Gillian Leng: Yeah, I'm happy to answer that. It's fair point that it is a bit confusing. Just as a piece of context, we are doing a review of our products so that we can in future clarify some of that. But in a nutshell, guidance is a generic term that we use for anything that we issue with evidence-based recommendations. Guidelines is reserved for historically clinical guidelines, but they now cover public health and social care. Some of the

recommendations that we've made around valproate, for instance, have come from our guidelines. They are broad recommendations covering big topic areas. They aren't mandatory, but professionals are expected to take them into account.

There are various ways that their use is reinforced, for example by the CQC and the GMC and medical defence unions. But they are advice. Clinical guidelines are advisory, but clinicians are expected to take them into account. Where people think of NICE and think that our guidance is mandatory, that relates to guidance from our technology appraisals programme so where we look at new drugs - not valproate because it wasn't a new drug, but where we're looking at, say, a new cancer drug, it goes through our technology appraisal programme. The mandate there is that if we recommend it, it should be funded. Hence there is some confusion that people think what NICE says has to be followed, but the mandate relates to that.

The other bit of guidance that it's worth highlighting - because again it's somewhat different - is the interventional procedures guidance that Kevin's responsible for. It looks at safety and efficacy. It's our only programme that really looks at safety. Again it's not mandatory, but when it was first set up, it was seen as a core standard.

At the time, we had core standards about safety and developmental standards. The core standards were reinforced by the inspector at the time. I think it was the Healthcare Commission, but it might have been the one before then. It didn't have a funding requirement, but it was quite strongly reinforced in the system and the Healthcare Commission supported that. But since the demise of the Healthcare Commission, it's not had quite such a lot of weight.

We've been working with partners in NHS England to reinvigorate the requirement for it to be taken really seriously, because it's looked at safety. It's, of course, very relevant to the conversations around mesh as to why there wasn't more notice taken of the Interventional Procedures Programme. That is somewhat set aside because of its focus on safety. There's more information, I think, in the submission that we put around various ways of assistance trying to follow that.

Julia Cumberlege: Can I get this quite clear in my mind? I hope it would help patient groups. The guidelines are mandatory. There are other people who have to take them into account - the public health, social care, GMC and so on. You're shaking your heads and saying they're not mandatory.

Gillian Leng: Not mandatory, no.

Paul Chrisp: Not mandatory.

Julia Cumberlege: They're not mandatory, right.

Gillian Leng: No, guidelines are not mandatory.

Julia Cumberlege: The guidelines are not mandatory. But you look to other people to implement them, to put them about, to communicate them so everybody knows that they exist and this is what you suggest should happen.

Gillian Leng: Yes.

Julia Cumberlege: The guidance then, if it's technology appraisals and requires funding and all of the rest of it, that is not simply good to have. That is mandatory.

Gillian Leng: The funding of it is mandatory.

Julia Cumberlege: Just the funding.

Gillian Leng: Just the funding, so there's no obligation for a clinician to prescribe something that we've recommended. But if they wish to, in conjunction with the patient, if they think this is the right drug, the commissioner can't then turn around and say, we're not paying for it, which of course might happen otherwise.

Julia Cumberlege: If the commissioner says that they can't afford it, what happens then?

Gillian Leng: They shouldn't, because there's an obligation, a legal obligation to provide funding for it. If that doesn't happen, there are ways that we would advise the patient and the clinician to challenge the system. Most of the drugs that come through that programme are actually funded through specialised commissioning, funded directly by NHS England. We have close links with them. As far as I know, the funding does follow, because they budget for it.

Julia Cumberlege: You don't take into account the commitment that the organisation may have in other fields, but you're not doing a sort of options appraisal as it were. You're saying that they have got to fund this particular drug or whatever.

Gillian Leng: What we do do is work closely with NHS England in relation to products coming through. We look at the pipeline and we talk to them about where the cost pressures might be so that it's planned for and in the budget and isn't a sudden surprise that would be a challenge for the system, because they'd have to take money from something else. I would say, 10 years ago, we might have been more in that position. But with the relationship with

NHS England, by and large, the planning is in place, so there is no sudden surprise in relation to funding.

Valerie Brasse: Does that mean it's serving the system rather than the patient if the need is there and you're saying, well, now we're having conversations with NHS England as to when we should have a look at these?

Gillian Leng: I don't - it's not about when we look at them. It's providing an alert to NHS England far enough in advance so they can plan for the funding. We have a requirement to issue a recommendation on a drug within 90 days of it getting its product licence. We stick to that, nothing to do with NHS England. But we just let NHS England know what's in our pipeline so they can plan for the funding. They don't tell us not to do it or to slow it down. We stick with that requirement.

Julia Cumberlege: It could be a cancer drug that actually takes priority over a mental health issue or something that the particular organisation wants to develop.

Gillian Leng: Most new drugs come through specialist commissioning, so there's a specialist pot of money to commission those specialist services. Mental health is usually commissioned at a different level.

Julia Cumberlege: Well, I was just thinking of other services that could be there.

Gillian Leng: Yeah.

Julia Cumberlege: No, I'm going to ask Cyril if he wanted to comment.

Cyril Chantler: No, I won't actually, because I don't think this is directly relevant to what we're here to talk about, interesting though it is.

Sonia Macleod: Can I just ask, one of the things, when you produce your guidance - okay, so you talked about [unclear]. One of the things we've heard is about skills shortages. When you do your guidance there, for example with non-mesh surgery, do you take into account the skill base required to deliver it?

Gillian Leng: The short answer is yes. I know more about the clinical guidelines programme and conversations that we're having with Health Education England. But over the years - specifically within interventional procedures, Kevin - we've been very aware that we're making recommendations that might say, as for mesh, you need specific skills and training to use this new procedure. We've had conversations with the colleges about providing that, so perhaps I can pass over to you to provide some detail.

Kevin Harris: I think that's exactly right. We don't modify the guidance in the context that we think there are people out there who can do it, because we're not

able to judge whether that's the case. But we might in our guidance make a specific recommendation that says, for example, this must be done by people who are appropriately trained in this procedure. We often make comments about patient selection related to that needing to be done through a multidisciplinary team. We might suggest what the composition of that team would be. But we look to the system to ensure that, when they implement the guidance, those things are put in place except, as Gill says, we can't mandate that to happen.

Cyril Chantler: You don't go into training needs and say - can I go very particularly to the placement of transvaginal tapes and so forth? I was trying to think of any other area of contemporary medical practice where a trocar is inserted into the body without guidance. Certainly when I started doing renal biopsies many years ago, you didn't do them with guidance, but you do now. Can you think of any other area where you place a trocar into the body blindly?

Kevin Harris: I can't off the top of my head.

Cyril Chantler: No.

Kevin Harris: I think you're right. I think most procedures now would be done with some [unclear].

Cyril Chantler: When you're placing it through the obturator membrane blindly, in retrospect do you think proper training programmes should have been thought through?

Kevin Harris: I'm not sure that I'm really in a position to answer that, because I'm not responsible for the training.

Cyril Chantler: No, but you are responsible for interventional procedures.

Kevin Harris: But we made it very clear that people who undertook this procedure should have undergone the appropriate training in order to do it, but we didn't define what that appropriate training was.

Cyril Chantler: Yeah. When you wrote the letter to the *BMJ* in November in response to the leading article on mesh, you talk about interventional procedures guidance aims to protect safety for patients, recommend it should be seen as mandatory, not just advisory. What does mandatory actually mean in those? If you mandate something, how can you, NICE, be sure that it actually happens?

Gillian Leng: Therein lies the challenge of the recommendations that we've issued over the years, because we don't have any powers to require anyone to do anything. We've worked with other partners in the system who do have the

ability to either require or encourage. As I said at the start, when interventional procedures guidance first came out, it was phrased as a core standard, as something that was seen as an essential thing that everyone followed. But as other organisations changed, that was lost. I personally feel there needs to be a much stronger requirement for the system to follow our Interventional Procedures Programme, because it's about patient safety.

Julia Cumberlege: Do you think the system is broken?

Gillian Leng: I don't think it's all broken. I think there's some really good stuff going on. But I think in relation to adherence to that guidance, it needs to be clear.

Cyril Chantler: Who are you mandating? When you use the phrase [unclear] I understand guidelines.

Gillian Leng: Yeah.

Cyril Chantler: I understood and appreciated NICE for 20 years, I suppose, now. I understand how useful guidelines are. I understand my responsibilities of when I was a doctor with relation to guidelines. But I do have a problem about what you regard as mandatory, because I want to know who is responsible for making sure it actually happens. You say the system. Well, specifically who, what, how in the system?

Gillian Leng: What happened originally, which seemed to work, was that Trusts were required to have a register of interventional procedures that we'd recommended so that they were - or not recommended, interventional procedures that we'd followed, so that they were - sorry, I've used the wrong word. Interventional procedures that we'd considered so that they knew what we'd said and they knew where they needed to put special things in place, like audit or training. The Trust would oversee that through their clinical governance committee. They were also supposed to look for clinicians who wanted to perform interventional procedures that we hadn't looked at and refer them to us for a view on safety.

There was a responsibility of the Trust and clearly within that a responsibility of the clinician, which would be to the trust, to the patient but also to their professional body. That was in the days before revalidation. Nowadays there might be something you could put in place around appraisal and data collection. That was reinforced by the Healthcare Commission who, as part of their inspection, were to check around their core standards that the Trust had those mechanisms in place. They used to give us reports. The last report I remember said something like 95 per cent of Trusts had that process in place.

Cyril Chantler: I see. Would that apply to the private sector too? Because a lot of this activity has taken place in the private sector.

Gillian Leng: Yeah. I don't know whether it's strictly applied. But informally from conversations I had with the private sector at the time, they were keen to be following what we'd said, because they wanted to demonstrate that they were in line with best practice as part of demonstrating the quality of the service they provided.

Cyril Chantler: Doesn't the CQC fulfil the same function then?

Gillian Leng: It has a different approach to inspection. I had a conversation about six weeks ago with Ted Baker, who's the Chief Inspector of Hospitals, specifically about this issue and whether there was more that they could do in the way that the Healthcare Commission had. He didn't immediately say, yes, that's fine. He said that they might be able to consider looking at some individual pieces of interventional procedures guidance. I understand it's because of the different approach they take to inspection at the moment. But whether they could do something more robustly, I don't know.

Cyril Chantler: Yeah, because we're not here blaming people.

Gillian Leng: No, exactly. It's different.

Cyril Chantler: We're just trying to understand that when you go through the last 20 years, you've been issuing guidance and yet this has happened.

Gillian Leng: Yeah.

Cyril Chantler: One of the questions which we've asked quite a few people we've seen - and we'll ask others as well - is we've met a lot of people who've been really damaged. It's been them and the associations they've created and their representatives in parliament that have brought it to our attention. As a doctor, I feel really bad about that...

Gillian Leng: Absolutely, yeah.

Cyril Chantler: ...because I'd have thought we would have found out about it earlier than we have done. The system's failed and so the question is to try and understand how it's failed and what can we do to recommend a better way forward? Perhaps you could just muse about that, Gill.

Gillian Leng: There is, of course, another element that could help for the future. That's the element of routine data collection and a requirement for that, which would be really important for NICE in our review of those procedures. Kevin, again I don't know if you want to add to that.

Kevin Harris: Yeah. I think that you've - it is very clear that women have suffered as a result of this. That is enormously regrettable. I think it is difficult not to conclude that people didn't follow what we had thought we were asking them to follow. I think that that operates at the level of how they performed the procedure and on whom they performed the procedures. I think the other big deficit was because we did, by and large, recommend data collection audits and reporting. It is evident that that didn't happen to the standard that it should for a number of probably different and understandable reasons.

But the one thing I think that would make the difference moving forward is if we had robust, rigorous, interrogatable systems for recording the outcomes not only of devices - it's easy to think of this as devices - but actually of procedures that we do to people that are properly longitudinally linked. Our systems, with some notable exceptions I think, in the medical profession by and large are not up to delivering that at the moment. It particularly falls down, in my view, over the long-term follow-up. We might be quite good at recording for a procedure - I don't know - 30-day mortality or something. But five-year outcomes for a patient who's been discharged to primary care, they can be analysed, but it's enormously difficult.

Cyril Chantler: When we met the president last week of the Royal College of Surgeons and the Royal College of Obstetricians and Gynaecologists, we put to them the notion that there should be a digital database.

I'm not talking here directly about a register - that comes secondly - but a database so that whenever a surgeon completes an operation note or a procedure that - you and I might have done a renal biopsy - that that is registered on a database with all the essential bits of information that go into the operation note anyhow, including of a device. [It's] put in the barcode of such device. That then becomes an interrogatable database which is held nationally, which registries can then link to and outcome data can be associated with by whatever system is in place for picking up when things go wrong. Would you favour that sort of...

Kevin Harris: Well, absolutely. Arguably, of course, there is a database of procedures through HES. We can argue about how effective it...

Cyril Chantler: Yeah, but the difference here is that instead of it being completed remotely...

Kevin Harris: Yes.

Cyril Chantler: ...and by a third party, this would be done at the time when you do the operation, because you're going to do it anyhow. It would just be done digitally. Away you go.

Kevin Harris: Well, absolutely. That would clearly be very helpful. The other thing from our experience in looking at procedures in general, as I say, is this link to the longer term outcomes which aren't always known to the secondary - so we have to be very clear about how the data flows through into primary care recording of data where often there are some very significant outcomes for the patient, which might not necessarily bring them back into the attention of the hospital.

Cyril Chantler: Well, that's why frankly - and I go back in history, because I was involved, as was Baroness Cumberlege, in the NHS Number. That's what it was intended to achieve.

Kevin Harris: Yes. It is a frustration to us when we come to review guidance that getting that meaningful data is extraordinarily difficult.

Simon Whale: But 16 years ago in 2003, NICE called for long-term observational data in relation to TVT. As you've just acknowledged, that and other guidelines that you've issued in relation to the use of mesh have not been put into practice. What do you do when you're concerned or you are aware that your guidelines are not being observed?

Gillian Leng: We routinely talk to the key partners in the system, at a national level particularly, to remind them of what we've said, to encourage them to take note, but we don't have any powers over them.

Valerie Brasse: Who does? Who's holding the rein?

Gillian Leng: I suppose the system stewards at the moment are the Department of Health and Social Care and alongside them NHS England.

Simon Whale: If you were concerned, as you have been - and I think we detect your frustration.

Gillian Leng: Yeah [laughs].

Simon Whale: If you were concerned that your guidelines were not being followed - and despite informal conversations with others in the system, they're still not being followed - do you write to the Secretary of State for Health and tell him about your concern? If not, why not?

Gillian Leng: We haven't done that. We have started, over the past 18 months, publishing every other month, an impact report in topic areas like cancer,

mental health, setting out in public for the board what we know from the data that's available, what's happened to our recommendations, highlighting what's working and where there are still gaps. We've used those to raise awareness of where things should be happening that isn't at the moment taking place. Part of the problem is we don't have a huge resource to do more of that data analysis. It's, if you like, a sideline.

Our core role is the evidence, issuing the recommendations. But underpinning that, we know we need to do as much as we can to get those recommendations implemented, so we produce these impact reports. I now co-chair something that's called the National Clinical Audit Partners Group so that, through that, there's a way of implementing things in the national audits linked to NICE guidance that haven't happened. But because we've been going for 20 years this year, there are a lot of things over that time that we've recommended that aren't being optimally put in place. It's a large task for us.

Simon Whale: In your opinion, has that compromised patient safety?

Gillian Leng: It may do. There are obviously examples that - specifically the mesh example that we know that has done.

Valerie Brasse: Let's talk specifically about those impact reports, so how many have there been in relation to mesh and in relation to sodium valproate? How many have been going back to the department and over how long?

Gillian Leng: It's a relatively new activity for us and so that's about 18 months. They haven't been focused on narrow topics. They've been focused on broad topics so that we can give an overview. It's not enough, I would argue. We don't have resource to do more detailed analysis.

We are investing in data scientists, because for the future we need to be working more with the data that's being collected to track what's happened to our recommendations. But we have - and this isn't a plea for more money - but we haven't got the resources to do all of that. That's why we work with people like the regulatory system in the past where they're looking at data around what's happening, because it is a gap. It's a gap around awareness of NICE, knowing what's good and where there are challenges, and then for us to have the capacity to - whether we write to the Secretary of State or we speak to royal colleges, there is a...

Simon Whale: I think we understand the point about needing resources to be able to do more of things as you've described. That's understood. But if you've got a concern that people are being put at risk because your guidelines are not being followed, presumably, as responsible people, you would want that

concern to be lodged at the highest possible level. The question is has that happened? Specifically in the case of mesh - because that's one of the things we're looking at - has that happened in the 16 years since you first said that there should be long-term observational data? Has NICE voiced those concerns to ministers?

Gillian Leng: I think - again I'm looking at you, Kevin. I think the first point that we became aware of the challenges around implementing our advice on mesh was when it was raised by the patient groups that were also alerting everybody else anyway. I don't think we sat on any information and didn't do anything with it. In fact...

Kevin Harris: No, we didn't, certainly not.

Gillian Leng: ...I'm absolutely sure that we didn't.

Julia Cumberlege: But isn't it extraordinary that it's the patient groups that brought this to your attention?

Gillian Leng: Yeah.

Julia Cumberlege: How can we in the future do better? How can we listen to these people? How can we identify what's going wrong, the suffering that Cyril talked about and all the rest of it? Can you think to the future what sort of mechanisms we ought to do to ensure that the patient voice is heard? Because these reviews come too late. It's the forecast that we really need. Is that in your remit at all?

Kevin Harris: I suppose this is a personal view really. But I think Sir Cyril's comment about the need to collect prospective data which is meaningful and related to outcomes that matter to patients - and having systems in place which analyse that and are capable of flagging to us at an early stage that there's an issue - would have gone a long way to helping with this problem, because when we did update all of our guidance in '16 and '17 on procedures related to mesh, it was still amazingly difficult to find any objective data that related to how common or how rare these issues were. There's absolutely no doubt that they happened, but to be able to quantify that and assess it in an objective way was very difficult.

In terms of how we produce our guidance, that tends to force us back to looking at the randomised controlled prospective published data, which I don't think is the appropriate way forward.

Julia Cumberlege: I go back to the question that you're there once the stable door is closed and the horse has bolted.

Kevin Harris: Yes.

Julia Cumberlege: I'm just wondering, do you commission research? You must pick up sometimes things that you just feel are going wrong. Do you commission any research?

Gillian Leng: In relation to research, we regularly issue recommendations for where research is needed. We feed that into NIHR, the National Institute for Health Research. They do their best to prioritise it. Some of that comes through and we look at the results. That's our contribution is generating the research recommendations. We don't have the ability or the funding to commission the research.

Can I just go back to your question around what could we do more to find out sooner the problems that patients might be having? We talked, didn't we, about having a more robust database or registry or whatever we call it for collecting that information? That's obviously important. Challenges are the Yellow Card system that we have, healthcare professionals filling in the information, women alerting their healthcare professionals about symptoms that they might not think are important.

If we think laterally, I wonder if we need something that's more straightforward for patients to directly engage in relation to their symptoms rather than thinking it's got to be a formal system. I'm not a great expert on social media, but there are all sorts of new ways that you can find out what people have been worried about through analysing Google statistics. You can highlight flu epidemics, can't you? I'm just trying to think a bit laterally about how might we find out what's bothering patients...

Cyril Chantler: Sort of crowd intelligence, yes.

Gillian Leng: ...without it being through one of our formal systems.

Cyril Chantler: Could we just explore that a bit more? I don't want to overrate this, but our profession is essentially conservative and rightly so in some ways, because you don't want to do things without properly investigating them. We're always a little sceptical about new things maybe. But the system itself doesn't seem to be very responsive to the patient voice. This would be an interpretation of what we've learnt going around the country.

Is there a need for some agency within the National Health Service - or within healthcare generally, because the private sector's involved - that is actually focused on listening to patients and drawing to the attention of politicians - because they are important in this - and the professions and

the National Health Service what is happening to patients out there so they can be investigated and the patient voice can be heard? We used to have a patient safety organisation. It's now part, I think, of NHSI.

Gillian Leng: NHSI.

Cyril Chantler: But maybe it needs to be much more independent than that.

Gillian Leng: Yeah.

Kevin Harris: Yes. Anything we do, of course, we're - I think the medical profession is probably trying to do it for the benefit of the patients, so getting their view on whether they've benefited is clearly the key outcome that we have to consider. Historically I don't think we have been good at that. We've looked often at technical successes for things. There are a number of [unclear].

Cyril Chantler: Not the problems [unclear] just the [unclear] clinical outcome measures, not the patient functional experience.

Kevin Harris: Absolutely. I think Gill is absolutely right. I think there are potentially new ways that we could begin to sample the patient voice in a much more timely and earlier way and using social media. We have tried to look actually internally within IP, as an internally generated research project, whether you can sample social media - not in a mesh-related context - in a way that might be meaningful, because there are people who...

Cyril Chantler: Yes. When NICE was set up - and I remember it well as someone who's argued for such a body that would be advisory about what the value of an intervention was. Was it safe? But also was it affordable? What's the cost benefit and all that? The notion was originally that it would be advisor in government and the department decide. But its independence was fundamentally important as I recall and still is, no doubt. But don't we need something that really expresses the patient interest, the public interest independent from the service?

Julia Cumberlege: Can I just say that years were taken off my life when I took part in the 2012 *NHS and Social Care Act*? It took a huge amount going through that particular legislation. You know we had a pause in that and all the rest of it. But one of the things that we were determined to do in that act was to introduce Healthwatch. I just wonder if that is something that comes across your desk at all.

Also, I wondered if you had any sort of relationship in a wider sense with the ONS? Because they seem to produce quite a lot of very interesting information and also research. They do research. I appreciate you're having

to deal with all these different arms-length bodies that were set up through that act and also, of course, the major NHS Improvement and all those other ones. I just wondered if you have thought about that.

Gillian Leng:

There's a few angles to take. One is in relation to our specific process around developing all the guidance. We always have patients on the committees. Sometimes we have people just coming to the committee to talk about their experience as individuals. Over the years, we've tried to get more summarised perspectives of the patient view, because otherwise it relies on one or two individuals. It's not been easy to make that happen systematically, again because it's quite resource intensive. Some charities provide it, but it's not a routine part of what we do, that sort of patient evidence that draws it together. I think it would be good if it were there, but it isn't there. That's why it's resource intensive. We do that in relation to guidance development.

At a sort of cross-cutting level, we do have links with Healthwatch. I don't think Healthwatch has ever contributed to our guidance. They seem to be more interested in their local systems and do advocate on our behalf to get guidance used. Our local field team talk to their local Healthwatch representative, so it's more flowing out rather than data back to us. We've got some links with ONS, not extensive ones but are building links because of our developing data and analytics work that I've mentioned.

We had links years ago with something called HealthTalkOnline. I don't know if that's still going. It was set up in Oxford - I can't remember who set it up - as an evidence-based way of bringing patient experience to life, with a patient audience though. It wouldn't have been aimed particularly at NICE, but they did some really good work of bringing together the patient experience.

We did have a lot of input to NICE's work through our Citizens Council. I don't know if you're familiar with that. But that was less the patient voice, more the citizen voice, 30 people representing the general demography of the UK to give us a view on the importance of key things like how much we should prioritise somebody young over somebody old. They said we shouldn't. It's those sorts of key questions they gave us input to.

To say is there a gap, I think that there is a gap. We do a lot of work around shared decision-making and work with lots of partner organisations. It's clear that the research around what matters to patients sometimes comes through individual trials but often is missed. For instance, breast cancer, clinicians seem to grossly - let me get this the right way around - overestimate how important it is for women to avoid mastectomy.

Whereas if you actually talk to women, they are not as bothered as the clinicians think they will be. It's that sense of what really matters to patients that we've spent quite a lot of time thinking about, probably less about getting that feedback after we've issued a recommendation - which is key to this inquiry, I know.

Sonia Macleod: Just on that theme, when you're drawing up your guidance, if you've got evidence coming in from charitable groups or from patients, from individuals and also obviously randomised controlled trials [unclear], how do you weight those different types of evidence?

Gillian Leng: It's a really good question. I suppose the short answer is we don't have any formal weighting system. I've got diagrams that I use for explaining how NICE works where we put the science, if you like, the randomised controlled trials and other published research in the middle. There are other perspectives that we then bring to it, obviously very importantly the patient perspective, but it's a perspective that we build around the evidence.

That's where our independent committees are really, really important. They include the patient as well. They have to take a view on all of that and decide what the recommendation should be. It's not an exact science, so there's no weighting. We have thought over the years about should we actually try and make this more scientific? But it's really not straightforward.

Valerie Brasse: Is there any internal coherence? Groups are coming together and weighting things differently. If one was to look at a spread of this, would we find internal coherence?

Gillian Leng: It's a fair point, because sometimes we have different committees that would look at something originally, then another committee would update it. The mitigation to that consistency check is that we have a quality assurance programme and we have external consultation with the stakeholders. That consultation, although time-consuming, is really important to do that system check. People will very quickly tell us if they think we've got it wrong.

Valerie Brasse: Can I go back and ask about evidence base? Because one of the things I think you were saying is it's very difficult to know whether you objectively got the evidence that we actually need. I think when it comes to efficacy, it's quite clear that you look at peer-reviewed literature and you'll look at registries. It's different for safety, but that's what I understand from your evidence to us.

I suppose my question to you is in relation to mesh. If we have substantial doubts - and the patient groups have expressed this very coherently - that we're not picking up all the adverse outcome measures. The literature is not doing that. We don't actually have registries, because we haven't got to that place yet. I'm left asking, what is the evidence basis for deciding that mesh is efficacious?

Kevin Harris: I don't think that's really what we said, was it? I think if you look at the recommendations around mesh, we were always very cautious about its use, and made it very clear that for the vast majority of the procedures that it had to be used cautiously with the risks of potential side effects being explained and the uncertainties around the procedure being explained and the requirements to collect more data moving forward.

Valerie Brasse: I suppose for me it's the evidence base you're looking at, because as I say, we're now disputing that the literature actually does what it's supposed to do...

Kevin Harris: Yes.

Valerie Brasse: ...i.e., come up with all the adverse outcomes. There aren't any registries, so I'm not now sure where you're looking to for your evidence to be able to say anything conclusive about mesh.

Kevin Harris: Clearly there is published literature...

Valerie Brasse: I know there is.

Kevin Harris: ...that people have called into question. We do try and get patient feedback from people who've had the procedures, actually. That's quite a difficult thing to - or it's difficult to get any quantity of patient feedback for that. If you look specifically at the patient feedback that we obtained for mesh, much of it was positive actually. Not all of it was positive. All of that would have been put to the committee. In terms of the internal consistency for interventional procedures, the committee is the same at any one point in time for every procedure [although] clearly it changes with time as people demit and are recruited on to the - but it's the same committee that looks at all procedures. The intention is they weight all the evidence in the same way.

Simon Whale: Am I right that evidence related to safety can come from any source?

Kevin Harris: Yes.

Simon Whale: It's not specifically from peer review or RCTs or anything [like that]...

Kevin Harris: That's correct, yeah.

Simon Whale: ...including unpublished sources?

Kevin Harris: Yes, that's correct.

Gillian Leng: Our future vision - Paul and I were at a meeting before we came, thinking about how NICE should work for the next 20 years if we get 20 years. The vision has to be that we're issuing these recommendations and that the feedback loop is drawing on data that's routinely being collected so that it's not just reliant on the published research which might not have answered the question. But there's a link back to the data systems. Hence lots of conversations, the burgeoning analytics team. But when we actually reach that state, I'm not sure, because it's partly what we do at NICE but also having the system geared up in a position to do that for us.

Simon Whale: But on the point about unpublished data related to safety, obviously that could be a channel, as it were, through which patients could provide information. That could be very helpful...

Gillian Leng: Yeah.

Simon Whale: ...because it's clearly lacking at the moment. But it's also potentially a channel for someone to assert that something is safe.

Gillian Leng: Yes.

Simon Whale: If you go back to SERNIP days, our understanding is that SERNIP changed the categorisation of mesh based on unpublished data received from the manufacturer.

Gillian Leng: I don't know.

Kevin Harris: Well, I can't comment on that.

Simon Whale: Is it possible that something like that could happen today?

Sonia Macleod: Our understanding is that the data that was presented was conference abstracts, so it hadn't been peer-reviewed and it was presented by manufacturers.

Kevin Harris: Within the IP interventional procedures process?

Sonia Macleod: This was back in SERNIP days before...

Kevin Harris: Yes.

Sonia Macleod: Yeah.

Kevin Harris: That couldn't happen in interventional procedures.

Sonia Macleod: But that couldn't happen now?

Kevin Harris: No, absolutely not.

Simon Whale: Sorry, just to be absolutely clear, so any manufacturer of any device that you're considering as part of your decision-making processes, if they come along and say, we've got such information that demonstrates that this product is safe - not just efficacious but safe - how would you treat that approach from that manufacturer?

Kevin Harris: If it was anecdotes, we - effectively they were just telling us that, we would ignore it.

Simon Whale: If it was a presentation from a conference [unclear].

Kevin Harris: The only reason we would ever look at that evidence is if they said it was unsafe and then we would report it.

Simon Whale: Right.

Kevin Harris: That's true for any source related to safety. If when we're looking at a procedure - the medical literature on most procedures, of course, does list safety and adverse outcomes. If there was something that someone told us about a safety concern that wasn't already reported in the medical literature, we would specifically comment on that in addition to what the literature had told us. It's usually done in a style of a committee comment. The committee was informed that this was also a safety concern.

Cyril Chantler: Could you just tell us about this committee? Who's on it?

Kevin Harris: It's a standing committee of NICE with 24 people, which consists of - roughly half are doctors who do interventional procedures. There are people from the regulatory bodies such as the MHRA. There are managers from the NHS and there are patients. There are statisticians.

Cyril Chantler: How many patients?

Kevin Harris: Two. Well, patient representatives actually. They're not [unclear] they're patients or not [unclear]. It's a standing committee which looks at all procedures. Their job is to look at the evidence, not to be experts on that individual procedure.

Cyril Chantler: Does it have any relationship with your Citizens...

Gillian Leng: Council.

Cyril Chantler: ...Forum which I - I remember when you set up, that was a very important part of...

Gillian Leng: Yeah. The link is that the deliberations of the Citizens Council formed a set of value judgements that all our committees abide by, so there's some wider context for how the committees take decisions. That's the link.

Cyril Chantler: Does your committee give equal weight to patient-related outcome measures as it does to clinical outcome measures?

Kevin Harris: It gives equal weight to all the evidence that it can look at. It frequently, in fact usually, would comment - because they're often missing - that what is needed is relevant patient-related outcome measures.

Cyril Chantler: When you make that decision, how do you then affect - how do you get an answer to the question you've raised? Go to NIHR? Is that how you'd do it?

Kevin Harris: That might be a route, yes, certainly. But we don't - we can't send all of our topics to NIHR, but the relevant, important ones we do try and escalate to them as research priorities.

Julia Cumberlege: You put out information in a draft form, guidelines or whatever, and then it's out for consultation...

Kevin Harris: Yeah.

Julia Cumberlege: ...for three months or something like that.

Kevin Harris: A little bit shorter than that, yeah, but yeah.

Julia Cumberlege: Sorry?

Kevin Harris: It's a little bit shorter than that, but yes, I think - but yes.

Julia Cumberlege: What do you do when you get tremendous response to that in perhaps a way that is not helpful to those who've been on the committee?

Kevin Harris: I think the responses are always helpful to the people on the committee. Actually, I can't think of an instance where that wouldn't have been the case. After consultation has closed, all of the consultation comments are tabulated. They're all sent to the committee who discuss each of the consultation comments one by one and agree over a response to them.

Cyril Chantler: Can I be very specific about mesh?

- Kevin Harris: Mm-hm.
- Cyril Chantler: We've been told going around the country that the outcome measure which everybody thought was important was whether or not women were continent. But the patients said to us, what about all the other things we've had to experience? The pain, dyspareunia, those things, nobody asked about those. If you've got a committee that's looking at the effectiveness of an intervention and it - shouldn't it have more patients on it who can actually talk about the outcomes that matter to them, not just the outcomes that might matter to me as a doctor?
- Kevin Harris: The patients who are on it are certainly not - they're certainly not afraid to comment on the things that matter to them would be my observation. We do, as part of the evidence gathering, try and get responses from people who've had the procedures if that's at all possible. I would be the first to say that the responses to that tend to be relatively small in number and are potentially open to bias actually, of course.
- Gillian Leng: Decent research should have picked up those adverse consequences. It's a bit worrying if it wasn't...
- Kevin Harris: Sure. To specifically answer your question in mesh, those are adverse events that we described in our literature reviews of mesh actually. They weren't new things that people told us that weren't already in the literature.
- Simon Whale: Can I just ask about sodium valproate? Are you, between you, confident that the Pregnancy Prevention Plan is assisting women in making informed choices and avoiding risks and harm to their children?
- Gillian Leng: You're best placed to do that.
- Paul Chrisp: Yeah. Again, the Pregnancy Prevention Plan was an MHRA recommendation as you know. What we do is we reflect those signals and the information that comes from the MHRA about the restrictions placed around general medicine and reflect that as quickly as we can in our guidance. I guess the remit and the actions that were taken by the MHRA and the CHMP on what would be an appropriate mechanism to protect girls and women of childbearing potential from harmful effects of valproate, that was their recommendation, which we reflected in our guidance.
- Simon Whale: Do you have continuing discussions with MHRA about the effectiveness of the PPP?

Paul Chrisp: We have regular contact. Yeah, we have a regular meeting every three months. We track past guidelines where there's been a safety signal. We look forward as well for any guidelines that are on our books that may have a medicine which the MHRA can say, well, actually we know that the Pharmacovigilance Risk Assessment Committee is looking at a medicine in this space. We keep in close contact so that we're able to respond quickly on any signal, any safety signal and reflect it in...

Simon Whale: Have those discussions with MHRA, specifically the discussions about valproate, included the voicing of any concerns about the effectiveness of the PPP?

Paul Chrisp: They haven't.

Simon Whale: As far as the MHRA are concerned and your own position in your conversations with them, you don't see any problems with the PPP?

Paul Chrisp: No, we reflect on what the Pharmacovigilance Research Advisory Committee - because they're charged with looking at the safety of the medicine.

Simon Whale: Are you aware of patient group surveys about the effectiveness of the PPP?

Paul Chrisp: No.

Simon Whale: Do you think you should be?

Paul Chrisp: Well, again I think that's - those safety signals, when we - when we look at our guidance, we look at any safety signals that would have an effect on our recommendations, be that from the MHRA or published in the literature, that would make us stop and think and conduct a review of any of our extant guidance and update them as appropriate.

Sonia Macleod: Your guidance effectively reflects the PPP? You would say so?

Paul Chrisp: Yeah, our - we take a steer from the regulator on medicines.

Sonia Macleod: If your guidance is being implemented, the PPP should be being implemented fully without problems.

Paul Chrisp: If our guidance is being implemented, then women and girls of childbearing age should only be offered valproate, as you know, if there's no alternative for...

Sonia Macleod: According to [unclear] conditions.

Paul Chrisp: Yeah, exactly, so that's our recommendation.

Sonia Macleod: Yeah, so you have no follow-up on knowing if that guidance is being implemented. Is that what you said?

Paul Chrisp: I guess we've got soft follow-up, by which I mean we've got a number of channels out to prescribers and clinical pharmacists. We have a network of 80 medicines and prescribing associates who we work very closely with and alert them as to any safety or indeed efficacy changes in any of our guidance related to medicines. They are part of their local health economy, so it's a method for getting messages out to the frontline quickly on any changes to our guidance. We haven't had any feedback from them on the Pregnancy Prevention Programme and valproate.

Gillian Leng: It's a challenge, because NICE isn't charged with policing the system if you like. That's not our responsibility. In the early days, the chairman of NICE thought that we shouldn't be doing anything after our guidance was issued. He did change his mind. Hence, we started that wider engagement around how do we get traction for what we've recommended? What are the levers in the system that we can use?

But our approach has been one of working with partners and looking for where there's something new that means we need to change our recommendations, so it's been historically more about when has there been new publications. We're gradually moving into the 'let's see what the data says' space. But it's a transition for us and again a challenge because it's not our role to...

Simon Whale: No, and I think we understand the silos.

Gillian Leng: Yeah.

Simon Whale: That's part of the problem perhaps that you're all in silos. There isn't a joined-upness about that, but there's a risk of there not being [one]. But in the case of the Pregnancy Prevention Plan, it's rather like patient-reported problems in relation to mesh. But if a patient group, as they have done, had conducted a survey of women and they found that women are still not being warned - women of childbearing age are not being warned about the risks of valproate in pregnancy and they're not being asked about PPP, then whose job is it to do something about that? What do you think in terms of whose job it should be?

Paul Chrisp: We can help. We can certainly help. But again, it's that collective responsibility which I know we've mentioned before. But I think it is. It's working with - if the MHRA are saying this is when this medicine should and shouldn't be used and these are the mechanisms we've got in place, then perhaps the expectation would be there is some feedback loop based on

that. Again, we can then react to that and get it into our guidance as quickly as possible and into the BNF. To me, the pieces might be there, but it's joining them up in a more effective way.

Simon Whale: Who should do the joining up?

Paul Chrisp: I guess it goes back to the point we made earlier about who has oversight of four different arms-length bodies?

Julia Cumberlege: I'm not at all convinced about collective responsibility. It seems to me that it's a very good way of passing the buck to somebody else. Is it not possible - and I appreciate the position you're in. It must be very frustrating for you from time to time. But working with these other agencies, isn't there something you can negotiate with them without breaking the law - and I'm not asking for that, but is there not an opportunity for you to ensure that one of the organisations takes the lead in this particular area and another organisation possibly takes the lead in another area? At least we the citizens have some knowledge of where the responsibility lies and who is going to do what, because at the moment we don't know.

Gillian Leng: I think that's a really important challenge for us. It's an important piece of work we need to take forward. I'd be very keen to get involved, because I've spent years trying to get the system to work together. I guess I worry that there's not the capacity anywhere to really make that happen, because it's such a complex system. Yes is the short answer.

Cyril Chantler: It's quite an interesting exercise to write down on a piece of paper all the people and agencies and bodies that might take part in this play.

Gillian Leng: Yeah. There is, of course, the new patient safety work that's being led by Aidan Fowler. I think we talked about patient safety work. He wants to set up a committee overseeing patient safety. Whether that will have the capacity to do this, that might be a good place to oversee it.

What NICE is wanting to do for the future is to bring all our advice together, because it is quite diffuse. You started off asking me, what's the difference? It is confusing, so we want to bring it together. We want to highlight some of the areas where there are safety concerns, because one way of dealing with the fact that valproate's being prescribed without the conversations happening is making sure there's always an alert. People ignore alerts, but if you've ignored an alert and something goes wrong, it should be professional misconduct, one might argue.

Simon Whale: But it's also a learning opportunity, isn't it?

Gillian Leng: Yeah, learning opportunity.

Paul Chrisp: Yeah.

Gillian Leng: Yeah.

Simon Whale: That's not just for the individual but for the system. If a pharmacist or a doctor is still supplying valproate to a woman who then goes on to become pregnant but she's not been told about the importance of Pregnancy Prevention Plan, it's not just about hanging them out to dry if that's appropriate. It's as much if not far more about how do we learn from that and make sure it doesn't happen again?

Gillian Leng: Yeah.

Paul Chrisp: I think that's really important. We touched on the point of being responsive to the patient voice and Healthwatch. It's funny [inaudible] Healthwatch volunteer.

Julia Cumberlege: Oh, right.

Paul Chrisp: Yeah. But there's a whole cultural change I think in this about - so it's related to the patient voice. I guess the other cultural aspect is that learning from mistakes. I know this is a very NICE response, but we have a guideline on medicines optimisation, which is all about reducing the hazards in medication prescribing. It's about how to get safe effective medication, working with patients, getting their values and preferences and ensuring that they get the right medicine at the right time that's right for them. It's important for what matters to them so they don't get tons of medicines that they don't particularly want or need. It's about building a culture of learning from mistakes. That's one of the recommendations that we came up with for that guideline.

Again, there's another - driving that into the system about how you can have effective medicines optimisation - including sodium valproate, but less controversial drugs, can we say - because that's how medicines should be delivered. To do that, you need that culture. It's working with other agencies to try to build that culture. Sorry, I get quite...

Simon Whale: Are you confident that that medicines optimisation guideline is being followed?

Paul Chrisp: Yeah, I think because it was also a push from our colleagues at the Royal Pharmaceutical Society as well, so it was a two-pronged approach. The pharmacists' professional body was leading on it. We developed a guideline. It's front and centre of the way clinical pharmacists think. It's

how do we - and I think it's - again it's another opportunity with a long-term plan of getting pharmacists into GP practices about how you can start to influence it at that point in the system. It sounds like a cop-out, but there is this - it is a cultural change. It's a change from the relationship between doctors and pharmacists. It's a change between patients and their relationship with clinicians. I think you can start to see that happening.

Valerie Brasse: Can I ask then a very direct follow-up to that?

Paul Chrisp: Yeah.

Valerie Brasse: The learning experience as a result of that, how has that influenced the way you approach guidance and guidelines in relation to the next generation of antiepileptic drugs like Keppra? Has it had an impact?

Paul Chrisp: Okay, so we're updating our guidance on epilepsy. I think that's scheduled for next year. Yes, I think what - when we look at a guideline, scoping is the first - I'm not going to get into too much of the detail of it but getting the scope right is really important. That's where we can also get patient views and healthcare professional views and commissioner views. Have we got the scope right on this? Are we asking the right questions? What's your experience of the management of epilepsy as a patient and as a clinician? From that, you can start to frame the research questions in how we look for the evidence, make our recommendations and highlight where there are evidence gaps.

Valerie Brasse: Has it changed as a result of what happened with valproate? We're looking at the new guidelines. We're just trying to work out what the practical changes were.

Paul Chrisp: I can't say definitively yes, but it will - I can't give you specifics, but it will have, because valproate was such a signal - sentinel medicine. That learning and the management of epilepsy will be within the scope of our guidance.

Valerie Brasse: One of the things that you said earlier was about your research recommendations going to NIHR.

Paul Chrisp: Yeah.

Valerie Brasse: Do you know - can you tell me what proportion of those recommendations actually get funded?

Gillian Leng: I haven't been given a recent number, but I have heard in the past. It's not huge. It's around about five, 10 per cent, I would suggest.

Valerie Brasse: Coming from NICE recommendations, maybe only five, 10 per cent actually get funded.

Gillian Leng: Yeah.

Paul Chrisp: But we do meet with NIHR - and at the moment, I think it's - well, it is, it's annually - and discuss what those research [unclear] are and help to prioritise from the research community's perspective and our perspective in terms of all of the research recommendations we found. When we go through our guidance, we can often find lots of gaps. Which ones should we be prioritising? When we do find one, we work closely with the research community to try to get that evidence into the guidelines as quickly as possible.

There's one example from last year where we - this may sound like a long time, but it was a year between the research being published and it appearing in the guideline. Now that's actually quite rapid. It may not sound it, but it is quite rapid in terms of the fit between the impact of the research making its way through the guideline development process.

Julia Cumberlege: Sir Cyril and I just want to go back to mesh. Can I just ask this question and then pass you over to Cyril? In the current guidelines, transvaginal mesh is used only in the research. That's the current guidelines. It's used only in research. But it appears to have been omitted from the draft guidelines. We wondered why this change was made.

Gillian Leng: This is the guideline, not...

Paul Chrisp: That's the guideline, yes.

Gillian Leng: Yeah, that you're [unclear].

Cyril Chantler: It's the one you put out to consultation.

Paul Chrisp: Yes.

Cyril Chantler: Consultation's closed.

Paul Chrisp: Yes.

Cyril Chantler: But having previously said that as a result of the trial you would not recommend placing mesh through the vagina, you've not put it in the - what you've sent out to consultation. We couldn't understand that.

Paul Chrisp: It will have been because of the evidence that the committee looked at that they felt that, in that indication, it should only be in...

Cyril Chantler: Are you sure it's just not been left out? Because the FDA has had a whole-day event on it last week.

Paul Chrisp: I can't imagine it would be because it's just been left out.

Cyril Chantler: That's strange...

Gillian Leng: Really strange.

Cyril Chantler: ...because the trial was pretty clear.

Paul Chrisp: Yeah.

Cyril Chantler: Will you check that, please?

Paul Chrisp: Yeah.

Cyril Chantler: Can we then go to mesh, back to your guidelines on mesh? You've gone out to consultation. You'll be coming in with your definitive advice sometime soon?

Paul Chrisp: April.

Cyril Chantler: In April, okay. But it's very much about stress urinary incontinence. We're also wrestling with rectopexy and things of that nature. Are you involved in that at all? Because we talk about the need for research. Unfortunately they've not been able to complete the trials that are underway, because there are problems with equipoise and numbers. But there's still a very great need to get more information to guide patients and surgeons as to what's to be done, so are you involved in that?

Kevin Harris: We have been. I think we published guidance on mesh rectopexy. We are, from time to time, notified about other procedures that involve the use of mesh. Most recently, for example, we looked at mesh hernia - mesh stoma reinforcements in parastomal hernias. Again, the process, from our perspective, is exactly same.

Cyril Chantler: If there was a need for more research in this area, which...

Kevin Harris: Yes.

Cyril Chantler: ...I would suggest there is - and we've been talking to the people involved, the [unclear] Society, Association of Coloproctologists and so forth. Would you be involved in putting a proposition to NIHR about funding for that sort of work?

Kevin Harris: We certainly could be. We haven't been to date.

Cyril Chantler: No.

Kevin Harris: I would need to go back and look exactly what we said about mesh rectopexy, but my recollection is that we did recommend data submission to their register, I think.

Cyril Chantler: Yes. Okay.

Sonia Macleod: One of my questions, your guidelines throughout for stress urinary incontinence have said that there should be submission to registers, the voluntary registers. But those registers by their nature are voluntary. They're run by the societies. The one thing that's very clear is that data capture isn't complete, so how can safety recommendations flow from such an incomplete source?

Kevin Harris: I think you've made a very good point really. I believe that originally when those recommendations were made, they were made in good faith, believing the registers to be functional actually. One of the things that we've clearly learnt is that - and I alluded - we alluded to it in our published literature that when we've reviewed some of the registers, not just related to mesh, that we've recommended over the years, many of them haven't been functional.

Cyril Chantler: Well, they don't collect patient identifiable data, because they're worried about GDPR.

Kevin Harris: Yes.

Cyril Chantler: But in fact, that could be dealt with. But they don't and therefore the notion of being able to trace out from a database things that are going wrong with long-term complications doesn't exist.

Kevin Harris: In relation to the [unclear] research registers, no.

Cyril Chantler: Well, to the registers that these sort of committees should have.

Kevin Harris: One of the things we have learnt is that not all registers are equal in this regard. There are some which I think are highly functional and produce very useful outcome data.

Cyril Chantler: In the mesh area?

Kevin Harris: Sorry, no, in general I'm talking - no, absolutely not.

Cyril Chantler: [Unclear].

Kevin Harris: Yes, and [unclear] and so on I think have been very effective. The committee was actually minded to making specific comment in its updated guidance on one of those procedures about how disappointing it had been about the performance of data collection through the registers. That's not helpful really. In a way, what we actually need to move forward to is a position where we have functional systems as we've discussed.

Cyril Chantler: As we've discussed.

Kevin Harris: We would absolutely support that wholeheartedly. We recognise that there are some challenges to that and not least resourcing it appropriately. But I think everybody, certainly the Interventional Procedures Programme [unclear] the Interventional Procedures Advisory Committee, would value that enormously.

Sonia Macleod: Going forward, you're clearly people who rely on registry data, so in some ways you're possibly some of the best placed to say, this is what we want from a registry. What would you say were the absolute key things that you want?

Kevin Harris: At the moment, we have four or five criteria that registers have to comply with. This is relatively recent. We ask them to self-declare that they perform against that. Again we are learning about what makes a good register actually. One of the things that is clear is its ability to be appropriately resourced and - so it's very easy to say we will collect data on all devices related to this procedure. We will analyse the data. We will abide by data protection legislation and so on. The actual key is whether they're resourced adequately to do it. I think in retrospect when we look at the ones we recommended with mesh, it was clear they weren't resourced adequately to do it.

Simon Whale: One of the things that NHS England told us in their written evidence is that registries are very expensive. They go on to say that and presumably they do link the two points - we'll ask them when we see them shortly - that it would therefore be better to have fewer of them but each registry covering a wider range of procedures. Would you agree with that?

Kevin Harris: I have a personal view. It is a personal view. I think, to a certain extent, they're right. To have a register for every single procedure would be an astronomical cost that probably couldn't be met. To have a more smart linked-up system that uses data that we already routinely collect and that properly analyses it, I think - it's a personal view - is a more achievable goal.

Simon Whale: If there was a gynaecology register, for example, as broad as that obviously is, would that be a sensible way forward?

Kevin Harris: To be honest, I think there's an argument for going broader than that. Many procedures are uniquely identified through HES coding systems. If you can link the patient who has had that procedure all the way through their clinical manifestation, outcome, I think that ultimately is something - I don't want to underestimate, because I'm not an expert in this, how difficult that might be in terms of legislation and technical things. But it would give you the ability to look at things that might really matter to patients and to look at things that you might not anticipate are related to that procedure.

I'm giving you a fictitious example here. But if you have a procedure that you've labelled as gynaecology and an outcome measure which is actually very important to patients isn't obviously a gynaecological one, just within a gynaecological register, that could be very easy not to identify.

Simon Whale: Where's the boundary then within the - I mean, is it just a register of every single procedure that happens across medical practice? Are we just having one national registry for everything? Because you're right. I think we'd agree with you that the point you've just made is absolutely right.

Kevin Harris: It becomes semantics about what - so the - at least in my view. The traditional view of a register is that somebody's got a database somewhere. Everybody submits data to that with predefined outcomes and then somebody analyses against that. I think there is an opportunity - well, I've always thought there was an opportunity - again it's a personal view - that we have got a National Health Service. Everybody is identified by their unique identifier. We have a service which actually delivers [unclear] rather tritely call cradle-to-grave medicine for most people. If we could join that up properly, we could get some meaningful data.

Julia Cumberlege: We've heard from the president of the Royal College of Obstetricians and Gynaecology that actually if we had a proper database that affected the life course so that when a woman had a difficult birth and later on became incontinent, then you could actually relate it and see really some of the causes and how to put it right and all the rest of it. It seems to me that we're actually just entering a new world. It could improve patient care hugely if we adopt it in the right way and put in the right infrastructure and the right resources, because it is going to be really, really important.

With maternity - which Cyril and I are involved in - it's very interesting that that is a cohort of women who absolutely understand the new technologies. They will say to us, my life is on my iPhone. Where are you, NHS? You're in the dark ages. We've got to get further forward onto the

right foot and introduce all this. I think it would improve safety and just the way that patients are now looked after, cared for, et cetera.

Gillian Leng: I would agree. I think that registries shouldn't be too narrow. We should be thinking about a future where we've got good quality data routinely being collected. Some of the more techy people I speak to are thinking of a world where it's all the voice-activated technology. That will just be able to pick up the information and code it seamlessly. I've got Alexa. That's about as far as my voice activation goes. But you can see the potential of that. Perhaps in the future we'll be able to draw upon this.

Paul Chrisp: I think it relates to the earlier point about working with the Office for National Statistics as well, because that is - as Gill mentioned, we are doing some exploratory work with them to see if we can track a signal across different recommendations on relatable pieces of information if you see what I mean, across our guidelines. I'm not explaining that very well.

Our guidelines are discrete pieces of information. But if you can link a signal over here and track it across in a quick way that says this recommendation is related to that and is related to that, then it's similar to your life course database. You can start to draw on data and not go through a process which is prone to error. You can start to employ technology to identify where that signal could impact on NICE guidance and other people's outputs and regulatory framework, however it might be. It's all about how we code and capture and make the bits of information talk to each other and relate to each other, I think.

Gillian Leng: Because that's another challenge. There might be a fragmented system around implementation of patient safety, but it's also fragmented in relation to data, data capture and analysis.

Simon Whale: But it comes back to who holds the ring on all of this.

Gillian Leng: Yeah.

[Laughter]

Simon Whale: You're saying it's the Department of Health who ultimately would need to make this happen for you.

Paul Chrisp: Part of it. I mean, even that is a - yeah. For us, for our world in healthcare and with the MHRA and our assistant partners, yes. But again, you could say, well, how is that linked to the ONS? Because that's another bit of the world that's not DH.

Simon Whale: It's one step at a time.

Paul Chrisp: Exactly.

Valerie Brasse: Just a couple of questions from me. One of the bits of information that you draw on when you're looking at the guidelines is [MORD] data, the American equivalent to our Yellow Card. I just wondered what your view was about that, because the patient group said to us they would like to have a MORD system here. They've got Yellow Card. What's your view?

Kevin Harris: Again, it's a personal view. I think it's better than we've got here, but probably has a number of infections.

Paul Chrisp: Yeah.

Valerie Brasse: We're looking at systems. Let's just see what else is on offer.

Kevin Harris: Any system that relies on reporting rather than collection of data is inevitably going to be a challenge and incomplete, isn't it? Because we know people don't report things.

Valerie Brasse: No, because it's much more open and transparent.

Kevin Harris: Yes.

Valerie Brasse: You can certainly interrogate it whereas you can't do that [unclear].

Kevin Harris: Yes, so all of those things I think are true.

Valerie Brasse: From your perspective sitting in NICE and how you use that data, is it better data? Are you getting more than you would be from the other [unclear]?

Kevin Harris: I think the signals are stronger certainly, but are they complete? I don't believe they are really.

Valerie Brasse: Okay, so the signals are stronger. That's a good one to take away. My other question is translabial scans. I know that in the guidelines, the consultation document, it's mentioned there as part of the mechanisms for investigating [unclear] mesh, but you don't place it in any sort of hierarchy. Patient groups tell us that's really important, that they would like to see a lot more of it. There just aren't centres where they can go and get translabial scans.

Kevin Harris: That's a clinical guideline question.

Paul Chrisp: Yeah, that should have been picked up in the consultation comments and \ [unclear] consultation closed in November. If people feel that strongly about it, you can look at that. As Kevin said...

[Over speaking]

Paul Chrisp: We respond to every stakeholder comment. We change recommendations on the basis of comments. That's why we do it.

Gillian Leng: What we would do if it seems like there's a gap in a facility or a service is to flag that up with colleagues in NHS England. As I said before, we can't do more than raise it with them. We have no power. But we do routinely talk to them about what's coming through the guidelines and what's new so that they know.

Paul Chrisp: Yeah.

Julia Cumberlege: I'm going to draw this session to a close. But before I do, I need to ask my colleagues if there's any further question they'd like to ask, and then also to you, whether there's anything you'd like to ask us. Sonia.

Sonia Macleod: I just had one question and it's actually historic. It's to do with mesh. When SERNIP reclassified mesh, it went from category C, which was safety and efficacy not proven, two jumps up to category A which was safety and efficacy proven. Would jumping two categories be normal for the guidelines or guidance?

Gillian Leng: [Unclear] it doesn't sound...

Kevin Harris: I can only speak for the Interventional Procedures Programme.

Sonia Macleod: Yeah. I do realise this is historical. I'm not asking for...

Kevin Harris: That would be a very unusual thing to happen. If you take our four levels of recommendation, to move two levels would be unusual.

Sonia Macleod: Yeah. The other thing is that we have heard that SERNIP reconsidered its classification at the request of manufacturers. What's the role with manufacturers in terms of requesting changes to NICE guidance?

Kevin Harris: No one can request, if you like, a change to NICE guidance. Anybody can ask us to look at any of our guidance again or indeed newly notify procedures to us to look at for the first time. That includes manufacturers. It includes patients. It includes clinicians. Historically, most of our notifications or requests for updates come from clinicians actually, but manufacturers do do that as well. We then have a process to consider with an update. It has to be based on new available evidence. They can't just ask us to update it because they'd like us to update it. To be fair to many manufacturers, sometimes they will produce new published evidence which they would like us to consider. That's often viewed as a legitimate reason for doing that.

Sonia Macleod: Okay.

Julia Cumberlege: Okay. [Unclear].

Cyril Chantler: No.

Simon Whale: No.

Julia Cumberlege: Valerie, no. Over to you. Anything you'd like to ask of us?

Gillian Leng: Do you have any questions?

Paul Chrisp: I don't.

Gillian Leng: No?

Kevin Harris: No, thank you.

Gillian Leng: No? Thank you for the opportunity to come and talk to you. If there is anything that can be done to encourage a stronger mandate for the system to respond to NICE guidance, especially in relation to safety, that would be great. Anything to facilitate a fit-for-purpose mechanism for data collection that we can use as well would be fabulous. Thank you.

Julia Cumberlege: Well, thank you so much and for spending all this time with us, over an hour and a half. Thank you very much indeed.

Paul Chrisp: Thank you.

END OF TRANSCRIPT

Session 3: NHS England

START OF TRANSCRIPT

Julia Cumberlege: Keith I don't know if you're going to start - saying who you are.

Keith Willett: Okay so I'm Professor Keith Willett. I'm - my role is as Medical Director for Acute Care and Emergency Preparedness in NHS England. I was the chair of the mesh working group and the mesh oversight group.

Keith Ridge: I'm Keith Ridge and I'm Chief Pharmaceutical Officer. I think it's important that I point out that my role extends beyond NHS England. So, it's system wide. Including for the Department for Health.

Julia Cumberlege: Thank you very much indeed. One of the things that's quite difficult in the present set up that we have, the systems that we have to work - because there are so many agencies, groups that are free standing groups as it were. One of the things I'd like to tease out to begin with is really who is responsible for procuring safe and effective services? Across the NHS? So where does this responsibility lie? Because we've got all these arms lengths groups and all the rest of it.

I don't know if - I'm going to call you Professor Willett because it's a distinction between the two of you. Would you like to start with that?

Keith Willett: Well in terms of overview, the - so NHS England's role as an arm's length body is to assure that the services are provided within the NHS, but the majority of those services are actually commissioned by Clinical Commissioning Groups. Or where they have been superseded by some more recent events. But essentially by Clinical Commissioning Groups. So, for instance in terms of stress urinary incontinence and prolapse, the say, routine - the local service delivery for those services in the past would be the responsibility of the Clinical Commissioning Groups to commission.

NHS England oversees those. Doesn't direct them. But oversees them. NHS England does have a role in directly commissioning services where they are specialist. Or they are directly commissioned. So, services to Armed Forces personnel, prisons and secure institutions, in combination with CCGs, primary care. Then there are the specialised commissioned services as well.

In the context of mesh, that would now be the complex gynaecology which would be around the removal or the management of complex cases or complications of mesh.

Julia Cumberlege: Right. Thank you very much. That's very clear indeed. But I'm just thinking - you've only got the oversight really of the CCGs who are commissioning these services. If you feel they're wanting, if you feel that they're not commissioning the right things or in the right way, what do you do about it?

Keith Willett: So, there is an oversight of them. They are monitored. There's an assurance process that goes on with CCGs on a regular basis. NHS England will be managing those and stepping in at a regional level where they are seen to fall short. The level of failure - if you like, that would be necessary for NHS England to step in and take control, would be at quite a high level, because most of that would be addressed by putting in contingencies to help the CCG and move them forward.

In terms of where they will sit in assessing the services, many of the services are based around standardised national contracts. Which are - if you like - templated nationally and then adopted locally by CCGs. But actually, the procurement - who they procure services from; how they assure those services. Those processes belong to the CCG.

Then they will sit within the framework nationally of - and they will say if you like - be steered by the regulatory bodies and advisory bodies. So, for - you have the MHRA quite clearly - as one of the regulatory bodies who would - they would work within those. We have NICE as the organisation that sets clinical standards and guidance. So, they would be working with those.

In most part - if it's outside of those areas - individual patient safety issues are dealt with by the patient safety team, which is part of NHS Improvement. Not part of NHS England. They pick up incidents as they occur. They're usually outside the scope - very often - of the other regulators. So, they would tend to pick up things that perhaps are not under their guise - under the sort of cover of the other regulators. I don't know if Keith wants to add to that.

Keith Ridge: I just thought it might help if we say something about primary care. Whether that would be helpful. So, for primary care and the sort of direct commissioning responsibilities of NHS England. So, for primary care contractors - and I guess we're specifically interested in community pharmacy and general practice in this instance. But there might be others, I guess. [I gather too] but I suspect those are the two main ones.

So, for community pharmacy then it's - there is a Community Pharmacy Contractual Framework which is negotiated and agreed at national level

and an assurance process which is based largely on self-assessment. Although it's a bit more than that. It's associated with the Community Pharmacy Assurance Framework. It's a process by which - in order to determine what is covered.

For general practice then there's - it's delegated effectively to CCGs and then obviously the role of CQC. It's probably also worth mentioning the role of the General Pharmaceutical Council. I know that's already appeared, I think. Duncan I'm sure would have explained to you the role of the General Pharmaceutical Council - not just in terms of registrants – of which there are two professions in pharmacy but also their system regulatory role in the form of their regulatory role around pharmacy premises and owners of pharmacies.

So other than that. I give you Keith?

Julia Cumberlege: Thank you very much.

Keith Willett: It perhaps adds a bit of clarity to what I've said. So, the regulator like MHRA - will be responsible for regulating and overseeing where a device or medicine is used appropriately but then there are consequences. Whereas the patient safety team will be where there is an inappropriate use or it's outside of the zone of the regulator. If that makes any...

Julia Cumberlege: So, the patient safety team is NHS England?

Keith Willett: NHS Improvement.

Julia Cumberlege: NHS Improve - sorry. Right can I...

Keith Willett: We work closely with them, but it is NHS Improvement.

Julia Cumberlege: Right. Thank you very much. Can I ask you. So, when you put a CCG into special measures. That can be on various grounds. I imagine. It could be financial. That they're not meeting those targets. Or it could certainly be on safety or it could be that they are not very effective in their commissioning. What do you do about that? You described about helping them. But if they're being put into special measures they may be a bit resistant to help. How do you actually deal with that situation?

Keith Willett: So that's not something either of us actually are directly involved in. We're clinicians in NHS England here to really represent the clinical perspective. But the - when going to special measures, it would be a combination. So, they go into special measures for a variety of reasons. CQC can put them into special measures. That usually would involve a significant direct input into the CCG to support them from the regional team. Depending on what

the issue was, what that support would necessarily be. Whether it was financial or managerial or whatever.

In many cases you will see a change - maybe a change in the board occur as a result of that. You may change certain roles within the organisation. So, it's a - it's sort of the last step measure that would be undertaken. But it is undertaken where there is an individual commissioning failure.

Julia Cumberlege: So, can I ask then. The CQC - it gets involved in assessing some of this. So where is their relationship? Between NHS England and it's particularly perhaps in primary care. With pharmacy [unclear]. Because two of our issues of course are medications.

Keith Ridge: Okay. So, with pharmacy - just to be clear about that - CQC's remit is quite limited. Because the system regulatory role lies with the General Pharmaceutical Council. I mentioned earlier, they regulate professionals and premises. In relation to primary care - more broadly in terms of general practice - then yes, then it's the CQC. Indeed, in preparation for this I've been discussing with aspects of what they have started to find in relation to Valproate. I think their inspection process is clearly documented in the normal way.

There's a memorandum of understanding between NHS England and the CQC in terms of how that works. Indeed, there are memorandum of understanding between - for example the General Pharmaceutical Council and the CQC in order for them to have information sharing and what have you. It's that type of relationship.

Julia Cumberlege: So, if you have a medical practice that is still giving women of child-bearing age Sodium Valproate - something like that, for epilepsy - but they haven't considered the Pregnancy Prevention Programme. How do you (a) find that out and (b) what do you do about it if you find that in fact, they're not doing what is expected of them?

Keith Ridge: I don't think we do find out at NHS England.

Julia Cumberlege: Sorry? You don't think you do know?

Keith Ridge: I don't think we do find out individual cases like that. I think that's something we all ought to consider. That would be my view. I think the CQC look for - and my discussions with them have been more about what they've found in general. I guess CQC will be appearing or have appeared. In my - for Valproate at least - there seems to be a bit of a mixed finding in general practice. Around this particular issue.

Simon Whale: How do you mean mixed?

Keith Ridge: So, I - I think that they are finding examples of good practice and examples where perhaps systems could be better, would be the summary of it. In the detail I've seen which is - well detail - it's quite broad. I'm happy to make some general comments in a broader way if that would be helpful at some point.

Julia Cumberlege: Wouldn't you be really concerned that patient safety is actually at a premium here - where the general practice is still doing what we know can cause harm?

Keith Ridge: I am concerned. When I look at the sort of - as the evidence base has increased around issues associated with Valproate and the sort of - how the regulator has responded, the Medicines Regulator in particular. The system in response to that in each [assisted] organisation as we've mentioned. Clearly, I'm representing NHS England in particular. But I guess - as I mentioned at the beginning, I do have a broader role. Then I think there are some things that could improve.

We've got to the point now where we are a year in from Sally Davies' letter. I just - where I am in my mind is that I think there's a need to just take stock about where we're got to with Valproate. To do that across the system. Happy to talk to you about why I think that more broadly if that would be helpful.

Sonia Macleod: Who should take stock?

Keith Ridge: Yes. That's a good question. As far as ultimately the Medicines Regulator has chosen - on the basis of evidence no doubt. Not just at a UK level but internationally - of the sort of risk benefit basis of Valproate and its usage comes down - at the moment, to use in pregnancy. Or use in women of child-bearing age, to be supported by a Pregnancy Prevention Programme.

I guess from their point of view they're then looking on the basis of that for organisations to react and professionals and professional bodies and the like to react accordingly. When I look at what has happened, then I think - so I mean I - the pharmacy world, I think the General Pharmaceutical Council has reacted appropriately, .in terms of their duties and their inspection role of both registrants but also premises and owners. I know that they have put in extra responsibilities, or extra sort of monitoring around inspection. Their inspectors monitoring.

I look at the IT systems. In terms of flagging a warning, and you can see that having sort of looked through what's happened then it feels to me that

general practice IT systems have reacted appropriately. Community pharmacy IT systems ditto. Where I think there might be a gap is in hospitals actually, where there's more flexibility to what is - what can be flagged. What is and isn't flagged in terms of prescribing and dispensing systems.

When I look at the GMC - then in terms of their reactions so far - then clearly, they are there to regulate professionals and have prescribing standards expected for people to respond to. I just wonder whether there is more to do. That's the discussion I'm having internally right now. To sort of say, I think it's time to take stock.

Sonia Macleod: You've just gone through and you've basically said each of the little constituent parts have acted appropriately. But we've heard reports...

Keith Ridge: Let me...

Sonia Macleod: ...that the system isn't working.

Keith Ridge: Yeah. So, let me carry on then in my analysis if you don't mind. I think in terms of NHS Improvement and their responsibilities as Keith has outlined - issuing a safety alert. One wonders - and I know that a new patient safety director will be coming to talk to you in due course. One wonders whether - what goes beyond issuing a safety alert.

So, you sort of - you get to the point where you sort of think - in the function I currently occupy - should I be thinking about - so we've got to this point. We're not clear. I'm not clear on just how effective all of that has been. Whether we should at this point take stock. As I've said. That's where I've got to.

Cyril Chantler: Did I understand your concern is particularly in general practice rather than in pharmaceutical practice?

Keith Ridge: There are - so some of - as you may know the new GP contract has specifically within it now - but obviously yet to be implemented - a quality improvement programme, which includes Valproate and the requirements around Valproate. Which is obviously a step in the right direction. We're in the process that we're going to be deploying thousands of clinical pharmacists into practices but that will take time. For me that's also a step in the right direction, including in terms of dealing with this.

But, yes. I think there is still more to do. I think for me I need to have some clear evidence as no doubt you do - that this is being as effective as is intended.

Simon Whale: Have you seen evidence that at least one of the patient groups in Valproate has shown us, which is that the PPP is not being followed in those clinical settings that we've just been talking about. GP surgeries and pharmacies.

Keith Ridge: I've seen the survey - I guess - in pharmacies. Clearly, I've reacted to that all in - you know with the other chief pharmaceutical officers. Who you will see now later I'm sure. The GPhC I think have reacted to the - you know - the Company Chemists' Association have reacted. They - it feels to me - which is what I said - that they have reacted appropriately.

But when you're dealing with something which - you know the risk benefit balance of the drug itself, in a difficult to manage condition, which has been established - the use of the drug - for many years, ingrained in medical practice, I think,

then it's a sort of - you can see how you get to this position where the Medicines Regulator has reacted in an appropriate way. But you get to the point - I think - where you have to think again about the risk benefit balance around here. Because in simplistic terms for me you know Valproate is - Valproate's been around for a while. There are alternatives. There are ways of managing, switching from one anti-epileptic to another.

So hence it's time to take stock.

Simon Whale: That would suggest the risk of exposing a woman of child-bearing age to Valproate is entirely avoidable.

Keith Ridge: Is entirely?

Simon Whale: Avoidable.

Keith Ridge: I think – see, the aim is to - of the programme - the PPP - is in part at least to ensure that there is not just - you know, sufficient information, there's sufficient information for people to make the right decision. Ultimately, the decision as to whether a drug is on the market or not or is contraindicated or not is not mine. It's the Medicines Regulator. A decision to prescribe is not mine. It's the individual prescriber with - working together with their patient.

It feels to me in what is such a serious matter that we should all at this point I think take stock. Several times.

Simon Whale: Is it possible to put your finger on who holds the ring in relation to responding appropriately but also suitably rapidly to the patient - to safety concerns. Who holds the ring on that? Because as you - as Professor Willett described at the beginning - there's an awful lot of organisations

involved. They sit inside of - they've got discrete responsibilities. Who holds the ring between all of the different players to ensure that patient safety concerns are responded to? Whether it's Valproate or mesh or anything else for that matter?

Keith Willett:

So, I think if you look at the components then we can pull that together. There is already within the system the responsibilities I declared at the beginning there. Then we have a national reporting and learning system across the NHS. That is a voluntary system, but it is encouraged to be open and forward and that is something that works pretty well across mental health and hospitals, but that works less well in the community and in primary care.

There's a commitment in the long-term plan to improve the safety because there is a recognition that that is a deficiency. That system will be replaced, I think it is 2020, with a new computerised system which will have artificial intelligence, machine learning - whatever - in order to pick up trends and elements which we wouldn't otherwise be able to do, simply because you don't collect it. If that becomes automated, then we will start to get a sensitivity around things that we didn't have before.

You've obviously also got the patient safety team which I've talked about - for the incidents. You've got the regulators then. On top of that you've also got the Serious Incident Framework which has been established for a good time. But that really - there's not clear criteria about when you fall into that. But it's when it's recognised to be a very serious incident where a patient's life has been seriously affected by an event or there was an episode that could well have resulted in that. Or there's [unclear] patient death.

That Serious Incident Framework is very well established. The organisation that has the serious incident is required to report it within 48 hours to the commissioner. The commissioner of that service is the one that is duty bound to investigate, ensure that standards have been met and lessons have been learnt. Only they can close that incident. There's also a requirement in that Serious Incident Framework to inform all the other parties that would be regulated within the system, whether that's the CQC, MHRA or anybody else.

So those things at sort of the sharp bit work. NHS Improvement has the overall responsibility for ensuring all those things are in place. So that's where the safety oversight sits in terms of the mandate coming down from DHSC. But I think the bit that Keith is alluding to and I would share - and having been through the mesh investigation now for seven years. I think it's

been in my - I've been involved with it. Quite clearly when you get to those things where there's an accumulative rising tide of issues which aren't specific, which aren't - there aren't sort of [loci] of them where you can rapidly identify that Trust as being the problem and there's obviously a bad team or a bad surgeon or something going on.

It's that sort of stuff which I think is much more difficult. If you then add to that the issues that Devices and Clinical Teams which we will talk about in a moment, I'm sure about mesh. Actually, it's a different sort of rising tide of events. How it might happen. I think we do recognise that there is a - we have to be better at trying to spot that. That's going to come - I'm sure we'll get to that in a moment. But I think there is - in that part of the safety system - it does still feel like it requires on a lot of voluntary - people standing up and saying, there's a problem. Putting that together. Collecting it.

That doesn't feel the most solid way of doing it.

Valerie Brasse: So, can the system as currently constituted deliver?

Keith Willett: I think it can. But it's got to be wound up to be really sensitive and committed to do it. The problem is these things happen across so many fronts. There are - I mean I'm in - I'm doing EU exit as you may know at the moment. For my - I mean [unclear] I am. But there are 72,000 medical devices and clinical consumables that were used in the NHS last year. There are nearly half a million that are on the catalogue.

Now, if you imagine all of those - given the rate of technology changes - modifications and changes - new versions of those will be coming through in their thousands a year. Some of those will have a long lag period before the problem may develop. I mean if it's a joint replacement, you've really got to go about 15 years now before you know that the joint replacement you've just turned to wasn't as good as the one you were using.

By the way, it's - the manufacturer's changed it three times like your washing machine will upgrade, your airline has been upgraded. Your car's been upgraded. All these things - so it's a very different model in order to pick that up. Clearly, I think there are real opportunities with the collection of data. We all know the issues around that and linking data - to put ourselves in a better position to understand that. But I think there has been a commitment to start to move down that process in the long-term plan which I think is very positive.

But I think there's a - this is a - these incidents I think have been wake-up calls for those involved in safety and for the regulators as to whether or not their tentacles in the system are as sensitive as they need to be.

Julia Cumberlege: Can I just ask you - thank you very much for that explanation. I do want to say we are hugely grateful for the work that you did introducing the pause which we recommended should be done. I know that you had to work very closely with the Department of Health in order to achieve it. Clearly, it's been very warmly welcomed by the patient groups.

I want to go back to the patients and the patient groups. Because we've had all this enormous amount of evidence from them. Listened to them and the problems that they've had. Just looking back a bit to 21 November 2012, when you sent out a letter with Sir Bruce Keogh at that time. He was then the Medical Director for England. You both signed that letter. You wanted to draw the attention of medical directors to the publication of a report from the Health Economics Consortium of York University.

The concerns that you had that time about common adverse events associated with vaginal mesh. Now, that was 2012. It took to 2017/18. Eighteen was it? Eighteen. Thank you. When we introduced the pause. Why does it take so long? Because you were clearly concerned at that time. In the intervening period a number of women have been seriously damaged.

I just - listening to what you've been saying to Dr Brasse. I mean it is clear it is a very complicated system we have at the moment. Getting all these dots joined up is extremely difficult. But nevertheless, surely when you were really concerned about what was happening in the introduction of surgical mesh, vaginal tapes et cetera for stress urinary incontinence. Why didn't you with your colleagues introduce a pause at least in 2012, 2013?

Keith Willett: I think because there wasn't evidence and the sort of evidence that is relied upon. In 2012 - you know how I became involved in this. I just happened to be walking through the department when they needed a doctor on a call because a regulator was talking to government officials and I was put on to the call. I listened to the call. At the end of it I was concerned that I was hearing things that the evidence wasn't sort of talking about. I need - I just felt we needed to understand it.

So, when we became NHS England and we appointed a national clinical director for maternity and women's health, I asked that national clinical director to start some work to explore this. To see if we could get to it. Because - I mean - I know as an academic I do research. I understand it. The

York Report. Really very poor scientific literature out there. As - and this is not unique to mesh. This is - this occurs across the board when new devices - unlike in medicines they have to go through a rigorous four phase testing process with substantial research behind it.

That's not the case for medical devices and implants. For some of the reasons I discussed earlier. When you looked at the evidence that had been accumulated at the request of the Chief Medical Officer, I think it was. The MHRA I think requested that. The evidence was - as it often is at that stage in the evolution of a device that's used - it is short follow ups. They're often case series. They often come from departments and units that are enthusiasts or they're designers.

But that doesn't mean it doesn't work. That doesn't mean it's wrong. Because that's how they've all started. In fact, my grandmother had Sir Geoffrey Charnley's third total hip replacement. Which became - you know - and was a standard for 25 years. It lasted three weeks. From the age of 40 until she died, she walked with two sticks and a large built-up shoe.

Now if we'd stopped total hip replacement on the back of a complication and surgery and the use of things that are always associated with complications. No medical intervention, pharmaceutical or devices is without complications. What people have to determine is secure the evidence. That is a balance between the evidence that you can get which is numerical around clinical trials, around follow up about the complications and the severity of the complications.

Also, that's sort of a population cohort evidence but then you have what you have experienced. A lot of - I know in the Review is that individual personal catastrophe. But if we go back to that stage, there just wasn't the evidence there.

Now Scotland in their independent review, they went down the route of looking at all that evidence. I have to say I didn't adopt that. The role I took was to try and bring the parties together which were not close together. At the beginning. I think I made that clear in the report. In fact, even the patients who we brought onto that group were not close together. In terms of a common cause.

What I spent the working group period doing was to try and broker through the middle of that an understanding about what we did know. What we didn't know. What the signs of the problem might be and the impact. Then to say, right let's be pragmatic. Whilst we are waiting to get evidence that says yay or nay. This is the size of the problem. Then let's make sure that

we are putting in place all the things we should do. What are the things we need to put in place? You know, we needed to put in place better quality.

So, we needed to make sure that the surgeons that were doing it were properly trained. That was a part of their appraisal. That we knew that, well actually the women who are going to surgery that they were in safe hands as it were. We needed to make sure that where there were registries those registries should be open so that the data could be collected on every case.

We also made it part of that national reporting structure. We devised that. We, importantly for me - because the - what had happened with mesh - and again it happens with new devices and I guess with new medicines, is that the - if there's a series of operations that aren't very successful and that was undoubtedly the case with stress urinary incontinence and prolapse, that had been for many years not very successfully reported. If they were working, then they often failed in the short to medium term. Along comes a new operation which appears - in those early studies - to be highly effective. It clearly was in the early studies.

What happens then is there is a shift in clinical practice. There is a shift towards what seems to be a strong new intervention. That carries with it a degree of - you know people want to be upfront and they're going to their continuance and professional development meetings and they're learning about the new techniques and they want to take them and offer them to their patients.

But because it was also a technically really rather straightforward operation compared to something like a colposuspension which is a very significant undertaking - and in the best of hands still wasn't the most wonderful procedure, then suddenly what you've done is you've bought in to an operation which is great. More surgeons are capable of doing it technically. It becomes the operation and therefore the second thing that happens is - which I'm - because I think a big factor for me in my understanding and - you know, in reflecting back is that the threshold to offer patients the procedures went from being - we know in the UK there's probably two million women at any one time that have significant incontinence. The figures are from the - as I recall - from the Review, that about 330,000 have it at a socially disabling level. They can't leave the home. They are forever having to pad or change or whatever. Whereas the major operations being undertaken would have been focused on the groups that were really very, very severely affected by incontinence or by prolapse, because the operation was now technically more straightforward and appeared to be successful, the threshold would have come down. Because it was available

more, by more surgeons in more hospitals and it became a sort of almost a day case - well it was. It became a day case procedure. That is what happens. That's not unique to mesh. That happens in surgical interventions. What you then see the consequence of is, where complications arise, the impact for the patients are much more - not more devastating - because they're devastating whenever you get the complication. But if you are - to the other extreme if you were dying of a condition and someone offered you a procedure which was really quite high risk - but it gave you a chance of survival - you'd probably take it.

If you go to something where you've got a totally disabling condition that you can't leave home. Your whole social, family, personal life is destroyed, and it doesn't work. Okay. That was bad but that was - that's within what a patient would anticipate being a potential. But if it's someone who just has a degree of incontinence which has been far less than that and then they get a devastating complication late down the line, that is somehow just much more unacceptable I think from a patient safety perspective.

Those sort of things have gone on. So, the other part of that was to make sure in that working group - the other thing we agreed unanimously between all the parties - was that we had to improve the consenting process and the information process. So, that's where the patient leaflets were promoted, that's where we went down the route of informed consent with a leaflet alongside it. We came to a conclusion - and I know you have read the working group report - which came to a whole series of recommendations that need to be made.

We were working - not with - but we were communicating all the time with the Scottish group that were looking at this, because clearly, they were doing a scientific review. Which valuable as it is, it is always difficult to really hang your hat on research which is not of the highest quality. So...

Julia Cumberlege:

I just wanted to ask you about the research. Because you've said of course that mesh was seen as a highly effective device and I can understand that. But I think what the query is with the patient groups is why wasn't there some real research done first of all in sort of pilot schemes or whatever you - the words you use in research. So that you could actually track it?

Because their feeling is that they're actually part of a research project now as guinea pigs and they really do resent that very strongly. They felt that the proper research should have been done before it was taken on by the whole of the NHS.

We know. We've heard of, women tell us that some of the surgeons were just there to have a go. Now, you know. What you were describing. The safety measures and that we adopted when we had the pause. You've put those into place. We were - some of my colleagues will question you perhaps on that. But it just seemed to us extraordinary that there wasn't any attempt to do some real research before it was rolled out.

Keith Willett: So, very - good reason for that. The process by which devices come on to the market is completely different to medicines as you know.

Julia Cumberlege: I know.

Keith Willett: The notifiable body structure. The regional implants that were even taken into that structure went in on a grandfather clause. In that they'd been in use for a long time therefore by de facto they were safe. True or not. Manufacturers - depending on the type of device - have to go through a series of checks. But most of the things that they have to go through to get the CE mark are things around the material testing qualities. The biocompatibility. They aren't required in any way to do the same level of FDA type approval research that's required with a single formulation of a medicine.

There's - and you can understand why that is. Because - as I described - these devices - when they come onto the market, they will be modified and modified and modified. Every year or two each device will be updated. Now, if that's the case does it mean every time you make a new version or you make a modification or you change the surface characteristics or you change the pore size in the mesh, you have to go and do a trial? If you're going to go and do a trial, then trials are exceptionally expensive.

Now I'm not saying money's the problem here. But, a trial - I run clinical trials. So, if I run a clinical trial and I run clinical trials of implants versus no implant surgery you'll be pleased to hear. Those trials - involving sufficient patients to give you the answer that you're looking for - will cost one to two to three million a trial.

For most of the things that I would test in a trial, the outcome is for the patients and for what we need, would be gleaned within six to 12 months. We very rarely need to run trials longer than that. If you're talking about devices here where the complications have occurred down the line - and I know from talking to the many of the women who have had - who've been harmed in this, the complications have arisen later. In fact, some of them well down the line. Well how long do you run those trials for?

They would be inhibitorily expensive, and we know that the decay in the numbers of patients who will continue to take part in those trials will mean it becomes futile after a while because you just haven't got enough numbers to make it statistically significant.

So, it is exceptionally difficult. So, the idea that you can do randomised controls in some of the medical devices is probably unrealistic, but there are other methods that you could use by which you could assess in longer term trials. But the difficulty is, how long do you wait? You will be aware that we only have to pick up the local newspapers or the national newspapers for the headline to be saying, 'new wonder drug blocked by NICE'. Or new thing on the market.

We had the Innovations Bill that was through the - attempted to go through the House which was about accelerating things on to the market because patients wanted access to them before they had gone through the full trials process.

So, we have to sort of bear that in mind as to what is the realistic - so I think we have this dilemma with devices, as to how we ensure the checks are happening in. So there have been - and the MHRA have worked and I know have developed and you'll need to question them as to where they have got to with alternative ways of monitoring.

Now, you will recall that in the orthopaedic world there were problems with hip replacements. There were some that failed. Early. Rather than lasting - you know, 15, 20 years we would expect a hip replacement to last. They were failing inside three, four, five years. The British Orthopaedic Association took the professional steps to set up a programme which is an example of how it can be done called Beyond Compliance. In other words, over and above what the CE mark and the notified bodies would do.

What they did, they got with industry and agreed with industry that a much more granular data collection would occur for the first period of time that implants were made available. The opportunity there is you only put them in to reference sites that are collecting that additional data set. So, patients have the opportunity for the new stuff, but they recognise they're part of that period. At the end of that - or during that period - for the hip replacements, which is what it was designed for they considered that - my understanding is - that they were pretty sure by three years whether this was a sound device or not.

There is the opportunity to that. But all of that is obviously quite a major undertaking when you talk about the numbers of devices there are on the

market and that come on to market every year. I think there are opportunities there but that's the space I think we are still relatively weak in and that the regulators could look perhaps more constructively at how they manage that. At the moment they're obviously constrained by the EU regulations. I say at the moment because we don't know where we will be on 29 March.

Julia Cumberlege: Yes. Well thank you very much for that. But I mean it is interesting isn't it? That the full pelvic organ prolapse, that is now - has to be a research project if you're going to implement it and all the rest of it. So...

Keith Willett: Although now it is actually quite difficult - and the other thing is it's quite difficult then to get patients to consent to join the research programme.

Julia Cumberlege: Yes.

Keith Willett: You know, it may be - and I don't know - but the meshes that were used originally. We know they were brittle. We know they didn't - they shrunk. We know they had problems. That's - and in some people they caused an issue. Clearly in many they didn't. But they did in some. As technology improves are there going to be meshes there that actually do what is wanted but don't have the complications? That evolution is the sort of thing that would normally happen in a device when it was being used.

I know it feels like the patients are the guinea pigs but that's the evolution of everything. You know, car safety's the same. The evolution in car safety has occurred by learning about accidents that have occurred in vehicles. You can't say that's the right way to go but we have to understand that this is no way near as straightforward as testing medicines in animal experiments and then doing dose dependant testing and then doing - okay so now we've worked out it doesn't harm you. Now we've worked out a dose that might work. Let's see if it actually changes the outcome of the disease. Which is what the medicines process would be.

That's very different in devices.

Keith Ridge: Indeed, with Valproate we've got to the point where there is considerable evidence of the risks. The issue for me is, are those risks being managed appropriately. Has the intervention worked and to be frank we haven't got the evidence yet to know whether the intervention has worked. That's where I am. So as Keith said it's a sort of very different situation.

Valerie Brasse: But isn't this one of the problems? We keep talking about not having the evidence. We might have had different evidence. You in 2012 talked about setting up the registry to capture the data. We can go back even further to

the NICE Guidelines in 2003 that talked about setting up a registry, capturing the data for stress urinary incontinence data. So, for 15 years collectively the system has been saying this is what we needed to put in place. Somehow it didn't happen.

Keith Ridge: Fifteen years was that?

Valerie Brasse: Well 2003. NICE Guidelines talks about setting up a register to monitor the long-term outcomes. In fact, one might say if that had been done the story of mesh might have been very, very different. Let alone how many women might not have suffered as a consequence. But the problem that I have - the Groundhog Day moment here - is you're looking at this from the outside and saying this is a system that's supposed to protect and ensure that the [unclear] is safe and provides effective safe services.

NICE are saying it, if NHS England are saying it and it doesn't happen, [unclear].

Keith Willett: So, I fully accept that. I think we've certainly reached the point where the pause was the right thing to do. We had those discussions. The process of going through setting up the registry is underway. As you're aware, the DHSC have commissioned that work through HQIP. Had we gone back and had registries - who knows. May well do. What I have to say is though we still don't have. We - you, you know - and I fully appreciate that you have interviewed many, many, many women. Far more than I have spoken to. Although I have spoken to a good number.

But what I was - I was trying to help understand the magnitude of the problem in order to make the arguments as to what we should do next. That's why once - I'm very grateful for the patient groups again to have gone directly to the department because they did allow us to generate the request which was accepted and take Secretary of State direction to do that retrospective review of the data since 2008 through to - sorry 2009 through to 2017.

We went to those data to try and understand what the real complication rate was because I fully accept that you've had the interviews and there are clearly many women whose lives have been devastated by this. But it would appear also we don't - what we don't know, is how many of that 100,000 women who had tapes for SUI who haven't appeared back in the system as an obvious complication. I'm not saying they haven't got complications because primary care we know are particularly - have been particularly poor in this area at identifying them as mesh--related complications.

But if we look at the partial or full removal rates - and that was the first time we had the opportunity at an individual patient level - which was not what the Lancet papers or the other papers of research could do - at an individual patient level, where it could track a patient from their primary operation as to when they next appeared in the system, if they did appear in the system for either a removal operation or whatever. We were also able to track on the treatment function codes when they appeared in a variety of clinics. We built in all the clinics that we thought were mesh-related complications, including orthopaedics and trauma for leg pain and all the other things.

We looked at those data and those were published by NHS Digital. That was an independent review by NHS Digital. The best estimate of an accumulative problem that resulted in mesh removal was less than four per cent for SUI as you know from the report and less than 1.5 per cent for use in prolapse.

If we looked at the attendance rate at a clinic for individual patients who've gone through that, it also showed that there was no difference, and they were higher than the average age for that - for the age and for the gender and age match groups. If they had mesh or no mesh but they'd had a procedure for SUI or for prolapse their attendance rates at the clinics were the same.

The only group that had a higher attendance rate were those who had colposuspension. That was true right through and right through the nine years follow-up. That was - you know there was 100,000 patients in SUI group. With the mesh and non-mesh and the prolapse again there was over 150,000.

So, that's not conclusive data. But we've got to put all this in the mix to understand that - I'm entirely supportive of the pause as you know. We enacted that. Did recognise that some patients would necessarily still require surgery because for some patients there was no alternative. Patients clearly had to be fully informed about that. That is now undertaken, and we need to do and are still monitoring the rate of use of mesh. It continues to decline time and time.

But I hear what you say about the registry. That was a recommendation in the - from the working group. We came into this with a fresh eye. I wasn't involved in this in 2003 so I can't say why it didn't happen.

Cyril Chantler:

Can I just stay on this for a bit please? We - obviously our Review is in different parts. At the moment we're trying to understand what happened.

Not because we're trying to blame people. We're trying to understand it. We will be of course looking forward and I understand that your role has now changed. So, we've now met your colleague who's taken over from you. We are in the process of working through with her and with officials how that goes forward not just in the area of stress urinary incontinence but also in terms of secondary commissioning of services for mesh removal. In the whole vexed area of rectopexy and so on and so – and pelvic organ prolapse. But, just looking from the 2012 to 2018, looking back with the benefit which is wonderful of having hindsight. Would you have done anything different with hindsight now? Over those last six years? Because that may give us some indication about where priorities need to go.

Keith Willett: It was too slow.

Cyril Chantler: Hmm?

Keith Willett: It was too slow. I mean I have to say it was - the process was too slow.

Cyril Chantler: Yeah.

Keith Willett: I mean. I drove it. It wasn't going to happen - it wouldn't have happened. I'm not taking any personal credit for that. But it probably wouldn't have moved if I hadn't said there was a problem. I think it was very difficult with the working group, but we got there. I think what we would - I think in retrospect some of the - what I did was - the oversight group was formed. I formed the oversight group for the very reasons that we're discussing here. I was concerned that things - because how many times have we seen reports or reviews come out - I'm sure yours won't be one of them - where things don't change?

That's, you know - and I've been around long enough in the NHS to have witnessed many of those. So, the reason for forming the oversight group was in the working group report you will see that we identified the organisation [unclear] responsible.

Cyril Chantler: I don't want to lose my train of thought on this and yours as well. You have a reputation of getting - making things happen in the National Health Service over very many years. So, if you say it's too slow then we have to say, well if Professor Willett couldn't make it work, how could it be made to work? What we've been conscious of as we've gone up and down the country is a lot of people in the various areas that we've been given the task of looking in to have suffered.

Lots of people have worked very hard to try and help them. But the system seems to have failed them. So, if the system has failed them and somebody

with great energy sees the problem and says it's too slow then what do we have to think about within the system to try and reduce the risk of this sort of thing happening in the future? There may be technical things to do. But are there any systematic structural strategic things we need to be thinking about?

Keith Willett: I think we discussed it where we haven't even added in the central alerting system which is another of the safety measures. But I think actually I - what I tried to do in the working group - at the end of it. For each of the things we needed - we said needed to change, we identified a responsible body to do that. In my oversight group was me keeping those people in the room for the next 18 months, making sure they delivered on that. I think we did. On all bar the registry which has taken longer for all sorts of commissioning and funding reasons.

But on all the others – so, NICE who initially were not rushing forward to redo the guidance because it wasn't that old, they stepped up to the mark. MHRA also you know we - they stepped up to the mark and we did hold them to account. So, I think for me there is something about clarifying the architecture for how this response - and I'm sure this is a - I would suggest this is a key output for the Review is how do we spot these rising tides and when we do what's the process we put in place in order to identify the magnitude of this rising tide? The severity.

Or whether in fact it isn't. It's just a phase of early learning and getting used to it and in fact it isn't a long-term problem. What's the process that goes in place for that? Who is responsible for it? That's probably got to be a joint responsibility but there clearly has to be somebody who's leading it. The job I did doesn't exist for someone to be put in unless it's someone who is sort of identified to put in. Then having got that, ensuring that all - because it will be a multifunctional solution, I'm sure - that there is clear lines of accountability for who is responsible for delivering each of those.

Cyril Chantler: But you mention NICE and we've met colleagues from NICE already today. They wrote to the British Medical Journal after the leading article on mesh last October. In November, going through answering criticisms which they had accepted that they'd made in that article, it's quite clear that talking to them - and in their published letter- that there were things that they would have wanted to happen but which they had no way of making happen. They talk about mandatory guidance but it's not clear what mandatory means in this sense. Because they can't actually mandate it to absolutely happen.

Keith Willett: No.

Cyril Chantler: So, we're conscious that a lot of people have been doing lots of useful things, but the fact is the operations have gone on, people have continued to be damaged. As you say it's too slow. So, how are we going to deal with that?

Keith Willett: So, I think there are - I think it's got to be - again there's a variety of interventions I would suggest. I mean, I think there needs to be a - and I do think you need to take medicines and devices separately...

Cyril Chantler: Yes, I understand that.

Keith Willett: ...because they are just completely, completely different. I think the approach is quite difficult to describe in devices. Obviously, I've been round this in my head many times. I think it is quite difficult to encompass it. Interestingly I'm not - the registry we must do. It's the right thing to do. But actually, we can't do that for every single version of every single device that comes on to the market. I mean the data collection load, unless it was automated.

Cyril Chantler: Well there's a difference between - if you don't mind me saying so - between a data collection system and a registry. We've already talked to the College of Surgeons and the College of Obstetricians about this.

Keith Willett: No, I agree. But the systems that we have that we could automate which would be ideal.

Cyril Chantler: Yes.

Keith Willett: Would not have most of the patient outcome data in which would be critical for patients.

Cyril Chantler: No.

Keith Willett: That's what we've learnt from the patients when we had the - when we were at the - we ran the workshop with patients recently on the registry. They were very keen to be able to own a contribution to their entry on the registry. But if we were to set that up for every device that goes in nationally. I think there are real opportunities around IT and information collection though. The scan for safety concept I would strongly support. I think it's quite primitive but nonetheless it has the - it's the real - when you can.

Because, you know for the whole of my career as a trauma surgeon, I have watched my theatre staff take a sticky out of the implant that I'm about to put in the patient, stick one in the theatre register on a paper sheet and stick one in the patient's records. But the chances of those ever being

referenced again, let alone with a barcode scanner and let alone ever connected to anything else is I would imagine next to zero.

So, there's real opportunities around that. With the things that have been brought up in the long-term plan, there's a real - and what we must try and do is to automate as much of this as possible. That will mean patient consent I'm sure, for their information to be shared across. That was the one thing that we were able to do with the last Secretary of State. Was to get that direction. On the basis of the risk of patient harm that we could link patient data. On a safety issue.

I think then under the - whatever the architecture is for safety surveillance and response in the NHS we have to build a system that will do that, where possible. I don't think it will ever be perfect. I think it's a really difficult area. I do think the regulator... I think it's quite clear which regulator is responsible for which bit though.

Julia Cumberlege: It is clear.

Keith Willett: I think it is clear from the regulator perspective. They're quite clear. But I think they are - MHRA - and you will have spoken to them. I think they're quite hamstrung in many ways by the constraints on them and by the structures that have been around them. Now I know there's been a lot of changes and they are trying to move that forward. But I did get the feeling they couldn't do all they would like to have done because of constraints.

The issue around the pre-market checks and the post-market surveillance. The post-market surveillance is the area where I think there is the greatest opportunity. But it's what data? How do we collect it? How do we make that manageable and how do we ensure that we pick up the outcomes - the detrimental outcomes that the patients wish to put forward?

Simon Whale: Just on the point about data collection. I mean I think in your written evidence you were saying - as you've just said that - I mean, separate registers for multiple different devices over interventions is impractical and would cost a lot of money. You talk I think about having - or suggest perhaps the way forward in this area would be a gynaecology database. So, the concern that I would have, and I think.

[Interruption]

[Laughter]

Simon Whale: But the concern I would have - and NICE were reflecting on this this morning and sharing the concern - was - which is that if you have a

gynaecology database, where you're trying to pick up patient-reported outcomes and experiences, you will pick up gynaecology outcomes and experiences. But as you've seen in mesh, it's not just gynaecological issues that arise. Would you end up saying what we should have is a sort of old-fashioned NHS cradle to grave, every person database that just follows everyone all the way through? Is that even practical?

Keith Willett: Well it - I guess it's practical. It's whether it would currently - without consent - would not be possible. Patients would have to consent and that's the - you know we've been down this before with discussions about patient data and sharing it and linking around all of the issues that have been had before.

I do think you could probably - you know if you - you should be able to have a reasonably good idea about what are the likely complications that would occur with most devices. Whether they're heart valves or hip replacements or whatever. But I think you may well be able to construct some sort of linked databases that would do that. But it's - you know it's not an easy ask to be comprehensive.

Keith Ridge: If I could sort of just - just a couple of thoughts really. So, it may or may not help. When I was chief pharmacist in the Glasgow hospitals, I can remember turning up on the first day and finding myself not just responsible for medicines but for the medical devices world as well. It was interesting. I reasonably quickly got it to the right person. But the sort of - it was interesting sort of - when you compare the systems there are in place for medicines. Not just regulatory and monitoring of various types and what have you.

But the more day to day systems. Like formulary management and the various things that go through that - go with that. Embedded in my world - embedded pharmacists in medical teams to help and ensure the right things are happening. Those sorts of things. Various other things.

They were - they're just absent in the world of medical devices. Simple sort of a formulary being a catalogue of limited choice and the controls that go in around that. When I think about some of the things I've been thinking about around Valproate. About consultant only, specialist only, named patient only. Is there - should we be thinking about making it - having the regime of a controlled drug?

Those sorts of things are sort of - okay some of those are regulatory in nature. But some of them are - they've grown up in terms of practice and systems around how medicines are managed. I think there probably are

some things - if I can help Keith a little here - to say that could be transported quite easily I think into the world of medical devices.

The only other thing I would mention is whilst on the - with Valproate then we need to get to a point where there is no doubt. If it's going to continue to be used, then there's no doubt that the right thing has happened in terms of explanation et cetera, understanding the risks and things.

Talking to various people in another piece of work - there's this sort of phrase which people are talking to me about. Which is about knowledge dissemination. How do you put in place the type of knowledge dissemination system which will actually lead to behavioural change and what have you? There's quite - there's a lot of thinking around that and experience in - very clever academics and things in terms of how that could be done.

So, there's a - you know the Safety Bill Legislation type of approach and all of that. But there's ultimately, I think in terms of the influencing behaviour - then there's this sort of concept of knowledge dissemination is probably quite a helpful one to explore.

But in devices I think there are some things actually which could be learnt from systems which have been in place in medicines for many years. Albeit sometimes they don't work very well.

Julia Cumberlege: Can I just ask Professor Willett. How long will it take you to establish - and I'm not sure it's your responsibility now - but how long would it take to establish a really good database for?

Keith Willett: So, the work HQIP have done - is to put in as you're aware - an interim database which will - as I understand it - the last [unclear] involved with it, was to draw data from the three professional databases that already exist. As a minimum data set, to at least give - to ensure that we have the opportunity for every use to be logged. Also, for the procedures to be logged that are not mesh related but for treating the same condition.

That - my understanding is - I haven't - I don't think the final report's come out from HQIP yet but that was expected to - that was looking at whether NHS Digital as the sort of independent host, would manage that. So that in the short term the clinician's returns and how the data was submitted would continue. But that they would be able to hold something whilst a full registry was commissioned, because that has to go through a commissioning process, tendering and approvals process, meeting the HQIP standards.

That's usually a two-year process. I think it can be accelerated in part by different commissioning and contracting arrangements. But in essence it can - that's usually a two-year process. The number of national clinical audits we have is limited. That's based on the number. So, I think the money that was - the cost was about two million I think for the registry to be established and run for a period of three years.

Julia Cumberlege: I'm not talking about the registry. I'm talking about just database.

Keith Willett: So, the data. That database is there...

Julia Cumberlege: Two years did you say?

Keith Willett: No, no. The registry would be established in - well the... So, and it would be a national clinical audit registry. Yes. So, the registry would be two years. But actually, a database drawing from the three organisations is what HQIP has been asked to look...

Cyril Chantler: That's not comprehensive. That's probably only a third of all the cases.

Keith Willett: Yes. Yes. Yes. Yes. But then it's how you...

Cyril Chantler: But that wouldn't fulfil the requirements of the pause.

Keith Willett: Of...

Cyril Chantler: The pause.

Keith Willett: Of all cases being logged.

Cyril Chantler: Yes.

Keith Willett: Yes. So that would - once that's in place there. We can't mandate. We don't have the legal powers to mandate. So, we - as an organisation - can write out and we can work through the colleges and special associations. We can work through the GMC. We can work through the CQC. Everybody recognising that that is the thing to do. The strongest lever we have in the system which is what the working group came to the conclusion of - was actually the appraisal process and revalidation and the responsible officers.

Because if doctors, surgeons, can't revalidate because they haven't submitted data. That's part of their process. Then clearly that is a threat to them.

Cyril Chantler: I don't want to put words into your mouth. So, tell me I've got this wrong. But I had thought that you'd pointed out - or somebody pointed out - that

one way of ensuring that every operation is logged on a database - I'm not talking about a registry - is that it's a requirement to get paid.

Keith Willett: Well that would be something I might have said to you.

Cyril Chantler: Did I make that up?

Keith Willett: Sir Cyril. I might have mentioned that to you. That isn't government policy and that isn't NHS England policy so. But clearly, I have had success working with tariff payments in securing...

Cyril Chantler: Well actually you're not the only person who's raised that possibility with us seriously.

Keith Willett: I mean that is something that has not been used before.

Cyril Chantler: We also have the support now of the Royal College of Surgeons for new devices, such that a database should be established which would be 100 per cent accurate because the surgeons would do it themselves. You heard me say that.

Keith Willett: We've had experience of that as an incentive. The best practice tariff model that we introduced to support the implementation of the major trauma networks, major trauma centres. Also, to improve the hip fracture pathway for elderly patients - that the - with that there was 20 per cent or thereabouts of the income per patient on the tariff was penalised or rewarded whichever way you look at it. By returning the data. That payment wouldn't be made until, or sorry... the last 20 per cent wouldn't be made until that data had been entered.

That was very effective. Not 100 per cent. Nothing's 100 per cent.

Valerie Brasse: So why isn't it being proposed for this?

Keith Willett: Because the payment models have changed since then. That isn't payment.

Valerie Brasse: There's no way of doing it?

Keith Willett: Well I'm not saying there's no way of doing it. I'm not the finance director of the NHS.

Julia Cumberlege: We might not be able to do the perfect. We might try and do the best we can. So, we need a database. Everybody is agreed. We need a really robust database. But it may not be 100 per cent perfect. We understand that. How long would it take to actually get one established? Bearing in mind that you can't mandate. But at least we would then get something...

Keith Willett: Well I think that what you're talking about is a comprehensive registry. Which is the same as the national clinical audit. Which is the two-year timeframe. Which is what HQIP are working to. What the interim was just to make sure there was an opportunity that all cases could be logged. Particularly going forward because we don't want a period of time when we're not having patients logged who are going into the system because that would be really important. We don't want an interruption...

Julia Cumberlege: I thought a registry was much more complicated than just a database?

Keith Willett: Well. So, a database is just a collection of data.

Julia Cumberlege: Yes, well that's...

Keith Willett: You choose the points.

Julia Cumberlege: That's what I'm asking for.

Keith Willett: But actually the - a national clinical audit is one whereby you build in the outcomes and you build in the clinical specific things which are, some of those may be more - softer if you like - in terms of what's been done. They're more pathway orientated than just about how old was the patient? When did they have their operation? When did they next appear?

Then a registry is what you would normally attribute to just logging the implant, rather than...

Cyril Chantler: We must be really careful here, Keith. We're going to end up with not understanding each other because we don't define the terms in the same way. A database for the purpose of where we're thinking about it - it doesn't mean it's right. But the way we're thinking about it. A database is something where you create an entry into a digital database for every time you do the operation. Right? That - as I understand it - does not require, under GDPR, patients' consent to go on a database if that is mandated legally through the system.

However, you do require under GDPR patient approval to establish them on a registry. The registry could interrogate the database and would do all the other things that the registers you and I have been involved in our clinical careers over many years do.

But at least once we've got the database established and running, it's ticking. So that as time goes by the registry can interrogate it. One year, two years, five years, 10 years out.

The pause as I understood it was about - among other things - making sure that we're logging all the operations so we can interrogate them for long term outcomes when the time comes. Is that clear?

Keith Willett: Yeah.

Cyril Chantler: Thank you.

Simon Whale: Can I just ask about the same in relation to medicines or Valproate specifically? At the moment - Doctor Ridge correct me if I'm wrong. But at the moment there isn't a - we don't have a means of tracking what happens to a woman who takes Valproate while pregnant and then has a - goes on to have a baby. There is no way of tracking that. Should there be and how do we set it up?

Keith Ridge: Okay. So, as I understand it - so the MHRA are looking at that as I understand it. I think they're coming before you later in the month, I think. So, it's probably best to hold that. I - the concept of registry in this space is the same it seems to me - I know the MHRA are looking at that right now.

Simon Whale: Do you think from where you sit that that would be a useful addition to the system?

Keith Ridge: So, in order to - my view on it? In order to - if we accept that there's a risk associated with this drug, and that the regulator over - and the regulators - medicines regulators - over the years have judged that risk benefit correctly, and that prescribers - and indeed dispensers I guess - but also patients themselves are understanding of those risks, and that it's being monitored appropriately in the way you describe, then yes. Of course, you would.

But it's a - that's part of the jigsaw I guess, Simon, isn't it? That there's other parts which, all of that needs to work.

Simon Whale: Yes. In terms of the mechanics of it. If - I mean how complicated do you think it would be to create such a database?

Keith Ridge: When I look at the prescribing data which I have then and see - so I think the figure which is quoted in Sally's letter is 27,000 patients. Then it should be doable I would have thought. It should be doable.

Simon Whale: I suppose the same question arises as in the case of mesh. Should it have been done before now?

Keith Ridge: My view, when you look at the risk associated with this particular medicine, given if we're talking - well we are talking about four out of 10 women in

terms of teratogenicity, and one out of 10 being - in terms of neurological development... One out of 10 in terms of abnormality, then that feels significant to me. Therefore, being able to track that - the progress associated with people on this medicine seems important.

So, my view would be yes.

Cyril Chantler: Can I ask a question - I don't understand. But I ought to because my grandfather was a pharmacist.

[Over speaking]

[Laughter]

Cyril Chantler: When a prescription is issued on the National Health Service, it goes to a clearing house doesn't it? So, the pharmacist can be paid and some sort of...

Keith Ridge: Yeah. It's called the BSA. Yes.

Cyril Chantler: Is it at that point possible to register that I've received this medicine as a patient on some sort of [factor] databases?

Keith Ridge: So, community pharmacy is - that's what you're describing there is the reimbursement system.

Cyril Chantler: Yes, but using the reimbursement system to log that Valproate and me with my - who I am and my demographics.

Keith Ridge: Yes, is the answer to your question. So, at the moment we do have data. Looking at the subset of people, of females within a particular age group - child-bearing age and the prescribing date. Or sorry, should I call it the reimbursement data and how that is changing over time.

At the moment - I don't know if you've seen that. But it is coming down. So, the answer is yes you can. We've also done some work recently in another area to link patient number with individual prescribing. So, this is part of the work I did with the former Secretary of State on medication error.

Cyril Chantler: Using the NHS number?

Keith Ridge: Yeah. So, it is possible. In primary care.

Simon Whale: That could be done quite quickly in primary care. Because those mechanisms exist now.

Keith Ridge: Possibly. Worth exploring.

Julia Cumberlege: It's the will to do it.

Keith Ridge: Yes, there is a will. I'm quite determined [laughs]. But I've - I come back to what I said originally. In many ways Keith is an example of it, isn't he. He has clearly taken the initiative and I think it's going to require someone to take the initiative. To ensure that the intervention is working well or not.

Simon Whale: Do you think it should be the Chief Pharmaceutical Officer?

Keith Ridge: The Chief Pharmaceutical Officer would be willing to do it, but I think whether that's the most appropriate thing or not, I don't know. I guess that will come in due course. We have a new Patient Safety Director as well. One would imagine that wherever it says a - you know a problem with that sort of thing, its just - it's pretty obvious that we need to be clear.

Julia Cumberlege: Professor Willett, can I just return to mesh? Again, thank you for what you've been doing. I appreciate you've been working extremely hard in this field and that you no longer have the responsibility. So, this may be an unfair question. In which case just tell me. But, can I ask you how you see the future of the pause. Where we are on it, and any other comments you've got on it?

Keith Willett: So, I think the pause has been very effective. We have clearly seen as a result of - and I'm grateful for everybody that contributed to that from the clinical arena and around describing what was a patient appropriate and clinically sound way to introduce the pause. With both the restriction and the high vigilance. Because that allowed us to do something.

It also allowed us to test something I think that may allow us to take it forward. In that the high vigilance - so even if we perhaps have - in terms of what has been achieved in terms of meeting the requirements of the pause - we have an opportunity to maintain the high vigilance process in place. Which I think is quite useful. Having now established. It's been accepted. In fact, was recommended by the profession. I think that has been very useful.

I think we can [unclear] that. It's a bit like I said about the reference centres when a new device comes in. It's like they should go into a high vigilance process. In a certain number of centres, for a certain length of time. Then when people are comfortable that this looks right, you can go back to the normal sort of process. So, I - clearly, we're dependent on the NICE Guidance publication. We're also dependant on HQIP with reports coming out.

So, they're all going to come out at the same time. There just needs to be a rain check at that point taken with your recommendations as to how this now sits. So, for me I think this has been a useful reflective period. There's a lot of things have gone on. We've got those things coming. We'll have your position from the Review. We'll have the HQIP. What it takes in terms of the database registry. National Clinical Audit. We'll have the view from NICE.

So, we will have sort of a - I think there's a point in time where we will sit down and say, okay, so now what's the right and proper thing to do to take this forward? What is - is there a role for mesh? What is the role for mesh? If there is a role for mesh, how is it scrutinised or whatever.

I think that is the right thing to do. I don't think I can - until I have seen all that and that's been put down and thought about - given the context of what's gone on. I don't think I will be able to give you a view as to how it goes forward. I would imagine though that there will be a case for some ongoing use of mesh in a highly restricted and monitored capacity which will be part of it. Clearly, I believe Specialised Commissioning for NHS England are going to give evidence to you as well.

Another part of the working group was obviously to ensure that we set up the centres and commissioned the complex gynaecology centres who would address the complications of mesh. Because that clearly was something where the system did let patients down. Because a lot of people didn't realise that the problem was mesh. Didn't realise that removal was an option. We certainly didn't get referral patterns right there.

So, I think that also will have been addressed. I think we'll be looking at a bit of landscape to be quite honest about it. I think it will be sensible at that point for everyone just to sit down and reflect on what is the next step forward.

Julia Cumberlege: So, in the meantime it will stand as it is now?

Keith Willett: Well, I think it does - it stands until those are completed. I don't think there's a problem with that. I think the system has got used to it. We asked the numbers from the - in fact the figures are due out today I believe from NHS Digital or in the next month. I haven't seen it yet. But I think the numbers of - the number of episodes of mesh being used has continued to sort of decline steadily over that period.

I think we're seeing now a much more highly selective group of patients. That may be the appropriate - that appropriate group. The number of removals has stayed about the same. We're not seeing any rise in the

number. So, we're still - it looks like we're still addressing those that have - are coming forward with problems from the past.

Valerie Brasse: Are we making bigger inroads into what's happening in the private sector? Do we have a [unclear] on that?

Keith Willett: So, we - as part of the NHS we don't have that. So DHSC remit in terms of private sector. But clearly you didn't expect me to ignore them. So, I did meet up with all the medical directors of the major private companies and hospitals. In fact, I would say they were very, very keen to ensure - and I'm sure for lots of reasons - reputation as much as anything else for commercial organisations - that they put in place the responsible officer role, ensuring that the surgeons were returning data.

We've seen that before. We saw that in the hip registry. The hip replacement registry. The independent sector was right on to that very quickly. My understanding is the same has occurred this time around.

Sonia Macleod: One of the things you've just said is that removal rates haven't changed substantially. But we've heard from quite a few women who say they have difficulty accessing removal services. So, is the removals rate actually reflective of the number of people who want their implant removed? Do you have any...

Keith Willett: I can't - I have no figures on that.

Sonia Macleod: Okay.

Keith Willett: So, we wouldn't know those figures. Specialised Commissioning may do because obviously that removal now fits under the Specialised Commission Complex Gynaecology Contract. They've gone through the consultation process on that. That's closed. They're now identifying the centres.

Simon Whale: One of the other things that we would need to ensure is that surgeons are able to offer women an alternative form of surgery to mesh surgery.

Keith Willett: Yes.

Simon Whale: Obviously one of the things that's happened since the growth in the use of mesh is the decline in Burch Colposuspension and other alternatives. Therefore, a decline in the knowledge and skills out there to do them.

Keith Willett: I'm not sure it's a decline. Mesh has been around long enough now that most practising surgeons who were not trained in any other technique.

Simon Whale: So, what do we do about that?

Keith Willett: So, that was why I brought in the high vigilance process in to the alternative operations as well because the last thing we needed was the mesh complications being diminished and then us having a whole lot of new complications of equal magnitude or worse. Because people were trying to do operations that they hadn't done previously.

So, there is then a [unclear]. So, which is why I think this - there's a pause at the end of the pause as it were. Everyone says, right where do we go? Because if we're now talking about changing competencies, we're talking about new training programmes. You know, there are still surgeons around who can do those procedures. But they're technically very difficult. I mean, I am a pelvic surgeon. But not for gynaecological reasons. The tissues in an older person - and not necessarily very old - but in an older person. Some people - we're all just as much different on the inside as we are on the outside.

Some people have really poor tissues and with the best will in the world, trying to do an operation to reconstruct tissues is just not possible. In fact, the colposuspension procedure, actually you generate all - you almost create a mesh with - rather than polypropylene with another form to - which is what was the colposuspension operation is not actually a million miles away from it. Because - and then what happens is the anchorage in that tissue fails.

The same thing applies to the - things like retropubic sling where you're using fascia. You know, if the fascias pull down in the pelvic floor, it's usually pulling the abdominal wall. The tissues - and because they're natural tissues they decay or are broken down, they lose their strength and so they become incompetent. Which is why you can understand why tape came in in the first place. Because people were struggling to give patients the sustained outcome that they wanted to give them.

Simon Whale: One of the points that's been put to us about colposuspension though is that it was - and could have continued to be - an evolutionary technique. But that mesh got in the way of that?

Keith Willett: Well mesh was the evolution really. It sort of took that sort of - it was - in colposuspension you're almost sort of building like a trampoline of suture material on to the tissues that were good to hold the pelvic floor. I mean I'm not a gynaecologist so I'm - if this is being videoed and watched by gynaecologists they'd be - I'd be getting numerous letters I'm sure. But the - so mesh was the sort of the obvious way to do it. Rather than make lots of sutures. Let's put a mesh there. Which essentially does it. Tie the mesh in so we've got the inherent strength and more anchor points.

So that was the logic. So, it was an evolution. You know, the evidence around biological alternatives - and I mean by - sorry biodegradable alternatives. The evidence for that is - you know, quite clear from NICE. That only really should be experimental at the moment. Because they appear not to have a sustained benefit. Because you're not trying to just do something temporarily and then it's going to be fine. You're actually trying to build an architecture that will last long term.

There are two ways you do that, either with inherently the strength within the mesh itself or in the reaction to a foreign material which is what you get which creates scar tissue. Which is a good form of creating an alternative layer of tissue. So, that's why it came in. I can't give you an idea as to whether a colposuspension would evolve in a different way if mesh hadn't come through. I just don't know. Not my specialty.

Julia Cumberlege: Can I go back to the beginning.

Keith Willett: Please.

Julia Cumberlege: Where we were talking about mesh and patient groups. I mean, one of the things that's come out so strongly is that patients really do feel that they're not being listened to. We've heard of individual cases where surgeons have been totally dismissive of the women's worries and concerns. So how do you in the future ensure that the patient voice is heard, and that people take it seriously? I have to say there is also a gender issue here as well that we've come across.

But I'm not going to go into that because I could be here for two weeks talking to you about that. But I'm not going to. I just really want to know how can we ensure that the patient voice is heard, respected and actioned?

Keith Willett: That's why - so you know you're balancing this cohort of patients who have a problem. These recorded numerical complication rate that some study has shown versus that collection of individuals who've had a devastating effect. That's a really difficult one to - so we have to create a model. I talked about what we put in as an alternative. That's got to be one which is biased towards the patient.

We have to give the patients voice. Because the patients may not be as articulate. They can certainly be bamboozled by surgeons and by regulators and by everybody else. But also, they are - they have a betrayed trust. Already. That makes them often very reluctant to step forward into those arenas. So, I think it is very difficult. So, you have no choice. But I think to

intentionally bias the patient voice to be heard. Which means you have to create a structure in which that is prominent.

It's almost like you have to have an evidence to disprove the problem rather than prove the problem. I don't quite know how you do that. particularly given it's such a number of things and be - given the longevity of the problems. Because you may have just - literally just a few things in the first few years. Then suddenly you start to get the problems with metal on metal hip replacements. You know, batteries failing in pacemakers. You know, we've got - there's a list out there aren't there?

So how you describe something that encompasses all of those, I do think is very difficult. It probably needs a lot of people to do a lot of hard thinking with as many inputs as possible. I think the - you know, what we've gone through with Valproate and with mesh has got us some way forward in doing some of that thinking.

Simon Whale: But I think one of the consistent messages that we've heard from other people that we've spoken to - and this applies to Valproate- affected families as well - is that they have had to fight to be listened to and to receive the kind of care and support that they need. In some cases, they fight but they don't get it. In some cases, they're lucky enough to get it. But it is almost a case of luck.

Keith Willett: Part of that was lack of information and ignorance on the clinician side. That there even was a problem. That this could be. Hence the work we did on the GP communications and sort of - you know, informed consent. So, there was a big - but I can't believe any gynaecologist or urologist out there now doesn't know that there is a potential problem. There's a whole series of complications that can be attributed to mesh.

Simon Whale: We are - we're told every time we speak to women affected by mesh [unclear] that some of them are still today currently battling against denial from their surgeon.

Keith Willett: I'm mortified to hear that because I just think the amount we've done. How that is the case I struggle to understand, because anybody who cares for their patients - you know, none of us want our operations to go wrong. None of us want to see complications. It does require a bit of bravery to stand up and say, it's gone wrong. I'm really sorry. But you know, we've all been there. Things do go wrong. We try desperately hard and we have to learn from it.

But to not be aware that those complications could now occur and be attributed to what's gone on I think - or even if you are not to then refer

the patient on for a second opinion if you generally believe where the patient is clearly seeking that advice, I think is poor. Very poor. So, I think we have to bias the system in the patient's favour and then disprove - if you like - disprove that there's a problem rather than the other way around.

So, I think the idea that we can do something around that. But that really sits within that [postmark], it's surveillance, regulatory responsibility I would argue as the home. As part of the safety structure within the NHS.

Sonia Macleod: To do that, the patient has to be aware of the implant they've had, and they have to make the connection between the implant and the symptoms. So, it always requires the onus being on the patient.

Keith Willett: Yeah and that's really difficult. I don't know whether you were listening to the news but there was the whole issue in the news last night about white goods catching fire and the recalls. We buy the white goods and apparently less than a third of the registrations are completed by the public. This is white goods. You know. It's only - all they have to do is literally you know, send a card off in the post. Which is a free post or go online. We don't do it. Then when the manufacturer has a problem and wants to recall them all, they can't get hold of them.

So, you know. That's - how we do that. Because we'd all love to say you know patients should own as much of their care and responsibility as possible. But in reality we're going to have to have a symptom prompt. So, for me things like the scan for safety we talked about earlier. That barcode says on this patient. So, when that NHS - sorry when that NHS number appears in general practice anywhere, somebody knows that patient...

Cyril Chantler: It's logged centrally. Not just in the University of Leicester

Keith Willett: Correct.

[Over speaking]

Valerie Brasse: Can I just ask is there - I think we talked about this before. A sort of BME dimension to some of what we're trying to do - or you've been trying to do. Both I'm thinking about the Valproate and you've got the mesh. But just broadly about how to reach harder to reach groups.

Keith Willett: There's bound to be. I would say. Any harder to reach group - and it's not particularly BME. It's you know - it's vulnerable individuals in society. Always a real challenge. There we are reliant very much on the system being the spotter of where the connection might need to be made,

particularly where it's people who are often not registered. They don't have registered GPs. They rely on using A&E departments.

We can do this for child protection. Very well in the acute sector. Anywhere you appear. If you're on the register, the flag goes up. GP systems actually have very good flagging systems. Although they flag so many things.

Cyril Chantler: That could take years. By the way, the child protection [unclear]. That took 10 years.

Keith Willett: Yeah no. No.

[Over speaking]

Keith Willett: So, seven years is not too bad.

Keith Ridge: Prescribing generally you do see variation like many other things. Across the country. But in terms - I'll give you an example. The use of particular types of medicines in more deprived areas. You do see differences. One wonders what the explanation is. I think just to say on the sort of - on Valproate specifically in terms of patient engagement and you're obviously aware of the group that the MHRA and others [unclear] met yesterday. I understand there's an ongoing discussion. But I would be - given how long Valproate's been on the market, then if a consultant neurologist doesn't know the issues associated with Valproate, I would be very surprised.

But I guess on the other side of that coin is you would - you sometimes feel that the risk associated with this medicine - which is considerable - has sort of become engrained into practice. Engrained in to practice over the best part of 30, 40 years.

My understanding - given the nature of epilepsy for example and what it would mean to people as individuals - practically and otherwise to have controlled epilepsy becoming uncontrolled. My impression is that there are some aspects of the use of Valproate which clinicians find also helpful. For example, the sedatory sort of element of it and what have you.

Then I think it's a sort of - it becomes a sort of - you begin to wonder just whether it's such engrained in practice that the regulatory decision I'm sure is always right. But you start to put in place a range of mechanisms. Now we're into the Pregnancy Prevention Programme. At what point do you sort of say, well actually we need to go to the next stage. Whatever that might be. So that's where the - where I am.

Simon Whale: I think one of the problems with the Pregnancy Prevention Programme we've certainly heard is that neurologists will tell us that they don't feel comfortable talking to women about contraception. GPs on the other hand - if you ask a GP [unclear] they feel that that is the job of the neurologist. I don't know where the pharmacists sit in that.

Keith Ridge: So, the pharmacists should be - as you all know - they should be discussing each time that Valproate is dispensed with the patient. Even if - I think the CCA work has shown something like 40, 50 per cent of patients aren't actually collecting their medication if you see what I mean. It's someone else collecting it for them. All the difficulties that that sort of leads to. But they should be discussing.

So, I - you know, it is disappointing to hear that and hence my sort of thing about there's an intervention that's been designed. We need to check whether that is working or not. If it's not working to put in place the measures that need to make it work.

Sonia Macleod: But in terms of looking at the intervention. I mean, with the Pregnancy Prevention Programme, it reminds me of the Accutane programme in the US. The smart programme which consisted of various similar sort of system to manage Accutane related teratogenicity. It was again stickers on boxes. Negative pregnancy tests. Pharmacists. Everyone had to agree to two forms of contraception. It frankly didn't work.

Now that was put in in 2002. They then switched in 2006 to a new online system the FDA approved. I just kind of look at it and say well, if other countries have done something similar and found it didn't work, why do we not seem to be learning from that example? Why are we sort of putting in place something that looks very similar to what they had? Rather than moving on to a system they've now had in place for a decade. Which actually hasn't been as effective as they'd hoped it might.

Keith Ridge: So, you have a point. I think you know that's - I think from - as much for the regulator as for the NHS to respond to. I guess I'll say it again - where I've got to in my mind is, we need to check whether the intervention is working. Given the nature of what we're dealing with.

Keith Willett: I wonder if I could be excused. I have another meeting to get to I'm afraid.

Julia Cumberlege: Right, okay.

Keith Willett: I'm very happy to take other questions by written if you - if you have any other for me.

Julia Cumberlege: I'm just going to ask my colleagues if they've got any more questions.

Multiple Speakers: No.

Julia Cumberlege: Thank you so much. Thank you both very, very much for coming and thank you for the work that you do do which I'm sure you don't get much appreciation but it's certainly - we value the work that you do. So, thank you for that.

Keith Willett: Thank you. Appreciate it. Thank you.

END OF TRANSCRIPT

27th February 2019

Session 1: Medicines and Healthcare products Regulation Agency (MHRA)

START OF TRANSCRIPT

Julia Cumberlege: Okay, so if I could just remind you that we are videoing this and I hope that's all right for you. Because the one thing we've been very, very, very keen on is that we should be very open and transparent. There's been a lot of fear about, there's been, I think, a few myths and other issues, but we have been very anxious that the patient groups should really know and see and hear what we're doing, so nothing is hidden. Nobody can come back to us and say well, we didn't realise, et cetera.

So having taken the evidence from you, the written evidence, having had one session on alerting systems, we now want to go wider, as I say. So it would be very helpful for us if you could just say who you are, your name and your position in the MHRA, because this needs to go onto the video so that the patient groups and many, many others, when they're watching this then can picture what's happening. Then I'll introduce our colleagues around the table. So if you'd like to start.

Ian Hudson: Hello, I'm Ian Hudson, the CEO of the MHRA.

June Raine: I'm June Raine, I'm the director of vigilance and risk management of medicines at the MHRA, responsible for monitoring safety of medicines in clinical use.

Jane Woolley: Hello, I'm Jane Woolley and I'm a unit manager within the benefit risk management group.

John Wilkinson: I'm John Wilkinson, I'm director of devices at the MHRA, responsible for all aspects of regulation of devices in the UK.

Sarah Morgan: Hello, I'm Sarah Morgan, I manage the benefit risk management group which is within the vigilance and risk management of medicines division at the MHRA.

Julia Cumberlege: Right, thanks very much and I think you've got an observer here today, so welcome to you as well. So I'm Julia Cumberlege and I've been asked by the former Secretary of State whether I would undertake this Review into the three items that we've just been talking about. On my left is Sir Cyril Chantler and he's the vice chairman of the Review. The third member of

our panel is Simon Whale and Simon has been concentrating particularly on communications.

Then, of course, we need good people around us and so Valerie Brasse, Dr Valerie Brasse, is our secretary and Sonia Macleod, Dr Macleod, who is our senior researcher. So, if I could start the questions, if that would be all right, or is there anything you want to say first?

Ian Hudson:

If I may, I'd just like to say a few opening remarks, if I may. First of all, to say thank you very much for the opportunity to give evidence to this very important Review, we're very much looking forward to seeing the conclusions at the end of the Review. We and everyone else are very keen to ensure that patients get the right products at the right time with the right information, so informed decisions can be made. I and my colleagues have been very moved by the testimony from patients who've been affected by these three interventions: mesh, valproate, hormonal pregnancy tests. I started my professional life working in paediatrics actually and prescribed valproate to children with epilepsy.

I find these stories very moving and appreciate the challenges sometimes on deciding on treatments at the individual patient level. I think this is very moving testimony from the patients, as what the three interventions have in common, although scientifically the issues are a little bit different between them.

I did want to make, if I may, six points in relation to work that's going on in the agency that's relevant to the Review. The first really relates to patient input, but within the MHRA we have to make objective, evidence-based decisions, taking into account the totality of the evidence available to us. We weigh up the risks and benefits in reaching that judgement and get expert input from independent advisers in doing that. But patient evidence is part of the totality of the evidence that we will consider and indeed, patients can be very helpful in helping us put into context some of the evidence that we receive.

Within the agency we've got quite a number of mechanisms already for ensuring patient input into our work, whether it's open board meetings, whether it's lay members on our advisory committees, or our patient group consultative forum, or the meetings we have with various patient stakeholders. Or we may consult patients, we have consulted patients, for example, when we want to promote the yellow card scheme, to get their input into that.

We recognise - I and the senior leadership team within the agency have been discussing this on a number of occasions, including board discussions. We recognise we need to do much more in this regard and really are planning a much more systematic approach to ensuring patient engagement in our work. That includes better support internally for our staff, in terms of being better able to do that, but also horizon scanning, identifying areas at an earlier timepoint where we want input from patients and identifying issues perhaps at an earlier timepoint so we can discuss with them. Then really much more systematic approach to patient engagement.

The second area I wanted to cover was really the cross-system working. Our role within the MHRA is the regulation of products, not people, not healthcare assistants, so we need to work closely with others across the healthcare system to effect change when there is an issue where change is required. Now, we already do quite a lot in terms of cross-sector work. We have regular meetings with many different players, whether it's GMC, General Pharmaceutical Council, NHS Improvement, the NHS, the safety officers and Trusts.

We do a lot of that, but we recognise that there's more that needs to be done in that regard and really to understand the levers to how to make things happen across the healthcare system. Some of these levers, or many of these levers are not within the control of MHRA, but we have to understand these levers and work out how we can, across the system, work together to effect change. I think whether we get into - I'm sure we'll discuss this later, but as our, or National Patient Safety Committee or something like that, we must really focus on this area, I think and improve its effectiveness across the system.

The third area I wanted to touch on was transparency and openness. The agency is committed to transparency and openness and I think has come a long way in this regard, but also recognises there's more that can be done. We're very keen to be as open as we possibly can be. We've done a lot in terms of our communication, social media, we've talked about the patient groups. We'll also be pushing for much more transparency through regulation or indeed voluntary agreements internationally and things like device incidents, making sure that they're available at an earlier timepoint.

The fourth area I wanted to touch on was regulation itself. Regulation has changed considerably over the years since some of these interventions were first introduced. Regulation will continue to evolve, regulation should follow science and clearly, as we move into the future, will continue to change. I think we'll have far better tools in the future with things like

more registries, databases, artificial intelligence tools, et cetera, to be able to mine databases such that we have better information at an earlier timepoint to be able to make informed decisions.

The fifth area was to say that the agency strongly supports innovation, but safe innovation, for new products to be developed, brought to patients for the benefit of public health at an appropriate time. But balanced with that has to be appropriate monitoring, appropriate safety, such that innovation can be introduced safely into the healthcare system.

Finally, I wanted to mention that we must work with our colleagues internationally. Many of these issues are international in nature, the same drugs and devices are used internationally. Indeed, in the European Union context things like valproate have to be handled through the Pharmacovigilance Risk Assessment Committee of the European Union. So we do have to work closely with our European colleagues.

So really that's all I wanted to say by way of introduction, apart from to come back to at the end of the day we're here for UK patients, to make sure that they get the right products at the right time, with the right information. If things do go wrong, to react promptly across the system to make sure appropriate action is taken, including listening to their voice. So that's all I wanted to say by way of introductory remarks. I don't know, June, I think you wanted to say a few introductory remarks as well.

June Raine:

Well, certainly to echo your thanks to the Review for enabling us to focus on valproate and Primodos hormone pregnancy tests. I've mentioned that my role involves monitoring benefit risk in clinical practice and the challenges around that we'll no doubt delve into. But as Ian has said, things have moved on very substantially with the availability of real-world data and better methodologies for doing analyses to get robust results from that data. Ian's highlighted the role that patients play at every stage in this, when we consult our Commission on Human Medicines patients are there.

If we need to set up an expert working group, as we'll be talking about with HPT shortly, the patient voice is heard throughout at every step and that is integrated into the decisions that are made. So it's a challenging process, integrating all available data. We rely on our independent expert advisory committees and clearly they advise ministers who take a decision. Ian's mentioned the European nature of the regulatory framework we operate and the need to ensure that Europe also is involved in some of the important decisions and we'll no doubt talk about that in relation to valproate.

I think overall, the key issue is that when we have a robust regulatory position, moving that into action and into clinical practice is something we're really looking to the Review to test our thinking on. Yes, we involve the clinical leadership, the regulators and bodies involved in compliance. But what it really takes is for all of those to work consistently together and we do have some examples of when that coordination and consistency has been achieved, then we achieve prompt action. So I think the models of success should, I hope, involve our lens as we look at where we are now with the important products you're considering in the Review.

Ian Hudson: I think, John, you wanted to comment.

John Wilkinson: Yes, I just wanted to pick up on the evolving regulatory system, particularly in the devices area. The regulatory system's evolving very rapidly. It's worth bearing in mind that the regulations we are using at the moment were first generation European regulations, brought in in the early '90s and clearly they were really due a substantial review and upgrade. That indeed has been happening. That said, we haven't sat on our hands in that period and the agency's been driving a number of changes in the European system, along with other colleagues around Europe.

But even under the current legislation, we've introduced joint audits and notified bodies. There was variability in performance in notified bodies. They are supervised nationally and by definition, nationally supervised bodies might suffer from variability of interpretation rules and inconsistency of performance. So that's changed and we've now a joint audit scheme which involves both European Commission and several member states simultaneously. The other big area that we've moved forward is around clinical evidence and evaluation and it was fourth generation guidance there, which is substantially different from the guidance and expectations that were set in place at the start.

Both of those are being consolidated in new regulations, which as you'll probably be aware, come into force in 2020. They also bring substantial increased obligations on both manufacturers and ourselves in terms of monitoring performance of products in the market. So a number of the frameworks that we introduces in '93, '94, are being underpinned with much more substantive and substantial measures to ensure that products are tracked and their performance monitored in practice. I think the other piece, which we've already alluded to I think in our previous visit, was around transparency and (1) there is going to be better transparency of clinical evidence.

But sadly the new regulations didn't go as far as they might have done in terms of transparency around adverse events and other issues, which we're pushing to change. So I think broadly speaking, the legislation is changing. We, in the background, have been working on something that's highly pertinent to the meshes case, which is around data acquisition and high-quality data, so that we can compare the performance of products and indeed, interventions across the system.

So we were heavily supportive of Scan4Safety and the introduction of UDIs, unique device identifiers, which allows you to electronically connect patients and the products that might have been put into them. We've been working on global standards in that area so that we can pull data internationally. Clearly in a digital age there's lots of scope for exploiting new data sets which previously were less than accessible to us. So that includes registering this information into the registries and getting it out in useable form to help us in informed decision-making.

So specifically in relation to mesh, I think that whole area about relative outcomes and relative performance of part of the system has been particularly challenging. These are complex, often very debilitating conditions with complex presentations and the picture is far from clear. That could be clearer if the data that we were able to accumulate and analyse would help us make decisions in the future in perhaps a more timely manner than we have done in the past. I'm talking about the system as a whole when I say that.

I think the long-term implications of all implants are issues of considerable concern. One never knows how any intervention is going to perform over very long-term periods unless you test them for 50, 60, 70 years and of course, that would exclude their being available. So I think monitoring the performance of particularly implanted products needs to be enhanced in the future.

So I think the final thing I wanted to say is that we have extensively interacted with, as you're aware from the evidence, a lot of inquiries, clinical expert groups across a period of time. Largely, the advice we've received has been substantially consistent, but there is a place for these products in the patient pathway. But the monitoring of performance, I think, needs considerable improvement. Thank you.

Julia Cumberlege: Well, thank you very much indeed. If I could just pick up one or two things from your presentations, I just want to say on data acquisition we are, are we not, entering a whole new era now, where we're going to be able to get much more information. It'll be technological and people will be able to

assess much more clearly the trends and what's going on. But a comment was made to me by a patient yesterday who said to me 'data is important, but please don't forget in our case there are children involved. It isn't data; it is people, it is children'.

So I want to go on then to the patients and I do understand and I think, if I may say, you're very slow in the game on this one, but never mind, you clearly want to do things differently in the future. But I'm very conscious that although I'm sure you have extremely good patients on your groups and they listen and they give you advice and everything that they feel that you should hear, but my experience over many years in the National Health Service is that you get the favoured child, you get the favoured person. You get the person who actually in the end is not perhaps as decisive, is not questioning, because they get encompassed into the organisation.

So just looking at what happened in Scotland on their review, certainly that ended in great difficulty because they only had two patients on the group. What we have done - and I really do recommend it and we've done it in maternity services as well as with this Review - we really need to go out and listen to a lot of people. It isn't just the ones you trust; you have to hear all the story.

I hope that in the future you will actually do much more of that, because that is what has come through so strongly to us. It is not just one or two people who are very well-informed and I have to say the patient groups are - they do a lot of research, extremely articulate, very good, but actually you also need to hear from a whole range of people. So I hope that's something that maybe in the future you might consider.

I just want to ask you about one of the issues that certainly patients have brought forward to us, is about how much you are in the arms of the manufacturers. There really is a feeling about that, that you are hugely influenced by them. One of the things that clearly we would like to know is really how much the MHRA is funded by manufacturers. Also, if your funding is from the pharmaceutical and the medical devices industries, should you not have a conflict of interest register, which other organisations do have, not least my own, which is the House of Lords.

Ian Hudson:

If I can answer the factual element of how we're funded and then we can talk a little bit about conflict of interest and how we manage that. Funded - we operate as a trading fund as the agency, where we receive money from a variety of different sources. On the medicine side, we are virtually all funded through the pharmaceutical industry, that's correct.

But on the devices side, we are 95 per cent funded through the Department of Health for the work we do on devices. There's some funding for clinical trials and inspections of notified bodies, but the vast majority of it comes from the Department of Health. This is a model that many of our similar bodies around Europe and other regulated sectors also follow that the regulated pay, but certainly the device side is more direct government money.

We have very stringent conflict of interest policies and we use external experts a lot also, who don't have interests in the particular companies or products as well. So all our staff have to complete annual declarations of any interests. None of our staff can hold shares or have financial interests in the pharma or devices industries. We do employ people who come from industry, but then they can't work on that company's products or related products for a period of some two years. If they've been particularly closely involved in a particular product, that goes on indefinitely.

I think it's right that we do - we are able to employ people from industry, because we need the expertise to be able to do our job. But it is a very strict conflict of interest policy in terms of what we do. Similarly, we have external advisers through the Commission on Human Medicines and its underpinning external advisory groups. On the device side, a device expert advisory committee, again very stringent conflict of interest policies here.

The CHM, for example, won't allow any interests in the pharma industry in the expert advisory groups. People who might have relevant interests can't participate in the subject under discussion or competing interest. So we work on the basis of managing those interests, rather than excluding completely anyone coming from industry, et cetera. That, I don't think, would be right, but we do manage them very carefully.

Julia Cumberlege: I think that is encouraging, but these conflicts of interest, are they very transparent? Are they on websites? Can patient groups, individuals get hold of them and know exactly who is paying for what?

Ian Hudson: Certainly the funding of the agency is entirely clear in our annual reports and accounts, where it comes from, the different sources, that's clear. Things like our advisory committee structures are the members of CHM, for example, that's all in the public domain in terms of their conflict of interest and the policy there. So yes, that's all available.

Julia Cumberlege: That's encouraging. Can I just ask you a very general question, then I'm going to pass onto my colleagues. Who are you accountable to?

Ian Hudson: I personally report to the Permanent Secretary, in terms of my reporting relationships. I also have a board within the agency and I have a dotted line, if you like, to the board, but a formal accounting relationship to the Permanent Secretary.

Julia Cumberlege: Right, so do you meet regularly? What is the relationship like between you and your accountable organisation, which is clearly the Government through the Permanent Secretary?

Ian Hudson: Yes, well the agency is an arm's-length body of the Department of Health. There is a sponsored team within the Department of Health and one of the director generals there and directors underneath that who are responsible for us from an agency point of view. We have a huge amount of interaction between our sponsor team and the agency on an ongoing basis. Yesterday we had our quarterly accountability meeting with our sponsor team, where we go through issues, et cetera.

I meet with the Permanent Secretary regularly. I also meet with the Chief Medical Officer regularly. I also meet with the devolved administrations' chief medical officers and chief pharmaceutical officers regularly. But formally I have an appraisal with the Permanent Secretary once a year, but I meet him in between times, but the day-to-day stuff is done through the sponsor team.

Julia Cumberlege: Right, okay, thank you very much. I'm going to then pass on to Cyril.

Cyril Chantler: Thank you. Can I say I welcome your opening statement, because it dealt with a number of issues which have emerged and which you've clearly been thinking about. Just to emphasise it, because last time I think I mentioned, it's been a great concern that three things have gone really quite terribly wrong and people have suffered. Yet it's required the patients and the politicians to bring it to the attention of the system. My profession hasn't brought it to the attention of the system, the system hasn't acknowledged it, so there is something we've got to go away and think about there.

One of the bodies that gave evidence to us, the Epilepsy Society, said I think it would be right of you to consider whether medically qualified professionals gave sufficient weight to information provided to them in part, because this source was from non-medically qualified people. How do you respond to that? Do you think the system and the profession have not given adequate attention to what they're getting from patients?

Ian Hudson: I think the three interventions are a little different, but I think as I said in my opening statement, what is common is this deeply moving testimony

from patients across all three. I think that's right, I think we do going forward have to make sure across the whole system we do more to listen to patients. Certainly on valproate, I know, June, you've said to me that when we - early on when we were meeting patient groups, they really brought the neurodevelopmental delay home to us in terms of what it actually meant in terms of a figure of IQ on the scale versus actually what this really means for a person affected.

Absolutely we've got to do more of this, absolutely we've got to listen to patients more as part of the process. We've got to look at the totality of the data, of course we have and we've got to weigh up the risks and benefits, but absolutely the patient voice has to be heard, because it really can bring it to life what it actually means for someone.

Cyril Chantler: You mentioned the notion of patient safety, SAR, in your interests. Is that because the MHRA really relates more to the manufacturers and the industry, rather than the patients? Do you feel there's a gap there?

Ian Hudson: No, I don't. It's more because - and indeed, I look at the people in the agency, many of whom have got a healthcare professional background, physicians, pharmacists, et cetera and really the motivation for people working in the agency is to do the right thing for patients and the public. But the question - I think the challenge for us all is how to effect things across the whole system so that if an issue arises, how to make sure it happens across the whole system such that action is taken. So when a patient sees the doctor, they have the appropriate information, the appropriate conversation and action is taken at that level.

So what I'm really thinking about is what are the mechanisms for joining up the different players in the system such that we can act in a coordinated way, such that if we identify an issue, we are not the person sitting in front of the patient when they come and see their doctor. If it's an epileptic, deciding on whether to prescribe valproate or not. But to make sure that the system is joined up so that action is taken. So it's not so much our way of facing, it's much more joined up...

Cyril Chantler: When we had a meeting about - which we'll come to later on today - about registers and the pause, I asked a question at that meeting around what happens if there's a concern about a product. Do you raise that with the patient agencies? The answer I got, which I may have misunderstood, was that no, the MHRA can't do that. They have to go to the industry and talk to them about it. I said well why don't you share it with the patient, I understood them to say well no, that's not what we're allowed to do within the law.

Ian Hudson: Well, what we are able to do and what we will do - and it's a little different, the legal situation for medicine devices, but we take safety issues from patients through the yellow card system and I think are they the single biggest reporting group now, patients above health, certainly above GPs and doctors.

Julia Cumberlege: Is this the yellow card?

Ian Hudson: Yes, through the yellow card. We will take reports of issues from patients. We have on a number of occasions over the years in both - well, many occasions of valproate and also mesh, met with patient groups and HPT as well, met with patient groups to talk about the issues, get their involvement.

If we identify an issue, we'll want to look at the totality of the data. Totality of the data, yes, we'll go to the manufacturers and say 'could you tell us about what you know about your product and safety information?'. We may also look at literature reviews from wherever they come from. We'll look at the yellow cards which will come from patients or clinicians or pharmacists or whoever they come from. We'll look at the totality of the data, we'll then consult with our external advisory groups as...

Cyril Chantler: If you had an issue which wasn't about whether the device itself was properly manufactured and safe, but its use in the system and patients were in any form at risk, what would you do?

Ian Hudson: We would talk to - I think it depends where it's coming from, but if we're aware of an issue with a particular device...

Cyril Chantler: It's coming from patients?

Ian Hudson: It's coming from patients, but I think then we would then need input from a range of different people and then to discuss with a range of different people. That would, yes, include the manufacturers, it would also include the professions, the surgeons, for example, if appropriate. To date we have met with patient groups in some of these areas, but this is an area that we plan to do more systematically for issues at an earlier stage.

But we have met early on with Meshies United and patient groups there, but we will do this more systematically. But we'll talk to whoever we think is necessary to discuss the issue, decide who needs to do what and then provide advice. That may be joint advice between ourselves and the profession, or it may come directly from us, it depends what it is.

Cyril Chantler: Right, well perhaps we can return to this when we talk about mesh this afternoon, because it's particularly relevant there. Can I ask you one other question? You will be aware that *The BMJ* at the end of last year carried an article from the society of investigative journalists about lobbying to block European safety checks of dangerous medical implants, and Simon Bowers wrote a report. What's your view of that?

Ian Hudson: Well, I think the devices regulations have evolved over time. We've had a set of regulations that have been in place for quite a number of years. We've renegotiated and there came into force a whole new set of regulations in 2017 that are in a transition phase, coming in. They address a number of areas where regulation needs to move on to deal with new approaches, new technologies, need for further, greater vigilance, et cetera. So I think the new regulations address many of the areas that have been highlighted as concern by us in the past. So we are in the phase of transitioning to those new regulations. I can go through what some of the changes are, but it's not...

Cyril Chantler: The particular point, as I understand it, is that actually lobbying has actually interfered in some way with the process of approval and non-approval of medical devices.

Ian Hudson: I'm not aware of that, Sir, at all.

Cyril Chantler: You're aware of the paper?

Ian Hudson: I'm aware of the paper, but my experience within the agency is we've always taken a data driven approach, we've always then a scientific driven approach with expertise as required.

Sonia Macleod: I don't think it was criticising you; I think it was saying that when they developed the new regulations...

Ian Hudson: Oh, I see.

Sonia Macleod: ...the lobbying made an impact on the shape of the regulation.

Ian Hudson: Well, of course industry - the regulations went out for consultation, of course, industry would have had a view, but in fact it was - many aspects of the regulation are things that we, UK, have been wanting and pushing for, for some considerable period of time. So of course industry will comment on the regulations, other groups also are expected to comment on the regulations. But these are areas where we've been pushing for some considerable period of time. I don't know, John, if there's anything you want to add on that.

Simon Whale: Well, can I just underline that point? So are you comfortable, are you content that the regulations that are to be brought into effect in 2020 are as you would wish them to be? Do you want to go further?

Ian Hudson: By and large, yes. I think the one area that we talked about earlier was the openness and transparency bit, where I think we'd have liked to have seen a little bit more in terms of the ability to talk about some signals at an earlier timepoint formally. But other than that, I think by and large, yes, I think the regulations are good regulations and will be appropriate.

Simon Whale: On the transparency point, you've often found yourself saying that there are things you can't disclose to people who approach you because of confidentiality agreements with manufacturers. Is that a frustration or just a fact of life?

Ian Hudson: It's not a confidentiality agreement with the manufacturer; it's the legislation that says that basically whilst things are at an early stage in an investigation, there is a duty of confidentiality to manufacturers. John, is there anything you want to add on this?

John Wilkinson: No, I think we are often embarrassed by the fact that we have to, if you like, appear to hide behind article 20 of the Medical Devices Directives, which preclude us disclosing the nature of conversations we're having with manufacturers at any one time. I think there's some merit in not being completely transparent about every interchange that happens while you're doing an investigation, otherwise that investigation could be compromised. But ultimately, those provisions go too far and certainly the provisions around publication of adverse events and the information around those, I think there is no reason why those shouldn't be in the public domain.

Cyril Chantler: So do you have specific proposals for changing?

John Wilkinson: We have been working with industry to introduce a voluntary scheme outside of the legislation. That is showing promise, there seems to be in principle agreement that that would be a good idea from the major industry players. That would be a fairly powerful lever potentially to change the legislation in due course. So I think we're doing everything we can outside of the constraints of the legislation to try and [unclear].

Cyril Chantler: Do you have a public position on that that we could see?

John Wilkinson: I think I'd be very happy - and I'd have to consult with my colleagues who are working on this. We've put a number of papers into the European Commission and the European system in support of this...

Cyril Chantler: Because you did mention one of your points was more openness.

Ian Hudson: Yes, sure. Shall we write to you on this specific point?

Cyril Chantler: Yes, I think that would be very helpful.

Sonia Macleod: Can I just ask, in terms that this is something you would obviously like to see. There has just been an overhaul of the regulations relatively recently, so what prevented this being incorporated into the new regulations?

John Wilkinson: Well, I think you have to bear in mind that the development of European legislation is a tripartite activity. The Commission put out a consultative document at the front end and at the back end, everybody has to agree. The Commission are the facilitators, if you like, but the Parliament which has 28, 29 - I get confused at the moment in terms of - 28 member states, net of ourselves, you have the Council of Europe which is all of the member states and ultimately all have to agree on the nature of the provisions.

Clearly that's a complex process. So while we may have strong opinions, if that's not shared by other member states and if indeed the Parliament, then we have limited influence. We try to influence as much as we can on things we think are important, but ultimately it's a political process.

Cyril Chantler: Thank you very much.

Julia Cumberlege: Can I just ask on the volunteer element, so you could have just one or two manufacturers saying we will join in with this and then you're left with a larger number who don't want to.

John Wilkinson: I think it would be difficult to proceed if you didn't have a substantial core of large manufacturers. It's the large manufacturers that put, in terms of volume of products, the majority of products on the market. So you could go a very long way towards the goal with an agreement with the large manufacturers. I think that would increasingly pressurise the others to fall in line as well. So I think the approach is to seek a start to break the logjam and move the thing forward. Hopefully that will move quite quickly.

Julia Cumberlege: Well, it sounds a good idea.

Simon Whale: Can I just ask about something you mentioned in your opening statement? I think you said that there's a need for better cross-system working. That's certainly something that we've got a view on as well. Who's responsible for ensuring the system acts in a more coherent way?

Ian Hudson: That's a very difficult question, and we've been having discussions with NHS Improvement in relation to this and indeed, across the bodies through

the Department of Health, having some discussions here. Ultimately at the moment, we all have different roles and we either come together in some sort of overarching committee that has all the elements there to effect change, or we end up with another structure.

But I think the difficulty at the moment is our responsibility is clearly defined, but it's not the whole system. Other people have other responsibilities. So what I want to see is certainly if we say there is an issue and communicate it extensively through the system, then that system picks it up and somehow mandates that a change happens with CQC monitoring at the end to ensure that it has happened.

Simon Whale: Is there a ringmaster or a conductor of this orchestra?

Ian Hudson: Well this, I think, will be one of the key areas for your Review and recommendations, I think, to reflect on the best way of doing this. Whether it is some sort of overarching committee that has responsibility for this or some other route.

Simon Whale: But at the moment, are you saying there is no...

Ian Hudson: I think this is something...

Simon Whale: Nobody sets the direction of travel on how to ensure best cross-system integration?

Ian Hudson: Well, my expectation had been where we communicate on an issue, valproate for example, and we send out the materials, pregnancy prevention plan and all the rest of it, but immediately everyone would take action. What I'm deeply troubled by is stories that sometimes that isn't getting everywhere across the system and this is the basis of some of the patients' testimony that we've heard.

Therefore, I suppose the question I'm trying to ask is how across the system with all the players, with the levers that are there, can that system be made better and is it some sort of overarching safety committee? That might be the answer and certainly we've had some discussions with NHS Improvement in relation to they're creating NaPSAC, this National Patient Safety Committee, to accredit alerts going out. Whether that then changes into an overarching safety committee for the system, that might be a way forward.

Simon Whale: But today as it stands...

Ian Hudson: Today, I think it's difficult...

Simon Whale: ...if you've got a concern about something that's not working, something that's not happening as it should, where do you take your concern?

Ian Hudson: Well, what we have done here is we've communicated ourselves, then we've enlisted the support of chief medical officers. Or we've gone round to - things like valproate, I and the chair of the agency have gone round all the Royal Colleges and said please would you reinforce this with all your members. We've issued alerts with NHS Improvement, for example, a joint one, the Chief Medical Officer's done that. We've also got the chief pharmaceutical officers to write to the pharmacists with myself on areas that perhaps we felt more needed to be done. So at the moment it's a little bit - we go to the bodies that we think will work with us to effect change. I think this is an area that I would like to see improved going forward.

Simon Whale: How would you describe the Department of Health and Social Care's role in the system at present?

Ian Hudson: Well, I think they have a key role because they're responsible for all the parts of the system, putting it together. So I think they'll need to describe their own role in this, but certainly we had a meeting recently with the Department that the Department pulled together with the various players. I think that's a very welcome step.

Valerie Brasse: Has it ever been different?

Ian Hudson: Has it ever been different?

Valerie Brasse: Different, pulling the room together.

Ian Hudson: What I found challenging is the stories from patients where they're saying they didn't know. I've been doing this in one form or another for a long period of time and that really deeply troubles me that somehow it's not getting through. Now, is that I wasn't aware of it not happening before? Or is that more a new phenomenon that everyone is - I think everyone is trying to do their best in a very busy environment.

Valerie Brasse: But I think this is part of the problem, you see, we're hearing this from you and we've heard it from others and one's left thinking after all these years it's still not working. Every time there happens to be a problem, it's this ad hoc who do we speak to, let's try to get this sorted. It just bothers us a little bit that we've taken so long to say right, we need to get the system to play together, lead the orchestra to sound together.

Ian Hudson: Well, I think the NaPSAC, National Patient Safety Committee through NHS Improvement is a welcome advance, where we'll be all operating the same way in terms of the alerts going out, in terms of who they go to, the board, et cetera. There are other players, of course, the healthcare system, the HSIB investigatory branch as well, looking at particular topics and setting them out.

Valerie Brasse: Why is it taking so long?

Ian Hudson: Yes, well, I'm not sure I can answer the question why it's taken so long. What I would say is I'm pleased to see that some of the changes and some of the things we've proposed now.

Valerie Brasse: Can I just ask one other question? The CHM, I've been looking at their terms of reference. They are not, as I understand it, responsible for investigating regulatory failings. Who is?

Ian Hudson: The agency's remit is really public health issues. Now, I don't think that's an agency issue, nor a CHM issue to look at that. So I think a separate mechanism would have to be put in place to investigate regulatory failures. I think it would...

Valerie Brasse: So we don't have anyone at the moment who should be responsible for looking into regulatory failures?

Ian Hudson: Well, I think the focus certainly on our current work is much more on dealing with the issues and going forward, rather than going back over things in the past. So no, I don't think that's...

Valerie Brasse: But I ask the question...

Ian Hudson: Of course legal systems, of course, but outside of that there isn't a body that would now be looking back and saying did the system do the right thing or not, is that a failure or not, no.

Julia Cumberlege: Do you think there's a role there for Parliament in that respect? Because there are other agencies, like the ombudsman's agency, where they report to a select committee which is responsible for the work that they're doing. One of the great difficulties with all this is we have so many different agencies and different component parts to the health service as we know it, not least triggered by the 2012 Act which actually made arms-length bodies and all the rest of it.

So there's always a temptation to say well actually bring it all together, if we have another overarching body. Then in the end we sort of deepen the bureaucracy, which is actually not what we want. I'm just trying to think of

things that would be of help to you and to all the other agencies in trying to bring it much more together and perhaps more accountable. It seems to me there could be an accountability to Parliament in terms of having the select committee that deals with some of this, but you may think that only deepens the bureaucracy.

Ian Hudson:

Well, formally the licensing authority is the Minister, the Health Minister, Secretary of State and we are acting on behalf of ministers and indeed, many things are sent up to ministers for their agreement. We also have an accountability to Parliament. I have appeared in front of a number of select committees, particularly on certain topics and indeed, if the health select committee wants to look at something then we may well be asked to go and appear in front of them and account for what's been happening. There are a number of all-party parliamentary groups as well that we meet on a regular basis to talk about areas of interest to the Review.

So there is quite a lot of parliamentary activity and responsibility now. I think the question you come to is another overarching body versus a coordinated committee. I think it's difficult. I think another overarching body, as you say, adds a layer of bureaucracy, but maybe an agency cross (relevant) body committee with specific responsibility for safety and ensuring action is taken, that doesn't create another tier, if you like, may be a way to go. I don't know, I think that's the challenge.

Julia Cumberlege:

Thank you. Shall we go onto Primodos, is that all right? Well, you know the history here of Primodos and the tragedies that have occurred. Of course, it is now very much in the past, thank goodness, but we are still meeting the young people, or even getting on in years a bit, who've been affected by this medication that was given to patients, given to women who were being tested for pregnancy of course, whether they were pregnant or not. So patients have actually been saying to us where was the warning? Why wasn't there a warning that women were told at the time that this could have had an effect? Was it simply that there wasn't the information there? Was this just thought to be a good idea? How did this all come about?

Ian Hudson:

This was what was being done at the time, this was the way of diagnosing pregnancy, if you like, at the time, until the alternate tests came along and replaced the hormonal pregnancy tests. There was conflicting data at the time in relation to these birth defects and there was a warning added of possible birth defects and new tests came along in due course. What we've done since then on a number of occasions - and I think you've spoken to Dr Gebbie and the expert group. But the agency has and then ministers asked for an expert group to be convened to look at the totality of the data and

to see really basically whether the hormonal pregnancy test was causing the birth defects.

I think you've seen both our written evidence and heard from Dr Gebbie in terms of their findings. So clearly these are tests they used in the '70s, in the conditions of the '70s and not now, but certainly our role more recently has been to review the totality of that data and then to listen to the expert group that was convened and their findings. They didn't find that the totality of the data supported causal association between the...

Julia Cumberlege: So we will learn from that, what?

Ian Hudson: Well, I think the expert group also came up with a number of recommendations in relation to medicines in pregnancy more generally. These recommendations are across a broad range of areas, I think there's something like 13 different recommendations and we're working very hard to take those recommendations forward. I should also say that regulation has moved on a long way since hormonal pregnancy tests were first introduced in the '50s and '60s and until they were eventually withdrawn in 1978, I think. June, is there anything you want to add on this?

June Raine: Yes, certainly. Baroness Cumberlege's question goes to warnings and of course there's a historic element here about how they would have reached anybody. But I think the heart of the question is, a warning should be based on the evidence of safety. I think the important point is that that question has been looked at on a number of occasions, but the review that we've done is the most rigorous ever undertaken.

I think the reason that we devoted such care and attention to sifting thousands of pieces of evidence is that it was a very important question for the women themselves. So we fully recognise what you've been seeing and hearing and to involve the patient's perspective right throughout that, as every piece of evidence was looked at, was our commitment. I hope that shines out of the report.

I think your second point about learning from this, yes, we've learned a very great deal about how the patient perspective is involved. We did our best to make sure that their involvement was not a difficult one, but we knew it would be daunting and despite best efforts, there were elements of distress that we deeply regret and would wish to move on to do things rather differently.

I think we learned a rather important message about the communication of science and the science isn't what people expect to hear. That, I have to say, is one of the big challenges and not alone for this class of medicines.

We see vaccines in other areas where the basis of our work in rigorous stance is really critical to public health. The findings of your report, your Review are so important here.

Then I think the third area is what Ian has just mentioned, and our cross-sector group, which is a model in a way of what we've just talked about, to bring together all parties with a commitment to improve medicines in pregnancy. Whether it's from the very first development, how we test for teratogenicity, whether it's the modelling of the dose the woman should have. It's an astonishing fact that only five medicines have been tested for their effects in a pregnant woman, so the confidence a woman has when she takes what her doctor orders for her infection, whatever, just isn't there and we're going to do something about that.

We have an information consortium of all the information providers who are going to ensure that wherever a woman turns to for information or advice, she'll get clear and well-constructed advice for her. Every signal that happens in a pregnant woman will be looked at. So I hope I've conveyed that this is really happening and it will only happen if the clinical world, science and academia and funding bodies come together to fill this gap. The concept, as we did with paediatrics, of filling a really important gap.

I think we're on the right track because the National Institute of Health in the US is on the same track and we'll work with them. So this report should be seen as a really important contribution to women's health for the future. While there are very difficult aspects of the science that was looked at by the experts you've talked to, our mind is open to all further evidence that accrues, as you would expect from a scientific body.

Julia Cumberlege: Thank you very much.

Sonia Macleod: Can I just ask on that basis, in terms of going back and saying we were looking at warnings, one of the things that struck me is that the committee for the safety of drugs weren't entirely comfortable with hormonal pregnancy tests, but they didn't consider them sufficient evidence. I haven't seen a risk benefit analysis in the way that I would have expected to have seen it. Certainly in terms of the benefits of hormonal pregnancy tests, given there were alternative tests available, how was it weighed and how would that have changed in the intervening time?

June Raine: I think we were focusing on the context at that time. What we understand is that the society aspects weren't as wanting an instant diagnosis perhaps as much as we do now and the use of the alternative test was very time

consuming and probably not very accessible to most people. Which is why when the tests that you get now, with a simple urine test in the pharmacy or wherever, has made such a difference.

The other context was the regulatory context itself and I'll turn to Dr Woolley on this, there was never a licence for these things. The only licence that was ever granted was for the amenorrhoea indication. So all the rigours of what we would do now simply weren't there. We would have said, as we would do with any investigation, that this is a healthy person having something for which - it's a test, knowledge is an important thing but it's still a test. Therefore, the benefit risk would be rather finely balanced and any risk unacceptable. May I ask Dr Woolley just to clarify the points you'd like to raise on that?

Jane Woolley: No, I think you've covered it all and I think the indications removed in 1970 and at the time it got its licence.

June Raine: Yes, we were the first along with Norway.

Sonia Macleod: Absolutely, although it wasn't committee for the safety of drugs removed the indication, was it? It was the McGregor Committee.

Cyril Chantler: Do we know why the McGregor Committee - it's very difficult going back over a generation, I do understand that, and it's sterling work doing it if we can learn something for the future. Do we know why the McGregor Committee did remove it in 1970?

Jane Woolley: It might have been because it was a diagnostic test and they didn't reimburse diagnostic tests in those days. So they said you can only have this drug in the proprietary index if you remove that indication.

Cyril Chantler: So is it likely that's the reason that patients wouldn't have been informed at the change?

Jane Woolley: I think so, because I think it was just a commercial decision at the end of the day by Schering, certainly from documents that I've seen. But based on that recommendation by the McGregor Committee, they thought it wasn't worth having that as the indication.

Cyril Chantler: Difficult and hypothetical questions to direct it, but given the fact that the committees discussed the possibility of the teratogenic effect between '67 and '75, do you think in the modern world - and I was a doctor then, I know doctoring has changed hugely over that period. Do you think nowadays it's likely that their anxieties would have been shared with patients, rather than suppressed on the basis that we shouldn't - I'm not trying to feed you...

June Raine: No, shared decision-making is the way that medicine is practised now. I think in those days - and I wouldn't want to use words like paternalistic, but there was a very great deal that the doctor would then decide what a woman needed to know, in a sense, taking her role. It was particularly apparent, I think, in obstetrics and gynaecology, if I may say, but nowadays this would be unthinkable, that somebody didn't have a part to play in that decision and know the pros and the cons.

We have to put our minds back to the time when particularly, I think, in obstetrics and gynaecology that there was a rather more need-to-know basis. Particularly there was one quote that came to mine, if a woman is pregnant she needs to hear it from a doctor. So that, I think, tells you that the whole idea that a woman might wonder if she was or not and be able to find out for herself was really not there.

Cyril Chantler: Thank you, going back to what you were just saying about the future. The EWG recommended the MHRA should systematically monitor outcomes, after taking important regulatory action to protect patients from harm from medicine, use this information to inform action. Does that mean that the MHRA holds the ring in this area? Because we've just had a conversation about who holds the ring in other areas in patient safety, but you are in charge.

June Raine: The really important framework change, when the vigilance of safety monitoring regulations were overhauled in 2012, was the responsibility, a power that we welcomed, to monitor the effectiveness of risk minimisation. It meant a whole change in emphasis with the pharmacoepidemiology team and data sources that would enable us to do this. We'll talk about some of the challenges, particularly with valproate, in how we approached this in getting the right data, the right parameters to inform judgements on whether risk minimisation is working.

So that, I hope, tells you that for the holding the ring on a regulatory decision on safety, then flows through to monitoring that. In a cyclical way, taking steps to improve it if necessary. We always strive, I think, to be proportionate, it's simply a phrase, because we never want to deprive someone who is going to benefit from the medicine, from over-restricting it. So it's a case of judging the populations in whom the benefit risks may be in question and approaching that in a way that we can measure whether it has achieved the right public health outcome.

We've published a bit about this approach with some key decisions and I think our wish now - and I think I did mention it last time - is to be very systematic about the goal of a risk minimising step and when it's achieved.

Sometimes a change in clinical practice will require many factors to deliver that public health goal and we're getting better at using new disciplines, like implementation science, to identify those goals and to have the data streams and studies that will help us. So when we talk about valproate, I hope we'll talk about some of the studies that are happening in Europe right now, but I know the Review will reflect on the timeframes for those.

Cyril Chantler: But that would also reflect the need to pull all these conversations to involve the patient as well as patients.

June Raine: At the very beginning, on the judgement as to what risk minimising efforts are acceptable and what the goal is the one they see as appropriate.

Cyril Chantler: When you come to prescribe, you would expect the prescriber to discuss these with the patient.

June Raine: Yes, indeed.

Julia Cumberlege: I have to say one of the real tragedies, the legacy of all what went wrong, is that when we've met a lot of women and their husbands and partners and everything, the feeling of guilt, the guilt in the woman that she caused this disablement to her child is very real. We just have to think about what we can do about it, because we try and persuade them you are not guilty, but they don't believe that. So it's really...

June Raine: Yes, yes, we understand.

Julia Cumberlege: We've obviously got to go forward in medicine, I understand that, and in devices and other things, but actually we do have to think about the harm that's been done as well. Simon...

Cyril Chantler: Can I have one more? This is my last one. We've talked about this to the EWG, the sponsor of EWG was you or the CHM?

Ian Hudson: Did the minister ask for an independent group...

Cyril Chantler: I am used to - I know there are other ways of doing it, but I'm quite used to the notion that the National Academy of Medicine in Washington [unclear], when they do report they also put a peer review group in place to look at the report before it's actually released. This didn't happen in this case, though it could have done, there are similar places in this country that could have happened. Do you think that was a mistake?

Ian Hudson: Well, the expert advisory group did do their work and produced their report and then it was reviewed by the Commission on Human Medicines.

Cyril Chantler: I know it was but...

Ian Hudson: So that is one of the ways of...

Cyril Chantler: Yes, that's the answer they gave. But as I say, in other jurisdictions a separate committee would have been established, for example, at the Institute of Medicine, which is now the National Academy of Medicine, to peer review the report before it was released.

Ian Hudson: Well, June, you may want to comment, but certainly the process of the nine experts looking at all of this were eminent people. Then an independent review by the commission feeding into the commission who were...

Cyril Chantler: Okay, you said they're the sponsor of it.

Ian Hudson: Well, the sponsor of it, but they're not the people who wrote the report.

Cyril Chantler: No, I know that, but it's still the sponsor.

Ian Hudson: They did scrutinise it and that was the advice that came through. So I think it's a robust process, very robust process. June, do you want to...

June Raine: I think we need to reflect a little further, there are aspects of our work, particularly on access to medicines, where we would do a public consultation on a proposal and get wider input into it. I think we probably need to reflect...

Cyril Chantler: So you could have asked the Academy of Medical Sciences to...

June Raine: There's no doubt that the CHM provided a very rigorous review.

Cyril Chantler: Thank you.

Julia Cumberlege: Thank you, Simon.

Simon Whale: Can I just talk a bit or explore a bit more about warnings in relation to - specifically in relation to Primodos but obviously the wider context. So in the case of Primodos, there were concerns about the product and those concerns were voiced informally, I think, from the late 1960s through into the 1970s. But as we've discussed already, the science then and the science now doesn't reach a consensus on causality.

So I'm trying to understand at what point - if you were to wind forward to today and you had a similar situation where you've got concerns that are raised, including in that case by certain individuals within the company that manufactured the product, at what point should the receiver, the recipient,

the patient, the woman in this case, be made aware of those concerns when science isn't overwhelmingly in favour of causality?

Ian Hudson: I think the world has moved on considerably and the practice of medicine's moved on considerably since the '70s. June, you were referring to the perhaps more paternalistic approach then, but I think now in any pregnant woman and a decision to give her a medicine or not would have to be a careful consideration of all the available evidence and a proper discussion whether that's the right treatment for her at that time.

Simon Whale: But as you've mentioned, there's limited scientific knowledge about the effect of medicines given to a woman while she's pregnant.

Ian Hudson: Sure, so if there are uncertainties that has to be part of the discussion.

Simon Whale: So it would be today...

Ian Hudson: Absolutely, yes.

Simon Whale: ...and it wasn't then.

Ian Hudson: I wasn't practising medicine in the '60s and '70s but...

Simon Whale: Well, the women we've spoken to who took Primodos and who then subsequently had children who were damaged, certainly weren't - what they've told us is that they were not warned of any risk or any concern that existed at the time. They took the pill on that basis.

Ian Hudson: My expectation now is if there's a pregnant woman - and indeed non-pregnant women or men or whoever, in terms of any discussion about the risks and benefits of a treatment before they embark on that treatment, in the context of the disease they have. I think medicine has moved on tremendously in that respect from certainly when I qualified, which was 1982, I think, but from then onwards it was much more paternalistic and a view of not being quite so forthright in terms of information to now, where I think there's a much, more greater - and rightly so - expectation that people are properly discussed and a shared decision-making.

Simon Whale: Do you think there's a willingness for people in the system, clinicians included, maybe specifically clinicians, to say to a woman who's pregnant who they think needs to take a certain medication, I do not know what effect this might have on you or the unborn child?

Ian Hudson: What I expect them to say is that clearly you've got this condition, you need this treatment, this is what we know about it and this is what we don't know about it.

Simon Whale: Do you think that happens?

Ian Hudson: I'm not the best person to judge that.

Simon Whale: Who's the best person to judge that?

Ian Hudson: I think the people who are treating patients are the best people to judge that, but that's what I would expect should happen.

Simon Whale: Who within the system is best to judge that?

Ian Hudson: Well, I think the people who are actually treating the pregnant lady...

Simon Whale: So the individual clinician?

Ian Hudson: Yes and the professional societies should be the people who perhaps are best able to answer that question.

Sonia Macleod: Surely the person in the best position to judge it is the recipient of the information, because they are the person who should know if they've received that information.

Ian Hudson: Yes, I agree, it should be a joint decision, if you like, between the healthcare professional and the patient.

Simon Whale: In the system, which part of the system then knows that the patient has been given the information that they needed in order to make an informed decision and therefore, the system is operating as it should? Which organisation within the system is responsible for knowing that that's happening or isn't happening and taking action to ensure that it does?

Ian Hudson: I think there's a professional responsibility on the healthcare professionals to go through a consent process. Now, for surgical processes that's recorded and written down, et cetera, but if you're prescribing something, even if I go to my GP with something, I expect there's a professional responsibility there. Certainly if there are then issues with that, that's going to come up through complaints, revalidation, all of that side of things, if there are issues relating to that. But I think it's primarily a professional responsibility to ensure that there is proper discussion of risks and benefits of any intervention. June, do you want to...

June Raine: Perhaps I could add something about thinking about what we can add to this. We're very conscious and have been for a long time that the leaflet and what we call the summary product characteristics probably isn't as helpful as it could be. In fact when the legislation was overhauled in 2010

to 2012, there was a commitment by the commission to look at the shortcomings.

We did a bit of a study ourselves, looking at what we call a risk management plan, which is a document that covers what is known, what isn't known, what might be expected to happen with a particular medicine. In fact, patients preferred that kind of information to the standard, what's been in place for a long time leaflet or SPC. The opportunity exists, I think the European Agency hasn't quite maximised that opportunity, to publish these.

So in a way, in an ideal world, the health professional would be informed by that distilled knowledge of what's known and what's not known and be able to just talk through it with a woman, saying I'm in my first pregnancy, what do you know about people in their first - and they'd have that system at their fingertips and be able to say well, we've studied 1500 and this is what we know, these are the gaps. I think that whole dialogue could be informed by a distilled embodied piece of information, that would be really what we would like to work towards.

Valerie Brasse: Can I ask you a specific question about the summary product characteristics and just tell me if I've got this right. Because I think that you cited in your evidence this is based on European Commission guidelines, that adverse events without at least a suspected causal relationship should not be listed in the SPC. So, if we look now at a modern-day contraceptive pill which we found that contains both norethisterone and ethinylestradiol [unclear] pronouncing those, but anyway, they're the same components of Primodos, albeit of different constituents, ingredients, different concentrations.

This particular product characteristic information sheet lists pregnancy as a contraindication and gives a special warning that an increased risk of congenital abnormalities has been reported following the use of six hormones in pregnancy. So does that mean there is the causal or suspected causal association because it's there?

June Raine: Let's go back and take it in steps, if we may. I think the European guideline, unlike what happens in the US, states there should be at least a reasonable...

Valerie Brasse: Suspected.

June Raine: ...likelihood that there's a causal association, so we don't just put everything that happens. However, because many of the updates that we put in this summary and product characteristics emanate from the US,

many companies will be following the guidelines there. So we have quite a job to do in Europe to make sure that what the information to the woman is has a reasonable likelihood of helping her, rather than just being a coincidental thing that happens.

In terms of the contraceptive pill - and again I'd like to turn to Dr Woolley on this, we have to understand too that there are certain aspects of use of these hormones that may result in a change to the foetus. That may not be quite the tests that we're applying to Primodos here today, because of the other aspects that you might like to talk about, [unclear] and so forth. So could I pass to Jane to tell you a little bit about that?

Valerie Brasse: Yes, because obviously you can see there is a confusion and...

[Over speaking]

Valerie Brasse: ...square with the findings obviously of the EWG report.

June Raine: Yes, it's a slightly different question.

Valerie Brasse: Yes, well, not least because actually there is somewhere in the summary - and I'm sure that I have read this right, no doubt you will tell me if I've got it wrong. That in fact there is a statement in the EWG report that says findings of the review for HPTs, including Primodos and a possible association between exposure in pregnancy to HPTs and adverse outcomes in pregnancy do not have implications for any current licenced medicine.

They are in fact considered to be reassuring for women, who may inadvertently become pregnant while taking these hormones for contraception or gynaecological conditions. Yet here we have a modern-day contraceptive which is saying very specifically a contraindication for pregnancy and actually there is the reported association with malformations.

Jane Woolley: Yes, I think that that warning refers to virilising effects of norethisterone...

Sonia Macleod: No, it doesn't.

[Over speaking]

Sonia Macleod: ...congenital heart defects [unclear].

Jane Woolley: Okay. I can't - I don't know [unclear].

June Raine: We'd like to look into that and provide you with a full explanation. I think the other context is that clearly the expert group would have been aware of some other studies, where women did take one of these pills

inadvertently throughout pregnancy and did not have an increase. So we'll look into the context for this particular pill. I would say I'm glad you've raised it, because it is so important that women are confident in what advice they get.

Julia Cumberlege: Can I just tell you that in fact we've heard from the Association for Children Damaged by Hormone Pregnancy Tests that actually when they came to give evidence to the Expert Working Group, they felt that actually they weren't treated very well, that they felt that there could have been better interaction between the Expert Working Group and also the patient group. Are there ways that you could do this sort of thing differently?

June Raine: Absolutely and we want to. The understanding that this would be daunting was fully appreciated and the understanding that people needed time to tell their stories and feel that there was an engagement. Interestingly, when we look at if you like the evidence that we have, it's that people did have a reasonable amount of time and did have some questions to show - not to show, that indicated the engagement and the interest.

I think we do need to go further than that, and I speak in my former life as someone who was privileged to take two public hearings and there's probably nothing more daunting than that. The preparation that was individualised that the European Agency was able to give meant that women could come and feel very comfortable and deliver what they wanted to get across. So that's the big message, and Ian has spoken about how we will be training our staff, we will setting them goals, so that anyone who comes to visit us to give their views and their experiences feels totally comfortable. That the surroundings and the daunting nature of the experience doesn't impede them or upset them.

I can only say that yesterday I was meeting with a patient group, and the conversation - and Mrs Morgan was with me - was of equals, was of information we needed to share to pursue the goal that we all embrace. So it can be done, the resources, the time, the training will be put into that and I'd like to give you that assurance.

Julia Cumberlege: Thank you very much. Anybody else before we move on?

Sonia Macleod: Just one question, one of the things that we've had raised quite consistently from patient groups is that the indication for the hormonal pregnancy test was removed in 1970, but until 1975 there were contraindications added. Just really questions about that gap and is that gap normal, why was there a gap? Should there not have been such a large gap?

June Raine: We would like to say that today there wouldn't be such a gap, absolutely not, but the rigours of the procedures and the standards of performance that we have now were certainly not even imagined then. Jane?

Jane Woolley: I think obviously I've only seen minutes and extracts and putting things together, but I think the CSM at the time wanted to be sure of their own data. That's why it took until 1975.

Valerie Brasse: Just as a follow on from that, it's rather odd, because of course if the indication had already been removed, it's slightly odd five years later to put a contraindication on the drug it's a pregnancy test if it's already been removed.

Jane Woolley: Well, I think that's because it was still used in secondary amenorrhoea and so women could have actually been pregnant and taken it for a different reason. So they wanted to make sure that...

Valerie Brasse: Yes.

Jane Woolley: So I think women were supposed to have a pregnancy test first and then take it.

Valerie Brasse: Then take that, because of course that raises the other point for me, was the actual dosage for the treatment of secondary amenorrhoea and indeed the way it was licensed is exactly the same as taking the test, pregnancy test, as taking the pregnancy test. So one's left wondering whether anyone could have known that it had stopped being used as a pregnancy test, because of course when you do a prescription you don't actually say what you're putting it on for. It's exactly the same difficulty.

Jane Woolley: I think that was one of the big complaints as well, that people were still being prescribed it even though it wasn't licensed for that indication.

Valerie Brasse: No one would have been able to check them because no one would have known that's what it was licensed for.

Jane Woolley: Exactly.

Simon Whale: Can I just ask a question about the Expert Working Group, we've already discussed? Some of the concerns that have been raised with us by patients, patient groups, are around the conflicts of interest of the EWG members. I know we've talked about conflicts of interest within MHRA, but this is a specific point about the EWG itself. What was your role in commissioning and selecting those members of the EWG?

Ian Hudson: They were selected by CHM, weren't they?

June Raine: The Commission on Human Medicines would have approved the membership. When someone's name is discussed as a person who has the right expertise and experience to add value, given the question that the group is going to answer. They are sent the clear statement of policy on this and asked to provide information about their own activities. That's at the moment when they're asked if they would be available to serve. Jane, did you want to add...

Jane Woolley: The only other thing to add was that the Expert Working Group themselves could also at the first meeting be given an opportunity to state if there were any areas they felt were lacking, that needed to be filled. Also Mr Dobrik was an invited expert as well at the request of Mrs Lyons. So she also had some input into the membership too.

Simon Whale: We've been told that one of the members of the EWG has been paid to do work by Schering Bayer. I don't know whether you can confirm that or not.

Jane Woolley: I can confirm it but we didn't know that at the very first meeting. Mrs Lyons did tell us and we looked into it. He confirmed it and then he stepped down.

Julia Cumberlege: Should you not have enquired about their conflicts of interest?

Jane Woolley: We did and they had to sign a form.

Julia Cumberlege: They didn't declare a conflict of interest?

Jane Woolley: No, I don't know if there was a misunderstanding, but no.

Simon Whale: There's another member of EWG who was at university with a prominent Schering scientist.

Jane Woolley: I don't know about that.

Simon Whale: That didn't come to light either.

Ian Hudson: Well I'm aware that there were allegations of two conflicts of interest. One we found, investigated and was of no substance, we felt and that person could continue. The other was one that you've just referred to, that was removed.

Simon Whale: These both came to light because the patient group representative raised them, not because of any due diligence done by others.

Jane Woolley: We knew about one of them because it was very clear that she had - what her role was. We didn't feel that was a conflict and the group didn't feel that was a conflict, but the other one we didn't know about and it wasn't...

Simon Whale: The underlying wider point here is about trust, isn't it? The patients and those representing patient interests have to have trust in the process. It's quite difficult to trust a process where something like that comes to light only through the diligence of the patient group. Would you agree with that?

Ian Hudson: Well we ask people before they join expert advisory groups to declare things. Usually at the start of expert advisory groups the chair will then again ask anyone to declare any conflicts of interest. You then have to rely on people to declare conflicts of interest. Clearly if things come to light then of course we have to work through it. It's rare for that to happen, it's unfortunate that it happened on this occasion, absolutely, but that's - we always ask, we always get people to declare that.

Simon Whale: So you're confident in the process?

Ian Hudson: Well, clearly we need to reflect also what - if there are cases where conflicts do emerge - I'm talking in general terms, if conflicts do emerge, is the process sufficiently robust, what additional steps should be taken. Certainly I've been in discussions at a European level through the European medicines board in terms of should there be a more formal go and investigate, rather than just rely on people's self-declarations.

Simon Whale: What's the answer to the - what was the conclusion of that discussion?

Ian Hudson: I think still the basic premise is to rely on people's self-declaration and honesty. Clearly if things do come to light, rather than a formal go and investigate absolutely everyone - but I think if things do come to light, clearly action has to be taken. But it's a challenging area.

Simon Whale: The problem here is that - another wider point is that the patient groups feel that they're the ones who have to prove things, fight for things and make things happen and no one else is doing that. This is one small but significant example of that. It was only the patient group who found out about this conflict of interest and that the individual then stepped down. It was a significant issue. If it wasn't for the patient group, it wouldn't have come to light and that's concerning, isn't it? Should they not be learning from that...

Ian Hudson: Yes, definitely and I think that's...

Simon Whale: ...and action, not just...

Ian Hudson: Yes, I think that's very fair. We need to look at this to make sure that satisfying the process is sufficiently robust.

Simon Whale: My last question, one of the other things that you said in relation to the Expert Working Group, that both the one that looked at [unclear] and the one that's going to be looking at Carl Heneghan's work, is that you're committed to continue to examine evidence in the future. So if new things come to light or new work is done, you'll do that. Is there any limitation on that in terms of how long you're going to continue to do that for in the case of Primodos? What type of evidence do you need to see examined by EWG or other bodies?

Ian Hudson: I think it will depend on the nature of the evidence that comes forward and if it's substantive, then we will continue indefinitely. If it's not substantive then we'll have to form a judgement. Certainly here we had considerable discussions, when new evidence comes along we discussed with ministers and took a view that it was entirely appropriate to get the expert groups, a European one and another national one, to look at this because it was a major piece of evidence.

Simon Whale: Okay, thank you.

Julia Cumberlege: All right, so shall we go on to valproate now? When valproate was first licensed it did carry warnings to doctors about its use in women of childbearing age. Yet we know that women were still being given Epilim when they were expecting children, or were thinking they might be pregnant. So how did that actually happen? Because the warnings were there and yet the women were still - their babies were still being harmed.

Ian Hudson: I think, as you said, from the very beginning the warnings have been there, from 1972 the warnings have been there. We should also understand that valproate is a very effective drug and for some women it may be - or some men, for some people it may be the only effective antiepileptic. But it does trouble me and certainly as the evidence has built, it does trouble me that women are still being exposed, or women of childbearing potential are still being exposed despite the building evidence, despite the very extensive communications that have gone on, despite all the meetings, et cetera.

I think that the question I keep asking myself, I keep asking June, we talk across the system, is how really with the ever increasing regulatory steps that we've taken, ever increasing communication that we've done, getting all the professional societies involved, ministerial meetings, bringing everyone together, lots and lots of ways out into the system, how can we - it comes back to the question of the levers in the system that we were talking about earlier, how can we really pull the levers with everything, pregnancy prevention plans, et cetera, all in place to make sure that women don't say that they haven't heard.

Julia Cumberlege: It's a huge dilemma, isn't it? Again, it was the patient group that did a survey that showed us that the pregnancy protection plan really was not working. It was they that brought the information to us. Now, should you not be doing surveys like that to see what action you've taken is effective?

Ian Hudson: Well we certainly have been looking at information to look at the exposures of women in terms of women of childbearing potential, who's getting during children, who's starting on epilepsy, have been collecting that data through clinical practice research datalink. We've also been working with General Pharmaceutical Council and asking them to go out to the pharmacists and check in terms of things there. We're working with CQC to build that into their audit of practices to make sure that the appropriate regulatory measures are being taken into account. So we've been doing a lot in terms of the enforcement of this, but June, do you want to add to this?

June Raine: I think it's a very important point that the patients have been able to, by their rapid ability to collect experiences, move this on rapidly. Ian has talked about when a review - and this was a European review, two European reviews in fact, finishes, there's work underway to look at the behaviours of health professionals and how the drug is being used. Particularly the effects on, if there are other aspects of these effects on pregnancy. But I think the ability of patient groups to get feedback very quickly through the internet, it's an online survey that's been done, has been invaluable. I think that's a message going forward.

If I could perhaps pause on your first question though, I think what has changed is the availability of alternatives. I think if we look back in time, the risks of valproate, yes, were known very clearly, it would have a really significant risk of harm in pregnancy, so did phenytoin. So the choices that a woman had would have been very limited for a condition that was life threatening potentially, at least would stop her living a healthy and productive life. So I think probably the understanding of the role of Epilim, valproate and its need in certain conditions is one of the key factors here.

But I also think that understanding the risk - and it's probably something that you're reflecting on too - is possibly not shared equally. This is why the women's experience of what that risk is like every day with a child who's been affected is in no way mirrored by points on an IQ scale or cohort studies or whatever our databases are showing us. So I think that's why things have changed and changed in the last six years. We need more activities like the patient groups telling us very quickly what is happening in practice.

Valerie Brasse: But on that front, the valproate network group didn't get up and running, the patient engagement didn't get up and running until five or six years ago. Yet here we have something with known effects for 40-odd years. So that comes back to how the patients get brought into the system to talk about that everyday experience of what it is like to raise a family when they have all these problems.

June Raine: It does go, I think if I'm welcoming your question, to this understanding of risk. It was really only until we had robust data around 2012/13 that the nature of effects on the children as they grew up became apparent. Now, earlier data on younger children were available, but what we tackled when we led the first review in Europe was the persistence and the permanence of that risk.

At that point, the judgements that were going to be made by health professionals and women were in the context of saying yes, there should be effective contraception. Then we had to move further to say there must be a pregnancy prevention programme. I hope I've stressed and we did in our evidence that we will be ready to go further. The Valproate Stakeholder Network has simultaneously brought together all parties...

Valerie Brasse: Not just the patients.

June Raine: ...the clinical leaders, the compliance bodies, the regulators, the academics and the researchers. We've had 11 meetings with probably about 30 to 40 in each one and I hope that this is finally achieving the acceptance of risk that needs to be in place. I think that has been the big challenge here with getting the change that we want to see happen.

Julia Cumberlege: Cyril?

Cyril Chantler: In the interests of time, 1973, the committee's response to the regulators said we'd better not talk to the patients, we don't want to cause fruitless anxiety. Well, I qualified in 1963 and I can remember the concern about phenytoin. So valproate came in 1973, you'd have thought they'd have been a bit more aware of the need to communicate with patients then. But I accept medicine was different then and the answer you gave to Primodos, it's very clear that this would not be acceptable now, we're agreed on that.

June Raine: It's interesting that only in 1999 did a leaflet in clear and comprehensible language for someone to be the basis to back up what the clinician had said in those moments when you're trying to absorb perhaps two or three messages that are fundamental to your life and health, your plans for your family. So that in itself tells you this is very recent, 1999, it's only now that

we're able to say people should get those - in the language they can understand - those messages.

Cyril Chantler: But we are agreed that what happened then would not be acceptable in this day and age.

June Raine: Absolutely.

Cyril Chantler: So that's common ground. Then going on to where we are now, it really is extraordinary that it has taken so long to actually - patients to understand the risk. Even now you're doing as many things as one can think you could do and still it's not working. When we last met, you suggested that maybe the way forward was a register and we're going to return to that, I think, in some detail this afternoon in another context. But 20,000 people taking valproate when they're in childbearing age, women, is that - could you say more about the register you commonly take and how much that could work?

June Raine: Yes, perhaps if I set the scene by saying I think we have common ground between us on what the challenge is. The regulatory position is robust and proportionate. To translate that into meaningful clinical change is where we are. We're building the registry, we've had two stakeholder meetings and common between us is the need for every woman on valproate, from girlhood or whenever she starts, to be tracked throughout her life, whether she switches to another treatment, has a baby or whatever.

Cyril Chantler: Would you do that through the prescription system? How would you do it?

June Raine: We are hoping to do it with NHS Digital to pick through, yes, but there are some obviously details that are still to be defined. Alongside that from the beginning of April there will be an incentive to general practitioners through the NHS quality improvement and this month...

Cyril Chantler: I just want to, if I may, just concentrate on the registry.

June Raine: Okay, let's do that then.

Cyril Chantler: We're very good at the what in the National Health Service, we're not so good at the how. How would this register actually practically work? Would you link it to the prescription and the clearing house for the prescriptions? How would you make it work?

June Raine: Yes and ideally - and we had those discussions with NHS when they were introducing it, that's why I mentioned the quality improvement framework, that at the time the GP is doing that he knows that all those details need to be on the registry. So that would have been part of it ideally, yes, the...

Cyril Chantler: But would you rely on the GP to register the patient? Or would you do it through the prescription which is cleared centrally and that would automatically - with a patient's permission which we of course would require under GDPR?

June Raine: Yes, that would be ideal, to make sure it's picked up through the prescription. But I think what we need to do is be sure that at every step that registry is - and the woman's updated details on it are people's responsibility.

Cyril Chantler: You're talking to NHS Digital about how technically that can be achieved?

June Raine: Yes, they've had experience with a couple of registries and we're reaching out to key people who have done that. I don't want to overstate where we are, we've had two workshops and you'll be given the details, to agree what the purpose and the principles and the various structural issues to do with leadership - which is not just structural; it's the whole passion that should go with delivering this registry and to make sure that the clinicians are totally behind it. So the actual how is going to follow on.

Cyril Chantler: Could you give us a briefing about what you've done and where you're trying to get to on this? It would be very helpful if you could.

June Raine: Absolutely, yes.

Cyril Chantler: Thank you.

June Raine: We will be providing you with that and most welcome for any of the team to come to any of the meetings.

Cyril Chantler: Thank you, yes, that would be very welcome.

Sonia Macleod: We were going to [go to] the last one, unfortunately it was just too short notice.

Julia Cumberlege: Okay, thank you very much. We've heard again from the patient groups that warnings were supplied to clinicians and patients, but these warnings were actually out of step with each other. Also, with the knowledge that was available at that time. We've heard that certainly there were potentially risks that were well known, especially some of the studies that were done on animals that was likely to cause huge problems.

I'm just wondering why were there discrepancies with the information that was given to doctors but not to patients, yet you had your patient information leaflets which actually didn't chime with the summary of the patient characteristics that doctors were given. It just seems to me that

again there really was a disconnect between even just the information that was given out.

June Raine: It's an important point, I'm very troubled by what you said because the leaflet by law has to reflect some product characteristics and every safety issue has to be mentioned in equivalent terms, even if the language may be slightly more accessible. I'd be very concerned and I don't know if Mrs Morgan wants to say anything, there would never be any deliberate step not to have a leaflet reflecting that.

Sarah Morgan: No and as previously, if you have examples to look at that would be very helpful and we could...

Valerie Brasse: This is going back over history, so when you're looking at the chronology you're just seeing that they're not moving in tandem. So we go back to 1994, it's the first time that the patients would have learned that there was a potential risk, in the patient information leaflet. Then thereafter they just don't marry up, so we've done that tracking exercise and they simply don't marry up as you go through to 2000, they're just simply not aligned. So for the patients, they'd be saying had we known, had we had the opportunity to have that conversation, we might have made different choices.

Ian Hudson: Could you give us the details of this?

Valerie Brasse: Yes, we need to compare and contrast, the exercise we've done.

Ian Hudson: Sure, very happy to look at that and then come back to you on that, because I think we are not - I am not aware anyway and I can't imagine why we've got any discrepancy.

Valerie Brasse: It's actually also something that Sanofi mentioned to us, because they said that there were times and occasions when they wanted to put more into the leaflets, but actually had come to meet the regulators and there was a different understanding of the science. So it's quite interesting, the debate about what they felt should have gone in, and then months later actually it does go in, but there was something about timing and your different understanding of the scientific evidence that...

Ian Hudson: Can we work through the specifics, if you give it to us...

Valerie Brasse: As official.

Simon Whale: Can I just go back to the current situation with the PPP? Can I just establish, what's your view on whether it's working effectively or not? Is it or isn't it?

June Raine: I think the implementation progress has been disappointing. We took stock of all the perspectives on 12 February from our stakeholder meeting and focused on the data presented by the patient group in fact, who gave us a further tranche from December to now. Their original data set had been over the summer, you'll recall that the Chief Medical Officer wrote in April, the legal change came into play in May and the patient group came to us in August with their data saying that, I believe, it was 58 per cent didn't get a leaflet and various other aspects of the implementation weren't working. We were very, very exercised about that, as was our former minister.

The latest set of data, which goes to your question, is slightly better but nowhere near where it should be. I think the figure was 40 per cent getting the leaflet. Very worryingly, 63 per cent not having had the annual review, which gives them a chance - women a chance to do that risk acknowledgement. Because it has to be annual in case a woman's situation has changed and many will have never thought of having children, then all of a sudden their lives change and they do. So that has to be done at least annually and in two-thirds that's not happening. So that is extraordinarily worrying. It's information that we're checking against other data sources, as Dr Hudson has mentioned.

We use the CPRD, we have the Business Services Authority data and we already know that there's what our patient groups called a postcode lottery, that you are twice as likely to get valproate in some parts of the country than others. So how systems change and we know that the NHS will have brilliant practice in some areas, but a slower change process in others. So at the heart of your question is, is it acceptable nearly one year on and I think none of us would disagree and say it's not acceptable, it is not acceptable.

Simon Whale: No, I'm sure you're right, I think we can detect your frustration.

June Raine: Yes.

Simon Whale: What needs to be done and how quickly does it need to happen?

June Raine: We asked all our stakeholders that on the 12th, 10 days ago, and I think there needs to be a tailored solution. But we looked at where the barriers are and where change isn't happening. I think clearly the specialists, neurologists and paediatricians, really have to deliver. The psychiatry profession has introduced very good guidelines, but all specialists - it is a specialist care drug - need to accept that. The second thing is to improve access to epilepsy nursing. The Association of Epilepsy Nurses really want

to do this job and they need the adequate resources to do it and are more than willing to bridge that gap.

I think then pharmacists need the training and the testing to be sure they are - they talked about women being valproate safe; we all need to be valproate safe. So the pharmacist needs to have the knowledge and be tested, because one of the findings of the women was that the people that they asked questions of couldn't help them with those questions. So there are answers and everybody needs to be very articulate about sharing those and being able to have a conversation.

There needs to be a digitally enabled form that is a method of communication between all parties and I think underpinning that - and it's probably the most challenging of all - has to be contact with those 20,000 women. We were informed early on that access to those names and addresses was not possible because of restrictions. We have checked with other - particularly with our colleagues in Ireland they have done it. So I think that is the fifth element, there needs to be a plan. I'm talking about proposals here. But from what we heard just over a week ago, I think we have to move this to a new level.

Simon Whale: I think a lot of what you've said we welcome. I suppose there's a question about the urgency of this. If the failure is as it's been reported by you just now, the numbers are high, two-thirds is a high proportion. That means that there are women today who could be taking valproate and are about to be pregnant or even are pregnant. They're exposing themselves and their child to be to enormous risk, a one in two risk. So the urgency is overwhelming, isn't it?

June Raine: It is, it is.

Simon Whale: What kind of immediate or radical action could be taken?

June Raine: We've obviously used communication tools, but I think we need this package, if I can say, a concerted action. If we can move forward promptly, it would be to contact people and at the meeting I'm referring to on the 12th, the Business Services Authority, was called into the frame as could we institute this contact. Women need a tailored plan. We're told by the specialists that many don't want to come forward because they are concerned that they'll be given advice and their lives are settled in the medicine that's keeping them well and productive. I think we do need to do that really rather in the coming...

Simon Whale: So that'll be taking information from the prescription form to enable you or others to contact those people directly?

June Raine: Yes and I think you've been discussing with colleagues in the NHS about this whole issue and I think people are ready to consider these matters now.

Cyril Chantler: I put it to you that the one thing that we can do which we've not tried, because we haven't been able to, is actually to put the patients more in charge of their care. Many years ago Baroness Cumberlege and I were involved in the introduction of the NHS number, and that was so you could actually link the system around the patients. So the register would enable that to happen and then the patients themselves and the organisations that support them, the whole system could then direct the care where it's needed.

So what this tells me is that if that analysis is correct, then the sooner we get this register up and running - and it's relatively easy to do this nowadays, whether you're talking about the DVLA, you're talking about the National Lottery, you're talking about - big registers are not difficult. So we need to get on with it, don't we?

June Raine: Yes, I totally support what you said and we have the key principles now as of the 12th. We have the model, we have the people and we have the goal. So with NHS Digital's experience, particularly where they've delivered to registries, I think we can then...

Simon Whale: Given the risk that women and children to be are exposed to today, because of the fact that the PPP isn't working, one thing that's been put to us by patient groups is that perhaps products should be, at least temporarily, withdrawn from the market, or this indication removed, to enable the system to put in place the safeguards you're talking about. So that you don't have this period where the system's trying to do what it wants to do to safeguard women and children, but while it's doing it women and children are continuing to be exposed to it.

June Raine: Yes, well that's course of action that as a regulator is always in our minds. When, I think I mentioned, activities around coproxamol failed to secure the appropriate use, it had to be done. Thioridazine was another one. In the end, it's the ultimate that here we have, as we understand from clinicians, a medicine that has a unique value for some people and that there are people who cannot live a normal, healthy, productive life without it, we have to accept that judgement.

So the question is how to be proportionate and ensure for a woman, as she moves into her childbearing years or beyond, has access to that tailormade care and planning so that she is actually fully informed and able to take the

decisions and will not have to suffer the consequences of the women and the families you've been talking to.

Sonia Macleod: Do we know what proportion of patients on valproate are refractory to other treatments?

June Raine: We're looking at data from all the other member states, which is what we can have access to, as a first start to say why is it used at the level that it is in this country and Denmark uses it to a much, much lesser degree. So this is a question we're raising as often as we can with our neurology colleagues as to how they can actually define in terms of history, investigation, prognosis, where these patients are. What is the irreducible minimum of colleagues, women who will have to make that choice, a very hard choice not to have a baby.

Valerie Brasse: Is the PPP attached to other drugs? The experience of using it elsewhere, it may be that those other drugs are much rarer and there's a much smaller defined population group. But I'm just wondering, is it a problem specifically with valproate, or have you had the same experience trying to make the PPP work when attached to other drugs?

June Raine: There is a PPP for other powerful teratogens, thalidomide is back on the market, as are other drugs for multiple myeloma, like lenalidomide, pomalidomide and isotretinoin as you'll know for the very severe skin scarring acne. The context is probably a little different and the longstanding, if you like, understanding of what has been the challenge with valproate, understanding what a neurodevelopmental disorder is has evolved over time. I think that question goes to how you change clinical practice when the judgements that have been made have been seemingly acceptable.

Valerie Brasse: But it's about how the PPP is working in with other drugs, so we seem to have a problem here around compliance. It's not being delivered as it was intended to be and yet you've got it working with other drugs, or not, your experience with other drugs might have led you to...

June Raine: We monitor how thalidomide, pomalidomide, lenalidomide, isotretinoin work in practice, and pregnancy prevention isn't for 100 per cent. There are always glitches or failures and we monitor very closely across the EU what the failure rate is and then take steps.

Valerie Brasse: Is the valproate PPP problem comparable to what is happening elsewhere, albeit dealing with a different population?

- June Raine: I think it is a unique set of circumstances in fact, because the populations who are having the drugs for myeloma, or very short term for scarring acne, have a very much perhaps more immediate efficacy component to do the weighing up and will be in those situations more likely to want to avoid pregnancy, rather than someone who's well on Epilim and wants to envisage a normal family life.
- Sonia Macleod: If you look at, for example, the international examples of those pregnancy prevention programmes for isotretinoin, the original smart programme was fairly similar to PPP in that it involved box stickers, it involved this acknowledgement, it involved checking the woman was on contraception. That was ineffective essentially and so it was replaced in 2006 by the iPLEDGE [unclear]. So internationally - I appreciate fully it's a different drug, it's a different cohort, but if you have international examples where similar measures haven't worked, how do you analyse those and then utilise them in working out how going forward we can make a PPP work?
- June Raine: Well we do look at these and we've looked very closely at iPLEDGE in fact and we have to consider obviously the environment. This was very much a US development. We might think it was over-rigorous in terms of the short, or relatively short-term use and the way a person has to be tested before they get their medicine. The whole point, I think, of these women who have a condition that's lifelong is to be able to live a normal life and not be constantly bearing the burden of intensive risk of immunisation. I don't know if Mrs Morgan wants to say anything about when we look across at other programmes for teratogens, what we've learned.
- Sarah Morgan: I think we try to take the learnings from particularly [unclear] there was a recent review of retinoids throughout Europe and the PPP. We've tried to take the learnings and include those in the considerations around valproate, taking into account the very different people context.
- Sonia Macleod: Yes, but I suppose one of the things that struck me about iPLEDGE is being an online programme, it's accessible not just by people who have access to that patient record, but also by pharmacists as well as GPs and everybody else. It effectively provides you with a register of women of childbearing age taking that medicine. Those seem to me like they would have been very, very valuable things to have.
- Sarah Morgan: I think that's where we want to get to with valproate and we've had discussions about the summary care record the pharmacist has access to and how the prescription itself can provide the link between the different health professionals. So that is where we want to get to with valproate.

Simon Whale: Can I just ask a question about the communication of risk? The mandatory warning went out, as you said, last spring, summer, from the CMO. That went through a central alert, I think I'm right in saying. At that point it would have gone to the CCGs amongst others and it would have been for CCGs to act on that, by presumably communicating with local GPs and community pharmacists. I presume no one knows how many CCGs did act on it.

June Raine: Our colleagues in NHS Improvement have that data. I haven't looked at it lately.

Sarah Morgan: We have, there was an NHS Improvement alert in April 2017 where we have feedback from the CCGs about the previous communications and the action taken on that. The alert that went from the CMO in April 2018 didn't have the feedback, it wasn't a patient safety alert; it was a letter from the CMOs. We've tracked through various mechanisms with the materials that Sanofi sent out to healthcare professionals, particularly to pharmacies, to ensure that the packages of materials to pharmacies were actually received and notified as received and the individual pharmacy have that information in terms of feedback.

Simon Whale: But what we don't know is how many CCGs received the CMO's letter and said themselves we need to tell GPs in our patch about what the CMO mandatory warning letter says. We don't know how many did that and how many didn't, is that right?

Sarah Morgan: I don't have that information. The CQC is inspecting GP practices, but we don't have the information of the cascade.

Simon Whale: Right, so we don't really know whether that letter had any - it comes back to Dr Raine's point about the failings of PPP. If the messages aren't getting through because they're being delivered to people who don't act on them, if that's the case, we don't know, you don't know, then that's clearly a part of the system problem. But not knowing whether it's a problem is also a problem.

June Raine: Yes, well we've assured that CQC has valproate as a test of the safety of the operations of whether it's a GP practice, a hospital or whatever. But then it's down to them making their findings more visible than when we hear about a practice being put in special measures. We did talk at our stakeholder meeting about much more visibility in that regard.

Simon Whale: The other thing we've heard, both from people representing neurologists and representing GPs, is a degree of confusion about who's responsible for what here. So neurologists have told us that they don't feel particularly

comfortable giving women advice on contraception, it's not what a neurologist does. On the other hand, GPs, I think the Royal College of GPs actually came to one of our hearings and said it's the role of the neurologist as the principal prescriber to inform the woman about PPP and make sure that that's understood. We've got two conflicting messages here, what's your view on that?

June Raine: Yes, the steps we've taken are to bring - and in fact our former minister brought all the players, all the leading clinicians together to perhaps resolve these and the deliverable is across Royal College guideline, which is in draft and is about to be agreed. So that should help, because I think it's not simply roles and responsibilities; it's everyone owning the issue and not always thinking it's someone else's. So, I think we're nearly there and across Royal College guideline, underpinned by the valproate guideline from NICE, they should be out in March, will help with that. It's bringing together from the clinical angle what the woman should experience as a pathway where everyone has the right advice at the right time.

Sonia Macleod: With respect, in terms of the Royal College of GPs, their membership does not encompass every GP. So although Royal College guideline, I think, is a fantastic step forward, how does that reach people who aren't members?

June Raine: Again, it's a good question and one that we're aware of. I think the incentive from the NHS, which will go into the quality improvement activities from 1 April, will I hope then foster the questions of well, I'm going to be incentivised, I am a very responsible professional, I look to find what guidance exists and we'll take away from your question how we can make sure that guideline is then made available. It's the need for the NICE guideline to be available to enable practices to qualify for those additional points.

Julia Cumberlege: Right, we're just coming to a close now, which I'm sure you're pleased about. But I want to ask just one final question, because it comes again from a patient group, which was very concerned about the anomalies that they saw in how valproate was originally licensed. I don't know if you want to come back to us on that, but clearly they felt that the information was available, it was licensed for one year and it was licensed on condition that the patients were monitored for efficacy and safety and so on. They just felt that actually that was an anomaly and they didn't want that sort of thing to happen again in another area.

Ian Hudson: Sorry, I'm not sure the question - maybe we should follow up in writing on this, but I'm not entirely sure I understand the question. Why it was licensed only for one year, or why...

- Sonia Macleod: No, I think the question was related to the fact that the licensing was slightly anonymous in that the usual clinical evidence base wasn't required. Instead it was put on a one-year temporary licence. So we are going back to 1971 or 1972...
- Ian Hudson: Yes, it was licensed in 1972, put on [unclear].
- Sonia Macleod: So I think there were question marks as to how that had happened and why that happened.
- June Raine: I think at the forefront of consideration was the teratogenicity and I think at that time a study was required to compare it with phenytoin alternatives is more...
- Sarah Morgan: Well I think they had animal data which were concerning at the time of licensing, which was why they - and also efficacy concerns, which is why they licensed initially to specialist centres for a period of one year to collect data to enable further licensing. From what I can understand, the decision to give it a full licence or to stop the restriction of specialist centres, was on the basis that it was equivalent in terms of teratogenicity to phenytoin. But we can look back to see if there's any further detail on that.
- Julia Cumberlege: Because I think the patient group also feel very strongly that there should have been some clinical trials. You will perhaps inform us whether there were or there weren't.
- Sarah Morgan: Okay.
- Julia Cumberlege: Anyhow, thank you so much for this morning, very, very grateful.

END OF TRANSCRIPT

Session 2: Medicines and Healthcare products Regulation Agency (MHRA)

START OF TRANSCRIPT

Julia Cumberlege: So I'd like to start off by just asking you does the MHRA still think that mesh is safe for use in pelvic surgery?

Ian Hudson: Let me start with that one. I of course remain concerned with all the stories that I hear from the women who have been harmed by the procedures, and they're very moving and very difficult stories. I think mesh still has a role in appropriate circumstances. It's not for everyone, and clearly it has to be part of an appropriate treatment pathway, with properly informed, consented patients. I think we have to separate out urinary incontinence versus a pelvic organ prolapse and then the different sorts of prolapse, et cetera. But I think as per the NICE guidance, it has a role in different treatment pathways. So yes, I think in appropriate circumstances, yes.

Julia Cumberlege: The NICE guidance has a hierarchy of treatments and it's the last resort. Would you agree with that?

Ian Hudson: I think clearly our role is the product end and then more broadly, NICE look at it in the context of other available options, et cetera, but I've got no reason to disagree with the NICE guidance. It's been something that's been very carefully thought through, at least in terms of pelvic organ prolapse it wouldn't be, and the PROSPECT trial showed that the results were, in terms of the beneficial outcomes, similar, whether it's native tissue repair versus mesh.

But more complications for mesh, therefore, based on that and the whole treatment guidance and looking at the whole pathway, I don't think it would be a first line treatment for most conditions. But there will be people who will relapse after that first line treatment, or for whom it doesn't work, or particularly complicated surgery. So I think it's still an option.

Julia Cumberlege: We do know that in New Zealand they've actually removed the supply of surgical mesh for the treatment of pelvic organs. Do you think that then the implantation and single incision on the mini-sling for the treatment of SUI? Because New Zealand seem to be having a difference of policy than we do and I'm sure you've been looking at it and discussing whether it's something you would wish to adopt or not.

Ian Hudson: John, you may want to comment on the specifics, but what I would say is since we became really aware of these issues, we've looked at this a whole number of times from 2010 onwards. We've provided you with the chronology of that. I don't think New Zealand have seen any evidence that we haven't seen.

Since 2010 the review - the whole various reviews that have happened, our own review, your report, the SCENIHR report, the one we did for the Chief Medical Officer, the NHS England review, the Scotland review, NICE review, all come to broadly similar conclusions that in certain circumstances, as part of an appropriate treatment pathway, with appropriately trained people, with appropriate consent, there still is a role. I think that still applies for mesh. John, is there anything specific...

John Wilkinson: Well I think Australia and New Zealand were in tandem on this and the transvaginal prolapse repair route was viewed as not appropriate in that context. But you have to remember that they don't have a NICE, who is able to support, if you like, the limitations and the guidance on the use of the product. So perhaps they're in a slightly different position to the UK, where they didn't have obvious mechanisms for defining the constraints in use of these products. They may have come to a different conclusion for different reasons.

Julia Cumberlege: There's a similar situation with the USA, in terms of the USA, I understand, also have different recommendations.

John Wilkinson: I think there are subtle differences in the USA in terms of what the FDA is putting out as guidance, but I'm not aware of any wholesale bans for any particular procedures in the US.

Valerie Brasse: I think it was just the decision to reclassify much earlier, so they came to a view much earlier that it should be classified as a class 3 device much earlier than the Europeans.

John Wilkinson: Well it's a class 2B device in Europe and I think the classification systems are slightly different. But yes, I think there's some evidence that the FDA recognised the particular risk here and took measures to increase the risk management around that. The difference between 2B and three, relative to American FDA two and three is not - well, it's a more significant difference between two and three in the US and 2B and three in Europe.

Julia Cumberlege: While we're on the reclassification, it's something that very much surprised the medical profession and others that the reclassification took place about a year after the mesh was first introduced. Now, do you not think that was quite a strange decision to have made? Because there wasn't any evidence

then of randomised control trials or the science you were talking about earlier on. Yet this reclassification was made from C to A implying...

Sonia Macleod: The SERNIP reclassification.

John Wilkinson: SERNIP, right, sorry, yes. The SERNIP significantly predates me and that was a voluntary mechanism that was put in place to look at interventional procedures. I think that was subsequently superseded by the NICE intervention procedures programme. So I'm not sure I'm qualified to comment on the processes that took place there, but it would be surprising that you would move substantially from one risk classification to another unless there was significant data to support that, I would have thought.

Julia Cumberlege: Well it did surprise the Royal College of Obstetricians and Gynaecologists and other very important people in our world that that had happened, because they couldn't see any evidence of why the change was made.

Cyril Chantler: They were alarmed at the evidence that seemed to have determined it came from the industry, so that raised questions of conflicts. All of this, you know, is set out in the October edition of *The BMJ*.

Sonia Macleod: Can I just take you back a little, when you said New Zealand and Australia don't have the equivalent of NICE so they don't necessarily have the same measures that define the usefulness of treatment pathways, we do but those - as you say, NICE wasn't in place when mesh was first introduced. So if you look back to when mesh was first introduced, what mechanism was there for determining its use? Because SERNIP's clearly voluntary and device regulation back then, we're talking the mid '90s so it's relatively early, so could you put that into a bit of context?

John Wilkinson: As I said earlier, the medical devices legislation, the first medical devices legislation that came into force in Europe was in the early '90s. There were patchworks of activity done by individual authorities, but medical device regulations is in some respects in its relative infancy. So the processes that defined what constituted safe or unsafe use was largely left in the hands of the clinicians who chose to or not use the products. So the products were put on the market with evidence in those days which wouldn't satisfy current levels of requirement, because the world's moved on and certainly won't satisfy the requirements of the new legislation.

But in reality, there were very few controls over how new products were introduced. We're seeing examples where there has been rather rapid introduction or adoption of new technologies which have not produced the results that have been expected, or have been adopted at a pace which is not consistent with training and learning in that process. So I think there's

certainly something around the regulation of products and the management of introduction of new interventions safely which requires some attention.

Julia Cumberlege: Yes, perhaps we could go on to that, because certainly the patient groups think it's very strange that risks were not actually explained to them. Earlier on this morning we had a conversation about risks and the explanation now that is given to women. We hope that is actually happening within the service, because we're still getting grave concerns from women that they're not being told exactly what the risks are. In fact with this insertion of mesh, very few of them are actually shown the tools that are going to be used, what they call the hooks which are actually quite substantial pieces of metal that are inserted into them. When they've seen that, they then have second thoughts; is this a good idea?

Now, it's the whole process that actually needs to be explained to them. They need to really see what is going to be inserted into their bodies and in some cases not at all. It's just a conversation from the surgeon who says I can get rid of your incontinence very easily, this is a really good solution and don't you agree it would be a good idea? Women have told us that some of them were having physiotherapy that was working, yet the surgeons were saying you don't want to bother with all this exercise and things, this is the answer. Now, that sort of behaviour is really unacceptable, it is damaging, it is damaging people. I'm just wondering where in your regulatory framework where you can influence that sort of behaviour.

Ian Hudson: Maybe I'll start and John, you may want to comment. Certainly with this whole issue since 2010, with our chronology you've seen we've worked with the professional societies, we've worked with them in terms of information sheets to be given to patients. The British Society of Urogynaecological Surgeons and BAUS have all got leaflets, et cetera, on their websites and are to be made available to patients. Our expectation is, I think, very much the discussion we were having this morning.

My expectation is that there's a proper discussion between the surgeon and the woman, that treatment pathways as per NICE, et cetera, are followed and it's a frank and honest discussion that weighs up the difficulty of the condition that the woman has, which can be significantly debilitating and the risks of the options in terms of treatment and the potential benefits, but also the risks as well. I expect that's the conversation that should be taking place, absolutely. We have a part to play in that in that we're regulating the products end of things and will work with the other

bodies, but we're not the ones sitting there in front of the women and the surgeons need to be having that conversation, absolutely.

John Wilkinson: I think we have a role clearly, when adverse events happen manufacturers are obligated to report to us and we want more and more clinicians and patients to report to us. But often the challenge we face is sifting out whether the product was the problem, or there was a process or procedural problem. But I think we do have a role in surfacing the issues, I think we have done historically in this area, to try and encourage the other parts of the system to take notice and act on what may be a problem for patients and in this case clearly was for a significant number of patients.

Julia Cumberlege: Because women feel that they are almost part of a trial. They talk about being guinea pigs, that they're just being used just to try out these new processes, new meshes. Of course, we've had a debate I'm sure about innovation versus harm, et cetera. So of course, as a society we don't want to stop innovation, but we've got to make sure it's safe. Really what we've heard was that there wasn't really the research necessary to give women that confidence.

Ian Hudson: Well it's clearly, as we've established, some women have been harmed by these procedures. Each of these, the device element did produce a package that was reviewed by a notified body. The regulations have moved on, we can talk about the new regulations and that was deemed sufficient and generally, I think, goes up to about a year of follow-up, that sort of length of follow-up that was in some of the dossiers. I think I'm very sorry to hear that women feel that they are being treated like guinea pigs and I think clearly we've got to learn from these messages.

I think as John has said, what is very clear is that we've got to - when new technologies are introduced in the health system, there's got to be appropriate monitoring, appropriate training of the people inserting these devices, appropriate vigilance reporting tools, et cetera, so it can all be done safely. I think that's clearly where we must get to.

Sonia Macleod: But is a year's follow-up enough for a device that can go in for a lifetime?

Ian Hudson: Well I think the challenge with all of this is at what point is it reasonable to introduce something and then you've got to weigh up the condition the person is suffering from, the alternatives, how much distress they are suffering with the condition, what is reasonable to ask for prior to CE marking in the case of devices and what mechanisms are in place for appropriate follow-up afterwards.

Sonia Macleod: So in terms of weighing up and balancing, where does that process sit? What's your role as a regulator within that process?

Ian Hudson: For products to be put on the market, devices to be put on the market, they go to a notified body who will assess them, including the whole package, and issue a CE mark. We will then have a responsibility in the marketplace, but in the future legislation part of the process will include a plan for monitoring the safety of the product in the marketplace, on top of the normal requirements that are there now for reporting that.

Sonia Macleod: What I'm trying to establish is okay, you have a product, you sit and you say okay, we've done this, we've got this much on clinical file, we've got a year's worth of data, is it the notified body that says that's enough, that's sufficient, we think you've shown, you've demonstrated sufficient safety?

Ian Hudson: The notified bodies issue the CE mark at that point, yes, that's correct.

Sonia Macleod: So it's the notified body that does that?

Ian Hudson: Yes, that's correct.

John Wilkinson: I think what has shifted, I think historically the amount of clinical evidence required to place products on the market was significantly less than it is now and will be in the future. That said, there's a clear need for post-market follow-up, structured post-market follow-up, because if you go back 10, 15 years, essentially post-market follow-up was we'll collect adverse events and if we get a noise, a signal from that that says it's not working as we expected, we will react to it.

I think we're moving very rapidly and the new legislation will accommodate that into an era where you say well that's not good enough. You actually have to have a structured post-market plan, and that needs to extend for the whole life of the product, because we've seen lots of examples where products are introduced into clinical practice, they work very well for a period and then they fail because this may be 10, 15 years down the line. So there's a balance between what is the appropriate amount of information that goes with putting the products on the market in the first place and what you collect in due course.

You have to remember, I think, that these are typical engineering products, if you like, so that they do iterate, they do develop. So the products that were on the market 20, 25 years ago have almost no resemblance to some of the products that are on the market now. I'm thinking of things like pacemakers and the like, they're completely different. So there's a need to manage collection of long-term data prior to putting the thing on the

market, with the need to get things into the market and developing from the knowledge of their use in clinical practice, which is what happens. It's a difficult balance to strike, there are no hard and fast rules about it.

Julia Cumberlege: I do have to say, the patients that we've met - and we have met a great many in the course of this Review. There are patients who've had mesh inserted in the last few months, the moment they have the operation they felt this excruciating pain, they knew things had gone wrong. They have had great problems in trying to find surgeons who can take out the mesh. When you're inserting it into this part of the body, of course, it's very, very vulnerable. You've got so many other organs around. Sometimes it's been badly inserted and we've heard some detailed examples of why that has gone wrong.

There are issues about the type of plastic, the polypropylene that's inserted and the mesh. There are all sorts of questions about the whole way of dealing with this particular problem of incontinence. This isn't something that's historical; it's happening now and we're getting the evidence from women who have recently had it inserted and are in a terrible condition. As I said, trying to get it removed is not easy.

John Wilkinson: We regulate the products, but in my mind clearly the implications of implanting products into people, which can't easily be removed, needs to be managed upfront by the manufacturers to an extent. They need to be thinking about that in the long term, but certainly the clinical community and those who are placing the products into patients. In terms of implanting devices, it's my understanding - and you've had many submissions from eminent clinicians who can speak much more authoritatively about the clinical issues. Clearly there is a sort of profile post-operatively where things will surface quite quickly if the initial procedure hasn't worked well and those need to be dealt with quickly.

Then there are long-term issues that may surface, and I think that just plays into the need for effective long-term follow-up. Two things, (1) effective long-term follow-up and (2) careful and managed introduction of new technologies, which I think sit in parallel with each other. In the introductory phase there are two components as well. There's what the manufacturers are obliged to do and then there's what the clinical community needs to do to support the safe, carefully managed introduction so that you build confidence, if you like, in a new intervention over time on the basis of good data about that...

Julia Cumberlege: And what the regulator does.

John Wilkinson: And what the regulator does, yes.

Julia Cumberlege: Or doesn't do.

John Wilkinson: No, we have a role in looking at the manufacturers' responsibilities, looking at the data broadly to see that things are performing as they're expected to do. If they're not, then we have an obligation to intervene.

Ian Hudson: I think it also comes to the appropriate discussion with the patient, with full insight as to the risks. The figures show that most women do derive benefit, but not all do, and the stories are the ones we've heard, you're telling us about. But the appropriate consent, appropriate discussion of the risks, taking into account the condition and the suffering of that woman before she gets to thinking about surgery, alternate treatments, et cetera. Then the provision of the service, the training of the surgeon, whether they're doing enough operations, et cetera and if things go wrong, what the provisions are for looking after the woman afterwards.

Julia Cumberlege: But we do often hear the surgeons saying this is the answer, this is the way, this will solve your problems, all the rest of it. There isn't a proper explanation, there isn't what could go wrong. I know in this country there are some exceptionally good surgeons and I absolutely appreciate that, but I have to say there are some that are so convinced of their own views that they are not expansive enough to women to tell them what could go wrong. We hear that, we hear that now, this isn't history; this is what's happening now. Sorry, okay, I'm going to go on to somebody much calmer than me. Cyril.

Cyril Chantler: When we've met the National Institute for Clinical Excellence and NHS England, various things have come through. One is how long it's taken to recognise that there was a problem, because yes, you're right, 90 per cent-plus seem to have got benefit. What nobody seems to have appreciated until we met the women is just how terrible the suffering is for those where that is not the case.

So when NICE responded to the *BMJ* article of last October, they said the systematic approach after our recommendations in 2005 could have identified more quickly and avoided many of the adverse outcomes of mesh. When Professor Willett gave evidence on behalf of NHS England, we said to him given all you've done, what would you say could have been better? He said it was all too slow. It honestly took us meeting these families to actually go back and say the recommendations of how to improve the service were actually sent round by the medical director of

NHS England in 2012 and again in 2017. Here we are in 2018 and it's not happening.

So we then went to the chief medical officer and eventually to NHS England and said to ministers, saying we think you should stop until such time as the things that need to be done, which are set out, have actually happened. I have to say, they've not happened yet and we need to talk about that later on this afternoon maybe. But why has it taken so long? Who is in charge of it?

Ian Hudson: I ask myself is there more that we could have done at an earlier timepoint and then I look back to see what we have done and when we started hearing about this in 2010, the commissioning of your Review then and all the other reports that we've been talking about to see the totality of the data, working with the various professional societies, et cetera, working with DH and all of this. I agree, it's taken a tremendous amount of time and I would have liked to have seen a considerably faster process, progress.

Cyril Chantler: But why should we think it's going to be any better with the next interventions? NICE said to us intervention procedures guidance aims to protect the safety of patients and its recommendations should be seen as mandatory, not advisory. So what does mandatory mean if there's nobody to make sure it is mandatory?

Ian Hudson: Well I think this gets to the crux of some of the issues we were talking about this morning, how to join up the systems such that if there's guidance, like the NICE guidance here or something on valproate we were talking about this morning, where the system is mandated to take action or follow the guidance or deal with it.

Cyril Chantler: Who can mandate it?

Ian Hudson: Well I think this gets to the questions we were talking about earlier, do you need some overarching safety committee that says henceforth it will be? Or does a body like NHS Improvement have the power to say henceforth the Health Service will do? Or is there a patient safety...

Cyril Chantler: Will your role change in the future in any material way? In this instance I understand what Mr Wilkinson has been explaining to us, but you're going to become a competent authority, aren't you?

Ian Hudson: We are the competent authority.

Cyril Chantler: Is that going to change when the new regulations come in, so that you will have more capacity to influence this?

- Ian Hudson: I think our role is on the product end of things, but to continue to monitor and if we continue to get lots of events coming in and hear the stories, then I think we still have the job of trying...
- Cyril Chantler: The [unclear] you get is in what way does it reflect the patient experience? We know that quite often success has been the clinical outcomes, you're no longer dry - no longer wet, but it's not including the other outcomes measures, the PROMs, the patient reported outcome measures, or the PREMs, the patient experience measures. So success may be success in terms of the primary aim, it's catastrophe in other ways. So who picks that up and is that within your surveillance, or is it somebody else and if so, who?
- Ian Hudson: Well, we still will be collecting safety data on an ongoing basis and if we're still hearing about major safety concerns, despite all the actions the system is taking, then of course we will have a responsibility to flag that concern.
- Cyril Chantler: But they never reported to you, or you didn't require from the system the fact that there was pain, or that they had dyspareunia, or did you?
- John Wilkinson: I think you're pointing to an interesting issue around the rules that sit under the regulation around reporting. It's evident from the numbers of reports that come from manufacturers that the bad outcomes for patients aren't necessarily linked to the product per se but are actually clinical practice issues. So the obligations on manufacturers are to report incidents which involve above a certain threshold of seriousness, but effectively that has to be linked to the performance of the produce per se. There is some grey in that interpretation, I would say.
- Cyril Chantler: So what reporting system comes to you, the yellow card system, which we gather is going to be approved and digitalised? How would you pick up things that may be a concern to the patients but not necessarily to the manufacturer?
- John Wilkinson: If we had more patient reporting it would make a significant difference. At the moment that's low, despite repeated efforts, we've increased the amount of patient and clinician reporting, but it still isn't at a level we would like.
- Cyril Chantler: I thought they were now the main cohort of people who reported to you.
- John Wilkinson: I'm talking in medical devices terms.

Valerie Brasse: Can I explore that a bit further, because it's my understanding that the medical advisers as a whole, the main mandatory reporting comes in from the manufacturers and that is your highest number of reports...

John Wilkinson: Correct.

Valerie Brasse: ...for medical devices overall. Then you get the healthcare professionals and below that you get the patients. When we look at mesh, pelvic mesh figures, on the other hand, it's completely different. There is this reversal, the order is completely different. So although the numbers aren't high, it's actually now the patients who are reporting more, then the healthcare professionals and at the bottom are the manufacturers. Is that because what the patients are reporting are the adverse outcomes of a procedure and how it's affected them and the manufacturers are only looking at was there a fault in the product? Is it a factor that...

John Wilkinson: I think that is essentially the issue that you're alluding to here. Actually when dealing with bad events, you need to look at them in the round, in my view. But as a product regulator, the manufacturers have particular obligations in relation to performance of the product.

Valerie Brasse: They're not reporting anything else.

John Wilkinson: They can't take responsibility for how people use them, although often we get useful signals from manufacturers' reports about usage issues, which we will use. But in reality...

Simon Whale: Aren't we linked to how the manufacturer markets the product? So if the manufacturer is persuasive, as they often are when they market their products, that in this case it is quotes and this phrase has been used many times in front of us, 'a gold standard product with a gold standard procedure, 30 minutes as opposed to an overnight hospital stay and so on, but think of the money your hospital can save'. Manufacturers using all these quotes and persuasive and on the face of it very credible arguments, then the result of that is that hospitals and individual clinicians are going to follow the manufacturers' line of thinking, they're just going to do it. So the manufacturer is creating a demand, not serving a demand.

John Wilkinson: I think it's true to say that manufacturers invest large amounts of money, I'm guessing, in producing products that resolve particular clinical issues and therefore, it's not unnatural that they would want to commercially exploit those. Equally, I think there is an obligation on all concerned - and a big part of our role is to ensure that the evidence that's put forward to support those products is consistent with the claims of their usage. The manufacturers are obliged to describe the conditions under which the

products should be used, but clearly it's a system issue in terms of what clinicians ultimately actually do with products and how.

So I think it comes back to this safe clinical guideline, safe introduction and managing introduction. Historically there might have been incentives to commercialise things as rapidly as possible, because that's the way - you've invested, you want to get a return on that investment. I think now that clearly is a flawed approach in many respects and the introduction of new technology needs to be managed stage by stage so that the assumptions pre-market are reinforced post-market to a point out in the future, whenever that may be, where you say actually we are confident that this works as it should...

Simon Whale: Do you think manufacturers would agree with you, that that way of doing things was flawed?

John Wilkinson: I think increasingly the enlightened ones are. If you look at some of the initiatives that are happening across the pond in the USA, it's certainly about long-term - it's about real-world data which is happening in turn, but I think that's what it's about. It's about how do you collect effectively data which reinforces your pre-market proposition or otherwise, but that effectively ensures that the assumptions that you put the product on the market with are borne out in practice. If they're not, you do something very rapidly to fix that.

Simon Whale: So as the product regulator, how do you enable yourself to be confident that a product that is designed to go into a human body for a lifetime, at least a very long time, is inherently safe?

John Wilkinson: It's increasingly a combination of what's the data that supports putting it on the market in the first place and what is the plan...

Simon Whale: Risk market authorisation.

John Wilkinson: ...to manage it in terms of post-market data collection.

Simon Whale: Doesn't it come back to Baroness Cumberlege's...

John Wilkinson: That would not have been the case 10 years ago.

Simon Whale: It comes back to Baroness Cumberlege's first question, doesn't it, which is, it's kind of understandable that women, in the case of mesh, would feel like guinea pigs. Because the only way in which you and the industry can understand whether this product is suitable for a lifetime in the human body is to put it in some human bodies and see what happens.

John Wilkinson: That applies to any intervention, whether it's pharmaceutical or medical.

Simon Whale: It's a fact of life, isn't it? So should the system, including every aspect of the system, the regulator, the manufacturer, the health professional, should the system not be a little bit clearer with people that this is the reality of innovation and medical progress?

John Wilkinson: I think you're absolutely right and I think conversations I've had with patients have often surfaced about they didn't realise that products were going to wear out. They do, hips and knees don't have an infinite life cycle. Products do potentially change across their life and those risks and the consequences of failures need to be played out very clearly for patients, because that's part of the risk benefit equation that the patient needs to understand in managing the conditions and the potential interventions that can resolve those.

Simon Whale: When you authorise a product, to what extent do you take into account the difficulty of removing that product from the body, should it be necessary?

John Wilkinson: I would say historically that's not been a focus of the regulatory system. I think it's been very much focused on a reasonable effect forward from the intervention. Some of the long-term impacts have not been fully considered, actually they're not fully understood in all cases because clearly some patients are outliving their interventions in ways that perhaps weren't anticipated in the days...

Simon Whale: Do you think it should be part of the decision-making process?

John Wilkinson: I do, yes, absolutely.

Simon Whale: Under the new regulations, is that possible? Are you enabled to do that?

John Wilkinson: The new regulations are very much more specific about requirements around post-market clinical follow-up. The old ones have words in that space but were really just talking about collecting adverse incidents and reacting to those. This is a much more proactive issue and I think it's very important that the long-term impact of these products on people is considered and those are weighed up at the time of intervention because they - and they are in fact in many cases.

If you think about hip replacement, for instance, a lot of the sometimes less than successful innovation has been trying to manage this need to intervene with ever younger patients. But in the knowledge that hips - we've just had some data last week - last 15, 20, 25 years. They don't last

forever and you don't have an infinite number of opportunities to revisit the operation in the first place.

Simon Whale: If you're talking about a piece of polypropylene inside the pelvis which in terms of removal has been likened by patients and by commissions actually when speaking to us, to removing chewing gum from the hair. Do you still think that there is a place for surgical mesh in pelvic procedures in the future?

John Wilkinson: We've consistently been advised by clinicians and a wide range of places that there is. I think we have to go on the clinical advice we have. There are intractable problems for which mesh remains the most effective intervention. So I have to go with the breadth of clinical opinion that I've received.

Julia Cumberlege: Can I just ask you, because as I understand it, when you're bringing a new medicine, a medication or whatever to the market, there's a huge amount of research that has to go on. It takes about nine years, something like that, from the very beginning to the product on the market. Where does devices fit into that? Because it seems to me that the regulators or whoever are far less rigorous in ensuring that the device is safe.

Ian Hudson: Maybe I can pick up that a little bit and then John, you might want to come in. Medical devices, of course, span anything from an Elastoplast all the way through to mesh and hips, so a very broad range of different things. The regulations are getting much more stringent with medical devices, requiring much more clinical data before they get the CE mark together with a plan of monitoring afterwards, plus additional pre-market scrutiny for the highest risk devices. So all of that will actually increase the requirements on device manufacturers to produce a larger dossier of evidence before a product is CE marked.

Clearly, each device or each medicine have very different circumstances, et cetera and it's got to be tailored to the circumstance. So I think it's right that the regulations, the new set of regulations, device regulations are increasing the requirements, particularly for the more complicated and invasive devices. It's right that that should happen.

Devices are different things to medicines, of course, devices continue to evolve, slightly change that, slightly change that. You can't do that with a medicine without having to go through a significant development programme. Then it's a question of tailoring the needs to the circumstances and how different is it to something else. But the

requirements are certainly going up for devices, perhaps more than they have been in the past. John, is there anything you want to add to that?

John Wilkinson: I don't think so. I think it's a balancing decision around risk, cost, a whole raft of issues relating to what constitutes a reasonable amount of evidence for placing the product on the market. What constitutes an effective follow-up and I think it's difficult to define precisely. There's no generality to it because some products are clearly very different from others in terms of the level of evidence that would be required and the consequences of getting it wrong, which is probably the most important component here.

Valerie Brasse: More regulation doesn't mean better regulation.

John Wilkinson: It doesn't, you're right.

Valerie Brasse: So this is around variability and CE marking up to now has obviously been a problem. Do you have confidence that having more regulation will mean better and that the means by which the governance arrangements and the processes of getting the CE marking will actually improve the concepts?

John Wilkinson: The legislation has clearly learnt the lessons of 20, 25 years of using the previous generation of legislation. But like all legal frameworks, the proof of the pudding is in the eating, as it were. The implementation of that legislation will be critical to its success.

Valerie Brasse: It's the variation in interpretation.

Ian Hudson: Perhaps I can come in just on this. I think if you're talking about the standard of the notified bodies, this is an issue that we have been addressing for a number of years. Following the breast implant issues, we've pushed for a joint audit programme of the notified bodies. So it's not just a single competent authority inspecting the notified bodies, but it's a broader - it's the commission and two member states, another member state involved.

Valerie Brasse: That's our routine?

Ian Hudson: Yes, and the notified bodies. So that's been in place for a number of years and we've seen actually a drop-off in the number of notified bodies from what, 80-odd to 50 or something.

John Wilkinson: Fifty, yes.

Valerie Brasse: What did that mean for the devices that they CE marked?

Ian Hudson: Well they're still in place but...

Valerie Brasse: So hang on...

John Wilkinson: Well perhaps I'll comment. If a notified body ceases trading there's a challenge that they have to find a new notified body. So most...

Valerie Brasse: So manufacturers would...

John Wilkinson: The manufacturer has to go and find a new notified body. The notified bodies as the recipients can either take on face value that the product has gone through the certification process, most or I would say all don't do that, because clearly they're taking responsibility. Legally they typically can transfer to another notified body. In reality, the recipient notified bodies are fully reviewing their products and we've seen post the introduction of the joint audits, we've seen a spike in the withdrawal of CE marks across Europe which I would interpret as certificates being removed because the evidence didn't support the products.

Valerie Brasse: What proportion of those were class 3? Any idea?

John Wilkinson: I'm not sure I can answer you that and I'm not sure whether I've got that data available, but probably relatively few because most of the notified bodies that have gone out of business have been the smaller notified bodies, which would probably not be doing class 3 products. But that's just...

Valerie Brasse: There's a lot of probably in that.

John Wilkinson: Well, there is because I haven't got the data.

Valerie Brasse: No and really that's one of the issues, isn't it? Not holding a central register of what's actually on the market.

Ian Hudson: Can I also follow up with the new regulations, John, I think it's true to say that all the devices that are currently on the market have got to go through a recertification...

John Wilkinson: Yes.

Ian Hudson: ...and the notified bodies have also got to go through a re-designation process as well.

John Wilkinson: Yes, historically when you change in a lot of regulatory regimes you go from one to another, there's a sort of grandfathering activity. There is no grandfathering in this; it's transition arrangements but no grandfathering. So every product that's currently on the market needs to go through a recertification to the new standards.

Simon Whale: Is it right that notified bodies should be, continue to be commercial companies?

John Wilkinson: I'm not sure that's a question that I'm in a position to answer.

Ian Hudson: I think the question...

John Wilkinson: Well, they vary in reality from publicly owned bodies, in certain member states they're part of two organisations like BSI in the UK, which have peculiar constitutions. They're a private body but with a public purpose, through to more commercial enterprises. They're all linked to conformity assessment bodies, standards bodies and the like, which in many sectors is deemed an appropriate way of approaching that, approaching ensuring that there's conformity and things are being put on the market and conformity with the legislation.

Simon Whale: I suppose certainly...

John Wilkinson: If they're managed effectively, I'm not sure that there's an issue around whether they're in public ownership or private ownership.

Simon Whale: Obviously the question or the issue that people have raised concerns about with us...

John Wilkinson: Yes, I understand that.

Simon Whale: ...is the role of the profit motive. So if the notified body is there to make profit and be a successful business, it needs to attract custom and to attract custom it has to know and serve its customer and its customer is manufacturers.

Ian Hudson: I think the question is rather than are they commercial enterprises, are they competent to do their job and I think that has been the thrust of the joint audit programme, the whole recertification of notified bodies, et cetera. The inspections of notified bodies by the competent authorities across Europe to make sure that they're competent to do the job. We talked earlier about the number of notified bodies reducing from 80-odd to 50.

Simon Whale: So the fact that the profit motive is involved is not a concern to the MHRA?

Ian Hudson: Profit per se is not the issue, it's whether they're competent to do their job and they do it entirely appropriately is the area we would focus on.

Cyril Chantler: I want to turn now to the how, we discussed this morning the what. One of the requirements for releasing reports which was set out, is that surgeons

report every procedure to an active database, a register of operations is maintained to ensure every procedure is notified and the woman identified has undergone surgery. So that is an agreed what, and it's been around for a long time. So what about the how?

When we met the president of the Royal College of Surgeons and the president of the Royal College of Obstetricians, we put to them the notion that there was a difference between a national database and registry. As far as the database is concerned, we would propose that every time a surgeon completes an operation, as part of the operation note which she or he always completes, that they would register a set of information which would include a device which has been inserted, maybe with Scan4Safety and a barcode but whatever.

That would then be reported to a national database, in other words, the responsibility for creating the database would be on the person who did the operation, not a third-party code or whatever. Was that a reasonable proposal? They said yes, they thought it was. It's in line incidentally with what the Royal College of Surgeons has said is the future of surgery. First question - and I've got three - the first one is would you support that?

Ian Hudson: Absolutely, yes.

John Wilkinson: I think one - there's evidence that coding is one of the critical areas and clearly, we've seen that in other jurisdictions. Accurate coding is one of the fundamental building blocks of anything that's going to work here and the surgeon who's done the procedure is the best placed to code the thing appropriately and correctly.

Cyril Chantler: My second question is who would be responsible for creating this database? Would it be you? Or would it be a new agency, which we've discussed more than once during this session?

Ian Hudson: Do you want to talk about the discussions we've had in relation to this?

John Wilkinson: Yes, I think we've got a lot of experience of registries on the devices front, particularly in the orthopaedic sector, because the National Joint Registry has been operating for a long time, very successfully and very effectively and has been a vital tool in allowing us to be the first regulators worldwide that...

Cyril Chantler: I'm talking of the database here, not a registry.

John Wilkinson: Right, okay.

Cyril Chantler: The database is the information which is - you used the word mandate and I think it could be mandated under legitimate [unclear] reason and GDPR to be collected. The registry is what then interrogates the database with the complicated [unclear] and that does, in my understanding, require quite properly patient participation in permission to do that. It would also, I think, reasonably involve people who are expert in this area, be they the Pelvic Floor Society, BAUS, [ISA] and so forth.

John Wilkinson: Well, I don't think the responsibility for putting large databases together, covering a variety of interventions across the system including those that involve drugs and devices or not, is the responsibility of the MHRA. We're a product regulator essentially, so I think the need for us to be engaged in that process, with that process and have access to certain aspects of information that surface is absolutely critical. So I think we are a very interested party, but probably not going the...

Cyril Chantler: That needs to be my third question.

Ian Hudson: Can I just comment on that? I think particularly if it can be linked with the patient notes, that would be the way, electronic patient notes, properly coded. Then maybe a body like NHS Digital that can extract them from the patient notes would be the way to hold the data. Then to put on top of that the analytics around a registry to...

Cyril Chantler: There are certainly GDPR issues and this and that which I'm not competent to discuss, because that gets into using it as a register and that does require the permission of the patients. Once you've got the database, you've got something which enables other people with permission as appropriate to link to.

You are one of those people, which is my third question, which is, given your responsibility for seeing whether medicines and devices are safe in the short and the long and the infinite term, if you've got one inside you as I have, then would you be able then to construct, theoretically at any rate, a linkage system which can link the yellow powered reporting system to the database so that you could facilitate, as I think you've just suggested, Dr Hudson?

Ian Hudson: We would certainly want to look to do that. We currently hold CPRD within the MHRA and we are exploring how we link yellow card data with CPRD to rapidly look at signals. June can maybe comment a bit more about that. So similarly, if we have a large collection of patient records effectively or patient data to be able to, with a signal or even look at this database for -

well, we'd need to think through the scientific merits of using it to confirm signals or not, but that's a separate issue.

But to somehow link the generation of a signal somewhere with interrogating the database rapidly to evaluate it properly, absolutely, that's the direction we'd want to go. We already link CPRD with about 12-15 different datasets, hospital and associated statistics, the number of registry type data for epidemiological type purposes. June, do you want to comment about the work you've been doing in regard to...

June Raine: Even a little step further is how to involve the patient voice, because if the patient is going to be asked please will you give your permission for us to do studies, et cetera, but the app that we've produced that we talked about for yellow card, we've got quite an interesting piece of work ongoing at the moment to link that data. It's called application programme interface work, but to link that in, so in an ideal world the patient would be able to add their experiences and feel a real sense of ownership of the monitoring of the treatment or the intervention.

So I think we start with simple questions, spontaneous data and this exposure monitoring through a registry or a database, then build the registry so that that has an opportunity not just for regulatory positions, but for other important public health uses as CPRD is.

Ian Hudson: I think the importance of a registry in this area deals with the product-related aspects, but it also deals with the clinical practice outcomes in relation to clinical practice. I think both are important elements to be able to monitor in a register.

John Wilkinson: I think our experiences of talking to people about registries and what's good and what's bad, we've done quite a lot of work. Clearly the governance around registries is important because the data needs to be available to patients, it needs to be available to manufacturers, it needs to be available to clinicians, there are a whole load of stakeholders that can benefit from the feedback loops that registry data allows them to use for the benefit of...

Cyril Chantler: You can do a lot with anonymised data and I think the law is pretty clear about that and the factors now. But it's not quite so clear when you're using patient identifiable data of their immediate medical circumstances and that we have to go away and explore. But in principle, you're alongside what I've just been saying?

Ian Hudson: In principle, we would very much value richer data sources such as the one you've been describing to enable better decision-making, absolutely.

Sonia Macleod: The other query alongside that is that obviously NHS data is linked into the NHS systems. Anything in the private sector doesn't automatically. So in terms of device systems, we've heard certainly a lot of mesh was done in the private sector first, because device availability, because of funding issues, is often then in the private sector first. Do you monitor relative difference in usages between private and NHS? Do you look at that data?

John Wilkinson: We don't have access to that sort of data and I think that's...

Sonia Macleod: Would it be helpful to?

John Wilkinson: I think it would be extremely - I think you have to consider the interests of patients in the round, not whether they've chosen to go into the private sector. Actually, I think obligations for data sharing broadly speaking between the NHS and the private sector should be similar.

Cyril Chantler: Do you have any connection with PHIN, the Private Healthcare Information Network? I should declare an interest, by the way, I'm a non-Executive Director..

John Wilkinson: I'm not aware that we do, no.

Ian Hudson: No, I don't think we do.

June Raine: I'm not sure.

Cyril Chantler: Maybe outside the meeting, that would be helpful.

Julia Cumberlege: Just because that's been raised, can I just ask you about the private sector? Because the private sector, of course, does a lot of work for the National Health Service. We just wondered, as you are the regulators, whether you analyse whether device implanting procedures are carried out at different rates in the NHS and in the private sector.

Ian Hudson: I don't know the answer to that, do you?

John Wilkinson: I don't think we have access to any information. We have anecdotal information, but that's the best we can offer in these situations.

Julia Cumberlege: But you are the regulator also for the private sector.

Ian Hudson: We're the regulator, yes.

John Wilkinson: We're the regulator for products that are used in the UK, whether they're used in the private hospital and increasingly it's neither the private sector nor the public sector; it's actually in the home and the like. So I think we are responsible for the thing in the round, but that doesn't necessarily

equate with having good quality information about what goes on everywhere in the system.

Julia Cumberlege: Do you think you should be finding out some of that information?

John Wilkinson: I think it would be very helpful to understand whether there are differences in clinical practice that sit in the various places, the differences in outcomes. Because clearly the risk profile to patients may be different according to the circumstances in which they are being managed, whether that be at home, in hospital, in a public hospital or a private hospital or wherever else, in a nursing home.

Julia Cumberlege: Is there a body that can do that?

Cyril Chantler: Yes, there is actually.

Julia Cumberlege: Right, well he knows, he knows everything.

[Laughter]

Cyril Chantler: We'll talk about it afterwards.

Ian Hudson: Okay.

Cyril Chantler: Forty-five per cent of their activity, as we've learnt, in the private sector is on NHS patients.

John Wilkinson: Yes, but I think there is a broader trend which means that historically, traditionally patients went to a hospital, they were managed by a consultant and they left. That breaking down in many respects, hospital stays are shorter and the amount of community care is changing. The sort of products that industry's developing are actually reflecting that as well. So the risk profile of managing the system is changing, I would say.

Simon Whale: Could I just go back to the discussion that Sir Cyril raised about databases? Bearing in mind your contact with, working relationship with manufacturers, you might know their thinking a bit better than we would. Do you think they would find databases of the kind that we've discussed now helpful from their own perspective?

John Wilkinson: My belief is the forward-looking companies want the best available data about the performance of their products. Historically they may not have necessarily wanted to surface issues in a timely manner, I don't know, it's hard to say. But the forward-looking companies now realise the consequences of the long-term continuing failure of a product to them, reputationally, financially, in every other respect. Clearly they don't

generally set up in business to damage patients; they're there to help patients.

So my view is that it is in the interests of everybody to have good data and to act upon it in a timely manner and that includes the industry. I think they'd be hard pressed to say otherwise and I don't think they would, from my experience.

Ian Hudson: Maybe I can add to that, John, to say I absolutely agree with what you've said, but clearly there are 20 device databases in the UK of different sorts already. There's a large number of medicines registry type things across Europe and companies use them to address safety issues with their products. June, you'll have seen through your various vigilance activities, a lot of companies producing medicines are using databases to...

June Raine: Yes, certainly the big shift, the new era started with the requirement of companies to have in place a plan to fill in the uncertainties, to actually conduct studies that would answer the questions that largely are predictable and to do so in a reasonable period of time. So that really has created a momentum and again European agencies have been doing quite a lot of work about how to have visibility, the best model for a registry and how to build interoperability.

Just as many of these things build from the passion of health professionals, the biologics for example, a marvellous registry in the UK, but others in other countries, can they provide an interoperable base so that when a safety question arises - I think one good example was when the question about brain tumours, for example, that you can get rapid answers rather than small snapshots. So this is now going to be the era of getting good data, robustly analysed from real experience which can be very different, however much we want good trial data, it is rather selective compared with the real world out there.

We always have to pay tribute to the extent the clinicians go to try and help their patient, even if perhaps the circumstances that patient's in are not quite ideal. So I think yes, it's the future and I think the companies who originally said when we introduced risk management plans, I can quote from experience, this will be expensive, then reflected how expensive it is, not just in financial terms but in human suffering to have not enough data soon enough.

Cyril Chantler: It's worth putting on the record, many of the clinical databases were established by clinicians who were trying to help patients and quite often they've had to find the funding themselves for the database. I personally

think it's time for the state to get much more involved in this and work with the clinical community and the patients to produce a better system.

John Wilkinson: One of the things worth identifying is one of the spinoffs of the National Joint Registry was an initiative called Beyond Compliance, which when it was set up was beyond compliance, but arguably post-2020 when the new medical advice regulations come in, it is just part of providing a service to be compliant. That would really very much target at this early introduction, ensuring that products were introduced into the market to a selective number of clinicians who are properly trained and committed to feeding back.

So the Beyond Compliance model, while having had a number of teething troubles on its way in, is a pretty good one to look at to see if that can be replicated elsewhere, I think. It needs some development, it's not fully mature, but in principle it's providing both the clinical community and manufacturers the sort of early stage feedback which should allow you to head off problems earlier, or indeed see opportunities for improvement earlier, if you like, perhaps two sides of the same coin.

Simon Whale: But there's an appetite amongst manufacturers, as opposed to just a willingness to go along with something. An actual appetite, I think, is what you're saying there is.

John Wilkinson: Yes.

Simon Whale: Then combined with your own appetite for that to happen and similar feeling amongst the relevant clinical bodies, then it ought to be possible to make it happen very quickly, is that right?

John Wilkinson: It ought to be and the UK is in a position to be a world leader in that. I don't think regulators worldwide are going to prescribe local data, but the manufacturers who are producing products for the world generally will need to find the data that's going to support their regulatory submissions worldwide. I think there are opportunities around that for the UK to show a lead.

June Raine: May I add to that too because, just quickly building on Dr Hudson asking if I'd like to comment and in terms of the experience that we have in the area of medicines, in proactivity studying safety once a product's in wide use, that can be extended to the device world. In order to, I think, perhaps have a leapfrog effect, have a very large advance in perhaps a shorter space of time than it's taken medicines, the innovative medicines initiative that's funding the world commonly, integration of data with us at the moment in

the application programme interface world has accepted that devices should be part of this.

So I think it's all telling you that you're absolutely right, the industry is beginning to realise that public health protection should span these different worlds of medicines and devices and build on the very best.

Julia Cumberlege: Can I just ask you, thinking about the industry, we talk about it as the industry but of course it's different companies. Those companies are in competition with each other, they are concerned about their share prices and all the things that go with the private sector. I'm just wondering, we were talking about how useful they may find data in terms of the robustness, the acceptability, whatever, of their products. But if they get that data, is there any requirement do you think in the future that they should make it public?

Because one of the issues that we've heard from patient groups is the secretiveness of the manufacturing industry. Personally I've had an experience with that, of actually just trying to go into one of their - with permission - one of their sites. It's like going into Fort Knox, they are very worried about people who are not part of the company actually coming onto the site. So I'm just wondering if we do as we're hoping to do with data and possibly later on registries, et cetera, but with the data, if the data is shared with the manufacturers do you not think that they should make that data public as it is influencing their marketing potential?

Ian Hudson: May I pick this up? Yes, absolutely. I think what should happen - we have this policy in relation to clinical practice research datalink which we have within the agency that studies done on it have to go through approvals, through our independent scientific advisory committee. We publish which studies have been approved and then there's an obligation to publish the study at the end. I think the owners of the database, if companies want access to that data, should be agreeing that any studies done on that data should be published. I think that's the way to handle it.

Julia Cumberlege: I think people would be very reassured by that actually. Right, any more?

Valerie Brasse: Yes, can I ask you if MHRA had to recall a mesh product, would you do it and how would you do it?

Ian Hudson: Well how do we recall - we can revoke a CE marked product and communicate, but go ahead.

John Wilkinson: We have powers to take products off the market if we feel there's a significant public health risk. When we do that, we do it on behalf of the

whole of Europe. That can by necessity make it a somewhat interesting process if other parts of the system don't agree with your assessment of the risk. But we have the powers to take a product off the market. There are recalls taking place on a regular basis as part of the routine workings of the regulatory system, there are batch-related product problems and such like which will generally be executed by the manufacturer. In fact, most of the regulatory action is executed by the manufacturer, because they understand their obligations and they do it. We will...

Valerie Brasse: So you tell them the particular mesh now has to be recalled?

John Wilkinson: Yes, we have the power to persuade manufacturers to take products off the market, in which case they take it off. We have the power to force them to take it off, which is a slightly different legal process. But if products are taken off the market, typically we will issue a medical device alert and galvanise the system to freeze inventory.

Clearly recalling products that have been implanted already is a different matter, so I think there's been a series of - and we saw this with, if you like, the guidance around metal-on-metal hips. You have to take very serious considerations of what's in the best interests of patients for the next step for an implanted product. So you're not going to say everybody has to have their mesh removed and replaced, because clearly that needs very careful clinical consideration.

Valerie Brasse: Part of the issue of being able to make that decision is locating where the mesh has been implanted, in which patient and where they are. Of course, without the unique UDI at the moment it's just the practicalities of how that would happen.

John Wilkinson: Well UDI in conjunction with Scan4Safety are the keys to, if you like, a Pandora's box of information in the future which will help us to manage these things, they're rather...

Valerie Brasse: That's the thing...

John Wilkinson: Well it's beginning to happen. We've got Scan4Safety, we've got UDI compliant barcodes on most of the high-risk products now. So that data is happening, it needs to be implemented in a more consistent manner and we need the datasets to be designed so that they can be interrogated effectively. So I think we're well down the road, but we have still a long way to go.

Valerie Brasse: But if you had to recall a product that was already implanted, where we're pre-UDI world, pre-Scan4Safety, can it actually be done? Can those

patients be located, found, brought in, had a consultation? Can any of that happen now?

John Wilkinson: It can and does happen, but it can be very clunky and you can have no guarantee that every patient...

Cyril Chantler: I think Valerie's asking can you do it for mesh.

Valerie Brasse: Exactly, yes, can you do it for mesh?

John Wilkinson: The probability is, I would imagine, not easily with mesh. With things like a heart valve or a pacemaker, I suspect the recording of the particular products and linkage to patients and paper records is more comprehensive than it would be for mesh.

Ian Hudson: I think the other thing though, part of a consideration to recall a product is what do you do with the patients who've got it implanted. A lot of the circumstances would be we don't put any more in, but the risks and benefits of removing a product that's already in and is functioning, appears to be functioning well, would be quite different to not implanting a new one. So that's part of the risk consideration at the time, when the decision is taken whether to recall a product or not.

Simon Whale: It's just that there's a practical issue before that, which I think you've just covered, which is that you just can't - it's not possible in the case of mesh to locate those people who had it...

John Wilkinson: I can't answer the question until you try. I think it would be very variable. I think you'd find certain hospital trusts have excellent recordkeeping and have historically collected the sort of data that's required. Others possibly not, I don't know is the answer. We have previous experience from the PIP breast implant issue, where it took a long time to reconcile the...

Julia Cumberlege: When you force a company to take their product off the market, presumably there's some sort of an appeal by the manufacturers for what you're doing, for taking it off the market. Are there issues where the manufacturer would actually take you to court? Would there be legal implications in this? Would there be compensation?

John Wilkinson: It's very rare for manufacturers to challenge decisions that regulators make on the medical device side. Particularly in Europe we've tried to take these actions in conjunction with our peers around Europe, which makes it more challenging. Generally, the data speaks for itself.

Ultimately, if a decision is made and the manufacturer wants to challenge it, national authorities like ours have a process where they can appeal it

locally, but ultimately under current legislation it has to go to the European Court of Justice for a decision. There is nothing in between, so there are no court appeal mechanisms which are more or less robust, not particularly legally sound, if you like, but very little between there and the European Court of Justice, would be my interpretation of the current system.

Sonia Macleod: And post-Brexit?

Ian Hudson: We do perhaps a bit more on the medicines side, we do end up in court sometimes with companies who do want judicial reviews against our decisions that we've taken. That is a fact of life, not very common but it does happen.

Julia Cumberlege: Right, any other questions?

Sonia Macleod: On another question, in terms of pharmacovigilance we are currently part of the EU, we currently operate [unclear] vigilance system. Guess the next bit, what's going to happen?

Ian Hudson: Are you talking medicines or devices or both?

Sonia Macleod: Medicines and devices.

Ian Hudson: June, do you want to...

June Raine: Well, I think we can be confident that actually what we do nationally will, largely speaking, continue. I think in terms of preserving powers for urgent action, then there we're talking in a way slightly easier decisions and urgent action on a device. You can suspend, revoke, compulsorily vary and urgent action will always be capable of being justified. I don't think in terms of legal action it's been more than once in my professional career that a scientific question has been asked. But to the future...

Sonia Macleod: Most of our pharmacovigilance capability, because we're a much smaller population in terms of numbers...

June Raine: We will continue to use all data sources from any parts of the world. We've got not just our European network, where we're planning and hoping to be partners, but international through the WHO and close relationships with FDA, TGA, Health Canada and so on.

So pharmacovigilance is truly sans frontieres, it is a global function and it's even such that a new flu vaccine being tested in Australia, our children will benefit from the knowledge that we get immediately, simply because their flu season is a bit earlier. So it is an international function, but no one is complacent and clearly the hope is for a close partnership to continue.

Nonetheless, I think we're absolutely ready to make our decisions for our people in good time, if that's not to be achieved.

Ian Hudson: I just wanted to reiterate the government's preferred position is continued participation in the European system. Clearly, that will need to be negotiated, but that is the preferred position. Do you want to comment on the vigilance side?

John Wilkinson: Yes, in devices the vigilance processes are less evolved than in medicines and the level of collaboration and pooling of data is nowhere near at the level it's been on the medicines side. Equally, we do have well established global communication systems and I've said many times to people if there's a public health problem post-Brexit, whatever the circumstances are, I'm still going to phone my peers in Germany and France and ask them (1) for help or if we can help them.

I think the community of regulators who are around the world will be disrupted in terms of our access to inform data channels, but we will continue to exchange information. So it's not ideal but it's far from disastrous, I would say.

Julia Cumberlege: I hoped we were going to have a Brexit-free zone this afternoon, but there we go. It is a huge issue, of course. Simon, any questions?

Simon Whale: I just had one other question really, which is this morning I think when you made your opening remarks you talked about MHRA's support for safe innovation. There's obviously a natural tension between those two, which I think represents a challenge for everyone in the future and it's something that everyone in the system and beyond the system needs to be thinking about, including patients. I suppose the question in relation to mesh is whether looking back as we sit here today you would say that mesh was a safe intervention, an innovative safe intervention.

Ian Hudson: Well I think again a new product being put on the market now, the need for the product in terms of the clinical need, the current treatment options, because I think the gynaecological surgery in itself has moved on a long way from when mesh was introduced. Mesh was introduced because of a high failure rate of existing procedures, but that's moved on. So I think you've got to look at everything in the context of where you are when you're introducing it. We've touched on this a number of times, what I'd like to see is clearly we'll have for new products coming along and for new regulations a larger clinical package, more monitoring put in place in terms of the post-marketing follow-up commitment, et cetera.

I'd like to see the Health Service doing its part in terms of thinking about early guidance in terms of how to introduce this in a safe way, Beyond Compliance, Scan4Safety, all of that, data sources to be able to monitor it. In an ideal world for me, you'd get all of that in place for new things coming in. You do always, as you alluded to, have to balance that, at what point is a reasonable point for a new product to be brought in for public use. Balancing what is known, what is not known, the degree of risk in the context of the condition that the patient is being treated for and what's the need therefore. There are demands for urgent treatments in high unmet medical need type circumstances.

So you've always got to have that balance as what's the right time. You don't want to hold up innovation where there'll be a clear benefit to patients. On the other hand, we want to do it safely, such that you get the right balance of what's known before, but monitored very carefully afterwards. Full openness, of course, we we've talked about earlier in relation to what's known and what's not known.

Simon Whale: Thank you.

Valerie Brasse: In that future world of openness, will we ever get to a place where we have a central database that shows all CE approved products there are on the market?

Ian Hudson: I hope so. We should have that...

John Wilkinson: Yes, EUDAMED 2 is in construction. Like all public sector IT projects, it's not easy, particularly at a European level. But the design and the intent is there. When it will arrive in completion, I don't know, but I think the intent's right and the components, if they deliver, will help us greatly because we will know what's on the market, which at the moment we don't.

Sonia Macleod: EUDAMED's been under discussion for years...

John Wilkinson: It has.

Sonia Macleod: ...and years and it still isn't there. Do we have an expected date when it will go live?

John Wilkinson: Well, the legislation, interestingly, includes a paragraph around what happens if it's not there. I think there was an assumption that elements of it would be late. To be fair to the Commission and people who are developing it, it is a mammoth exercise, but it needs to be completed. I don't imagine it will be completed on the dot in 2020 when the legislation

has to be implemented, but hopefully major components of it will be and it will be completed within a reasonable timeframe.

Julia Cumberlege: Right, now it's up to you, are there any questions you'd like to ask?

Ian Hudson: I don't think I've got any questions for you. Clearly, what we've spoken about today, the hugely important issue of making sure that across the system, ourselves, everyone across the system will listen to patients much more. Also, the second issue really about joining up the system to make sure the system is responsive when things go wrong and how we do that and the levers to pull. The third area is a real push for better data, better monitoring, et cetera. I think those are the three key areas for me in the areas we've been talking about to all of you.

Julia Cumberlege: Right, well, thank you so much.

END OF TRANSCRIPT

5th March 2019

Session 1: NHS Digital, Healthcare Quality Improvement Partnership (HQIP), Private Healthcare Information Network (PHIN), Professor Justin Keen

START OF TRANSCRIPT

Julia Cumberlege: So just before we start that, can I ask HQIP whether you've got any conflicts of interest because we haven't actually - I think - had anything from you on that?

Danny Keenan: We've no conflicts of interest.

Jill Stoddard: No.

Julia Cumberlege: Sorry?

Sasha Hewitt: No. No conflicts.

Julia Cumberlege: No conflicts of interest? Perhaps you'd be kind enough just to write that in to us so we've got a record of it. Because people do ask us, so that would be good.

Right. So, I'm Julia Cumberlege and I've been invited by the Secretary of State - the former Secretary of State - to do this Review. When one is tasked with an issue like this, the first thing you do is try and get the very best people about you - around you - advising you - and I have that. So, Sir Cyril Chantler is on my left and many of you will know Cyril and he knows many, many people within the NHS. On my right is Simon Whale and Simon has taken particular responsibility for communications - which as I have said previously is really important to us.

On Simon's right is Dr Valerie Brasse and Valerie is Secretary to the Review team and on Cyril's left is Sonia Macleod - Dr Macleod - who is our principal researcher. So that's us. So, then I'm going to ask you if you - because it's going to be on the record - if you can very briefly say who you are and the position you hold. That would be helpful. So, shall we start with you?

Manpreet Pujara: Yep. So, I'm Dr Manpreet Pujara. I'm a GP. I work for NHS Digital as the Clinical Director for Patient Safety and Clinical Governance. I also have a role as a lead at my CCG - leading on prescribing and GP IT.

Julia Cumberlege: Right. Thank you very much indeed. Yes, thank you.

Stuart Harrison: I'm Stuart Harrison. I'm the Head of Safety Engineering for NHS Digital. I work for Manpreet.

Julia Cumberlege: Thank you.

Jill Stoddard: I'm Jill Stoddard, Operations Director at HQIP.

Sasha Hewitt: I'm Sasha Hewitt. I'm an Associate Director at HQIP.

Julia Cumberlege: Thank you.

Danny Keenan: I'm Danny Keenan. I'm the Medical Director at HQIP and also Associate Medical Director at Manchester University Hospitals. I'm seconded two days a week to work with HQIP as Medical Director.

Julia Cumberlege: Thank you very much.

Matt James: Good morning. I'm Matt James. I'm the Chief Executive of the Private Healthcare Information Network.

Julia Cumberlege: Thank you.

Prof. Justin Keen: I'm Justin Keen. I work in the Faculty of Medicine at the University of Leeds.

Julia Lake: I'm Julia Lake. I'm - I was until a month ago - the Clinical Information and Outcomes Manager at the Leeds Teaching Hospitals and I'm now working with the EHR - the electronic health records - team [unclear].

Julia Cumberlege: Right. Thank you very much indeed.

I'm going to start with a question and just say that one of the things that we've been tussling with to some extent is about definitions, so that we really know what we're talking about. I think it was Voltaire who said, if you wish to converse with me define your terms. So, I'm going to start putting this question to you and just asking whether you agree with this. Because we have been thinking a lot about our terms and particularly what is a registry? Secondly, what is a database?

When we have been talking to people there seems to be some confusion about these two terms. So, I'm going to read this out and I'm just going to ask each of you if you agree with this definition because we really need to get this straight.

So, this is the International Medical Device Regulations Forum, and this is what they have suggested is a registry. 'An organised system that continuously and consistently collects relevant data in conjunction with routine clinical care, evaluates meaningful outcomes and comprehensively

covers the population defined by exposure to a particular medical device or devices at a reasonably generalised scale - e.g. international, national, regional, health system - with a primary aim to improve the quality of patient care'.

So, I hope you think that's - we know what we're talking about now when we're talking about registries.

A database. This is the *Oxford English Dictionary*. 'A database - a structured set of data held in a computer, especially one that is accessible in various ways'.

We're thinking as a Review Team - for our purposes - it's in relation to mesh - such a database might include the NHS number, the type of procedure, the operating surgeon, the healthcare provider, the unique device identifier, the date of procedure, the age of patient and the gender. Does that sound right to you for a database? Okay? So, when we're talking about databases, that is what we're talking about. When we're talking about a registry, it's something much, much fuller and more difficult - I would suggest - to establish but very important that we do.

So, if you have queries on that - and after perhaps you've had a bit of thought - if you could let us know that would be very good.

So, I'm going to ask first of all Digital and PHIN and I have to say it's good to see you here again Matt. Thank you for coming. We don't appear to have a clear understanding of how many people have been affected by the interventions we're talking about - Primodos, sodium valproate and surgical mesh. So, can you enlighten us at all about how many people you think have been affected by these interventions? Do you have any statistics on that material, anything to help us on that?

Manpreet Pujara: So, I think...

Julia Cumberlege: Shall we take Primodos first? Shall we go through the three? Primodos - do we have any information on that?

Manpreet Pujara: No.

Julia Cumberlege: No. Alright. Thank you. Sodium valproate?

Manpreet Pujara: I think that we can - we have figures as to the number of women of child bearing age who are taking sodium valproate - or who have taken sodium valproate in the past - based on statistics available from the BSA [unclear] and also could be based on information from GP IT systems in terms of repeat prescribing.

Julia Cumberlege: Right.

Manpreet Pujara: [Unclear].

Julia Cumberlege: So - you may want to write to us on this - but what sort of - what is the amount roughly? How many?

Manpreet Pujara: So, I think it's really difficult because this is a figure that I didn't bring with me. To have an - and it would not even be an educated guess for me to suggest what that number is. I think it varies. What I can do is I can put it in to perspective so that - when I did a search - an audit - in my own practice of 14,000 patients about three years ago. we had 14 women of child-bearing age who were taking sodium valproate.

Julia Cumberlege: Right.

Manpreet Pujara: So, the number from a practice perspective isn't huge. But obviously the total number will vary and within my CCG the work that we have done also shows that there is variation within practices as to the number of patients taking sodium valproate. Because valproate is used for a number of clinical indications it will depend on the [unclear].

Julia Cumberlege: Yes. I think we're talking about child-bearing age.

Manpreet Pujara: Yes.

Julia Cumberlege: In particular. Yes. Because we had a debate in the House of Lords on Thursday and people were bandying about different figures. Now we would like a bit more accuracy on that.

Manpreet Pujara: So, I could certainly take an action to provide those figures to you.

Julia Cumberlege: Thank you. That would be helpful. Surgical mesh.

Manpreet Pujara: So, again I don't have figures. I'm not an expert in the surgical mesh work that has taken place. But [unclear] are able to provide some details about the numbers.

Julia Cumberlege: So, is it possible then that you could write to us...

Manpreet Pujara: I certainly will [unclear].

Julia Cumberlege: That would be very helpful.

Manpreet Pujara: [Unclear].

Julia Cumberlege: So, if we haven't got the exact figures. If we haven't got - and we'll never get it exact - I mean, I do appreciate that. Because all the time things are moving. But we're just wondering would a full retrospective audit be needed? Would that be helpful - a retrospective audit?

Manpreet Pujara: I think it would be helpful - it comes down to what data is available to do that retrospective audit and I'm sure that we can certainly have a look at the data collections that we make at NHS Digital to see what information we can gather in terms of the numbers involved and factors. It will depend on accurate recording at each individual Trust and each organisation - which includes obviously the private sector and what access we have to that data in that situation. Mostly the recording of data - recording of information - for mesh may also have taken place in primary care if and when the details were provided accurately - the general practitioner is able to collect that information.

But this will not be happening in a consistent way across the -certainly the 7500 practices within England.

Julia Cumberlege: Okay. Can I asked PHIN also - if I could ask you - do you have any statistics from the private sector?

Matt James: I'm afraid the short answer would be no and that's for three principal reasons. The first is simply timeframe. So, PHIN is mobilising now to be in a position to collect data systematically across private healthcare on the same basis as the NHS and to be able to do that in the future. Which may help in any future scenarios like those that the Review is looking at going forward. But we simply don't have anything that came from the timeframe that most of the incidents arose that you've been looking at.

The second issue is that we have very much a secondary care focus. So, whilst vaginal mesh might fall within that scope, the other medicines and so on that you're looking at are much less likely to.

The third issue is that the way that we collect our data - which is really aligned to the principal ways that it's done within the NHS - very much has a procedure focus. So, we wouldn't look for vaginal mesh itself. We might look for stress urinary incontinence and if it was recorded that vaginal mesh was a feature of that procedure - a procedure undertaken to relieve stress urinary incontinence - then that may be recorded. However, what the reliability of that would be within NHS data - and going forward within our data - I think would need to be tested.

Valerie Brasse: Can I just ask would the private sector have the capacity to do a retrospective audit?

Matt James: Well...

Valerie Brasse: Or the capability.

Matt James: So, I think there are two things. I think if you look back at NHS Digital's data for stress urinary incontinence - provided that the related diagnostic coding was accurate - you would be able to make a reasonable estimate from that general data of the number of cases - of the use of vaginal mesh. It would only ever be an estimate, but it would be a reasonable estimate.

In terms of a retrospective audit - speaking very frankly - and I might be completely sort of out of school here. I'm not sure how that would be done other than going right back to original patient's notes or doctor's notes. Because I strongly suspect that the level of detail doesn't exist recorded in the system that one could easily access in order to be able to do that in any sort of centralised fashion. I might be completely wrong but...

Julia Lake: No, you're right. It would generally be held on a number of given databases so your mesh components might be in your stock inventory system, patient details elsewhere with your events and patient procedures. So, generally it's fragmented. Things are in different places and it's very rarely joined up all together.

Julia Cumberlege: But there are other conditions where we have a registry and it is very helpful to have those figures. Because we've been going around the country, we've obviously heard a huge amount from the patients who have suffered deeply - from particularly surgical mesh - but also sodium valproate and also Primodos. We are conscious that trying to actually get a handle on how many operations are done and how many result in complications when it's mesh - and disabled children in the other two conditions - is very difficult for us.

The more help you can give us on this really would be very much appreciated.

I think the data set would help us. It's quite strange in a way that this hasn't happened in the past. It seems to have taken us an awful long time to actually get to grips with this situation and there's a lot of learning - I think - to be done by that because the thing that patients certainly are saying to us - at the moment - we feel that we are actually a clinical trial. Why wasn't this done before? The speed of coming to understand some of these issues has been glacial. It has been awful.

So, I'm going to pass on now to Cyril.

Cyril Chantler: The reason that we raised with you the definition is because we've been rather confused about how different people have looked at this. So, can I just go into this in a bit more detail. What we're exploring is the notion that there could be a centralised database collected at the point of the surgery. When we attended the workshop, we raised this proposition. Which would have the necessary information centrally held and created by the person doing the operation - not by a third party - using the NHS number, which would then enable us to build registries connected to it and around it.

Now, can I ask you whether you think that's something that you would think's worth exploring? Perhaps ask all of you? I'm going to start with NHS Digital.

Manpreet Pujara: So, I think it is something that is worth exploring because we do have other registries which are effective. I think the key is that it needs to be mandated because - and I'm just - I'm not an expert on IG and GDPR let me just say. But patient consent to - whether they want their information on the registry...

Cyril Chantler: Can I interrupt you at that point - again so that we don't get confused. The proposal - which I really do wish you to - your review about - is that it might be possible - under legitimate usage on whatever section you're talking about - to mandate - if you like - that information for the database. But as I understand GDPR - and I could be wrong about this - to create a register does actually require the permission of the patient under opt out or whatever.

Therefore, the registry will be a secondary event which the patients would then agree to - in my experience because I've been involved in a registry - the European Dialysis and Transplant Association Registry - 30 years ago. Patients are only too pleased to agree because they want to improve the outcomes. But, Dr Pujara, is that a reasonable proposition?

Manpreet Pujara: I think so, yes. Because I think recording of an event needs to happen - [unclear] historical purposes and legal purposes. So, it is important that there is a record of the mesh that has been inserted. I think having a registry would be very helpful. The point I was making was just that very aspect, that you need to get the patient's consent for the additional bit to go on to the registry - which is what my understanding is.

Cyril Chantler: Okay. I want to come back - if I may - to your Breast Implant Registry in a minute but can we turn to HQIP now and say how do you react to this discussion?

Danny Keenan: Basically, where we are today is we've got a totally haphazard system - led to quite an extent by scandal or whatever. So, we have the joint registry which you're going to hear about which has been going for a long time. We've had other audits - whatever you might call them. For instance, the implantation of heart valves and pacemakers - which could affect using your definition of registry - which have been going for quite a few years.

Then of course we've got the breast scandal and that came along with a registry and possibly there's going to be something with mesh - but we'll leave that aside for a second. But if you think of the devices being implanted today - into human beings around England - there's an enormous amount of stuff going in. Cataracts, stents - every area of surgery and interventional medicine is putting things in. There is very, very little information on these.

So, the idea of developing a registry to do with devices is a good idea. But you have to actually say, well what is it you're wanting to do? Are you wanting to do device surveillance - which is on a safety area? Are you wanting to look at outcomes? I suspect that's what patients - they would want both of those. Mesh is a really good example of outcomes because the outcomes are actually - are very far out. So, where does the registry finish? Indeed that - in your definition - which we will answer to with the data set - outcomes weren't mentioned.

Yet outcomes going on out into the future is really important. Actually, the example we have of the joint registry - you probably saw the thing in the news a week or two ago - which incidentally didn't have the NJR on it. It was an international look at joint registries giving outcomes up to 25 years for survival of - et cetera - of joints.

Then on the other hand - to do with outcomes - we actually stuck on to the National Joint Registry patient outcomes like death which actually wasn't very good coupling together because death and surgery...

Cyril Chantler: Yes, I understand that, and it does actually talk about meaningful outcomes in the international definition. But at the moment, the distinction that I'm seeking your reaction to is the notion of creating a database to which properly designed registries to deal with all the issues raised - which I absolutely agree with not least because I have a heart valve myself [laughs]. It's that distinction I'm after. In principle, are you comfortable?

Danny Keenan: It has to be yes because you would say why haven't we been doing that so far? It has to be yes.

Cyril Chantler: Indeed. Before I turn to Matt, I must declare an interest because I'm a non-executive director of PHIN. Matt, your reaction.

Matt James: Well, I'm in huge agreement with what both Danny and Manpreet said actually. It is a totally haphazard system at the moment. I've been closely involved in the Breast and Cosmetic Implant Registry and worked closely with HQIP over the last few years. Whilst it is imperative that we are able to collect the sort of information that will provide a much, much better look at these issues and protect patients in the future - the manner by which we do it I now think is critical.

I would really like to see not just another stand-alone, problem specific, device specific registry created, but a much more comprehensive look taken at how devices, medicines and any other factors that are directly affecting patients - can be universally recorded.

I won't dive too much into the detail now because I'm aware of how short we are on time but as a principle that has got to be exactly right. In terms of information governance, I do completely recognise that a strong degree of mandation on various parties to do this would help enormously.

Because it has been PHIN's experience that despite the fact that we are very clearly legally mandated to do things, we must interact with other parties - including our partners NHS Digital, including the consultants who must review their own data before it's published - who are not legally mandated to do those things.

The process of obtaining permission or obtaining an end to end pathway of lawful basis to proceed is extraordinarily complex. It would also be my observation that currently every single registry takes its own bespoke approach to consent and confidentiality. If you go down the consent route, you're very much pushed in to being extraordinarily specific. The particular situation you could easily create is one in which a patient has to review three pages of closely typed text that says, yes I consent to this particular - my data being collected for the purpose of analysing this particular drug and for those purposes and no other purposes.

Then turns the page and then for this particular device that has been implanted into me and then for this particular outcome measure in respect of the surgeon's performance and so on. They're going to have to sign four or five different consent processes - each in ignorance of the other quite deliberately at the moment. We must find a better way through that.

Cyril Chantler: Yes. Well we are seeing the Rare Disease Registry and the Cancer Registry later today. Professor Keen - you've got huge experience in this area.

Prof. Justin Keen: I have some. [Unclear] Go first to Julia, then I'll come back to you.

Cyril Chantler: Okay.

Julia Lake: Just on that matter of consent actually I just did a little bit of analysis yesterday to look at cosmetic breast surgery. I looked at our HES data against what our consultants had submitted based on consent and it was only 40 per cent. So, you're omitting 60 per cent of patients with implants because they hadn't consented to it.

Cyril Chantler: I understand the consent issue but I just at the moment would like to concentrate on this issue about the difference between a registry and a database. Are you comfortable with the conversation we've had so far?

Julia Lake: Yes. Yes, I am.

Cyril Chantler: Professor Keen?

Prof. Justin Keen: Sorry. Thank you, Sir Cyril. The - so perhaps one of the striking things - just looking at some of the oral evidence - written evidence given to this team so far - is that there's a sort of - if you like - an outside hospital view. So, I wonder if there's some value in actually noting a third [type] if that's okay which is a data warehouse which would be familiar to people who work inside Acute Trusts. Because that may be where you could reconcile your notion of a database and a registry.

So, in very simple terms most Trusts will have what we call real time systems. So, systems that clinicians, doctors and nurses and others use on the ward for the direct care of patients. Then a data warehouse is - as it were - a very large repository that sits behind it offline as it were - which takes data from the Patient Administration System, the Electronic Record System and many, many other systems - dozens in terms of [unclear]. But it's sort of - if you like - it's an offline store where you can take databases - subsets of data - from the real time systems.

So, it's individual data sets and then link them together. So, one possible solution is to take data from - for example the Electronic Record System, link it to data that are filled in on a slightly different database - possibly concerned with a specific mesh implant procedure. But they could be linked together in the data warehouse and as far as I'm aware most Trusts...

Cyril Chantler: Yes, I understand that and also the need to [unclear] central and local. But I think what I'm proposing is a database - or we're proposing - is something much more like a central system run by NHS Digital. Like the DVLA or

something of that nature. I accept the need for local as well and that links, but again you've got the issues that Matt has raised about mandation maybe under 251 and opt out which is not the same as opting in through consent.

Prof. Justin Keen: I'll just say one more thing then which is that the - again just looking at some of the evidence that we've received so far. One of the things that I think can be underestimated - particularly if you're in a regulatory or other [unclear] national body - is there are - the simple fact you really need buy in from the clinicians on the ground to start with otherwise this just isn't going to fly. So - and I have to agree with you - it's just that I would emphasise the need to get that data capture buy in to clinic...

Cyril Chantler: I absolutely agree.

Prof. Justin Keen: ...first.

Cyril Chantler: We've already put this proposal - as you'll see - on our Review website to the President of the Royal College of Surgeons and the President of the Royal College of Obstetricians and Gynaecologists and they think it's a good idea.

Prof. Justin Keen: Good.

Manpreet Pujara: Sir, I just wanted to come back and say I'm being very simplistic about this because I find keeping things simple clearly helps. A medical device is like any drug that is prescribed. There is a legal duty and responsibility to record that information. If that information is recorded - and it should be recorded in a clinical system that is being used by the clinician, then that information can be collected and used on multiple occasions as necessary, as defined, and is legal to use, to ensure that actually the care of patients is improved, and safety is improved.

So - being a singleton - I would expect every medical device that is fitted is recorded. Actually, some of that information will come to us at NHS Digital - as the data guardians for England - and that information will be available for us. That information can be released and accessed through the legal processes that currently exist to ensure that appropriate research can be carried out.

So that we only have to do this once. We're not revisiting this and having to create multiple registries because it's a do once and actually use many times. It's the principle of devices being like drugs and an expectation there is a full audit trail and history of what has happened.

Cyril Chantler: Okay. Thank you.

Julia Cumberlege: I just want to ask about HES data because what I understand from people is that it's not very accurate because of the coding system. What we're suggesting with the database is that it's actually done by the surgeon in the operating theatre - or just in the building anyhow. So, do you think that would improve that? We won't be duplicating will we - HES data?

Manpreet Pujara: You should ideally only have to record things once.

Julia Cumberlege: Well I do agree with you but...

Manpreet Pujara: We need to ensure that the systems that are being used - and it will be a transition there is no doubt - that systems that are deployed record the information at the coalface and make that available to be used...

Julia Cumberlege: Okay.

Danny Keenan: Essentially if you produce a system that's easy for surgeons - as we're talking about - to use - they'll use it. But say for instance the cataract audit which we run today, at something like 60 per cent uptake and the reason probably is because it's not readily electronically available in the operating theatre. Now, if it's sitting there easy to use, it will be used. If there's - obviously bringing colleagues with us is the best thing but there is a bit of mandation about this and that will probably make it up 95, 100 per cent.

I think the ease of use and then the other thing is it mustn't go into a black hole. It must be used back so that it is used by colleagues to improve care. That's the real catch I think for colleagues.

Julia Cumberlege: Well I think we agree with so much of what you're saying, it's to get it to happen.

Danny Keenan: That's right.

Julia Cumberlege: That is always the challenge. Anyhow. Simon.

Simon Whale: Yes, can I just explore an associated issue. So, if - let's assume that the database that we're talking about - the kind of database we're talking about - does exist. Who should be able to access that database and how would they go about it? Does NHS Digital have a view on that?

Manpreet Pujara: At the moment data access I think happens through [unclear]. Again, I'm not an expert on [IG and DARS] but applications are made to the group to access that information. They are assessed and reviewed. If legally allowed, that information is made available to the researchers.

Sasha Hewitt: Can I just say one very important group that would need to have access to that data [through One] are the patients. So, patients - through the work that we've done - we held a stakeholder workshop and patients very clearly want access to information about the type of mesh device that they've had inserted. For that information to be readily accessible to them perhaps even higher - you know, an email or something that they can keep for a very, very long time.

Obviously, we need to make the data available to researchers and third parties but really it's the patient group.

Simon Whale: Yeah, I mean I think we completely agree with you. Should patients be able to enter information on to the database?

Sasha Hewitt: That's something that we did debate - again through those workshops that we held - and very much patients, clinicians thought that patients should be able to directly enter their outcomes. So, how they - you know, symptoms and how they are all doing before and after their procedure. That...

Simon Whale: Would you agree with that? I mean you don't see any problems with doing that?

Sasha Hewitt: I think there are other national clinical audits I can think of who do that. So, the National Early Inflammatory Arthritis Audit collects PROMs directly from patients. It provides patients with a secure login so that they can access that data themselves and record how they are doing. I think it's a very powerful way to involve patients more.

Simon Whale: What about manufacturers? What access should they have to this database?

Sasha Hewitt: I think the manufacturers do need access to this information so they can improve. They already have access to NJR data and that's very - I think one of the strengths...

Danny Keenan: Yes.

Sasha Hewitt: ...of the NJR.

Danny Keenan: The governance system that sits around the NJR is very good and has worked for a decade - longer than a decade - so I think any system that we might be bringing in, we already have a template for relationships between the information in warehouses et cetera and industry having the access they need.

Julia Cumberlege: Do manufacturers share their data with the NHS? With all these bodies?

Danny Keenan: I'm not sure I can answer that. I chair the indicator committee for NICE.

Julia Cumberlege: Sorry?

Danny Keenan: I chair the indicator committee for NICE. NICE has got a very good set up - you probably could hear it directly from them - as to the linkage between manufacturers - it's mostly to do with drugs and new devices. There are problems. There are problems with sharing data. I don't want to give you a second-hand version of that. I think it would be much better to get colleagues from NICE who are intimately involved in that developing guidelines and specifications for technology and devices.

Julia Cumberlege: Hm.

Simon Whale: Can I also just ask about the link with Yellow Card? So how - I mean this is a question for anyone and everyone - how would this database link to the Yellow Card Report?

Matt James: Sorry, I don't know what that is.

Simon Whale: Yeah.

Stuart Harrison: The concept around traceability of devices is good and I completely agree with the aspects of giving patients the ability to register and so on is taken elsewhere in the digitisation efforts around the NHS. But again, it fits in to other national strategies in that regard. In terms of the safety culture, it provides a more open and transparent view around devices, healthcare and so on. With regards specifically to the Yellow Card Reporting System, that has a traditional function. I think the linkages with other databases - or registries, as we define it - are technically possible.

The user view could be tailored depending whether it's patient, manufacturer or NHS or private access. All of these things are available currently.

Cyril Chantler: So, do you have a system in place to share information - or intelligence - between MHRA and NHS Digital?

Stuart Harrison: We do, yes. We have a data sharing agreement and we...

Cyril Chantler: Is that HES data or - it can't be...

Stuart Harrison: This would be patient safety related information regarding health IT systems.

Cyril Chantler: But at individual patient level?

Stuart Harrison: There are elements of the incidents that we work with that has - that do have patient outcomes or patient details on them, but with regarding the...

Cyril Chantler: Identifiable patient data?

Stuart Harrison: No. Not to that level.

Cyril Chantler: So HES data - which is non-identifiable?

Stuart Harrison: It's anonymised but it's similar to HES.

Cyril Chantler: Right.

Stuart Harrison: We focus purely on the health IT side.

Cyril Chantler: But it is anonymised?

Stuart Harrison: Yes.

Cyril Chantler: Yes.

Simon Whale: Does that include Yellow Card Reporting? Do you - do MHRA share Yellow Card Reporting in any form with you?

Stuart Harrison: Yes. Specifically around health IT and devices area. I believe you've had John Wilkinson in on a previous session - so that linkage is there.

Cyril Chantler: Right.

Julia Cumberlege: So, do you have an influence in ensuring that the Yellow Card System is more comprehensive? That it acts properly, that it is responsive to patients? Or do you leave that to the MHRA?

Manpreet Pujara: Maybe I should answer this one. So, you know we've been instrumental in engaging with MHRA and getting them to engage with the NHS App team so that patients can directly report the Yellow Card System. Obviously one of the reasons that I'm keen for the information about any devices being made available within the patient's record is so that there can be linkages should there need to be linkages.

So, we are working very closely to ensure that the Yellow Card option for patients will be simple, straightforward and as Stuart has said, you had MHRA come to your hearing, and I think that the volume of reports that they are receiving as a result of allowing patients to enter information has significantly risen as a result of that.

- Sonia Macleod: So, once the NHS App is in place, there's a Yellow Card reporting function that presumably pre-populates, that goes to [unclear]. What then happens to that information? Is it stored within that patient's individual NHS App record? Because we've heard of patients submitting Yellow Cards and then they can't find them under [unclear] number, things like that. So, would that provide the patient with an identifiable [unclear].
- Manpreet Pujara: So, again I'm not working on that on a day to day basis but what I would expect to happen would be a report to fire off to MHRA - although the note within the patient's record that a Yellow Card has been submitted. What level of details is recorded in the patient's records - or indeed if a full copy of that report is available for the patient to review - I could find out what the plans are if this is to happen. I don't know the [unclear] at the moment.
- Simon Whale: In terms of where we started in this part of the conversation around who should have access to the database and who - both input and read access - I'm just conscious that we've not heard from Professor Keen or in fact James or Julia. I wonder if you have any thoughts on it?
- Prof. Justin Keen: I agree with a lot of the comments that have been made, particularly by my HQIP colleagues and certainly stress the importance of patients having access. A lot of the rest of it -if you like - within NHS Digital and the information governance [unclear] are reasonable in general terms. So, it's again looking at [unclear] within the NHS then it's just current information - it's [unclear] patient access is perfectly reasonable.
- Simon Whale: Yeah.
- Julia Lake: So, what we've found with some places where we have external databases that our clinicians put - usually through a secure portal - is that within the Trust we don't have access to get that information back. So, we have some audits where we have a lot of assurance around it. So, the data doesn't leave our Trust until it's been signed off clinically, it's been signed off for data quality and all of those checks have been done and then it gets uploaded.
- What we found with some registries is that it goes offline, and we don't have that sense check internally, for our consultants to say actually I'm happy with all of that, and it's not until it gets published later we think, ooh something was missing. So, I think any kind of national database or registry needs the ability for us to re-extract our data for us to make sure that - and we have a period of validation - to make sure that what we're sent is as good, complete and accurate as it can be. Clinicians in our Trust are very

involved in that process. They like to have that reconciliation and that process in place.

Simon Whale: Okay, thank you.

Julia Cumberlege: Could I just ask you HQIP - and perhaps Professor Keen - we've talked a lot about registries. Can you just tell us what type of oversight you think they need and what sort of governance is required?

Prof. Justin Keen: Do you want me to go first?

Julia Cumberlege: You know, who should be responsible for commissioning it?

Sasha Hewitt: So, the National Clinical Audits that HQIP commission on behalf of NHS England - and [unclear] - all have their own governance structure. So, they all have an overarching project board composed of clinicians, health stakeholders such as - well local...

Danny Keenan: Trusts and CCGs.

Sasha Hewitt: Yeah. Very importantly patients, patient groups such as charities. They have steering groups. Sometimes - increasingly so, separate patient panels that feed into those groups. So, they've got their own governance in terms of overarching - oversight - where you're thinking about HQIP obviously manages those audits. We report any risks through to NHS England on a quarterly basis.

Jill Stoddard: So, we commission and contract manage the audits or registries or confidential enquiries. We contract manage so they - we appoint a host organisation that acts as a host to the provider team that manage the registry or audit and we contract manage that provider team within the host organisation. Then we upwardly report to the funders. So, in many of the cases it's NHS England and the Welsh government that we upwardly report to.

Danny Keenan: We have links - confirmed links between our outputs and the CQC and NHSI so that we have trigger points if an audit is showing something or whatever. That direct links are made between the audit results, the team leading it and the regulators.

Julia Cumberlege: It sounds a very cumbersome system. I mean, is it not possible to streamline it, simplify it, make it more effective?

Jill Stoddard: So, I think that we were actually asked by the Department of Health in August to undertake a rapid piece of work around looking at the three societies that are currently in place that host mesh data and that's around

a sort of short term, interim database solution. Because we are aware that it takes quite a long time to procure. Obviously if there's a certain amount of money involved, we have to follow legal frameworks for procurement. So, it can take up to a year to actually procure for a registry. Once the - a favoured person is given a contract, then it obviously takes them a period of time to set up teams and the IT platforms.

So, for a registry to be set up from start to finish actually takes quite a long time, which was one of the reasons why I think the Department of Health asked us to undertake a rapid piece of work around looking at the feasibility of an interim database solution. To sort of potentially suck data out of the society databases, to start collecting from big pre-existing repositories of data. We are very aware of the time trajectories involved because we want to get answers quickly for people, obviously.

But - so we could think about what's currently in place and then we'd have to think about for a registry - actually procuring and commissioning a registry - will take quite a long period of time to do because of the legal frameworks involved in doing that.

Danny Keenan: Can I just add to that. You have to remember that the systems we're using - we do use HES data a lot. But then say, about 70 per cent of the data going in is HES data but 30 per cent is bespoke. Actually, it does take time - and as we move digital and get into much more comprehensive electronic records, that will be helped. But the other point you heard about validation is really important.

So, if one of these things fires off and such and such a hospital is an outlier or an individual surgeon is an outlier, we have to be 100 per cent sure that that data is saying the right thing. That's why these validation exercises are really important. So quite a lot of the time is taken - not just internally validating data, but it comes up in to the [audit provider] and it gets cleaned so to speak.

It goes back to say is this right. So, there is a lot of that moving back and forth to make sure that the conclusions that are reached are accurate.

Julia Cumberlege: So, can we have a [cockshy] on how long this would take? First of all, to establish a database that's useful and secondly then moving on to a registry?

Danny Keenan: Are we talking about the whole thing? Not just to do with mesh?

Julia Cumberlege: Well, I thought we needed the database first - to get some facts and then...

Danny Keenan: Are we thinking of mesh or the whole?

Julia Cumberlege: I'm asking it in two parts. First of all, the database. How long - because clearly, you've got to gather the information and presumably it takes a bit of time to actually gather enough to be useful and then, drawing on the database, we then have a registry and I'm just asking the first part, how long would that take? The second part, how long would that take?

Danny Keenan: Okay.

Jill Stoddard: So, for...

Julia Cumberlege: Mesh.

Jill Stoddard: ...just mesh yes.

Julia Cumberlege: Hm.

Jill Stoddard: So, for an interim database we have just given the report in to the Department of Health - it's currently embargoed - and we are awaiting a decision from the Department of Health about a potential outcome from that. It depends upon what the decision is from the Department of Health about which potential model has been suggested that they would like to adopt. So, if it's possible to actually run with using data from the current societies, that would probably take a year to actually bring to fruition. That's a rough estimate.

For a registry, I would estimate - because of the legal frameworks involved - probably from start to finish, it would take a year for procurement and commissioning, a year for a host organisation to set up the teams and the platforms and start gathering data and then a year to get to a final report. So, you're probably looking at -this is a rough estimate - three years to get to a final report for a registry.

Valerie Brasse: But within that - and within your proposals - and obviously we're not asking you to talk through what's currently embargoed. One of the issues about the databases - as we know - is that the reporting is - well it's under reporting on all three of them. Do you therefore have proposals for how that would be moving towards 100 per cent reporting, even for the initial stage which is the database?

Sasha Hewitt: I think that depends on a few different factors. So, the first is whether or not this - what legal basis it's operating under and whether or not this is mandated. So, if perhaps - you know for instance - the Department of Health were to direct NHS Digital to collect data, that removes the

requirement to collect - to gather consent and obviously then it's a legal requirement for organisations to submit data.

Even under those circumstances, there still needs to be engagement in order to get people to use the system. It's very easy to build a database, very difficult to get people to use it and it does take time for those participation levels to rise. Even in national clinical audits that we've got where you suck the data directly out of EPRs, it still takes considerable time to build up participation levels.

Jill Stoddard: [Unclear].

Sonia Macleod: If you're sucking data directly out of EPRs, presumably that literally is just taking the data out...

Jill Stoddard: That is taking...

Sonia Macleod: If you've got a unique device identifier for each device, surely that will enable you to pull a data set of where these devices are.

Matt James: May I respond to that. I think what you've just said there could be the absolute key to getting this done very quickly. The question you asked at the beginning was - well actually you set out in setting out the differences between a registry and a database - what the components of a registry might be. Every one of those is a component of existing data systems and parts of the patient record with the exception of the unique device identifier.

If rather than focusing on rebuilding information - with all of its duplication and all of its necessity to build a database from scratch - we focused on the process of ensuring that the unique device identifier is recorded in every instance - and specifically is recorded and entered into the patient's record - then you would have a basis for finding the correlation between the use of a device and the patient in every instance and it could be done quickly.

You mandate its collection on the ground, and you mandate digital to handle that data - for example - then very quickly you'll develop a picture of which devices exist in which patients.

If on the other hand - we choose to build a registry from scratch. I mean, the Breast and Cosmetic Implant Registry I think is up to six or seven years and counting and is not sort of - it's basically operational now in collecting data but it's not fully operational in being able to analyse that and produce results. So that's an example. It doesn't necessarily mean that everything has to follow that pattern. But a far quicker way to it would be to make

sure that the device data gets into the patient record rather than creating [unclear].

Sonia Macleod: That requires electronic patient records and how close we are - I mean how close are we to having complete coverage?

Danny Keenan: We're not - we're not close. Manchester, where I know a lot about. We are actually tendering for an EPR at the minute. In fact, I read about it the other night - I think it's going to be the autumn before it comes out with the spec and it's going to be at least next year. So, we are quite a long a way off. The first thing - having said all that, is to get the NHS number into any of these areas. We haven't got that at the minute. So, if you have an NHS number going in and a device identifier, you've actually - those two things would give you a fair bit.

Cyril Chantler: The proposition that we're putting is that when the surgeon - or the clinician - pulls out the operation note which always happens...

Danny Keenan: Yes.

Cyril Chantler: that it includes this information. Certainly, maybe the barcode of the device and the NHS number among the other things. There's no reason - that goes into the patient notes - there's no reason it shouldn't go to NHS Digital. No reason why it shouldn't go directly to the patient. Then you've got the foundation to do all the other things which are necessary. That is the proposition.

Matt James: We've come from - registries were invented in the era when things were recorded on paper initially. Two bits of paper can't talk to each other, two electronic systems can. If we focus on making sure that the mandations, assessment rules, the lawful basis and the imperatives to join up electronic systems exist, we can get to an answer - I believe - far more quickly than if we continue to create what are effectively workarounds.

The question earlier around clinical confidence and the quality of HES data. I don't think clinicians do have confidence in the quality of HES data because it wasn't originally designed as a clinical system and yet is increasingly used for clinical analysis. I would strongly prefer to see that we address the clinical quality of the HES data which is one of the fundamental building blocks - precisely by ensuring that clinicians have input to it at the operational level rather than continuing to create workarounds. Where we collect all of that patient demographic data - the operation details again on a separate system - in order to then be able to build upon it with a few additional data feeds.

Cyril Chantler: Could you tell us something about the Breast Implant Register because I don't understand that. It's run by NHS Digital isn't it?

Manpreet Pujara: Yes. I'm really sorry to say that I'm not on a day to day basis involved with that.

Cyril Chantler: So, why isn't it run by HQIP?

Danny Keenan: We weren't asked.

[Laughter]

Cyril Chantler: But wouldn't it be natural for it to be run by HQIP?

Sasha Hewitt: So, we - well it...

Manpreet Pujara: No. Because we are the data guardians of the NHS and therefore by law, we are able to keep that information...

Cyril Chantler: I understand why you collect the data...

Manpreet Pujara: Yes.

Cyril Chantler: ...in the way we've been discussing, but why isn't the interrogation of the data and it's undertaken...

Manpreet Pujara: So, a request needs to be made...

Cyril Chantler: ...through HQIP?

Manpreet Pujara: ...to the DARS team in order to access...

Danny Keenan: Well we - there is a lot of history in this - I mean it's - you know, and we've already talked about clinicians and HES. I'm not stepping out of turn saying clinicians and NHS Digital - it wasn't a great relationship either. Now, it's fair to say that it is miles better our relationships - I'm talking as clinicians - with NHS Digital. It's obvious to all of us that there should be one area warehousing data. We can't have this system - which we do today - bits of data...

Cyril Chantler: HQIP, MHRA, NHS Digital and any organisations directed at - in patient safety - ought to all be doing their job but linked.

Danny Keenan: Sure. We do talk a lot to each other [laughs].

Cyril Chantler: Thank you.

Julia Cumberlege: Can I just enter another area now because we are concerned with GDPR and that crops up in all sorts of different situations and discussions. I'm just wondering how the interaction with GDPR would work with a database or a registry as well.

Danny Keenan: Sasha...

Julia Cumberlege: Can you explain that to us?

[Laughter]

Sasha Hewitt: My specialist topic. So, you're wondering how - what the GDPR requirements would be of a database or a registry? So - this is a really tricky one because we have obviously GDPR, which is the *Data Protection Act* essentially. All of the security arrangements that go along with that, but we also have the common law duty of confidentiality. Which is basically what everybody's talking about here when we're talking about consent and the legal basis to collect this information.

It's very easy [laughs] - I say very easy - turn off the camera when I say that. But it's easier to find a legal basis under GDPR than it is to find a legal basis under the common law duty of confidentiality - is my experience as an Associate Director at HQIP. However, there are lots of - you know, the GDPR is not brand new. The requirements within it largely have existed for a very long period of time. It's just more explicit in its requirements.

So, a lot of the things - like having a legal basis under GDPR - being transparent with patients, being secure - all of these things are really - they really are the same. It's just that its requirement to exercise individual rights is clearer. Organisations now need to be accountable and transparent in their processing. So, we did - in our report to the Department of Health - recommend that whichever model they choose there would need to be dedicated information governance resource available for whichever organisation is setting up an interim or a long-term registry to ensure compliance with GDPR and common-law duty of confidentiality.

Because certain things would need to be done, such as a data protection impact assessment. There would need to be a data protection officer appointed, transparency documentation would need to be developed, any consent materials. They would need to apply for a data security and protection toolkit with NHS Digital - which is the new IG toolkit. So, there would be lots of requirements, but I don't think any of that is insurmountable. It just takes time and resource and certainly our national clinical audits manage to do that quite well.

I think it would be possible.

Cyril Chantler: Why can't HQIP set up registries itself? Why does it have to go - get other people to do it? Because if you did it - with all those things covered - and you have a relationship with NHS Digital - which was transparent and open and proper information governance, and you deal with the opt out and Section 251. Why can't all that be linked in a sort of more efficient way?

Jill Stoddard: So, I suppose the easy answer to that is, we could do that - we have got the right people who could do that. It's about resources and being given a remit to do that.

Danny Keenan: We have been thinking exactly along those lines actually. Because those same ideas have gone through our heads as well as to - you know - just get on with this, because...

Cyril Chantler: I mean I must be clear. I think the involvement of the clinicians, of all sorts and patients in this exercise is vital.

Jill Stoddard: Absolutely.

Cyril Chantler: But I don't see why it all has to be done separately.

Matt James: Can I - to come back to [unclear] - I think what - the process that HQIP currently manages is an upfront exercise involving patients and clinicians in the design and the data to collect, and the objectives of a registry and how it's going to set out its purposes. There's an exercise which HQIP managed very well when they were involved at the back end of that which is to ensure that the right - correct processes with validating the data, checking the outcomes and enabling the clinicians to be directly involved with validating the outcomes and then publishing the analysis

There's this process in the middle, which is all about holding data, the consents around the data, obtaining the data and shuffling it around the system. Whilst the front end and the back end really do need customisation to a medical speciality or a particular issue and need careful governance arrangements, surely we can find ways to standardise that process in the middle.

So that unlike BCIR and PHIN and every other organisation that's been invented that's had to find its own way through the data protection rules and spend years doing so and face huge amounts of frustration and expense. It will at the end of day be huge amounts of taxpayers' money spent trying to navigate a taxpayer funded system around how the - you know the legal basis is managed.

If we can find a single approach to that on a common data platform, common data architecture and a common approach to the way that we handle those issues of lawful basis and consent then we will be in a far, far better place.

Sonia Macleod: But surely they apply across all the registries? It doesn't matter...

Matt James: Every one is bespoke currently.

Sonia Macleod: But that's the point. Why?

Matt James: Yes.

Multiple Speakers: Yes.

Sasha Hewitt: Well I guess they're bespoke because they each have - they're, each of them are trying to collect different types of data from different types of specialities, on different types of patients. They all have a unique methodology. So, they have to do that in a different way in order to collect the right data and produce the right outcomes. So, certainly my experience of audits is one size does not fit all. The best audits are the ones who are run by the clinical societies and organisations that deliver that patient care and can really drive the improvements at the end.

But I - my experience is not one size fits all. I don't know - you know, even within NHS Digital you've got your clinical audit platform. I would have thought there's still a need to bespoke and tailor that depending on...

Manpreet Pujara: I agree. But I think the key goes back to that - my simple message earlier on - which is about just collecting it once if there's that expectation that - dare I even say it - professional requirement - that actually you're recording this information and once it's recorded it should be able to be used on a number of occasions. It's about partnership working and ensuring that actually you may have different agencies that are involved, but actually that you collect it only once.

Danny Keenan: You have to think about the National Audit Registry - so a lot of the national audits are in chronic disease areas. We're talking quite a lot more to do with devices and the sequelae from devices. They're quite different. So, if you were to think of something like stroke or heart failure, they're actually - their requirements in there are quite a lot different to say a mesh registry or a joint registry. It's possible in the latter area that is a spec that would cover quite a lot of what's required, unlike the chronic disease area where actually there's different bespoke areas that need to be looked at.

Sonia Macleod: Absolutely. But I mean the overarching legal frameworks that...

Danny Keenan: [Unclear].

Sonia Macleod: They are the same.

Danny Keenan: Legally yes. Sorry.

Cyril Chantler: So, it would be possible to conceive - obviously all registers are different. The one I was involved in was for children across Europe who had kidney transplants or kidney failure and obviously that's very different. But they could all exist within an overall framework that did all the governance - both legal and information governance - and link in to the data collection systems and so forth. The whole thing could be integrated could it not?

Danny Keenan: I think the answer is yes. We've grown this thing haphazardly as well - the whole programme. If you think of microchips and cardiac things - they kind of came in with Blair et cetera [the death areas] and that's obviously how it all grew and then we moved along to chronic disease. But I think what you're coming at and probably it is time to look across the programme and say well what is common and there is - like certainly with legal basis [unclear]. But taking it forward, yes. There are common areas in these for sure.

Julia Cumberlege: I very much like Cyril's words of integration. Because partnerships is always a lovely, lovely idea. We know that even in the best practices now partnerships break up and they are very difficult, very time consuming. It depends really on the individuals involved - whether they want to work together or not. Although I think it's a lovely idea, I really think it's not strong enough, and that we need to think of something different in order to make this really work. I don't know if you'd agree with that? Probably not. Okay.

Simon Whale: Can I just take that point a little bit further. So is there a problem - in terms of getting to where we - I think we're all agreed we want to get to - the database and registry concept that we've described. There doesn't seem to be any dissent around the table from those here today. Is there a problem in terms of decision-making and leadership? I mean who's ultimately responsible for implementing the kind of thing that we're talking about?

Danny Keenan: Well [unclear] to the Department of Health and Social Services and obviously NHS England are very, very important in our work as well. In fact, the vast majority of our work comes from NHSE.

Jill Stoddard: So, in order for us to act we need to be given a remit. So currently we are waiting for a decision from the Department of Health or NHS England about a remit to do whatever, and funding. I don't know whether that's

something that they would want to do through HQIP as an organisation or a different organisation. So those are the decisions that we are currently waiting for.

Julia Cumberlege: Are you putting pressure on the bodies concerned to come to a decision?

Sasha Hewitt: I'm not sure that that's our role at the moment.

Danny Keenan: We are answerable particularly to the Medical Director at NHS England. That's our close link. Obviously with NHS England and I coming together that's going to make that easier.

Julia Cumberlege: See from a layperson's point of view, it always seems to me that there's somebody else that you're passing the buck to. That gets very, very frustrating. I understand that parliament was responsible for a lot of this in the 2012 Act - *Health and Social Care Act* - and I do understand all these different bodies. But anything that we can do in new innovations that actually supersedes all this and really gets to the grips and make HQIP make - it's understandable to people, would be really helpful. We need your help with that.

Danny Keenan: We met with Steve Powis - the Medical Director - the other day in fact. He would be the key person. He and Simon Stevens to be honest. But there's going to have to be money spent and it has to be that access.

Cyril Chantler: So, my understanding you get your contracts in effect from NHS England but the person to whom you're accountable is the Department of Health and Social Care?

Jill Stoddard: No. So, on this particular occasion - for the mesh work - we were approached by the Department of Health to ask - because of our expertise at HQIP - whether we could undertake a rapid piece of work. So, we said yes, absolutely, really important subject. We really want to be involved in it.

Cyril Chantler: It's an arms-length body.

Jill Stoddard: Extremely...

Cyril Chantler: You're an arms-length from NHS England are you? Not from the Department of Health?

Sasha Hewitt: So, we're not an arms-length body we're...

Cyril Chantler: Are you not?

Sasha Hewitt: ...a charity. So we're...[laughs].

Jill Stoddard: [Laughs].

Sasha Hewitt: I guess our remit is through the contract that we hold with NHS England and we have to go through a procurement process to win that contract. So, we are - you know a small healthcare charity.

Jill Stoddard: We have a National Clinical Audit and Patient Outcome Programme at HQIP. HQIP is the host organisation for that and we have the headline contract for that programme with NHS England and the Welsh government I should say as well.

Cyril Chantler: Thank you.

Matt James: May I speak plainly on this for a minute because I think Danny referred to some of these issues earlier. But we're coming from the outside. What we're trying to do desperately is bring the private healthcare data into alignment with the NHS. The question that immediately faces you in doing so is to which bit of the NHS shall we align because of lots of different bits going in lots of different directions. That is what has drawn me and our organisation in to trying to understand all of these different pieces.

The question that was asked earlier about why HQIP wasn't asked to run the Breast and Cosmetic Implant Registry. The organisation controlling the overall response to that was the Department of Health and Social Care who asked NHS Digital to run the registry end to end. Probably slightly to the surprise of some of the people who were participating in it up to that point. Because up to that point NHS Digital hadn't been greatly involved. In fact, the MHRA had been taking the lead in doing the work up.

But I think it doesn't really matter what that particular provenance was. It's illustrative of the point that if we continue to have a bespoke response to each issue that arises, we will get a different answer every time and we will end up still dealing with a multiplicity of projects at different stages with different governance arrangements and so on.

That's why - to come back to the same point - I think it's imperative that in framing recommendations, whoever is responding - whether it's the Department of Health and Social Care or NHS England - there needs to be an understanding that a level of co-ordination and alignment to existing processes and existing governance arrangements would be extremely beneficial to whatever comes next.

Cyril Chantler: Can I say this conversation - at least to me - has been hugely helpful, so thank you. Can I just move us to a different area now because it particularly relates to sodium valproate? We don't actually know how many women of

child-bearing age are currently actually receiving sodium valproate. But there ought to be a way of establishing a register given that we know where the prescriptions are going.

Is that something that you could do - Dr Pujara - through NHS Digital?

Manpreet Pujara: I think we do know the number of women who are receiving sodium valproate. I just don't have a figure to give you today. I must apologise.

Cyril Chantler: Okay. How do you know that?

Manpreet Pujara: Well we know that from one or two areas. A lot of that information comes from prescriptions that have been dispensed [unclear] with the BSA. So that is primary care prescribing on the whole.

Cyril Chantler: Yes.

Manpreet Pujara: With a small amount of secondary care prescribing where an FP10 prescription has been used. The information that we don't have consistently is about prescribing in secondary care. Whereas - bearing in mind that most sodium valproate is initiated by specialists but actually prescriptions continue at primary care - we can be fairly confident that the information...

Cyril Chantler: So, you can create a register linked to the NHS number? This is patient identifiable information? To know where the women are. You could do that?

Manpreet Pujara: We could get the information from the BSA who have the dispensing data and who are the holders of that dispensing data. That would provide us with an NHS number as well as the drug and the history in terms of prescribing.

Now as we move to a more electronic system - so as you will know, traditionally prescribing was - has been computerised for the last 20 odd years. But with actually the dispensing, the claiming has not been electronic. For the last 10 years we've been moving towards an electronic system - an electronic prescription service - which means that we also have information about what is being prescribed and what is being dispensed.

So, as the NHS moves more and more closer to fully electronic prescribing in primary care - and dispensing in primary care - the amount of information that we have will be significantly richer and fuller in the sense that we can compare what has been prescribed and what has been dispensed as well.

Simon Whale: You could start collecting that data now? Even though you haven't got full EPS.

Manpreet Pujara: We are not the holders of that data. The data is...

Simon Whale: It's with the BSA.

Manpreet Pujara: ...transferred from the GP system, to the Spine - where it stays for a transient period - and on the expiration of that prescription and then goes to the BSA or is discarded if the prescription hasn't been dispensed. So, at the moment we don't hold that data for an infinite period of time at all. Which is why we have to go to the BSA to find out the information about what has been dispensed.

Simon Whale: Is there anything to stop you doing that then?

Manpreet Pujara: No. So again - not being an expert on data and IG - I would say there is nothing stopping us from doing that. We would just need to ensure that it's legal and whether we needed a direction to be able to do that.

Sonia Macleod: But that gives us women of child-bearing age [unclear] parameters...

Manpreet Pujara: Yes.

Sonia Macleod: ...receiving valproate?

Manpreet Pujara: Yes.

Sonia Macleod: That doesn't tell us the number of children born, does it?

Manpreet Pujara: No.

Sonia Macleod: Can we do that?

Manpreet Pujara: I think if you - that would involve further linkages. If you were able to determine which one of those women are of child-bearing age are pregnant during a certain period of time, there's different ways of getting that information. But I think in today's world the most reliable probably is from the exemption certificate that pregnant women have. Because not all pregnant women now come and register with their GP if they fall pregnant. Most of that is done by the community midwives and so on.

So, sometimes as a GP I really wouldn't know that a patient is pregnant until they are well into their pregnancy. They don't have the...

Cyril Chantler: But technically - and there are issues of common law confidentiality and GDPR in this area - hugely so - to create a registry of women of child-bearing age who are taking valproate.

Manpreet Pujara: [Unclear].

Cyril Chantler: There are very significant issues there.

Manpreet Pujara: So, it's possible.

Cyril Chantler: But technically it is possible?

Manpreet Pujara: Yes. So as part of the work that we have done with the GP system suppliers - clinical system suppliers in general practice - we have made available audits for all practices to be able to run on a daily basis to see how many patients they have - how many women they have - of child bearing age who are taking valproate.

Cyril Chantler: Is that for all GP digital support systems?

Manpreet Pujara: Yes.

Cyril Chantler: SystemOne, Vision and EMIS.

Manpreet Pujara: All four of them.

Cyril Chantler: Which is the fourth?

Manpreet Pujara: Microtest. A small number of practices. That was enabled in all four systems early last year and reported in July to the stakeholder our [unclear] stakeholder network that that was all happening.

Valerie Brasse: That's a consistent across all the four suppliers?

Manpreet Pujara: Yes.

Julia Cumberlege: But isn't it important that we ensure that women are much better informed - of child-bearing age - because if you wait to see whether they're pregnant, it can take a few weeks. It can even take up to months for those who don't want to come to antenatal classes and things and the damage is done.

Manpreet Pujara: Yes.

Julia Cumberlege: I wondered if you had any views on the Pregnancy Prevention Programme. Because it does seem to be that that is not working very well at all. We've had surveys that are done by the patient groups to show that it isn't doing

very well. We just wonder why it takes so long to update some of the healthcare IT systems.

Manpreet Pujara: Thank you for that question. So, we have again worked with the system suppliers - between December 2017 and last year - to ensure there is a new, updated safety warning for any woman of child-bearing age who is taking sodium valproate. Which not only warns the prescriber, the user who's issuing the repeat medication, the authoriser about the fact that this is a woman of child-bearing age. But it also asks specifically, have you checked whether or not this woman is on a Pregnancy Prevention Plan? Whether or not they are - they'd had a review by a specialist in the last year as to whether they need to continue taking valproate.

There is a set of questions that appear on the screen. One of the things that we've done for the first time is encourage suppliers to ensure that that warning is consistent across the four systems wherever possible so that - with the way the workforce moves within general practice at the moment - with 40 per cent of [unclear] being salaried GPs [unclear]. It's important there is consistency in the systems.

We've also worked with the dispensing system suppliers so that when the woman is collecting her medication from the pharmacy that they also do the checks. They also have a similarly consistent warning to ask those questions. So, the system should be working better.

Julia Cumberlege: Yeah. What can you do then to ensure that it is as near foolproof as we can get, because we know at the moment it isn't? We are very concerned that more babies are being damaged.

Manpreet Pujara: So, I remain very concerned about what I would call alert fatigue amongst all of us. Because we're using the technology on a day to day basis in almost anything and everything that we do. We are used to moving on - shall I say - on occasions - not necessarily [reading]. I think it's really, really important to ensure that clinicians, prescribers, actually pay attention to the warnings that are there and that those warnings - the number of warnings are minimised to those that are relevant for that individual patient.

So rather than receiving unnecessary warnings which are not relevant for the patient - which then results in a clinician or user learning to switch off and ignore those warnings. Sadly, I've come across Trusts that have actually switched off their warning systems because of alert fatigue. We need to ensure that those warnings are very focused in those specific circumstances and to ensure that clinicians have a system and a way of

actually discussing those warnings. I would like to actually put the patients at the heart of this.

But the patient can actually also challenge the clinician. So, for me when I have a high severity warning, not only is it a red warning but the computer also beeps and I have a habit of discussing every single one of those warnings with the patient - particularly if I'm overriding that warning - as to why I am overriding it.

That needs to become the norm and I think what we need to enable – and I am hoping that patients will be able to access their [unclear] and [unclear] systems where they can actually look at the drugs that they're taking themselves and take charge of their care that they will be in a position to actually ask questions.

The key thing for valproate is at the initiation of the drug to ensure that the woman - or teenager or child - is aware - or their parent is aware - in those circumstances, of the risks. But also, now ensuring that those warnings are checked every time a prescription is issued. That's what we've enabled.

What we need to do is to ensure that it's a co-ordinated effort and it is a - I'm going to use the word partnership again - between the patient, the practice and actually the pharmacist - to ensure that they all understand why this drug is being prescribed, why it's being taken and what action have they taken to ensure that she's not going to become pregnant.

Sonia Macleod: One thing that strikes me is that warnings are there for a reason. So how is it Trusts can simply turn them off?

Manpreet Pujara: A very, very good question. I have no answer to that at all. I don't know Stuart if you want to...

Stuart Harrison: Some of the systems are inherent and configurable and so that's a feature and sometimes some clients will ask for that. I kind of agree with your train of thought that that shouldn't be possible and ultimately what Manpreet said is very much configurable to the clinical setting.

Manpreet Pujara: GP systems are configured in that way. So those warnings are there. But what we can't do is control the user - their behaviour.

Julia Cumberlege: Right, well I'm going to draw this to a close. Thank you very much indeed for coming. But first of all, I'm going to ask my colleagues if they have any further questions they want to ask?

I want to echo very much what Sir Cyril has said which is it's been enormously helpful to us. I do want to thank you. You're going to give us

some more information that we've asked about numbers and things like that. If there are other things that you think, oh my goodness they missed out on that, we'd love to know. Because we are very anxious to do a really good review and it does depend on people like you - who've got the knowledge and the expertise - to help us do that.

END OF TRANSCRIPT

Session 2: The National Congenital Anomaly and Rare Disease Registration Service (NCARDS) and National Joint Registry (NJR)

START OF TRANSCRIPT

Julia Cumberlege: Would you like to perhaps go along this way, and if you could say who you are and where you're working and what you're doing.

Elaine Young: Yes, thank you. I'm Elaine Young, and I'm the Director of Operations for the National Joint Registry, which is based at the Healthcare Quality Improvement Partnership who host us.

Matthew Porteous: I'm Matthew Porteous. I'm a consultant orthopaedic surgeon in Bury St Edmunds, and I've been working with the National Joint Registry since very soon after it started. I chair two of their committees and sit on just about every other committee there is, so I have a fairly good knowledge of it from a clinical side.

Julia Cumberlege: Lovely, thank you very much.

L Powers-Freeling: I'm Laurel Powers-Freeling, I'm the chair of the National Joint Registry Steering Committee. I'm a volunteer, but I have been the chair now for seven years.

Julia Cumberlege: Right, thank you very much.

Nicola Miller: I'm Nicola Miller, and I am Head of Registration for the National Congenital Anomaly and Rare Disease Registration Service. I am head of registration for the north of England.

Julia Cumberlege: Thank you.

Sarah Stevens: Hello. I'm Sarah Stevens. I'm a public health consultant and I lead the National Congenital Anomaly and Rare Disease Registration Service hosted by Public Health England.

Julia Cumberlege: Right, okay. Thank you. That's really helpful. One of the things that we've been considering, not only this morning when we had another group in, but we've been thinking about it quite a lot in our own discussions and testing it out on people. One of the things that we think is really important is to actually - when we're talking about registries, talking about databases, what do we mean by them? Because there seems to be a bit of confusion in these terms. So, if I could just read to you the definitions that we've picked up, and if you could tell us if you think this is about right, we'd be very grateful. Or if you say, look, actually you need to improve it, et cetera.

It's quite a lot to take in in one go, so we can easily send it to you, and you could make your comments later on.

For the purposes of this afternoon, we're talking about a registry as an organised system that continuously and consistently collects relevant data in conjunction with routine clinical care, evaluates meaningful outcomes and comprehensively covers the population defined by exposure to a particular medical device or devices, at a reasonably generalised scale, for example, international, national, regional health system with a primary aim to improve the quality of patient care. That's taken from an international medical device regulations forum, so that's where we've gone to for this definition. Do you think that pretty well covers it, for most [unclear]? So, this database, we're talking - sorry.

L Powers-Freeling: I suppose one of the questions in there is whether the data sets are comparable. So are you simply registering an incident or registering a procedure or a case, or are you trying to register something which you'll look across for comparative and analytical purposes?

Julia Cumberlege: I'd like to go on to the database now, because that definition is what we think would be the first step, as it were, to get a proper database, and then arising out of that would be a registry, which obviously would be more fulsome and include a lot more patient information. So, if I could just say the database - and this is the Oxford Dictionary - 'a structured set of data held in the computer especially one that is accessible in various ways'. For our purposes - this is the Review talking now. For our purposes, in relation to HES, such a database might include the NHS number, type of procedure, operating surgeon, healthcare provider, unique devices identifier, date of procedure, age of patients, and gender. That's how we would see a database - does that sound about right?

[Aside discussion]

L Powers-Freeling: At the risk of jumping ahead of something else, I suppose the nature of the device - I think in total we have about 5000 different items on the NJR database, so there's not a hip replacement, there are a wide range of options involved and that can be due to the metal that's been used. It could be something about the way the joint's constructed, et cetera. So, within the device definition, the specification of that was actually critical to understanding which ones...

Cyril Chantler: We do understand that.

L Powers-Freeling: Okay. I just want to make sure.

Cyril Chantler: You do run a very good joint registry which is why we're here to hear from all of you. What we're trying to do is to understand how you identify patients, and you do that with security that you're right, not secondary through HES or something like that. We want to separate just for the sake of conversation, so we understand what we're talking about, the registry which is a detailed piece of information looking at long term outcomes and all the complexity that [unclear]. My personal experience is that I was on the European Dialysis and Transplant Association Registry for many years, looking at children with end stage renal failure across Europe, and constantly interrogating the registry, asking questions, going back - but you've got to be sure you've got the patients right, to begin with.

So, what we are suggesting is that we think through NHS Digital identifying the patients - the question is then about GDPR which we're going to come to during the next hour. The notion is that a surgeon - if I may as a paediatrician put it this way - but when she or he carries out an operation and fills in the operation note, that that note contains the core information which we've just been through to identify the patient - the doctor's procedure, which is then probably mandated - not into the hospital notes but to a central register which - a central database - now I'm doing it.

A central database which the register will then interrogate in the more complex ways that they do that. We have to be thinking about all the different registers that exist and need to exist, and our particular issue is in relation to surgical mesh, where we don't have it, and we need urgently to have it as part - all the reason we ask for a pause in operations until we've got it. It's the question of how you set that up. As I understand it, again, we're going to be asking you this question - under GDPR, you can indeed mandate of the section 251, the collection of information for a legitimate purpose.

What is also clear is that if you run a register under the opt-out, you can opt-out from being on the register. Whether that relates to GDPR or the common law, due to confidentiality I'm going to ask you to advise me about that, because I don't completely understand it. That is the reason we've separated the two, and we've put to the press at the Royal College of Surgeons and to press at the Royal College of Obstetricians and Gynaecologists whether they would in theory support a practice whereby this core information is included in the operation note which would then serve as a database which can then be linked to proper registries. That is the background to this way of defining it. Does that make sense?

Julia Cumberlege: Good - thank you very much. If I could first start off then to ask you - could you describe what you consider to be the strengths of your own registry and how it could be improved?

Matthew Porteous: Okay, so we have got - we're the biggest registry of its kind in the world. We've got two and a half million records, so we have a mass - that sort of size is a beauty all on its own because you can really start digging down into the data. We add about a quarter of a million records a year now. We've got 95 per cent compliance which has gradually crept up. It was dramatically improved when the 2011 entry was mandated - before that it was voluntary, and if you're going to have a registry and you don't mandate it, you might as well not bother, in my view.

Then we have a data quality audit where we go back and check what's been entered against what's been put into HES. We've been running that for the last four years, so we're now very near 100 per cent compliance retrospectively. We do that retrospectively, about a year in arrears, to make sure we've got a good data set. We have really good - in the last few years we've really developed, and we've gone from being a registry that is looking particularly at devices, and whether or not brand X is a good brand or not, to a registry that actually supports good clinical practice.

That's the dramatic change we've had, so that every consultant that puts in a joint replacement gets access to their portal. They can look and see what they've been doing. They can look at all their performance. Now there is a clinical - the clinic consults a clinical report once a year that is downloaded. My report for example, runs to 32 pages of detailed information about my personal performance, and that we're also pushing for that to be mandated as part of appraisal. All the good people use it, but we know that actually about a quarter of surgeons don't download it and use it as part of their appraisal - but we're getting there slowly.

We have a - two years ago, we undertook a transparency and accountability agenda, so exactly how we do everything has been laid out. That's all available on our website, so that particularly for Alert and Alarm surgeons, hospitals, implants - all of that is laid out clearly so that people know how it works. We spend a huge amount of time laying out spreadsheets and charts and accountabilities and responsibilities for the - and standard operational procedures for all of those things. I think those are the main things from my point of view.

Julia Cumberlege: Thank you very much indeed. Can I ask then - you're saying that surgeons will look at their performance - can they look at other surgeons' performance?

Matthew Porteous: You can't see other surgeons' outcomes. You can see their patient demographics - those are published online by the NHS, so you can look at those for any surgeon. You can look at the surgeon, but you can't see what their outcomes are. What we do do for individual units is we send a you unit report which has individual surgeons marked. Those surgeons are anonymised in theory, but always in my unit, I know who they all are because you work out roughly how long they've been there and what the dots are. We very much encourage just - both us and the GIRFT initiative - encourage every unit to sit down every year and go through their unit report, and for each surgeon to discuss their personal report.

Cyril Chantler: Can you just - Getting It Right First Time...

Matthew Porteous: Get It Right First Time.

Cyril Chantler: ...for the audience.

Matthew Porteous: Sorry - Get It Right First Time Initiative which started in orthopaedics.

Sonia Macleod: There's no sort of benchmarking of individual performance against experience?

Matthew Porteous: There is a benchmark - very much so. You get a funnel plot. Each individual makes a funnel plot and they can see where they are on that funnel plot, and where everybody else is. Everyone else, of so many surgeons, is just a massive dot. We identify outliers and I'm part of the surgical performance committee where we identify surgeons who are outlying, and there is a whole process for managing surgeons who reach Alert and Alarm level, provided it's all done confidentially. So even in the committee, we don't know who the surgeons are. It's only when they break the code - that surgeon 7692 is the surgeon who has been outlying, then they get sent a letter. Does anyone know who they actually are?

Sonia Macleod: Essentially the funnel plot enables an individual surgeon to say, okay, I'm here, and not, these are all my contemporaries?

Matthew Porteous: Yes.

Sonia Macleod: So, there is a sort of comparator in there but it's a long line?

Matthew Porteous: Absolutely - and you can see where you are in relation to the mean and whether your performance is better or worse than the mean. We're very conscious of the fact that we don't want people ranked. To become an outlier at alert level, you have to be two-standard deviations worse than the mean. To become an outlier at an alarm level, you have to be three-

standard deviations worse than the mean. That's one in a thousand jumps and that is a statistical aberration that you're there.

Julia Cumberlege: So, the outliers know who they are?

Matthew Porteous: They do - and it's a whole process for managing those once they've been identified.

Julia Cumberlege: Could you tell us a bit about that?

Matthew Porteous: We write to them - this is for the individual outliers. We write to them individually and tell them they're an outlier. Almost without exception, they have actually had a letter. When you reach alert level - which is two-standard, you get a letter that we ask for as an acknowledgment to say, watch it, you're heading in the wrong direction, basically. We don't require any action to be taken. If you reach alarm level, then we send them a letter, and six weeks later, we send a letter to the medical director of the hospital informing them that they have an outlier there. We require them to send us back an action plan - it gives them an outline of what it is we want them to do and we want to know why they think they're an outlier, and we want them to tell us what they're going to do about it.

We then review that answer - very occasionally, it's not very satisfactory and we send it back again and say, no you've missed the point here. In the very rare occasions where we have major problems, we then go to the CQC and sit on our surgical performance committee - not because they can do anything about the individuals, but because we recognise that there may be a failure of governance mechanism within that organisation, which they will pick up on. Assuming everything is done according to the book, which happens 99 times out of 100, then we then actively monitor that surgeon to make sure that their change in performance occurs as they have promised us.

L Powers-Freeling: Do you want to say anything about the unit interventions and the visits?

Matthew Porteous: Yes, we have more recently tightened up unit outliers. We've had outlying units who've been outlying for years and they've never done anything about it. The British Orthopaedic Association have now set up a thing called an Elective Care Review, where a hospital that is having problems can invite an independent team - nothing to do with us - from the BOA, to go into that hospital and advise them as to what they need to do to improve.

L Powers-Freeling: We provide the information to support that.

Matthew Porteous: We provide the information to support that, and we have recently recommended a number of hospitals, who have been persistently outlying and have never really sorted themselves out, to have elective care reviews. Those who have - some of them take place and some of them never have to take place. Where the hospital has been resistant to that, the CQC have become involved, and told them that they need to have one.

Elaine Young: I think the strength of the system that we now operate looking at outliers [unclear] some surgeons, arose from the accountability and transparency modelling that we did. So that now, we're working with the specialist societies and the BOA, the regulators for implants, the MHRA - but for surgeons, CQC - and this didn't happen before. So, it's a really joined-up plan that I think is worth mentioning.

Julia Cumberlege: Can I ask two questions then - the first one is, do some of these outliers appear an outlier a year later when you're doing the process again?

Matthew Porteous: The answer is yes, but the reason for that is because of the way we calculate outliers. We use a thing called PTIR, Patient Time Incident Run incidents. That means that there's a huge drag on the system, so it's quite difficult to become an outlier, but once you've become one, your previous activity means that you're likely to remain an outlier for some time. What we like to see is a trend [talk] back down in the right direction. What you have to recognise with joint replacement is that it's a very slow game.

You can put a joint replacement in, and it might fail in the first year - we all get a few failures in the first year, but not very many. Then if you start to have failures at six and seven and eight years, that's probably because of something you've done, or you've selected a bad joint replacement. Really good joint replacements will last maybe 20, 25 years, so this isn't something where you put it in and snap, you're immediately an outlier. It may take some time for you to become an outlier.

Julia Cumberlege: In the meantime, those patients could be harmed.

Matthew Porteous: Well - absolutely, I would accept that, but what we don't know is - even now, we don't know what a really good joint replacement looks like until something new comes on to the market. There is a system now in orthopaedics called Beyond Compliance where those are much more closely monitored than joint replacements that have been around for a long time.

Because it takes a long time for joint replacements to fail, the best example we've had recently is metal on metal, with the ASR hip. It was perhaps seven years before we identified that there was a serious problem with

that hip, and that wasn't helped by the fact that some hospitals putting them in were poor to comply - we're going back to the beginning of the NJR now. I think we pick that up a bit faster now, but you're not going to identify a bad hip replacement really, really fast.

L Powers-Freeling: It's worth mentioning that the metal-on-metal hip - it wasn't that surgeons made a bad decision, so it was not about the capability of the surgeon, it was in fact recommended as a good prosthesis, but it took seven years to recognise that the wear on the hip was actually problematic. So, it is as much to pay attention to the implants themselves as it is to the surgeons that we operate the registry.

Julia Cumberlege: Seven years is a long time. A lot of patients would have suffered through that.

L Powers-Freeling: It is unfortunate, and it is a function of something that is intended to last 15...

Julia Cumberlege: Can you not speed up your system?

L Powers-Freeling: ...to 25 years.

Matthew Porteous: Sorry, I didn't hear you.

Julia Cumberlege: Can you speed up your system?

Matthew Porteous: We can speed it up if we improve compliance - we've done that now. So, the compliance at the time the ASR was happening was not - our numbers weren't big enough, because it's a statistical game you're playing really.

Julia Cumberlege: Yes.

Matthew Porteous: I think you have to recognise that all implants will fail. A hip replacement is great if it sees you out, but if you put them in to people in their 30s and 40s, they're all probably going to need revision, and they get told that at the time they have their hip replacement. Then it's a question of, is brand A better than brand B? So, it's not a question of, this is a really bad hip replacement. There are huge shades of grey in there. We don't always know which the very best hip replacements are for different groups as well.

So, an 80-year-old having a hip replacement might need a different hip replacement, because longevity is not that important if you're 80, because - very unlikely to live 20 years statistically. Whereas if you're 40 or 30, then that hip replacement might have to do 40 or 50 years, and that might be a different hip replacement which is a bit more expensive, or it might not be. We don't even know the answer to that yet.

Julia Cumberlege: Some advice then on surgical mesh - what should we be doing about that? Because that involves surgeons.

Matthew Porteous: It does - I was interested to hear the thing you said right at the beginning about the difference between a database and a registry, and we took the view in the NJR, when it was set up, that we don't try and interrogate records because that's too difficult - we require people to fill in a form and that goes into our data and it's completely separate from the patient record. In an ideal world, you could try and link the notes to the record and gather the data that way - I think you'll have a problem doing that because I don't think the systems are well developed enough in hospitals to pull all that information out.

Cyril Chantler: We want to mandate - and that seems to be the right word to use [unclear] you more or less said that, that every operation that involves a device at any rate, the surgeon, when they fill in the operation note, that record is then completed, goes to a central database, so at least you've captured it. Then we can talk about how you establish and ensure ratios after. Before you go on, could I just ask you - do you cover the private hospitals?

Matthew Porteous: No - at the NJR, we do. I don't do any private work.

Cyril Chantler: The NJR does?

Matthew Porteous: The NJR covers the private sector as well, and it is mandated - in fact it was mandated in the private sector before the NHS.

Elaine Young: From the outset, strangely.

Cyril Chantler: That's interesting.

Elaine Young: So, in 2003, independent sector was mandated but not the NHS, and as Matthew has said, that came in 2011.

[Aside discussion]

Simon Whale: Can I just ask Sarah and Nicola, in terms of NCARDRS, if that's an acceptable acronym to use rather than the full name, what do you think are the lessons to learn from the work that you've done in the registry, that you've accomplished? In terms of - thinking specifically about what we've got to do, or we think about, which is surgical mesh in this context, but your strengths - the strengths in what you've done and the lessons you would be able to impart to us would be really helpful.

Sarah Stevens: I think we've got four key strengths - one is definitely population coverage. We started congenital anomaly and registration and PHE in 2015, so in our

fourth year. At that time, there were regional registers covering parts of the population, but half of all births weren't covered at all, so there was no coverage in London and the south-east, and the eastern England and the north-west. In the last four years, we've moved these regional registers into PHE and then expanded to cover the whole population.

I do think where you're looking at rare conditions - obviously having that population coverage is a real strength. We are one of the biggest in Europe now. The other thing we've done over the last few years is build a single national data management system, so that cases are registered in exactly the same way, whether they're in Newcastle or in Bristol. We have standard operating procedures - they're coded and classified in the same way with clinical expertise in putting into that.

Simon Whale: Have you - sorry to interrupt. Have you developed those yourselves?

Sarah Stevens: Yeah, we fused - there's some international standards - the EUROCAT is the European registry's surveillance program, and we've used those - and what was happening before in the regional registers, but we've developed those as a standard nationally. I think that has been really, really important to do. The other thing is actually it's interesting the conversation about mandated data sets - we're not a mandated data set. It's something that would be good to explore, so we do rely on the goodwill of clinicians sending through this data.

Another strength of ours is taking a multisource approach. We get partial information from different places - from antenatal detection, so from a pregnant lady coming in through screening and we follow that postnatally too. As you all know, the information's fragmented - it's all got its limitations. So actually, taking this multisource approach and piecing that information together with key identifiers is the reason why we can increase our case ascertainment and coverage. That's been a real strength for us as well.

Sonia Macleod: Do you collect information on maternal illnesses as well - so do you collect information on epilepsy in pregnancy and medications?

Sarah Stevens: We do, yeah. Do you want to?

Nicola Miller: We do, yes - but we're probably better at that in the antenatal period. So, if an anomaly is detected antenatally we would be notified of that case and we would also be notified of maternal illnesses, et cetera. Where an anomaly hasn't been detected in the antenatal period, the anomaly would often be reported to us by paediatricians. We wouldn't necessarily be

holding [them to the] data at this point in time, so we need to go back and interrogate that for that case.

Sonia Macleod: How long do you follow the child through?

Sarah Stevens: Our aim is to follow the whole life course. I think at the moment we - definitely up to a year. Some regions have been going a bit longer than that when they have to.

Nicola Miller: We would follow through in terms of new diagnoses on the same patients. So that would come in and would be added to the case.

Sonia Macleod: Okay - so you have a lifelong track for anyone that's on your - interesting.

Nicola Miller: Yeah.

Cyril Chantler: Do you contact the families directly?

Sarah Stevens: No, only through the clinicians.

Simon Whale: Is there a disadvantage to not contacting the families and getting direct reports of experience?

Sarah Stevens: We don't get any self-reports at the moment. That is something we're looking at doing through rare disease work actually - enabling patients to self-report. For congenital anomalies at the moment, no, it's only through clinicians reporting or - another strength I think that we've achieved is actually getting electronic feeds directly from [unclear] genetic labs, from biochemistry labs, and using the routine data sources that are available.

Because obviously that reduces the burden on clinical time. So, we've moved to electronic reporting entirely and we give notifiers a number of different ways that they can report securely to us. We take the data in whatever form they are able to give it to us. We do have electronic notification forms that will take information if you already copied into an email for a referral - anything that we can do to keep the burden on clinical time as low as possible.

Simon Whale: Do you collect transgenerational follow-up data or not?

Nicola Miller: That's an interesting question. The way that we set up the data management system, we will be able to in the future. I don't think we've done that as regional anomaly registers, particularly one. Although you can see the links in the old legacy databases, but the way the new system is set up, you will be able to see links between women who have female children, and then those children having...

Cyril Chantler: You're obliged to give people the right to opt out?

Sarah Stevens: Yeah.

Cyril Chantler: Two questions - has anybody done that?

Sarah Stevens: Yes, we've had less than five in the last four years.

Cyril Chantler: What proportion is that?

Sarah Stevens: Less than five patients of [unclear].

Cyril Chantler: Yes - so it must be a tiny percentage.

Sarah Stevens: Yeah, very small.

Cyril Chantler: That must mean that you can contact the families - you know how to do that.

Sarah Stevens: Because we take this multisource approach, we do take identifiers - both of the mother and of the baby, and sometimes of the family. We would have their address, date of birth, NHS number, are normally the core ones.

Cyril Chantler: So, you could actually contact the families and get information from them if you wish to do that?

Sarah Stevens: We could - the reason why we use the clinicians is to ensure that the information that we have is up to date, so it's another validation, I suppose. Yeah, we could. The last point I was going to say about the strength which sounds very similar to the Joint Registry is actually about getting the data back as well to clinical teams, and the importance of doing that.

That's something that we've really worked on - and to patients in the public as well, we don't want this information to be going into a black box. It's about getting it back out in a timely way and using it to inform provision of care. Particularly for us, it's antenatal screening. So, every Trust that provides maternity care - it's 136 in England. They now get a tailored report on their antenatal detection rates, on their prevalence. That's been a new thing that has just happened in the last couple of years.

Cyril Chantler: Do you provide a [revised] service for patients and families - can they contact you?

Sarah Stevens: Yeah, all our information is available on the website. We do get patients contacting us and we work really closely with the patient charities and groups as well. So, we would do a lot of signposting to those groups.

- Valerie Brasse: The input's not mandated, so do you know how comprehensive your database is - do you have any idea?
- Sarah Stevens: It's estimated that around two per cent of all births in Europe are affected by a congenital anomaly. That's the findings from research that EUROCAT has which has been going since the early '70s. We know we're hitting that for those areas where we've got well-established regions, so that's why we think our case ascertainment is good. In the regions where we have just set up - so it's new feeds coming through - we're tracking those at the moment when we know there are gaps, and we're working on improving the quality of data there.
- Julia Cumberlege: I do understand that what you're doing is extremely sensitive and you have to be very careful how you go about what you're doing, but if there was an opportunity to contact parents, mothers, as Cyril has suggested, do you not think there's a huge advantage in that? Because we've met women who have had five deformed babies. If perhaps you had been able to contact them, then that might have prevented three of them being born disabled.
- Nicola Miller: I think there's an advantage to being very well known and allowing parents and families to contact us. I think the downside to directly contacting patients is that - obviously these are very sensitive situations and we need to be absolutely sure of what situation that family is in before we make contact with them. Obviously, it's very sensitive to be contacted by a service like ours immediately after being bereaved for example. So, I think that's why we tend to do any such contact using clinicians to make those kind of connections.
- Julia Cumberlege: Could you tell us a little bit about actual funding?
- Matthew Porteous: Go on, Elaine.
- Elaine Young: I'll just kick off that it's subscription - it used to be...
- L Powers-Freeling: We have two forms of funding.
- Elaine Young: Yes, exactly. There's a Trust subscription and there's a levy subscription from suppliers. That wasn't always the case - it was just through Trust, so this is a much fairer system. We calculate the subscription for every Trust based on the number of components that they've actually used that are logged with us, and procedures that they've done, so there's a calculation to be made on that. Similarly, for suppliers, it depends on their size as to the charges that are made. I think where it works out fairly is that the information that you can actually provide back to Trusts and to suppliers, I

think is key, if you're asking them to pay and financially contribute towards the registry.

So, units get their management feedback, their surgeons, as Matthew has described. They get their annual and clinic reports, a consultant level report, and suppliers have a system we call supplier feedback. They can go into the system, and they too, which I think is very important for a device registry, can actually monitor the performance of their devices. In actual fact, it's quite unique in the world, so that the manufacturers operate internationally - pretty much the same as manufacturers everywhere. They actually use NJR supplier feedback for regulation in other countries when introducing their devices. So, they kind of get a bit of payback as well, but it works very well in terms of funding.

Simon Whale: What kind of limitations do you put on suppliers' access to data if any?

L Powers-Freeling: They can only see their own data, so we don't allow them to see other manufacturers' data. Obviously, it would be commercially inappropriate to do that.

Simon Whale: Can they see data about surgeons' performance and outcomes?

L Powers-Freeling: No.

Matthew Porteous: No, but they can work out sometimes. If you're only supplying implant to four units and there's a problem in one unit you can probably - if you're that - you work out who it is.

Simon Whale: So, they can see the outlier profile, can they?

Matthew Porteous: No, but they'll know if - if there's a very limited number of people using something and somebody is an outlier, that implant will be creeping towards becoming an outlier itself with that one incidence alone.

Sonia Macleod: Can they see against the class of a product - so could they compare their individual product against the class generally?

Matthew Porteous: They can compare it I believe against - in hip replacement we have cemented and cement-less, so we divide up. We're having a big debate at the moment about whether that's appropriate. Whether actually a hip replacement is a hip replacement. If you're a patient you don't really care what this implant is, you just want it to last a long time. So that data is published anyway - we publish that in our annual report. For the high-volume implants, then there is detailed breakdown of those in the annual report every year.

Sonia Macleod: So, a manufacturer in effect can say, okay, this is my product within this class, and my product outperforms the rest of the class or underperforms?

Matthew Porteous: Yes, they do that. They use it in their advertising.

Sonia Macleod: Yeah.

Cyril Chantler: In the very helpful slides you sent us, I see that you're accountable - well, I think you're accountable or you're related to NHS England?

L Powers-Freeling: Yes.

Cyril Chantler: What is your relationship?

L Powers-Freeling: Well, the history was that we were set up after the metal-on-metal - after the [unclear] hip disaster, by Act of Parliament. The idea was that we were independent but that we would have a relationship with NHSE. So once a year, I go see the medical director of NHSE and talk about the products that we've made, the changes - what we need from them, how we think that we can develop the National Joint Registry to better serve.

Cyril Chantler: So why be part of HQIP?

L Powers-Freeling: Well, we are hosted by HQIP. We're hosted but we're not part...

Elaine Young: We're not managed by them.

[Over speaking]

L Powers-Freeling: We think of them as a supplier, I suppose, [unclear] to look at. We have three main suppliers - one is Northgate Information Systems and they basically hold all our data, and manage our IT infrastructure.

Cyril Chantler: Do you have any bad debts?

L Powers-Freeling: Sorry?

Cyril Chantler: Do you have any bad debts?

L Powers-Freeling: None.

Cyril Chantler: So the hospitals pay out regularly, do they?

L Powers-Freeling: Yes, we are solvent - in fact we have resources.

Cyril Chantler: I didn't mean to suggest you weren't. I don't quite understand why NHS England just don't cover your costs on the sort of [unclear] have to build.

L Powers-Freeling: It's a historical point.

Elaine Young: We are unique because our central funding comes down through the other audits that HQIP actually commission and manage. As Laurel said, we're actually just hosted by them because we're not a legal entity, so we have to have an umbrella organisation for contracts and be our data controller and that's the relationship. Historically, as Laurel said, from day one we have funded via a levy.

Cyril Chantler: Now you hold patient-identifiable data?

Matthew Porteous: Yes.

L Powers-Freeling: Yes.

Cyril Chantler: Therefore, you all entered the general legal requirement act due to confidentiality - common law due to confidentiality and GDPR, right?

L Powers-Freeling: Absolutely.

Cyril Chantler: So that means that - as I understand it - patients have a right to opt out?

Matthew Porteous: Yes.

Cyril Chantler: So, how do you deal with that - do you write to them?

Matthew Porteous: No - basically what we like to happen is that every patient is formally consented as part of the consent process for surgery for data entry into the National Joint Registry. There is a consent form - my practice personally is to do that at the same time as I take the consent for surgery. There's two forms - there's the NJR consent and there's the consent for surgery. I have to say I have never had anybody who has opted out. I've had one or two who've expressed reservations but when you sit down and spend five minutes explaining what it is, that they won't be contacted, that the data is confidential...

Cyril Chantler: However, as an organisation, you have the need to actually demonstrate that you're compliant - how do you do that?

Matthew Porteous: Well, first thing is that one of the things that has to be entered is whether or not consent has been obtained from the patient and there's a yes, no, and I don't know box. The good organisations will be 99.9 per cent yes, very occasionally, a no, and very occasionally, a don't know. We do have a - I don't know what the right word is. Not having been consented is regarded as yes, and we have a special dispensation for that. So, the only people who are, no, are the people who have actually said no.

Cyril Chantler: Because they've opted out?

Matthew Porteous: Because they've opted out. That is, I mean...

Elaine Young: Very small.

Matthew Porteous: It's tiny.

L Powers-Freeling: We also link to HES data, so we have a crosscheck on whether there is anything on HES that for one reason or another we haven't picked up, and we [unclear].

Simon Whale: How often does that arise as a discrepancy?

Matthew Porteous: What we've - actually, we've had all sorts of problems with HES as you probably know. There have been lots of issues - we had about four years in the wilderness where we weren't allowed to access HES data, so we just got on and did our own thing. What we've actually done for our data audits is we have linked to individual hospitals' PAS. We've asked them to send us a download of their PAS records which are one closer to the hospital than HES - hasn't been cleaned up in quite the same way. Then we compare the hospital's PAS for that period against what's been entered into the NJR.

You've got three outcomes - it's on PAS, it's in the NJR or it's in the NJR and it's not on PAS which means that there's a coding issue for the hospital. We've had some hospitals that have lost hundreds of thousands of pounds through poor coding. We've identified it too late for them to retrieve that, but they've tightened up subsequently, so it's useful for them to know. Or it's on PAS and it's not on the NJR, in which case we say, well please check. See if this should have been in the NJR, and then enter it retrospectively.

Cyril Chantler: However now you are working closely with NHS digital - you share information.

Elaine Young: Well we get the HES feed from them.

Cyril Chantler: Do you have a similar close working relationship with MHRA?

Elaine Young: Yes.

Matthew Porteous: Much closer.

Cyril Chantler: Can you explain how that works, please?

Matthew Porteous: The MHRA sit on our implant scrutiny group and...

Elaine Young: On our steering committee.

Matthew Porteous: ...on the steering committee. The implant steering group review the data on implants in the same way as the surgical performance committee review the data on surgeons and Trusts. We identify outlying implants or implants that are giving us cause for concern. They're discussed - we sometimes commission more detailed work.

Cyril Chantler: So, if I, as a patient, have got a painful hip and I think my hip replacement is the reason and I fill out a yellow card - how would that get back to you?

Matthew Porteous: It wouldn't, I think it would be fair to say. I haven't ever come across a patient filling out a yellow card. The yellow card is an alert device for medicines, but I didn't know...

Cyril Chantler: It's also for medicine devices too.

Matthew Porteous: Okay. Well, there you go - the ignorance of our orthopaedic surgeons on this. What does happen is that if there's a concern about an implant which doesn't usually come from a patient it normally comes from a surgeon, then they do discuss that.

Cyril Chantler: You see our problem is that in mesh it is a sad fact it's come from the patients so that's why we're so concerned.

Matthew Porteous: I can see that. We fairly regularly - I don't chair the implant scrutiny group, I sit on it. The chairman fairly regularly gets a communication from a surgeon saying I'm a little bit concerned about this combination or this hip or this knee. When that happens, he always brings it to the committee, and usually, by the time it gets to the committee, he's actually done a dive into the data and had a good look at it to see whether or not there's any suggestion in the registry that the implant is giving cause for concern.

Cyril Chantler: I'm trying to ask you a question without leading you to the answer. I have an artificial heart valve - do you think I am as safe as I would be if I had an artificial hip, in terms of outcomes and spotting what goes wrong?

Matthew Porteous: Well, the thing about an artificial heart valve is that when it fails, you're dead. I mean seriously - so that's a very definite endpoint.

[Over speaking]

Cyril Chantler: I promise you it fails slowly.

Matthew Porteous: Okay.

Elaine Young: Can I just step in, Matthew? Because I think I would say to you it's probably six and two threes because I think I'm right in saying that you have a registry. Cardiology has a registry that is...

Cyril Chantler: Yeah.

Elaine Young: Ah, okay.

L Powers-Freeling: They do for stents in things like that

Cyril Chantler: So that's why I asked you the question.

L Powers-Freeling: Yeah.

Cyril Chantler: It basically happened, but it does seem to me that I am much safer if I had an artificial hip because you insist...

Matthew Porteous: I didn't know that.

[Over speaking]

Cyril Chantler: I don't have an artificial hip.

Matthew Porteous: I think it would be fair to say that over the course of the registry and particularly in the last four or five years we've noticed a steady improvement in outcome. Because of the fact that we've got two and a half million records, and there's a huge lag that's quite slow to develop, but we have seen - we've got some data that suggests that there is a falling off, a dropping in the revision rate overall for hip replacement in the last four or five years. Part of that is the metal-on-metal getting out of the system - because of that we haven't put them in for 10 years now.

Actually, there's some data that suggests it's not just that, it's about people knowing what the best implants are, selecting them more. There's probably been - well we know there's been these improvements in surgical technique. The mortality rate for hip replacement since the beginning of the register has almost halved. That's got nothing to do with the register - it has to do with improvements in anaesthetic techniques, early mobilisation of patients, reduction in DVT rate - things like that. So, we are seeing a steady improvement in outcomes.

Valerie Brasse: Can I ask - the Beyond Compliance program, to what extent is that a contributor to better outcomes?

Matthew Porteous: I don't think that makes an awful lot of difference personally at the moment because the numbers are quite small against the whole registry. I

think what it's doing is weeding out implants, that aren't going to perform very well, getting into the system.

Valerie Brasse: That's a good thing?

Matthew Porteous: That's a thoroughly good thing. The number of implants that arrive and disappear again is very large - I did some work on that some time ago. Roughly six new hip implants have been introduced into the system every year for the last 30 or 40 years. Out of those, most of them just vanish away but the manufacturers only introduce them if they persuade people to use them. We do have this problem in - I think the whole of medicine, that people like things that are shiny and new, I call it Mr Toad Syndrome. Shiny and new we must have a go. Some people are made that way and will use them because they're like that and other people will say, no I want to use what's tried and tested.

The best implant combination in the National Joint Registry is the - if they're hips, it's the Exeter Hip. The Exeter Hip was first put in in 1971, and it remains the best hip replacement overall that we've got. I've used it my whole career. I sometimes ask myself, why do I want to use anything else? There are good reasons for that. I'm not saying that's the only good hip replacement, but you do have to wonder sometimes when somebody comes along with something that's a great new idea, and there's a great rush to use it. Metal-on-metal was a good example of that.

Julia Cumberlege: Can I ask you - you've talked a lot about surgeons and clearly their skills, et cetera. When you discover through your collection of information that actually you think that one of the manufacturers - one of the products they're producing is actually not as it should be or it is not as effective as it claimed to be, what is your position then? Do you go back to manufacturers?

Matthew Porteous: We have two levels - a bit like we do Alert and Alarm Surgeon, we have Alert and Alarm for implants. At alert level, they just get a letter. It's not as straightforward as it sounds because we have, for example, an implant that's only used in very difficult circumstances - it's not for use in straightforward knee replacements. So, if you've got an implant that's only being used for very difficult cases, it may actually be failing at a higher rate because you're not comparing apples and apples, you're comparing apples and oranges.

We write to them if it is a level one outlier, that is to say it's got a PTIR that is more than twice as bad as the class of implant in which it lies, then a formal letter is sent to the MHRA. Now the MHRA is well aware of level two

implants because they sit on the committee that decides what happens - what's a level one and what's a level two, anyway. So, they know what's going on, but we do formally communicate them if we get level one outlier.

Sonia Macleod: In terms of your interactions with the regulators and in terms of - one of the things we're interested in is a lot of the adverse events we had have been reported by women. So coming on the yellow card on their system, you're saying that you tend to get the professional adverse event reports but there doesn't seem to be crossover between those two. Is this formal communication for your outliers - is that where the crossover occurs?

Matthew Porteous: Sorry, I'm not - go on.

Elaine Young: No, I don't...

[Over speaking]

Matthew Porteous: We do not have a system in which patients can tell us about a problem, but our endpoints are only death and revision. So, we don't have a system that allows us to say, Mrs Smith has an implant that's not doing very well. We only collect revision data. We recognise that that is not perfect by any means but it's a really hard endpoint. It's a really easy...

Cyril Chantler: Are you thinking of moving into PROMs?

Matthew Porteous: We have - well, PROMs is not run by us except for shoulder replacement where we have our own PROM system that we do collect. We would really love to make PROMs work better than it does at the moment, and we would be quite happy provided we were funded to do it, to run PROMs and run it, I think personally, on every single patient basis, which is only very small samples at the moment, and if we were to do that, we would have a lot more information and we would be able to identify problems much earlier.

Elaine Young: Because the national PROMs actually measures at...

L Powers-Freeling: Six months.

Elaine Young: Six months.

Matthew Porteous: Six months.

Elaine Young: At the six-month point. Well, from [unclear].

[Over speaking]

Matthew Porteous: We do collect - the shoulder replacements, we are collecting our own PROMs and we're collecting it at - well, preoperatively, then I think six months, a year, two years and five years. So that is the way we think that that should happen, and I think if we did that, we'd be able to identify problems much earlier.

Simon Whale: Can I ask a quick question about sodium valproate? So, sodium valproate obviously can cause damage to the fetus and the child. I was wondering whether your registry is sensitive enough to pick up in utero exposure to a medicine like valproate. Is that something you're able to track or do track?

Sarah Stevens: It is - do you want to?

Nicola Miller: So, if an anomaly was detected in the antenatal period, we would highly likely be informed that the woman was epileptic and that she was on sodium valproate if that was the case. I think we would know if the clinicians were aware. I think what potentially the system is, once we have high quality data nationally, is that we can link with the prescriptions data and we could do the same thing backwards, so we can look at anyone who is on our register who has also been prescribed sodium valproate whilst they were pregnant, and see what they normally [unclear].

Simon Whale: So, you can do a retrospective audit?

Sarah Stevens: Section 251 gives us legal basis to collect information on suspected and confirmed congenital anomalies. At that cohort, we can link the - and the triangulation and the data I agree is really important, so again we use HES, PAS - we do have access to all primary care prescriptions through the NHS Business Authority. For known patients - for known cases if you like, we could go back and use that prescription data which has got very good coverage, it covers about 90 per cent of the population, but we can't do it the other way. So, we wouldn't know how many have been prescribed sodium valproate who then went on to have a normal...

Simon Whale: You've got access to BSA data now?

Sarah Stevens: It happened in the last 12 months.

Simon Whale: Right, okay.

Nicola Miller: Major congenital anomalies like neural tube defects - we're much more likely to collect data and be able to link those to sodium valproate. The smaller anomalies, like hypospadias, that may also be linked with sodium valproate - it's much more difficult for us to make that link because we're

much more likely to get that as surgical data postnatally, so baby data. That's why it would be really useful to be able to go back and [unclear].

Sonia Macleod: So, I'm guessing the neurodevelopmental data you wouldn't pick up because [unclear].

Valerie Brasse: One of the issues is obviously that that happened for women on sodium valproate. Then there's the next generation of anti-epileptic drugs, so the question is whether you're sort of alert to be looking for what the next generation might be delivering in terms of malformations in utero. I'm thinking Keppra and the likes, so I don't know whether you particularly look out for or try to pick up that sort of [unclear].

Nicola Miller: I think again we'd have to do that from the prescription data backwards. So, we would have to deliberately look at the class of drugs and look backwards to see who is on the database, and what the anomalies are around that. Otherwise, the danger is that you're looking for anomalies that you think are associated only, whereas if you go backwards you would see other signals, potentially.

Sarah Stevens: It's something we ought to do much more often.

Sonia Macleod: Yeah - have you done that?

Sarah Stevens: The linkage with NHSBA prescription data has only been more recent. It's actually because we sit within the same division as [cancer] registration, so they've been doing a lot of work on it - like the linkage there. We're looking to explore it further now, but it's relatively new, but I think it has huge opportunity actually.

Julia Cumberlege: I'm sure we could go on a lot longer but I'm afraid we've really come to the end of our time because we have another group coming in any minute. I'd like to thank you so much for coming this afternoon and for sharing all your expertise and advice to us. If there are other things that you think that we should have questioned you on or you want to tell us, please don't hesitate to come back to us and do that. Just to thank you for what you're doing for women, for the health service, for the hip replacements, and other orthopaedic replacements. Thank you very much indeed.

END OF TRANSCRIPT

Session 3: Association of British HealthTec Industries (ABHI)

START OF TRANSCRIPT

Julia Cumberlege: So just before we start that, can I ask HQIP whether you've got any conflicts of interest because we haven't actually - I think - had anything from you on that?

Danny Keenan: We've no conflicts of interest.

Jill Stoddard: No.

Julia Cumberlege: Sorry?

Sasha Hewitt: No. No conflicts.

Julia Cumberlege: No conflicts of interest? Perhaps you'd be kind enough just to write that in to us so we've got a record of it. Because people do ask us, so that would be good.

Right. So, I'm Julia Cumberlege and I've been invited by the Secretary of State - the former Secretary of State - to do this Review. When one is tasked with an issue like this, the first thing you do is try and get the very best people about you - around you - advising you - and I have that. So, Sir Cyril Chantler is on my left and many of you will know Cyril and he knows many, many people within the NHS. On my right is Simon Whale and Simon has taken particular responsibility for communications - which as I have said previously is really important to us.

On Simon's right is Dr Valerie Brasse and Valerie is Secretary to the Review team and on Cyril's left is Sonia Macleod - Dr Macleod - who is our principal researcher. So that's us. So, then I'm going to ask you if you - because it's going to be on the record - if you can very briefly say who you are and the position you hold. That would be helpful. So, shall we start with you?

Manpreet Pujara: Yep. So, I'm Dr Manpreet Pujara. I'm a GP. I work for NHS Digital as the Clinical Director for Patient Safety and Clinical Governance. I also have a role as a lead at my CCG - leading on prescribing and GP IT.

Julia Cumberlege: Right. Thank you very much indeed. Yes, thank you.

Stuart Harrison: I'm Stuart Harrison. I'm the Head of Safety Engineering for NHS Digital. I work for Manpreet.

Julia Cumberlege: Thank you.

Jill Stoddard: I'm Jill Stoddard, Operations Director at HQIP.

Sasha Hewitt: I'm Sasha Hewitt. I'm an Associate Director at HQIP.

Julia Cumberlege: Thank you.

Danny Keenan: I'm Danny Keenan. I'm the Medical Director at HQIP and also Associate Medical Director at Manchester University Hospitals. I'm seconded two days a week to work with HQIP as Medical Director.

Julia Cumberlege: Thank you very much.

Matt James: Good morning. I'm Matt James. I'm the Chief Executive of the Private Healthcare Information Network.

Julia Cumberlege: Thank you.

Prof. Justin Keen: I'm Justin Keen. I work in the Faculty of Medicine at the University of Leeds.

Julia Lake: I'm Julia Lake. I'm - I was until a month ago - the Clinical Information and Outcomes Manager at the Leeds Teaching Hospitals and I'm now working with the EHR - the electronic health records - team [unclear].

Julia Cumberlege: Right. Thank you very much indeed.

I'm going to start with a question and just say that one of the things that we've been tussling with to some extent is about definitions, so that we really know what we're talking about. I think it was Voltaire who said, if you wish to converse with me define your terms. So, I'm going to start putting this question to you and just asking whether you agree with this. Because we have been thinking a lot about our terms and particularly what is a registry? Secondly, what is a database?

When we have been talking to people there seems to be some confusion about these two terms. So, I'm going to read this out and I'm just going to ask each of you if you agree with this definition because we really need to get this straight.

So, this is the International Medical Device Regulations Forum, and this is what they have suggested is a registry. 'An organised system that continuously and consistently collects relevant data in conjunction with routine clinical care, evaluates meaningful outcomes and comprehensively covers the population defined by exposure to a particular medical device or devices at a reasonably generalised scale - e.g. international, national, regional, health system - with a primary aim to improve the quality of patient care'.

So, I hope you think that's - we know what we're talking about now when we're talking about registries.

A database. This is the *Oxford English Dictionary*. 'A database - a structured set of data held in a computer, especially one that is accessible in various ways'.

We're thinking as a Review Team - for our purposes - it's in relation to mesh - such a database might include the NHS number, the type of procedure, the operating surgeon, the healthcare provider, the unique device identifier, the date of procedure, the age of patient and the gender. Does that sound right to you for a database? Okay? So, when we're talking about databases, that is what we're talking about. When we're talking about a registry, it's something much, much fuller and more difficult - I would suggest - to establish but very important that we do.

So, if you have queries on that - and after perhaps you've had a bit of thought - if you could let us know that would be very good.

So, I'm going to ask first of all Digital and PHIN and I have to say it's good to see you here again Matt. Thank you for coming. We don't appear to have a clear understanding of how many people have been affected by the interventions we're talking about - Primodos, sodium valproate and surgical mesh. So, can you enlighten us at all about how many people you think have been affected by these interventions? Do you have any statistics on that material, anything to help us on that?

Manpreet Pujara: So, I think...

Julia Cumberlege: Shall we take Primodos first? Shall we go through the three? Primodos - do we have any information on that?

Manpreet Pujara: No.

Julia Cumberlege: No. Alright. Thank you. Sodium valproate?

Manpreet Pujara: I think that we can - we have figures as to the number of women of child bearing age who are taking sodium valproate - or who have taken sodium valproate in the past - based on statistics available from the BSA [unclear] and also could be based on information from GP IT systems in terms of repeat prescribing.

Julia Cumberlege: Right.

Manpreet Pujara: [Unclear].

Julia Cumberlege: So - you may want to write to us on this - but what sort of - what is the amount roughly? How many?

Manpreet Pujara: So, I think it's really difficult because this is a figure that I didn't bring with me. To have an - and it would not even be an educated guess for me to suggest what that number is. I think it varies. What I can do is I can put it in to perspective so that - when I did a search - an audit - in my own practice of 14,000 patients about three years ago. we had 14 women of child-bearing age who were taking sodium valproate.

Julia Cumberlege: Right.

Manpreet Pujara: So, the number from a practice perspective isn't huge. But obviously the total number will vary and within my CCG the work that we have done also shows that there is variation within practices as to the number of patients taking sodium valproate. Because valproate is used for a number of clinical indications it will depend on the [unclear].

Julia Cumberlege: Yes. I think we're talking about child-bearing age.

Manpreet Pujara: Yes.

Julia Cumberlege: In particular. Yes. Because we had a debate in the House of Lords on Thursday and people were bandying about different figures. Now we would like a bit more accuracy on that.

Manpreet Pujara: So, I could certainly take an action to provide those figures to you.

Julia Cumberlege: Thank you. That would be helpful. Surgical mesh.

Manpreet Pujara: So, again I don't have figures. I'm not an expert in the surgical mesh work that has taken place. But [unclear] are able to provide some details about the numbers.

Julia Cumberlege: So, is it possible then that you could write to us...

Manpreet Pujara: I certainly will [unclear].

Julia Cumberlege: That would be very helpful.

Manpreet Pujara: [Unclear].

Julia Cumberlege: So, if we haven't got the exact figures. If we haven't got - and we'll never get it exact - I mean, I do appreciate that. Because all the time things are moving. But we're just wondering would a full retrospective audit be needed? Would that be helpful - a retrospective audit?

Manpreet Pujara: I think it would be helpful - it comes down to what data is available to do that retrospective audit and I'm sure that we can certainly have a look at the data collections that we make at NHS Digital to see what information we can gather in terms of the numbers involved and factors. It will depend on accurate recording at each individual Trust and each organisation - which includes obviously the private sector and what access we have to that data in that situation. Mostly the recording of data - recording of information - for mesh may also have taken place in primary care if and when the details were provided accurately - the general practitioner is able to collect that information.

But this will not be happening in a consistent way across the -certainly the 7500 practices within England.

Julia Cumberlege: Okay. Can I asked PHIN also - if I could ask you - do you have any statistics from the private sector?

Matt James: I'm afraid the short answer would be no and that's for three principal reasons. The first is simply timeframe. So, PHIN is mobilising now to be in a position to collect data systematically across private healthcare on the same basis as the NHS and to be able to do that in the future. Which may help in any future scenarios like those that the Review is looking at going forward. But we simply don't have anything that came from the timeframe that most of the incidents arose that you've been looking at.

The second issue is that we have very much a secondary care focus. So, whilst vaginal mesh might fall within that scope, the other medicines and so on that you're looking at are much less likely to.

The third issue is that the way that we collect our data - which is really aligned to the principal ways that it's done within the NHS - very much has a procedure focus. So, we wouldn't look for vaginal mesh itself. We might look for stress urinary incontinence and if it was recorded that vaginal mesh was a feature of that procedure - a procedure undertaken to relieve stress urinary incontinence - then that may be recorded. However, what the reliability of that would be within NHS data - and going forward within our data - I think would need to be tested.

Valerie Brasse: Can I just ask would the private sector have the capacity to do a retrospective audit?

Matt James: Well...

Valerie Brasse: Or the capability.

Matt James: So, I think there are two things. I think if you look back at NHS Digital's data for stress urinary incontinence - provided that the related diagnostic coding was accurate - you would be able to make a reasonable estimate from that general data of the number of cases - of the use of vaginal mesh. It would only ever be an estimate, but it would be a reasonable estimate.

In terms of a retrospective audit - speaking very frankly - and I might be completely sort of out of school here. I'm not sure how that would be done other than going right back to original patient's notes or doctor's notes. Because I strongly suspect that the level of detail doesn't exist recorded in the system that one could easily access in order to be able to do that in any sort of centralised fashion. I might be completely wrong but...

Julia Lake: No, you're right. It would generally be held on a number of given databases so your mesh components might be in your stock inventory system, patient details elsewhere with your events and patient procedures. So, generally it's fragmented. Things are in different places and it's very rarely joined up all together.

Julia Cumberlege: But there are other conditions where we have a registry and it is very helpful to have those figures. Because we've been going around the country, we've obviously heard a huge amount from the patients who have suffered deeply - from particularly surgical mesh - but also sodium valproate and also Primodos. We are conscious that trying to actually get a handle on how many operations are done and how many result in complications when it's mesh - and disabled children in the other two conditions - is very difficult for us.

The more help you can give us on this really would be very much appreciated.

I think the data set would help us. It's quite strange in a way that this hasn't happened in the past. It seems to have taken us an awful long time to actually get to grips with this situation and there's a lot of learning - I think - to be done by that because the thing that patients certainly are saying to us - at the moment - we feel that we are actually a clinical trial. Why wasn't this done before? The speed of coming to understand some of these issues has been glacial. It has been awful.

So, I'm going to pass on now to Cyril.

Cyril Chantler: The reason that we raised with you the definition is because we've been rather confused about how different people have looked at this. So, can I just go into this in a bit more detail. What we're exploring is the notion that

there could be a centralised database collected at the point of the surgery. When we attended the workshop, we raised this proposition. Which would have the necessary information centrally held and created by the person doing the operation - not by a third party - using the NHS number, which would then enable us to build registries connected to it and around it.

Now, can I ask you whether you think that's something that you would think's worth exploring? Perhaps ask all of you? I'm going to start with NHS Digital.

Manpreet Pujara: So, I think it is something that is worth exploring because we do have other registries which are effective. I think the key is that it needs to be mandated because - and I'm just - I'm not an expert on IG and GDPR let me just say. But patient consent to - whether they want their information on the registry...

Cyril Chantler: Can I interrupt you at that point - again so that we don't get confused. The proposal - which I really do wish you to - your review about - is that it might be possible - under legitimate usage on whatever section you're talking about - to mandate - if you like - that information for the database. But as I understand GDPR - and I could be wrong about this - to create a register does actually require the permission of the patient under opt out or whatever.

Therefore, the registry will be a secondary event which the patients would then agree to - in my experience because I've been involved in a registry - the European Dialysis and Transplant Association Registry - 30 years ago. Patients are only too pleased to agree because they want to improve the outcomes. But, Dr Pujara, is that a reasonable proposition?

Manpreet Pujara: I think so, yes. Because I think recording of an event needs to happen - [unclear] historical purposes and legal purposes. So, it is important that there is a record of the mesh that has been inserted. I think having a registry would be very helpful. The point I was making was just that very aspect, that you need to get the patient's consent for the additional bit to go on to the registry - which is what my understanding is.

Cyril Chantler: Okay. I want to come back - if I may - to your Breast Implant Registry in a minute but can we turn to HQIP now and say how do you react to this discussion?

Danny Keenan: Basically, where we are today is we've got a totally haphazard system - led to quite an extent by scandal or whatever. So, we have the joint registry which you're going to hear about which has been going for a long time. We've had other audits - whatever you might call them. For instance, the

implantation of heart valves and pacemakers - which could affect using your definition of registry - which have been going for quite a few years.

Then of course we've got the breast scandal and that came along with a registry and possibly there's going to be something with mesh - but we'll leave that aside for a second. But if you think of the devices being implanted today - into human beings around England - there's an enormous amount of stuff going in. Cataracts, stents - every area of surgery and interventional medicine is putting things in. There is very, very little information on these.

So, the idea of developing a registry to do with devices is a good idea. But you have to actually say, well what is it you're wanting to do? Are you wanting to do device surveillance - which is on a safety area? Are you wanting to look at outcomes? I suspect that's what patients - they would want both of those. Mesh is a really good example of outcomes because the outcomes are actually - are very far out. So, where does the registry finish? Indeed that - in your definition - which we will answer to with the data set - outcomes weren't mentioned.

Yet outcomes going on out into the future is really important. Actually, the example we have of the joint registry - you probably saw the thing in the news a week or two ago - which incidentally didn't have the NJR on it. It was an international look at joint registries giving outcomes up to 25 years for survival of - et cetera - of joints.

Then on the other hand - to do with outcomes - we actually stuck on to the National Joint Registry patient outcomes like death which actually wasn't very good coupling together because death and surgery...

Cyril Chantler: Yes, I understand that, and it does actually talk about meaningful outcomes in the international definition. But at the moment, the distinction that I'm seeking your reaction to is the notion of creating a database to which properly designed registries to deal with all the issues raised - which I absolutely agree with not least because I have a heart valve myself [laughs]. It's that distinction I'm after. In principle, are you comfortable?

Danny Keenan: It has to be yes because you would say why haven't we been doing that so far? It has to be yes.

Cyril Chantler: Indeed. Before I turn to Matt, I must declare an interest because I'm a non-executive director of PHIN. Matt, your reaction.

Matt James: Well, I'm in huge agreement with what both Danny and Manpreet said actually. It is a totally haphazard system at the moment. I've been closely

involved in the Breast and Cosmetic Implant Registry and worked closely with HQIP over the last few years. Whilst it is imperative that we are able to collect the sort of information that will provide a much, much better look at these issues and protect patients in the future - the manner by which we do it I now think is critical.

I would really like to see not just another stand-alone, problem specific, device specific registry created, but a much more comprehensive look taken at how devices, medicines and any other factors that are directly affecting patients - can be universally recorded.

I won't dive too much into the detail now because I'm aware of how short we are on time but as a principle that has got to be exactly right. In terms of information governance, I do completely recognise that a strong degree of mandation on various parties to do this would help enormously. Because it has been PHIN's experience that despite the fact that we are very clearly legally mandated to do things, we must interact with other parties - including our partners NHS Digital, including the consultants who must review their own data before it's published - who are not legally mandated to do those things.

The process of obtaining permission or obtaining an end to end pathway of lawful basis to proceed is extraordinarily complex. It would also be my observation that currently every single registry takes its own bespoke approach to consent and confidentiality. If you go down the consent route, you're very much pushed in to being extraordinarily specific. The particular situation you could easily create is one in which a patient has to review three pages of closely typed text that says, yes I consent to this particular - my data being collected for the purpose of analysing this particular drug and for those purposes and no other purposes.

Then turns the page and then for this particular device that has been implanted into me and then for this particular outcome measure in respect of the surgeon's performance and so on. They're going to have to sign four or five different consent processes - each in ignorance of the other quite deliberately at the moment. We must find a better way through that.

Cyril Chantler: Yes. Well we are seeing the Rare Disease Registry and the Cancer Registry later today. Professor Keen - you've got huge experience in this area.

Prof. Justin Keen: I have some. [Unclear] Go first to Julia, then I'll come back to you.

Cyril Chantler: Okay.

Julia Lake: Just on that matter of consent actually I just did a little bit of analysis yesterday to look at cosmetic breast surgery. I looked at our HES data against what our consultants had submitted based on consent and it was only 40 per cent. So, you're omitting 60 per cent of patients with implants because they hadn't consented to it.

Cyril Chantler: I understand the consent issue but I just at the moment would like to concentrate on this issue about the difference between a registry and a database. Are you comfortable with the conversation we've had so far?

Julia Lake: Yes. Yes, I am.

Cyril Chantler: Professor Keen?

Prof. Justin Keen: Sorry. Thank you, Sir Cyril. The - so perhaps one of the striking things - just looking at some of the oral evidence - written evidence given to this team so far - is that there's a sort of - if you like - an outside hospital view. So, I wonder if there's some value in actually noting a third [type] if that's okay which is a data warehouse which would be familiar to people who work inside Acute Trusts. Because that may be where you could reconcile your notion of a database and a registry.

So, in very simple terms most Trusts will have what we call real time systems. So, systems that clinicians, doctors and nurses and others use on the ward for the direct care of patients. Then a data warehouse is - as it were - a very large repository that sits behind it offline as it were - which takes data from the Patient Administration System, the Electronic Record System and many, many other systems - dozens in terms of [unclear]. But it's sort of - if you like - it's an offline store where you can take databases - subsets of data - from the real time systems.

So, it's individual data sets and then link them together. So, one possible solution is to take data from - for example the Electronic Record System, link it to data that are filled in on a slightly different database - possibly concerned with a specific mesh implant procedure. But they could be linked together in the data warehouse and as far as I'm aware most Trusts...

Cyril Chantler: Yes, I understand that and also the need to [unclear] central and local. But I think what I'm proposing is a database - or we're proposing - is something much more like a central system run by NHS Digital. Like the DVLA or something of that nature. I accept the need for local as well and that links, but again you've got the issues that Matt has raised about mandation maybe under 251 and opt out which is not the same as opting in through consent.

Prof. Justin Keen: I'll just say one more thing then which is that the - again just looking at some of the evidence that we've received so far. One of the things that I think can be underestimated - particularly if you're in a regulatory or other [unclear] national body - is there are - the simple fact you really need buy in from the clinicians on the ground to start with otherwise this just isn't going to fly. So - and I have to agree with you - it's just that I would emphasise the need to get that data capture buy in to clinic...

Cyril Chantler: I absolutely agree.

Prof. Justin Keen: ...first.

Cyril Chantler: We've already put this proposal - as you'll see - on our Review website to the President of the Royal College of Surgeons and the President of the Royal College of Obstetricians and Gynaecologists and they think it's a good idea.

Prof. Justin Keen: Good.

Manpreet Pujara: Sir, I just wanted to come back and say I'm being very simplistic about this because I find keeping things simple clearly helps. A medical device is like any drug that is prescribed. There is a legal duty and responsibility to record that information. If that information is recorded - and it should be recorded in a clinical system that is being used by the clinician, then that information can be collected and used on multiple occasions as necessary, as defined, and is legal to use, to ensure that actually the care of patients is improved, and safety is improved.

So - being a singleton - I would expect every medical device that is fitted is recorded. Actually, some of that information will come to us at NHS Digital - as the data guardians for England - and that information will be available for us. That information can be released and accessed through the legal processes that currently exist to ensure that appropriate research can be carried out.

So that we only have to do this once. We're not revisiting this and having to create multiple registries because it's a do once and actually use many times. It's the principle of devices being like drugs and an expectation there is a full audit trail and history of what has happened.

Cyril Chantler: Okay. Thank you.

Julia Cumberlege: I just want to ask about HES data because what I understand from people is that it's not very accurate because of the coding system. What we're suggesting with the database is that it's actually done by the surgeon in the

operating theatre - or just in the building anyhow. So, do you think that would improve that? We won't be duplicating will we - HES data?

Manpreet Pujara: You should ideally only have to record things once.

Julia Cumberlege: Well I do agree with you but...

Manpreet Pujara: We need to ensure that the systems that are being used - and it will be a transition there is no doubt - that systems that are deployed record the information at the coalface and make that available to be used...

Julia Cumberlege: Okay.

Danny Keenan: Essentially if you produce a system that's easy for surgeons - as we're talking about - to use - they'll use it. But say for instance the cataract audit which we run today, at something like 60 per cent uptake and the reason probably is because it's not readily electronically available in the operating theatre. Now, if it's sitting there easy to use, it will be used. If there's - obviously bringing colleagues with us is the best thing but there is a bit of mandation about this and that will probably make it up 95, 100 per cent.

I think the ease of use and then the other thing is it mustn't go into a black hole. It must be used back so that it is used by colleagues to improve care. That's the real catch I think for colleagues.

Julia Cumberlege: Well I think we agree with so much of what you're saying, it's to get it to happen.

Danny Keenan: That's right.

Julia Cumberlege: That is always the challenge. Anyhow. Simon.

Simon Whale: Yes, can I just explore an associated issue. So, if - let's assume that the database that we're talking about - the kind of database we're talking about - does exist. Who should be able to access that database and how would they go about it? Does NHS Digital have a view on that?

Manpreet Pujara: At the moment data access I think happens through [unclear]. Again, I'm not an expert on [IG and DARS] but applications are made to the group to access that information. They are assessed and reviewed. If legally allowed, that information is made available to the researchers.

Sasha Hewitt: Can I just say one very important group that would need to have access to that data [through One] are the patients. So, patients - through the work that we've done - we held a stakeholder workshop and patients very clearly want access to information about the type of mesh device that they've had

inserted. For that information to be readily accessible to them perhaps even higher - you know, an email or something that they can keep for a very, very long time.

Obviously, we need to make the data available to researchers and third parties but really it's the patient group.

Simon Whale: Yeah, I mean I think we completely agree with you. Should patients be able to enter information on to the database?

Sasha Hewitt: That's something that we did debate - again through those workshops that we held - and very much patients, clinicians thought that patients should be able to directly enter their outcomes. So, how they - you know, symptoms and how they are all doing before and after their procedure. That...

Simon Whale: Would you agree with that? I mean you don't see any problems with doing that?

Sasha Hewitt: I think there are other national clinical audits I can think of who do that. So, the National Early Inflammatory Arthritis Audit collects PROMs directly from patients. It provides patients with a secure login so that they can access that data themselves and record how they are doing. I think it's a very powerful way to involve patients more.

Simon Whale: What about manufacturers? What access should they have to this database?

Sasha Hewitt: I think the manufacturers do need access to this information so they can improve. They already have access to NJR data and that's very - I think one of the strengths...

Danny Keenan: Yes.

Sasha Hewitt: ...of the NJR.

Danny Keenan: The governance system that sits around the NJR is very good and has worked for a decade - longer than a decade - so I think any system that we might be bringing in, we already have a template for relationships between the information in warehouses et cetera and industry having the access they need.

Julia Cumberlege: Do manufacturers share their data with the NHS? With all these bodies?

Danny Keenan: I'm not sure I can answer that. I chair the indicator committee for NICE.

Julia Cumberlege: Sorry?

Danny Keenan: I chair the indicator committee for NICE. NICE has got a very good set up - you probably could hear it directly from them - as to the linkage between manufacturers - it's mostly to do with drugs and new devices. There are problems. There are problems with sharing data. I don't want to give you a second-hand version of that. I think it would be much better to get colleagues from NICE who are intimately involved in that developing guidelines and specifications for technology and devices.

Julia Cumberlege: Hm.

Simon Whale: Can I also just ask about the link with Yellow Card? So how - I mean this is a question for anyone and everyone - how would this database link to the Yellow Card Report?

Matt James: Sorry, I don't know what that is.

Simon Whale: Yeah.

Stuart Harrison: The concept around traceability of devices is good and I completely agree with the aspects of giving patients the ability to register and so on is taken elsewhere in the digitisation efforts around the NHS. But again, it fits in to other national strategies in that regard. In terms of the safety culture, it provides a more open and transparent view around devices, healthcare and so on. With regards specifically to the Yellow Card Reporting System, that has a traditional function. I think the linkages with other databases - or registries, as we define it - are technically possible.

The user view could be tailored depending whether it's patient, manufacturer or NHS or private access. All of these things are available currently.

Cyril Chantler: So, do you have a system in place to share information - or intelligence - between MHRA and NHS Digital?

Stuart Harrison: We do, yes. We have a data sharing agreement and we...

Cyril Chantler: Is that HES data or - it can't be...

Stuart Harrison: This would be patient safety related information regarding health IT systems.

Cyril Chantler: But at individual patient level?

Stuart Harrison: There are elements of the incidents that we work with that has - that do have patient outcomes or patient details on them, but with regarding the...

Cyril Chantler: Identifiable patient data?

Stuart Harrison: No. Not to that level.

Cyril Chantler: So HES data - which is non-identifiable?

Stuart Harrison: It's anonymised but it's similar to HES.

Cyril Chantler: Right.

Stuart Harrison: We focus purely on the health IT side.

Cyril Chantler: But it is anonymised?

Stuart Harrison: Yes.

Cyril Chantler: Yes.

Simon Whale: Does that include Yellow Card Reporting? Do you - do MHRA share Yellow Card Reporting in any form with you?

Stuart Harrison: Yes. Specifically around health IT and devices area. I believe you've had John Wilkinson in on a previous session - so that linkage is there.

Cyril Chantler: Right.

Julia Cumberlege: So, do you have an influence in ensuring that the Yellow Card System is more comprehensive? That it acts properly, that it is responsive to patients? Or do you leave that to the MHRA?

Manpreet Pujara: Maybe I should answer this one. So, you know we've been instrumental in engaging with MHRA and getting them to engage with the NHS App team so that patients can directly report the Yellow Card System. Obviously one of the reasons that I'm keen for the information about any devices being made available within the patient's record is so that there can be linkages should there need to be linkages.

So, we are working very closely to ensure that the Yellow Card option for patients will be simple, straightforward and as Stuart has said, you had MHRA come to your hearing, and I think that the volume of reports that they are receiving as a result of allowing patients to enter information has significantly risen as a result of that.

Sonia Macleod: So, once the NHS App is in place, there's a Yellow Card reporting function that presumably pre-populates, that goes to [unclear]. What then happens to that information? Is it stored within that patient's individual NHS App record? Because we've heard of patients submitting Yellow Cards and then they can't find them under [unclear] number, things like that. So, would that provide the patient with an identifiable [unclear].

- Manpreet Pujara: So, again I'm not working on that on a day to day basis but what I would expect to happen would be a report to fire off to MHRA - although the note within the patient's record that a Yellow Card has been submitted. What level of details is recorded in the patient's records - or indeed if a full copy of that report is available for the patient to review - I could find out what the plans are if this is to happen. I don't know the [unclear] at the moment.
- Simon Whale: In terms of where we started in this part of the conversation around who should have access to the database and who - both input and read access - I'm just conscious that we've not heard from Professor Keen or in fact James or Julia. I wonder if you have any thoughts on it?
- Prof. Justin Keen: I agree with a lot of the comments that have been made, particularly by my HQIP colleagues and certainly stress the importance of patients having access. A lot of the rest of it -if you like - within NHS Digital and the information governance [unclear] are reasonable in general terms. So, it's again looking at [unclear] within the NHS then it's just current information - it's [unclear] patient access is perfectly reasonable.
- Simon Whale: Yeah.
- Julia Lake: So, what we've found with some places where we have external databases that our clinicians put - usually through a secure portal - is that within the Trust we don't have access to get that information back. So, we have some audits where we have a lot of assurance around it. So, the data doesn't leave our Trust until it's been signed off clinically, it's been signed off for data quality and all of those checks have been done and then it gets uploaded.
- What we found with some registries is that it goes offline, and we don't have that sense check internally, for our consultants to say actually I'm happy with all of that, and it's not until it gets published later we think, ooh something was missing. So, I think any kind of national database or registry needs the ability for us to re-extract our data for us to make sure that - and we have a period of validation - to make sure that what we're sent is as good, complete and accurate as it can be. Clinicians in our Trust are very involved in that process. They like to have that reconciliation and that process in place.
- Simon Whale: Okay, thank you.
- Julia Cumberlege: Could I just ask you HQIP - and perhaps Professor Keen - we've talked a lot about registries. Can you just tell us what type of oversight you think they need and what sort of governance is required?

Prof. Justin Keen: Do you want me to go first?

Julia Cumberlege: You know, who should be responsible for commissioning it?

Sasha Hewitt: So, the National Clinical Audits that HQIP commission on behalf of NHS England - and [unclear] - all have their own governance structure. So, they all have an overarching project board composed of clinicians, health stakeholders such as - well local...

Danny Keenan: Trusts and CCGs.

Sasha Hewitt: Yeah. Very importantly patients, patient groups such as charities. They have steering groups. Sometimes - increasingly so, separate patient panels that feed into those groups. So, they've got their own governance in terms of overarching - oversight - where you're thinking about HQIP obviously manages those audits. We report any risks through to NHS England on a quarterly basis.

Jill Stoddard: So, we commission and contract manage the audits or registries or confidential enquiries. We contract manage so they - we appoint a host organisation that acts as a host to the provider team that manage the registry or audit and we contract manage that provider team within the host organisation. Then we upwardly report to the funders. So, in many of the cases it's NHS England and the Welsh government that we upwardly report to.

Danny Keenan: We have links - confirmed links between our outputs and the CQC and NHSI so that we have trigger points if an audit is showing something or whatever. That direct links are made between the audit results, the team leading it and the regulators.

Julia Cumberlege: It sounds a very cumbersome system. I mean, is it not possible to streamline it, simplify it, make it more effective?

Jill Stoddard: So, I think that we were actually asked by the Department of Health in August to undertake a rapid piece of work around looking at the three societies that are currently in place that host mesh data and that's around a sort of short term, interim database solution. Because we are aware that it takes quite a long time to procure. Obviously if there's a certain amount of money involved, we have to follow legal frameworks for procurement. So, it can take up to a year to actually procure for a registry. Once the - a favoured person is given a contract, then it obviously takes them a period of time to set up teams and the IT platforms.

So, for a registry to be set up from start to finish actually takes quite a long time, which was one of the reasons why I think the Department of Health asked us to undertake a rapid piece of work around looking at the feasibility of an interim database solution. To sort of potentially suck data out of the society databases, to start collecting from big pre-existing repositories of data. We are very aware of the time trajectories involved because we want to get answers quickly for people, obviously.

But - so we could think about what's currently in place and then we'd have to think about for a registry - actually procuring and commissioning a registry - will take quite a long period of time to do because of the legal frameworks involved in doing that.

Danny Keenan: Can I just add to that. You have to remember that the systems we're using - we do use HES data a lot. But then say, about 70 per cent of the data going in is HES data but 30 per cent is bespoke. Actually, it does take time - and as we move digital and get into much more comprehensive electronic records, that will be helped. But the other point you heard about validation is really important.

So, if one of these things fires off and such and such a hospital is an outlier or an individual surgeon is an outlier, we have to be 100 per cent sure that that data is saying the right thing. That's why these validation exercises are really important. So quite a lot of the time is taken - not just internally validating data, but it comes up in to the [audit provider] and it gets cleaned so to speak.

It goes back to say is this right. So, there is a lot of that moving back and forth to make sure that the conclusions that are reached are accurate.

Julia Cumberlege: So, can we have a [cockshy] on how long this would take? First of all, to establish a database that's useful and secondly then moving on to a registry?

Danny Keenan: Are we talking about the whole thing? Not just to do with mesh?

Julia Cumberlege: Well, I thought we needed the database first - to get some facts and then...

Danny Keenan: Are we thinking of mesh or the whole?

Julia Cumberlege: I'm asking it in two parts. First of all, the database. How long - because clearly, you've got to gather the information and presumably it takes a bit of time to actually gather enough to be useful and then, drawing on the database, we then have a registry and I'm just asking the first part, how long would that take? The second part, how long would that take?

Danny Keenan: Okay.

Jill Stoddard: So, for...

Julia Cumberlege: Mesh.

Jill Stoddard: ...just mesh yes.

Julia Cumberlege: Hm.

Jill Stoddard: So, for an interim database we have just given the report in to the Department of Health - it's currently embargoed - and we are awaiting a decision from the Department of Health about a potential outcome from that. It depends upon what the decision is from the Department of Health about which potential model has been suggested that they would like to adopt. So, if it's possible to actually run with using data from the current societies, that would probably take a year to actually bring to fruition. That's a rough estimate.

For a registry, I would estimate - because of the legal frameworks involved - probably from start to finish, it would take a year for procurement and commissioning, a year for a host organisation to set up the teams and the platforms and start gathering data and then a year to get to a final report. So, you're probably looking at -this is a rough estimate - three years to get to a final report for a registry.

Valerie Brasse: But within that - and within your proposals - and obviously we're not asking you to talk through what's currently embargoed. One of the issues about the databases - as we know - is that the reporting is - well it's under reporting on all three of them. Do you therefore have proposals for how that would be moving towards 100 per cent reporting, even for the initial stage which is the database?

Sasha Hewitt: I think that depends on a few different factors. So, the first is whether or not this - what legal basis it's operating under and whether or not this is mandated. So, if perhaps - you know for instance - the Department of Health were to direct NHS Digital to collect data, that removes the requirement to collect - to gather consent and obviously then it's a legal requirement for organisations to submit data.

Even under those circumstances, there still needs to be engagement in order to get people to use the system. It's very easy to build a database, very difficult to get people to use it and it does take time for those participation levels to rise. Even in national clinical audits that we've got

where you suck the data directly out of EPRs, it still takes considerable time to build up participation levels.

Jill Stoddard: [Unclear].

Sonia Macleod: If you're sucking data directly out of EPRs, presumably that literally is just taking the data out...

Jill Stoddard: That is taking...

Sonia Macleod: If you've got a unique device identifier for each device, surely that will enable you to pull a data set of where these devices are.

Matt James: May I respond to that. I think what you've just said there could be the absolute key to getting this done very quickly. The question you asked at the beginning was - well actually you set out in setting out the differences between a registry and a database - what the components of a registry might be. Every one of those is a component of existing data systems and parts of the patient record with the exception of the unique device identifier.

If rather than focusing on rebuilding information - with all of its duplication and all of its necessity to build a database from scratch - we focused on the process of ensuring that the unique device identifier is recorded in every instance - and specifically is recorded and entered into the patient's record - then you would have a basis for finding the correlation between the use of a device and the patient in every instance and it could be done quickly.

You mandate its collection on the ground, and you mandate digital to handle that data - for example - then very quickly you'll develop a picture of which devices exist in which patients.

If on the other hand - we choose to build a registry from scratch. I mean, the Breast and Cosmetic Implant Registry I think is up to six or seven years and counting and is not sort of - it's basically operational now in collecting data but it's not fully operational in being able to analyse that and produce results. So that's an example. It doesn't necessarily mean that everything has to follow that pattern. But a far quicker way to it would be to make sure that the device data gets into the patient record rather than creating [unclear].

Sonia Macleod: That requires electronic patient records and how close we are - I mean how close are we to having complete coverage?

Danny Keenan: We're not - we're not close. Manchester, where I know a lot about. We are actually tendering for an EPR at the minute. In fact, I read about it the

other night - I think it's going to be the autumn before it comes out with the spec and it's going to be at least next year. So, we are quite a long a way off. The first thing - having said all that, is to get the NHS number into any of these areas. We haven't got that at the minute. So, if you have an NHS number going in and a device identifier, you've actually - those two things would give you a fair bit.

Cyril Chantler: The proposition that we're putting is that when the surgeon - or the clinician - pulls out the operation note which always happens...

Danny Keenan: Yes.

Cyril Chantler: that it includes this information. Certainly, maybe the barcode of the device and the NHS number among the other things. There's no reason - that goes into the patient notes - there's no reason it shouldn't go to NHS Digital. No reason why it shouldn't go directly to the patient. Then you've got the foundation to do all the other things which are necessary. That is the proposition.

Matt James: We've come from - registries were invented in the era when things were recorded on paper initially. Two bits of paper can't talk to each other, two electronic systems can. If we focus on making sure that the mandations, assessment rules, the lawful basis and the imperatives to join up electronic systems exist, we can get to an answer - I believe - far more quickly than if we continue to create what are effectively workarounds.

The question earlier around clinical confidence and the quality of HES data. I don't think clinicians do have confidence in the quality of HES data because it wasn't originally designed as a clinical system and yet is increasingly used for clinical analysis. I would strongly prefer to see that we address the clinical quality of the HES data which is one of the fundamental building blocks - precisely by ensuring that clinicians have input to it at the operational level rather than continuing to create workarounds. Where we collect all of that patient demographic data - the operation details again on a separate system - in order to then be able to build upon it with a few additional data feeds.

Cyril Chantler: Could you tell us something about the Breast Implant Register because I don't understand that. It's run by NHS Digital isn't it?

Manpreet Pujara: Yes. I'm really sorry to say that I'm not on a day to day basis involved with that.

Cyril Chantler: So, why isn't it run by HQIP?

Danny Keenan: We weren't asked.

[Laughter]

Cyril Chantler: But wouldn't it be natural for it to be run by HQIP?

Sasha Hewitt: So, we - well it...

Manpreet Pujara: No. Because we are the data guardians of the NHS and therefore by law, we are able to keep that information...

Cyril Chantler: I understand why you collect the data...

Manpreet Pujara: Yes.

Cyril Chantler: ...in the way we've been discussing, but why isn't the interrogation of the data and it's undertaken...

Manpreet Pujara: So, a request needs to be made...

Cyril Chantler: ...through HQIP?

Manpreet Pujara: ...to the DARS team in order to access...

Danny Keenan: Well we - there is a lot of history in this - I mean it's - you know, and we've already talked about clinicians and HES. I'm not stepping out of turn saying clinicians and NHS Digital - it wasn't a great relationship either. Now, it's fair to say that it is miles better our relationships - I'm talking as clinicians - with NHS Digital. It's obvious to all of us that there should be one area warehousing data. We can't have this system - which we do today - bits of data...

Cyril Chantler: HQIP, MHRA, NHS Digital and any organisations directed at - in patient safety - ought to all be doing their job but linked.

Danny Keenan: Sure. We do talk a lot to each other [laughs].

Cyril Chantler: Thank you.

Julia Cumberlege: Can I just enter another area now because we are concerned with GDPR and that crops up in all sorts of different situations and discussions. I'm just wondering how the interaction with GDPR would work with a database or a registry as well.

Danny Keenan: Sasha...

Julia Cumberlege: Can you explain that to us?

[Laughter]

Sasha Hewitt: My specialist topic. So, you're wondering how - what the GDPR requirements would be of a database or a registry? So - this is a really tricky one because we have obviously GDPR, which is the *Data Protection Act* essentially. All of the security arrangements that go along with that, but we also have the common law duty of confidentiality. Which is basically what everybody's talking about here when we're talking about consent and the legal basis to collect this information.

It's very easy [laughs] - I say very easy - turn off the camera when I say that. But it's easier to find a legal basis under GDPR than it is to find a legal basis under the common law duty of confidentiality - is my experience as an Associate Director at HQIP. However, there are lots of - you know, the GDPR is not brand new. The requirements within it largely have existed for a very long period of time. It's just more explicit in its requirements.

So, a lot of the things - like having a legal basis under GDPR - being transparent with patients, being secure - all of these things are really - they really are the same. It's just that its requirement to exercise individual rights is clearer. Organisations now need to be accountable and transparent in their processing. So, we did - in our report to the Department of Health - recommend that whichever model they choose there would need to be dedicated information governance resource available for whichever organisation is setting up an interim or a long-term registry to ensure compliance with GDPR and common-law duty of confidentiality.

Because certain things would need to be done, such as a data protection impact assessment. There would need to be a data protection officer appointed, transparency documentation would need to be developed, any consent materials. They would need to apply for a data security and protection toolkit with NHS Digital - which is the new IG toolkit. So, there would be lots of requirements, but I don't think any of that is insurmountable. It just takes time and resource and certainly our national clinical audits manage to do that quite well.

I think it would be possible.

Cyril Chantler: Why can't HQIP set up registries itself? Why does it have to go - get other people to do it? Because if you did it - with all those things covered - and you have a relationship with NHS Digital - which was transparent and open and proper information governance, and you deal with the opt out and Section 251. Why can't all that be linked in a sort of more efficient way?

Jill Stoddard: So, I suppose the easy answer to that is, we could do that - we have got the right people who could do that. It's about resources and being given a remit to do that.

Danny Keenan: We have been thinking exactly along those lines actually. Because those same ideas have gone through our heads as well as to - you know - just get on with this, because...

Cyril Chantler: I mean I must be clear. I think the involvement of the clinicians, of all sorts and patients in this exercise is vital.

Jill Stoddard: Absolutely.

Cyril Chantler: But I don't see why it all has to be done separately.

Matt James: Can I - to come back to [unclear] - I think what - the process that HQIP currently manages is an upfront exercise involving patients and clinicians in the design and the data to collect, and the objectives of a registry and how it's going to set out its purposes. There's an exercise which HQIP managed very well when they were involved at the back end of that which is to ensure that the right - correct processes with validating the data, checking the outcomes and enabling the clinicians to be directly involved with validating the outcomes and then publishing the analysis

There's this process in the middle, which is all about holding data, the consents around the data, obtaining the data and shuffling it around the system. Whilst the front end and the back end really do need customisation to a medical speciality or a particular issue and need careful governance arrangements, surely we can find ways to standardise that process in the middle.

So that unlike BCIR and PHIN and every other organisation that's been invented that's had to find its own way through the data protection rules and spend years doing so and face huge amounts of frustration and expense. It will at the end of day be huge amounts of taxpayers' money spent trying to navigate a taxpayer funded system around how the - you know the legal basis is managed.

If we can find a single approach to that on a common data platform, common data architecture and a common approach to the way that we handle those issues of lawful basis and consent then we will be in a far, far better place.

Sonia Macleod: But surely they apply across all the registries? It doesn't matter...

Matt James: Every one is bespoke currently.

Sonia Macleod: But that's the point. Why?

Matt James: Yes.

Multiple Speakers: Yes.

Sasha Hewitt: Well I guess they're bespoke because they each have - they're, each of them are trying to collect different types of data from different types of specialities, on different types of patients. They all have a unique methodology. So, they have to do that in a different way in order to collect the right data and produce the right outcomes. So, certainly my experience of audits is one size does not fit all. The best audits are the ones who are run by the clinical societies and organisations that deliver that patient care and can really drive the improvements at the end.

But I - my experience is not one size fits all. I don't know - you know, even within NHS Digital you've got your clinical audit platform. I would have thought there's still a need to bespoke and tailor that depending on...

Manpreet Pujara: I agree. But I think the key goes back to that - my simple message earlier on - which is about just collecting it once if there's that expectation that - dare I even say it - professional requirement - that actually you're recording this information and once it's recorded it should be able to be used on a number of occasions. It's about partnership working and ensuring that actually you may have different agencies that are involved, but actually that you collect it only once.

Danny Keenan: You have to think about the National Audit Registry - so a lot of the national audits are in chronic disease areas. We're talking quite a lot more to do with devices and the sequelae from devices. They're quite different. So, if you were to think of something like stroke or heart failure, they're actually - their requirements in there are quite a lot different to say a mesh registry or a joint registry. It's possible in the latter area that is a spec that would cover quite a lot of what's required, unlike the chronic disease area where actually there's different bespoke areas that need to be looked at.

Sonia Macleod: Absolutely. But I mean the overarching legal frameworks that...

Danny Keenan: [Unclear].

Sonia Macleod: They are the same.

Danny Keenan: Legally yes. Sorry.

Cyril Chantler: So, it would be possible to conceive - obviously all registers are different. The one I was involved in was for children across Europe who had kidney

transplants or kidney failure and obviously that's very different. But they could all exist within an overall framework that did all the governance - both legal and information governance - and link in to the data collection systems and so forth. The whole thing could be integrated could it not?

Danny Keenan: I think the answer is yes. We've grown this thing haphazardly as well - the whole programme. If you think of microchips and cardiac things - they kind of came in with Blair et cetera [the death areas] and that's obviously how it all grew and then we moved along to chronic disease. But I think what you're coming at and probably it is time to look across the programme and say well what is common and there is - like certainly with legal basis [unclear]. But taking it forward, yes. There are common areas in these for sure.

Julia Cumberlege: I very much like Cyril's words of integration. Because partnerships is always a lovely, lovely idea. We know that even in the best practices now partnerships break up and they are very difficult, very time consuming. It depends really on the individuals involved - whether they want to work together or not. Although I think it's a lovely idea, I really think it's not strong enough, and that we need to think of something different in order to make this really work. I don't know if you'd agree with that? Probably not. Okay.

Simon Whale: Can I just take that point a little bit further. So is there a problem - in terms of getting to where we - I think we're all agreed we want to get to - the database and registry concept that we've described. There doesn't seem to be any dissent around the table from those here today. Is there a problem in terms of decision-making and leadership? I mean who's ultimately responsible for implementing the kind of thing that we're talking about?

Danny Keenan: Well [unclear] to the Department of Health and Social Services and obviously NHS England are very, very important in our work as well. In fact, the vast majority of our work comes from NHSE.

Jill Stoddard: So, in order for us to act we need to be given a remit. So currently we are waiting for a decision from the Department of Health or NHS England about a remit to do whatever, and funding. I don't know whether that's something that they would want to do through HQIP as an organisation or a different organisation. So those are the decisions that we are currently waiting for.

Julia Cumberlege: Are you putting pressure on the bodies concerned to come to a decision?

Sasha Hewitt: I'm not sure that that's our role at the moment.

Danny Keenan: We are answerable particularly to the Medical Director at NHS England. That's our close link. Obviously with NHS England and I coming together that's going to make that easier.

Julia Cumberlege: See from a layperson's point of view, it always seems to me that there's somebody else that you're passing the buck to. That gets very, very frustrating. I understand that parliament was responsible for a lot of this in the 2012 Act - *Health and Social Care Act* - and I do understand all these different bodies. But anything that we can do in new innovations that actually supersedes all this and really gets to the grips and make HQIP make - it's understandable to people, would be really helpful. We need your help with that.

Danny Keenan: We met with Steve Powis - the Medical Director - the other day in fact. He would be the key person. He and Simon Stevens to be honest. But there's going to have to be money spent and it has to be that access.

Cyril Chantler: So, my understanding you get your contracts in effect from NHS England but the person to whom you're accountable is the Department of Health and Social Care?

Jill Stoddard: No. So, on this particular occasion - for the mesh work - we were approached by the Department of Health to ask - because of our expertise at HQIP - whether we could undertake a rapid piece of work. So, we said yes, absolutely, really important subject. We really want to be involved in it.

Cyril Chantler: It's an arms-length body.

Jill Stoddard: Extremely...

Cyril Chantler: You're an arms-length from NHS England are you? Not from the Department of Health?

Sasha Hewitt: So, we're not an arms-length body we're...

Cyril Chantler: Are you not?

Sasha Hewitt: ...a charity. So we're...[laughs].

Jill Stoddard: [Laughs].

Sasha Hewitt: I guess our remit is through the contract that we hold with NHS England and we have to go through a procurement process to win that contract. So, we are - you know a small healthcare charity.

Jill Stoddard: We have a National Clinical Audit and Patient Outcome Programme at HQIP. HQIP is the host organisation for that and we have the headline contract for that programme with NHS England and the Welsh government I should say as well.

Cyril Chantler: Thank you.

Matt James: May I speak plainly on this for a minute because I think Danny referred to some of these issues earlier. But we're coming from the outside. What we're trying to do desperately is bring the private healthcare data into alignment with the NHS. The question that immediately faces you in doing so is to which bit of the NHS shall we align because of lots of different bits going in lots of different directions. That is what has drawn me and our organisation in to trying to understand all of these different pieces.

The question that was asked earlier about why HQIP wasn't asked to run the Breast and Cosmetic Implant Registry. The organisation controlling the overall response to that was the Department of Health and Social Care who asked NHS Digital to run the registry end to end. Probably slightly to the surprise of some of the people who were participating in it up to that point. Because up to that point NHS Digital hadn't been greatly involved. In fact, the MHRA had been taking the lead in doing the work up.

But I think it doesn't really matter what that particular provenance was. It's illustrative of the point that if we continue to have a bespoke response to each issue that arises, we will get a different answer every time and we will end up still dealing with a multiplicity of projects at different stages with different governance arrangements and so on.

That's why - to come back to the same point - I think it's imperative that in framing recommendations, whoever is responding - whether it's the Department of Health and Social Care or NHS England - there needs to be an understanding that a level of co-ordination and alignment to existing processes and existing governance arrangements would be extremely beneficial to whatever comes next.

Cyril Chantler: Can I say this conversation - at least to me - has been hugely helpful, so thank you. Can I just move us to a different area now because it particularly relates to sodium valproate? We don't actually know how many women of child-bearing age are currently actually receiving sodium valproate. But there ought to be a way of establishing a register given that we know where the prescriptions are going.

Is that something that you could do - Dr Pujara - through NHS Digital?

Manpreet Pujara: I think we do know the number of women who are receiving sodium valproate. I just don't have a figure to give you today. I must apologise.

Cyril Chantler: Okay. How do you know that?

Manpreet Pujara: Well we know that from one or two areas. A lot of that information comes from prescriptions that have been dispensed [unclear] with the BSA. So that is primary care prescribing on the whole.

Cyril Chantler: Yes.

Manpreet Pujara: With a small amount of secondary care prescribing where an FP10 prescription has been used. The information that we don't have consistently is about prescribing in secondary care. Whereas - bearing in mind that most sodium valproate is initiated by specialists but actually prescriptions continue at primary care - we can be fairly confident that the information...

Cyril Chantler: So, you can create a register linked to the NHS number? This is patient identifiable information? To know where the women are. You could do that?

Manpreet Pujara: We could get the information from the BSA who have the dispensing data and who are the holders of that dispensing data. That would provide us with an NHS number as well as the drug and the history in terms of prescribing.

Now as we move to a more electronic system - so as you will know, traditionally prescribing was - has been computerised for the last 20 odd years. But with actually the dispensing, the claiming has not been electronic. For the last 10 years we've been moving towards an electronic system - an electronic prescription service - which means that we also have information about what is being prescribed and what is being dispensed.

So, as the NHS moves more and more closer to fully electronic prescribing in primary care - and dispensing in primary care - the amount of information that we have will be significantly richer and fuller in the sense that we can compare what has been prescribed and what has been dispensed as well.

Simon Whale: You could start collecting that data now? Even though you haven't got full EPS.

Manpreet Pujara: We are not the holders of that data. The data is...

Simon Whale: It's with the BSA.

Manpreet Pujara: ...transferred from the GP system, to the Spine - where it stays for a transient period - and on the expiration of that prescription and then goes to the BSA or is discarded if the prescription hasn't been dispensed. So, at the moment we don't hold that data for an infinite period of time at all. Which is why we have to go to the BSA to find out the information about what has been dispensed.

Simon Whale: Is there anything to stop you doing that then?

Manpreet Pujara: No. So again - not being an expert on data and IG - I would say there is nothing stopping us from doing that. We would just need to ensure that it's legal and whether we needed a direction to be able to do that.

Sonia Macleod: But that gives us women of child-bearing age [unclear] parameters...

Manpreet Pujara: Yes.

Sonia Macleod: ...receiving valproate?

Manpreet Pujara: Yes.

Sonia Macleod: That doesn't tell us the number of children born, does it?

Manpreet Pujara: No.

Sonia Macleod: Can we do that?

Manpreet Pujara: I think if you - that would involve further linkages. If you were able to determine which one of those women are of child-bearing age are pregnant during a certain period of time, there's different ways of getting that information. But I think in today's world the most reliable probably is from the exemption certificate that pregnant women have. Because not all pregnant women now come and register with their GP if they fall pregnant. Most of that is done by the community midwives and so on.

So, sometimes as a GP I really wouldn't know that a patient is pregnant until they are well into their pregnancy. They don't have the...

Cyril Chantler: But technically - and there are issues of common law confidentiality and GDPR in this area - hugely so - to create a registry of women of child-bearing age who are taking valproate.

Manpreet Pujara: [Unclear].

Cyril Chantler: There are very significant issues there.

Manpreet Pujara: So, it's possible.

Cyril Chantler: But technically it is possible?

Manpreet Pujara: Yes. So as part of the work that we have done with the GP system suppliers - clinical system suppliers in general practice - we have made available audits for all practices to be able to run on a daily basis to see how many patients they have - how many women they have - of child bearing age who are taking valproate.

Cyril Chantler: Is that for all GP digital support systems?

Manpreet Pujara: Yes.

Cyril Chantler: SystemOne, Vision and EMIS.

Manpreet Pujara: All four of them.

Cyril Chantler: Which is the fourth?

Manpreet Pujara: Microtest. A small number of practices. That was enabled in all four systems early last year and reported in July to the stakeholder our [unclear] stakeholder network that that was all happening.

Valerie Brasse: That's a consistent across all the four suppliers?

Manpreet Pujara: Yes.

Julia Cumberlege: But isn't it important that we ensure that women are much better informed - of child-bearing age - because if you wait to see whether they're pregnant, it can take a few weeks. It can even take up to months for those who don't want to come to antenatal classes and things and the damage is done.

Manpreet Pujara: Yes.

Julia Cumberlege: I wondered if you had any views on the Pregnancy Prevention Programme. Because it does seem to be that that is not working very well at all. We've had surveys that are done by the patient groups to show that it isn't doing very well. We just wonder why it takes so long to update some of the healthcare IT systems.

Manpreet Pujara: Thank you for that question. So, we have again worked with the system suppliers - between December 2017 and last year - to ensure there is a new, updated safety warning for any woman of child-bearing age who is taking sodium valproate. Which not only warns the prescriber, the user who's issuing the repeat medication, the authoriser about the fact that this is a woman of child-bearing age. But it also asks specifically, have you checked whether or not this woman is on a Pregnancy Prevention Plan?

Whether or not they are - they'd had a review by a specialist in the last year as to whether they need to continue taking valproate.

There is a set of questions that appear on the screen. One of the things that we've done for the first time is encourage suppliers to ensure that that warning is consistent across the four systems wherever possible so that - with the way the workforce moves within general practice at the moment - with 40 per cent of [unclear] being salaried GPs [unclear]. It's important there is consistency in the systems.

We've also worked with the dispensing system suppliers so that when the woman is collecting her medication from the pharmacy that they also do the checks. They also have a similarly consistent warning to ask those questions. So, the system should be working better.

Julia Cumberlege: Yeah. What can you do then to ensure that it is as near foolproof as we can get, because we know at the moment it isn't? We are very concerned that more babies are being damaged.

Manpreet Pujara: So, I remain very concerned about what I would call alert fatigue amongst all of us. Because we're using the technology on a day to day basis in almost anything and everything that we do. We are used to moving on - shall I say - on occasions - not necessarily [reading]. I think it's really, really important to ensure that clinicians, prescribers, actually pay attention to the warnings that are there and that those warnings - the number of warnings are minimised to those that are relevant for that individual patient.

So rather than receiving unnecessary warnings which are not relevant for the patient - which then results in a clinician or user learning to switch off and ignore those warnings. Sadly, I've come across Trusts that have actually switched off their warning systems because of alert fatigue. We need to ensure that those warnings are very focused in those specific circumstances and to ensure that clinicians have a system and a way of actually discussing those warnings. I would like to actually put the patients at the heart of this.

But the patient can actually also challenge the clinician. So, for me when I have a high severity warning, not only is it a red warning but the computer also beeps and I have a habit of discussing every single one of those warnings with the patient - particularly if I'm overriding that warning - as to why I am overriding it.

That needs to become the norm and I think what we need to enable - and I am hoping that patients will be able to access their [unclear] and [unclear]

systems where they can actually look at the drugs that they're taking themselves and take charge of their care that they will be in a position to actually ask questions.

The key thing for valproate is at the initiation of the drug to ensure that the woman - or teenager or child - is aware - or their parent is aware - in those circumstances, of the risks. But also, now ensuring that those warnings are checked every time a prescription is issued. That's what we've enabled.

What we need to do is to ensure that it's a co-ordinated effort and it is a - I'm going to use the word partnership again - between the patient, the practice and actually the pharmacist - to ensure that they all understand why this drug is being prescribed, why it's being taken and what action have they taken to ensure that she's not going to become pregnant.

Sonia Macleod: One thing that strikes me is that warnings are there for a reason. So how is it Trusts can simply turn them off?

Manpreet Pujara: A very, very good question. I have no answer to that at all. I don't know Stuart if you want to...

Stuart Harrison: Some of the systems are inherent and configurable and so that's a feature and sometimes some clients will ask for that. I kind of agree with your train of thought that that shouldn't be possible and ultimately what Manpreet said is very much configurable to the clinical setting.

Manpreet Pujara: GP systems are configured in that way. So those warnings are there. But what we can't do is control the user - their behaviour.

Julia Cumberlege: Right, well I'm going to draw this to a close. Thank you very much indeed for coming. But first of all, I'm going to ask my colleagues if they have any further questions they want to ask?

I want to echo very much what Sir Cyril has said which is it's been enormously helpful to us. I do want to thank you. You're going to give us some more information that we've asked about numbers and things like that. If there are other things that you think, oh my goodness they missed out on that, we'd love to know. Because we are very anxious to do a really good review and it does depend on people like you - who've got the knowledge and the expertise - to help us do that.

END OF TRANSCRIPT

Session 4: NHS Resolution

START OF TRANSCRIPT

Julia Cumberlege: So if you would like to introduce yourselves, that would be helpful.

Helen Vernon: I'm Helen Vernon. I'm Chief Executive of NHS Resolution. We handle indemnity schemes for the NHS in England and we also have a role in learning from claims to share that experience with the NHS for the purposes of safety improvement.

Julia Cumberlege: Thanks very much

John Mead: Hello, I'm John Mead. I'm Technical Claims Director at NHS Resolution.

Julia Cumberlege: All right, thanks very much. Just thinking about NHS Resolution, which I think has been going through some considerable reforms as an organisation in the last few years, what are the key reforms, do you think, for the journey that you've been through, and what objectives have been met? Would you like to say a bit about that?

Helen Vernon: Of course. A primary aim for us has been increasing our role in the period prior to a claim coming to us. That's involved a number of workstreams. One has been what we call an early notification scheme for obstetric brain injury. For the last two years we've been asking for incidents which fulfil certain clinical criteria which are likely to result in a child unfortunately having a brain injury following complications at birth. We've asked our NHS Trust members to report those incidents to us within 30 days of the incident rather than us waiting for the claim to come through, what can be five to six years after the event. The purpose of that is to enable us to share learning with the organisation directly more rapidly and then more widely with the NHS and our maternity Trust members.

Secondly, also to try to reach an early conclusion on legal liability and get any interim payments of compensation which might be merited at that point to the family as soon as possible. So meeting needs when they occur rather than several years down the line. That's been one workstream. The other has been refining our approach to how we learn from claims which are brought against the NHS in England, and we've done that by increasing the level of transparency of data to NHS Trusts.

We share it with them by way of scorecard information, but we've also been undertaking some deep dives into particularly prominent areas of claims, be that because they have high volume, so we've got lots of claims coming through in relation to the same sort of thing; or where they are of

high value, so they are particularly significant in terms of cost to the NHS. We've focused that on some main big areas over the last three years. So we did a report on examining five years of cerebral palsy claims where liability had been admitted. Then following that we did a report on mental health suicide. In the coming year we have a focus on emergency care claims, which are the highest volume speciality we receive.

The way we do this is by recruiting clinical fellows to come and work alongside our claims teams for a period of a year. For six months of that they spend their time looking in detail at the claims, and then for six months engaging with the wider system partners, such as the Royal Colleges to get buy-in and traction on recommendations from their findings. Then we've done some smaller deep-dives on specific areas like needle-stick injuries, cauda equina syndrome, pressure ulcers, those sorts of things which are common features of claims experience. That's been two things: one is the getting upstream in relation to maternity incidents, but secondly, refining our approach on learning.

That's very much a move away from our previous approach, which was one of inspection against risk management standards, and we discontinued that some years ago primarily because there was some overlap emerging with what the CQC were doing, but also because there was little evidence of either a correlation between the outcome of the risk management inspections and claims experience, but also Trusts were not progressing through the risk-management levels in the way that we had hoped. Then I suppose the third thing to mention is that we've been making our pricing for the indemnity schemes more sensitive to claims experience and trying to also use the pricing to incentivise best practice in relation to safety improvement.

We started that with maternity by incentivising 10 actions in relation to maternity safety which had the agreement of all of our arm's length body colleagues, and Royal Colleges, and using that as a way in which hospital Trusts could get a discount on their premium for fulfilling certain criteria. Those, I think, are the main areas where we've been focusing on in the last few years.

Cyril Chantler: Helen, how are you measuring the impact of your new patient safety role?

Helen Vernon: I think that's very difficult and challenging. We're trying to evaluate the impact of initiatives like maternity incentive scheme, but in doing that, we would have to untangle the impact of what we're doing from the patient safety efforts which are taking place across the system. That's quite hard because it's almost trying to prove a negative that by what we have done in

relation to learning or incentivisation, we have prevented an incident happening which would have occurred were it not for our...

Cyril Chantler: The way, as you and I know, it's happened elsewhere is that there've been fewer claims.

Helen Vernon: Yes, and I think because of the time lag that's historically existed between an incident occurring and the claim emerging, that's been something which has been difficult historically to capture, but by us being closer to the incident, I think in maternity brain injury in particular, we will now start to measure those incidents in real time, and hopefully that will accelerate our ability to evaluate the impact of what we're doing.

Cyril Chantler: You and I have talked about this so many times and I know it's not the purpose of today, but that's always been my concern about the need to intimately link the investigation to the family and the clinical team and to NHS Resolution to get the learning back and then rather hopefully you would see what's happened in Sweden, which is after maybe a lag of a year or two, that the number of damaged babies is beginning to fall. So are we setting up such a system for measurement like that, using Each Baby Counts, or whatever?

Helen Vernon: Yes, we are collecting data on those incidents, which now have to be reported to us in real time. We're also triangulating that data with the Each Baby Counts reports, and the reports to the neonatal database as well to make sure that the information is complete and accurate.

Julia Cumberlege: Can I...

Cyril Chantler: Well, only to go on to say that to extend that now to what we're currently doing here today, I know that you've had a number of claims in relation to mesh and maybe valproate as well. Has the learning from those claims been fed back immediately to the Trust of the individuals concerned?

Helen Vernon: I think in relation to the Trusts, those claims are very visible to them because of the information that's shared back with them by way of the scorecard. So they will see in real time as we do, the claims that they're getting through.

Cyril Chantler: Would you give an account for each one, because there haven't been that many, as to why you decided that the claim needed to be settled.

Helen Vernon: John, would you like to...

John Mead: Where a claim needs to be settled, we do seek the Trust's agreement to an admission of liability, and that will necessitate, usually, obtaining

independent expert evidence. So if our expert criticises the actions or inactions of the Trust, we will send a copy of that report to the Trust and say this is our independent view and what do you think? The Trust will have an opportunity to comment on that report. If they accept the conclusions, then fine. Those conclusions will constitute learning from the Trust in relation to...

Cyril Chantler: What about the individual clinicians?

John Mead: We don't have any direct control over that because our dealings are usually with the Trust's claims department or legal department. We can ask that these reports are fed back, and usually that does happen because people in the Trust's legal department are not clinically qualified, usually, and therefore they need...

Cyril Chantler: Wouldn't it be good to be sure that it happens?

John Mead: It would be good, I agree, but I can't think of an obvious way of us insisting upon it.

Julia Cumberlege: Can I just ask, thinking about the claimants, the people who feel they've been wronged, I understand it takes you about 14 months, the median term - time rather - to resolve those. It's now 40% longer than they were a decade ago. So I'm just wondering why it will take so much longer now to settle a claim.

Helen Vernon: Yes, we looked at this because as you know, the national audit office made some recommendations on the cost of clinic negligence and some of the drivers that lay behind that. They observed a lengthening time to settlement. Part of that is attributable to the time it takes for us to hear about the incident following its occurrence, and that might be because the claim has taken some time to come through, or it might be because the claimant lawyer has wanted to investigate it before reporting it to us. Then there's, part of the time is from the claim coming to us and that claim being resolved. What we've seen is that there's a number of factors driving that. One has been the volumes of claims coming through.

Another has been we've noted that sometimes when cases get into litigation, formal litigation, that can slow down the progress of the claim. We also saw from our data that an extending time to resolution was more a feature of those claims which we resolve without a payment to damages than it was for those with. So it's taking us longer to, I suppose explain to the injured patient where there was not an entitlement to compensation and then close the claim down, than it was on those cases where compensation was due to be paid. So there's a number of features driving

that, which we've been analysing and which we've recently reported back to the public accounts committee on two.

Julia Cumberlege: Right, so what are your plans for speeding up though?

Helen Vernon: We've focused on the brain-damaged baby cases because those have the longest period of time to resolving them, sometimes many years. Our focus there has been getting sight of them sooner so that we don't have that incident-to-claim lag. In relation to other cases, we've been discussing with the Ministry of Justice how we might speed up the court system, and we've also been focusing our efforts on keeping things out of formal litigation, because if that's where claims slow down, then clearly one way of tackling that is to stop them going into court proceedings in the first place. So we've been trying to increase the number of cases which are resolved without court proceedings being required.

We've also increased the level of mediation, which we found to be a very effective way of not only bringing matters to a head sooner, but also giving the patient a voice in the process, an opportunity to sit down with the Trust, with the clinicians involved, and for issues to be explored in more of a neutral, safe space than is possible with court proceedings.

Valerie Brasse: What's the uptake on the mediation process?

Helen Vernon: It's increased hugely, actually, particularly in the last 18 months to two years. We set ourselves a target of 50 for the first year of giving this a real push and we trebled that in that in the first year. We set ourselves a target of 80 for this year, and we've already more than doubled that. So I think as lawyers get more used to mediation as a process and more practised in it and can see the benefits of it for their clients and for patients and for healthcare staff too, it's getting more traction. So, certainly something that we see has benefit that we're keen to press on with.

John Mead: Yes, and it's particularly effective in those cases where there's something at stake more than money. So, it might be that the Trust hasn't apologised. It might be that the patient has particular concerns about something the Trust is doing or is not doing. Those issues can be addressed in a mediation with a Trust representative present, whereas in the normal mechanism for settling a claim, all we can do is offer money. But a mediation can offer a much broader range of remedies.

Julia Cumberlege: I think some of the advice you give to women, we've heard this through the mesh sufferers, is that they ought to be suing their surgeons. Now, has that advice come from you? Because certainly the women find they can't do that. They don't want to do that. They have been deeply disabled, hurt,

in real trauma because of the mesh case, but I just sort of think are there, you talked about mediation and I just wonder what percentage of cases you can resolve through mediation? Because that seems to me a better solution than actually suing your surgeon.

Helen Vernon: Yes, I would agree, and I think that in relation to your first point, the advice that's been given to women, that wouldn't have come from us because NHS Trusts are vicariously liable for the actions of all of their staff and we pick that up through our indemnity schemes through the Trust membership.

John Mead: Sorry, I think if I could add, what we do if a claimant is contemplating litigation and we can't get anywhere on the claim, we always advise claimants and their lawyers to sue the Trust. We never advise people who are involved with an NHS body to sue an individual clinician. It doesn't happen, for the reason that Helen's given. So I think that might, that advice might have come in the context of private treatment where an individual surgeon probably is not the employee of a private healthcare company.

Julia Cumberlege: Right.

Cyril Chantler: A lot of activity on NHS patients takes place in the private sector.

John Mead: It does, but most of that we cover under our indemnity scheme as well, including the liability of an individual clinician.

Cyril Chantler: So why wouldn't you contact the private hospital?

John Mead: We would in that situation, yes. What I was addressing was the Chair's comment that somebody has advised patients to sue surgeons. That has not come from us.

Cyril Chantler: But if you had concerns, I know how your indemnity scheme works with the NHS hospital Trusts, but how does it work with a private hospital? Where you've had concerns about the quality of care in a private hospital, how do you deal with that?

John Mead: Yeah, our clinical negligence scheme for Trusts covers certain private hospitals. It's voluntary, so the company may or may not choose to join. It covers those hospitals for their NHS contracts. So it covers both the organisation and the individual clinicians who are undertaking the NHS work at the private hospital.

Cyril Chantler: So if it's an NHS patient in a private hospital that is part of your scheme, your conversation will not be with the surgeon, it will be with the hospital.

John Mead: It will be with the hospital initially, yes, but it might with the surgeon additionally.

Cyril Chantler: So why wouldn't it be additionally with the surgeon in the NHS hospital?

John Mead: There's no difference. It's exactly the same. We will always go through the relevant legal department or claims department initially, and it might be necessary following that to have direct dealings with the surgeon, but normally we try to do it through the legal department as a smooth process rather than contacting thousands of different doctors.

Julia Cumberlege: So, if a surgeon has implanted mesh, might they have received financial support from mesh manufacturers if there is a case brought? Do you know any of that? We just wonder if there is some conflicts of interest that we would really want to know about, or patients would want to know about.

Helen Vernon: That's not a feature that we picked up in the claims. I don't know if John has any better information on that. It's not something that's crossed our radar.

[Over speaking]

Sonia Macleod: ...that you would ask?

Helen Vernon: I suppose in relation to - we would ask for disclosure of all relevant information in relation to the management of the claim. We'd want to see absolutely everything that might have relevance, and indeed, that will be disclosable to the patient as well and their lawyer would be entitled to full transparency to investigate. As I said, it's not something we've come across, but if it's a line of inquiry that was raised with us, we would certainly pursue it with the organisation.

Julia Cumberlege: Right, thank you.

Simon Whale: Can I just ask, there are some products, and sodium valproate would be an example here, that can give rise to both a product liability claim against the manufacturer, and a clinical negligence claim against the NHS. As we've been talking to people as we've gone around the country, people who have taken sodium valproate and are claimants have talked to us about their feeling that they get kind of passed from pillar to post between NHS Resolution and what you do on the one hand, and the manufacturer trying to, each of you trying to abdicate responsibility as it were, that's how they would describe it, to each other. So it's being passed from pillar to post and no one actually resolves the claim. Would you, that's their perspective. Do you agree with that perspective?

Helen Vernon: John, do you want to talk about the...

John Mead: No, I don't agree with that because if there has been negligence by one of our members, then we will pay the claim. We might want to pursue a further claim against the manufacturers; we might, we might not. But if there has been negligence, then we will deal with that claim on behalf of our member. However, if the claim is a product liability claim, then there is strict liability and law on, you know, strict liability on the manufacturer under the Consumer Protection Act. So that claim is probably against the manufacturer because the Trust has not made a product, usually.

Simon Whale: I think the problem in the case of valproate is that the argument would be that doctors didn't know what they should've warned because they weren't made aware of it at the right moment in time. So that's one defence that the claimant would be confronted with, and on the other hand, the manufacturer would be saying well, we did everything we needed to do. We put warnings on labels and on boxes and so on, so it wasn't us. So the claimant is left in a sort of no-man's land.

John Mead: Yes, I can understand why some claimants think that because of what happened in relation to the sodium valproate group litigation almost 20 years ago. We can't speak for the manufacturers, but as we said in our paper, we actually gave disclosure of our QC's advice in the context of transferring that claim from the NHS to the manufacturers, which we thought would be a more sustainable avenue for compensation for the claimants.

Simon Whale: I suppose from a simplistic point of view, which I'll take for the purpose of this conversation, if you're involved in a motor accident and there's a dispute about who is at fault in that motor accident, assuming you've got the appropriate cover, you as the driver of one of the affected parties, will get a pay-out. You may get your car replaced. The insurers will sort it out between themselves behind the scenes later. So the claimant gets an appropriate form of redress, compensation or pay-out or whatever you want to call it, and the two insurers can sort it out separately. Is there not some equivalent way of looking at things in relation to the point I'm making about product and medical negligence?

John Mead: There's always room for negotiation and discussion with other defendants, of course. We do that regularly where, for example, the Medical Defence Organisation's our co-defendant. That's always an avenue. But in relation to the sodium valproate claims, our defence in our view at the time was pretty clear, which was a defence based on the Boden principle, namely,

that it was considered at the time that sodium valproate was the best drug for many of those patients.

Simon Whale: Thank you.

Julia Cumberlege: Right.

Valerie Brasse: Yes, can I ask you about the indemnity scheme for GPs that you've been asked to set up, where you are with this and what that's going to look like? Is it going to mirror the negligence scheme for Trusts?

Helen Vernon: It's slightly different because we will be covering, it's a system level of coverage rather than membership level. So for example, for CNST, NHS Trusts are members of our scheme and they pay a contribution to us which is based on pricing methodology, which is weighted on experience and exposure. But for CNSGP, as it's now called, that will be centrally funded, and general practice, because it goes further than just the individual GPs, will be covered under that umbrella coverage from the first of April of this coming year. The regulations have just been laid for that scheme and we have been asked to be both the administrators and the operators of it in relation to incidents occurring after the first of April date.

Valerie Brasse: Is that going to cause you problems, being the administrator and the...

Helen Vernon: No, so now too, the other indemnity schemes, where we are both administrator and operator.

Valerie Brasse: What is your concern, obviously the NAO reported on the affordability of the other scheme, the Trust scheme. How is this going to be different? How are you going to be in a place that's considerably better than looking at a similar scheme?

Helen Vernon: I think that probably goes to the broader issue of the cost of clinical negligence, which on the basis that the calculation of damages settlements is the same, whether it's negligence in general practice or it's negligence in secondary care, then that is a broader issue for government. What the NAO highlighted was that it's not just an NHS Trust issue, in fact, it's not even just an NHS Resolution issue; it is a broader government issue, not least because the compensation framework is managed by the Ministry of Justice rather than health service. So that whole issue of the cost of clinical negligence to the system...

Valerie Brasse: Pay-out, rather than the cost of running the scheme or...

Helen Vernon: Yes, the cost of damages and the legal costs which are attached to the, recovering those damages.

Valerie Brasse: Are outside your remit, in that sense.

Helen Vernon: They are to a degree within our control, but the legal framework which governs the basis on which we make the payments is set by the Ministry of Justice.

Cyril Chantler: Helen, can I ask you a more general question? It seems to me the function of the NHS Resolution is two-fold. You may not agree with this proposition. That it is firstly to help the system reduce the amount of damage that patients incur as they go through treatment; and secondly, and maybe it's not in that order, to make sure that the taxpayers get the best value they can for what is a state-funded system. So you're balancing those two things. But the way you operate is determined within a set of rules established by Parliament. How would you like those to be changed to help you do your job better?

Helen Vernon: I think our aim is to get to the right answer as quickly as we can within the legal framework we operate within.

Cyril Chantler: Yes. So I'm asking whether you think in this day and age, because your legal framework is quite old, whether there are some things you'd like to see changed with that legal framework? There are one or two things from my recent connection with this area that it seems to me I wouldn't mind seeing changed.

Helen Vernon: I think two things come to mind. One is the way in which legal costs are dealt with and the Department of Health has run a consultation on fixed legal costs for claimant law firms. That's currently work which is with the Civil Justice Council, which we're contributing towards. We found that fixing legal costs has been effective in relation to the management of the defence costs side. Certainly our own boys have been working to fix fees for many years. So it's the legal costs side which is already under consideration by the Civil Justice Council at the request of the Department of Health. I think the second aspect is the once and for all settlement of damages, which is problematic, particularly in relation to the most serious injuries, where someone has lifelong care needs. Essentially what...

Cyril Chantler: Is this the *1948 Personal Injuries* we're talking about?

Helen Vernon: This is lump sum versus an annual payment for the rest of that individual's life. At the moment we have to make an assessment based on a point in time, and the expert evidence that we have to hand on how somebody's care needs might unfold, sometimes decades into the future. That's very difficult for both sides because for the claimant, clearly they want to ensure that that person will be cared for for the rest of their life. For the

defendant, we want to make sure that provision is adequate, that it's right, that it's appropriate, but not that it's excessive, bearing in mind that the cost ultimately falls to the taxpayer. So that once and for all snapshot is problematic.

That's one of the reasons that we've been accelerating the liability investigation and looking to make interim payments on the brain injury cases at a much earlier stage. So responding to needs when they occur, rather than trying to make a once and for all multimillion pound settlement at a point in time.

Sonia Macleod: But also if you're looking at lump sums versus periodic payments, presumably because of the changes in discount rate, relatively recent ones, will have a larger impact if you're, depending on which way you go.

Helen Vernon: That's exactly right. We've, for a long time, been able to pay those high-value settlements by way of periodical payments for life, but they are in themselves fixed at a moment in time. So it would be £100,000 for life irrespective of anything which might befall that individual during their lifetime. So their care needs might be worse than expected, or actually less than expected, and the payment doesn't adjust to reflect that. But we do have that advantage of being able to compensate in that way. Coming to Dr Macleod's point, there is the issue of a discount rate and the way in which that affects the value of lump-sum settlements in particular. So where we have a high-value claim where we don't have the option of making annual payments, the value of that will very much be affected by the court discount rate which is set at that moment in time. Of course there's legislation which has just gone through Parliament to address that issue.

Julia Cumberlege: Yes, so you say it addresses the issue, so do we now have structured payments? I thought there was something called structured payments, which actually is something that you can assess the needs of somebody, that it doesn't depend on a lump sum, but you can review their state, whether they need more care or less care. Doesn't that exist?

Helen Vernon: We do, as I've said, make structured payments. We call them periodical payments...

Julia Cumberlege: Sorry, does the structured payment then have to come from the lump sum, or can you change the lump sum?

Helen Vernon: No, we make a lump, when we make a payment for those very high value claims, we make a lump sum payment up front for immediate needs like accommodation and adapting accommodation and aids and equipment

and so on. Then we will make an annual payment for the duration of that person's life. The difficulty is that that payment is not reviewable in the event that their care needs are less or more than expected.

John Mead: If I could add, periodical payments and structured settlements are the same thing.

Julia Cumberlege: Okay, I think we'll draw this session to a close. I want to thank you very, very much for coming. If there are any questions that you want to ask for us that we haven't covered or any information you think we should have, we would really welcome that. But I'll just check with my team. Any last final...

Sonia Macleod: Just one, one maybe. It was really to do with the Duty of Candour and the implementation of Duty of Candour on whether you have seen any impact of that and whether you, in your claims, do you ask is this Duty of Candour, disclosure, and has it impacted on claims rates or anything like that?

Helen Vernon: It's something we've done some research on recently as well. We commissioned the behavioural insights team to look at the sorts of factors which led people to....

Sonia Macleod: Your [unclear]. Yes.

Helen Vernon: Yes, bring a claim following an incident or a complaint. Clearly one of those was, as we thought, when the patient hasn't had an appropriate explanation, when they've not been involved in the investigation, and so on. That validated what we've long said, which is that candour is absolutely critical when something goes wrong, that transparency and honesty is more likely to prevent than cause a claim. I've brought this with me which I'll leave with you, it's our Saying Sorry leaflet, which is widely distributed in the NHS, which makes that absolutely clear. In terms of how it's going, I think that its experience is variable. We're certainly seeing some examples of some fantastic practice in the service, but also examples of where it could be, things could be improved.

But it's certainly something that is a key focus of our work with our member Trusts to ensure that patients do get an explanation as soon as possible.

Sonia Macleod: On that theme, in terms of moving down a pathway to earlier in the claims process, I've noticed that you've got a memorandum of understanding with PHSO. How do they interact? How does that work in practice?

Helen Vernon: We are working very closely with PHSO to make sure that we give the same messages to our NHS Trust contacts because essentially we're dealing with the same claims and legal teams and it's important that we say the same things to them, particularly on an important issue like this, where we're absolutely aligned. So the purpose of that recent publication was to make that fundamentally clear, but also to explain, I suppose, how our two organisations interact and where there's areas of overlap, how that will be managed.

Sonia Macleod: Yeah, so I mean from a patient perspective, as a patient on that journey, do you think it's now clear where you need to go?

Helen Vernon: I think that guidance was aimed particularly at the Trust legal teams because they'd asked for it. This is the leaflet we use, which is both patient and organisation-facing. I think that in terms of patients being aware of their rights to a full explanation, their right to candour, I suppose it depends. In some Trusts there's a lot of direct support for patients in navigating the process and in some, perhaps it could be better. But it does need to be, it's very clearly an oft-repeated message through a variety of means.

Julia Cumberlege: Well, we've got no more questions at the moment, and I wondered if you had any questions for us?

Helen Vernon: I don't have any, but more than happy to provide any information following today's hearing if that will be of assistance to the panel.

Julia Cumberlege: Thank you very much - and John, can I thank you so much for coming.

END OF TRANSCRIPT

14th March 2019

Session 1: General Medical Council (GMC)

START OF TRANSCRIPT

Julia Cumberlege: I'm Julia Cumberlege, I was invited by the previous Secretary of State to do this review before he chose to leave, but there you go. On my left is Sir Cyril Chantler, who I'm sure you know and he's the Vice Chairman of the Review. The third member of our panel is Simon Whale and Simon particularly looks at communications and information and that side of things. On Simon's right is Dr Valerie Brasse and Valerie is our secretary. On Cyril's left is Dr Sonia Macleod, who is our senior researcher. Then we've got other people in the room who are just helping us run the session, as it were.

So we are recording this and I hope you appreciate that. It will go onto our website so people will be able to see what has happened through the session. Really it was our fundamental purpose to ensure that everybody knew what we were at, that nothing was hidden and people could understand where we'd got to in terms of the review.

One of the issues that came through when we met a lot of patients was that they thought that they weren't being listened to, they weren't trusted. They really felt that they should be taken more seriously, so that was why we are open, transparent and have a very important communication channel with them, particularly the patient groups. So we'll now record so that people will know who you are and what you do. So Professor, would you like to start?

Colin Melville: Yes, I wish I'd never said anything. So, my name is Professor Colin Melville, I'm Medical Director and Director of Education and Standards at the GMC. I am a registered medical practitioner with a licence to practise. I used to be an intensive care consultant, a role which I actually gave up when I took on this role in January 2017.

Julia Cumberlege: Thank you very much.

Anthony Omo: I am Anthony Omo, I'm Director of Fitness to Practise at the GMC and also general counsel, which means I look after all legal matters for the GMC.

Julia Cumberlege: Right, thank you very much indeed. As I was saying, one of the issues when we were going round the country and we were listening to a lot of patients, they were really very concerned about the consenting process. That when

they were going to be operated on, et cetera and especially when they were taking medications, they really weren't fully informed of the consequences of either the operation or of the medications.

So we were very concerned about that and we wondered really whether that's something that's come across your desks, how the consenting process is deemed to be by those who are having to use it, in terms of give their consent, that the thought was it is inadequate. We just wondered have you thought about that and if so, have you any measures to improve it.

Colin Melville: I think the first point that you made is that consent is a process and we would absolutely affirm that. So we do have guidance on consent, it's quite extensive. We have actually recently gone out to consultation to see whether there should be any changes to the guidance we provide. That only recently closed, so I'm not in a position at the moment to be able to tell you where we've got to with that, but we can certainly provide updated information later. We used - in terms of communicating, we had one of the highest responses we've had to any consultation and interestingly and I think helpfully, a good response from members of the public.

So we have very much got their view as well as those of professions and organisations. We launched it on social media with the hashtag 'deciding together' and what we're trying to convey is that consent is not about a moment in time when you sign a form; it is about a conversation, it is about presenting the information in a way that a patient can understand so that they can make an informed decision. I don't think we would say that there is anything fundamentally wrong with the guidance; it's about how that guidance is being used in practice.

I think there are some areas of practice where people perceive a greater clarity, so surgical operations where there is something in writing and something is signed. But on the issues of more general care and on prescribing, people probably don't think about it in the same way, even though it should be part of consent. In other words, consent is not just a process of signing something; it is a conversation which leads to shared decisions, whether they reach the threshold of needing a signature or not.

Julia Cumberlege: So you've been doing some research on this. What has that shown up? Have you received the sort of information that we have from patients, that actually they feel the consent process isn't good enough, isn't strong enough? You're quite right, it's not really about signing forms; it's about the way the information is given. It even goes to body language, we've heard women say that the conversation - when they took their husband or

partner, the conversation was between the surgeon and the partner and the surgeon never looked at the woman and expected all the answers to come from the other male that was in the room.

Colin Melville: Clearly that's disappointing. I wouldn't ever begin to defend that, either as a professional clinician or as a member of the GMC. That isn't what our guidance sets out. I think the difficulty here is the translation between, or the interpretation perhaps between what the guidance expects and how it's actually delivered on the ground. That is partly around how medical students and doctors are educated. Consent features very strongly in that process, but that doesn't help to answer individual doctors who you've obviously heard about where that is not seeming to meet what would be a reasonable standard of effectively communication, rather than anything else, and being compassionate and empathic towards the patient.

Julia Cumberlege: I'm very impressed with what you were doing on Twitter, which is hashtag 'deciding together', but have you used other mechanisms to get feedback from patients?

Colin Melville: Yes, sorry, I only used that as an example really to try and illustrate that what we're saying is that consent is not as a doctor I tell you what I'm going to do and you agree or disagree. It is about a conversation it's about presenting the information that will help the patient to make an informed choice. So it was only for that reason.

We used a number of avenues through our consultation, including engagement with some specific clinical and public bodies, patient representative bodies, so that we could hear that and we had a very good response. As I said, my team hasn't analysed it yet so I don't have that information, but there was a general support both from the profession and from the public for the changes that were in that guidance, which in many ways were more to try and tease out some of the smaller issues rather than the actual headlines of what the guidance says.

Julia Cumberlege: Because a conversation is between two people, and both parties have views and should be free to express them. But one of the suggestions we've had is that there could be an audio record of that conversation so that the patient, having heard what the clinician has been telling them, could take that away and discuss it with their family and then come back. Because there may be a lot of questions that they would have asked if they'd had more time to think about it. I just wondered if you had any views on that sort of an improvement.

Colin Melville: I don't think I have a specific view on audio recording, but there clearly needs to be a mechanism that a patient can take something away that in some measure summarises and allows the patient to come back and have further conversation or to seek clarification. I think the other point is that consent is not a once and for all decision; consent can be changed or withdrawn at any point. That might be something about patient public education as well as the profession to understand it. Just because on one day a patient made one decision, doesn't mean that the following day they might have a different view.

Julia Cumberlege: Right, well thank you very much. We might come back to that. Simon.

Simon Whale: Well just to pick up on something about consent, thank you for supplying various data to us, that's been really helpful. Just looking at cases that come to you that involve consent, I'm looking at your numbers, 2018 total of 120 cases, I believe. But 84 out of the 120 were either no further action before investigation or closed during investigation. It's quite a significant proportion that didn't get beyond that stage. Any comment you'd like to make about that?

Anthony Omo: Yes, obviously concerned with what we're hearing, which is bad, not good practice in any stretch and so we do take action when we get concerns in as the figure shows. So we have an investigatory process which has statutory thresholds and so it has to hit the threshold before we can investigate and then take action. So it's difficult for me to say in those individual cases what happened, but what generally happens is consent will be wrapped up with other issues and the more serious it is and the assessment of the risk the doctor poses to future patients, we would be more willing to take action, more able to take action.

If the consent is a communication problem rather than - and there are no other concerns about the doctor's practice, then they could get advice or a warning, which is before we actually get to a tribunal. So there's a variety of things in there around consent. We take it quite seriously, but the mechanism we have for taking action relies on what is quite a legal test of the fitness to practise of the doctor going forward, as opposed to what they've done in the past. That presents certain challenges for us, but we would investigate any concern of the nature you described, where patients - and particularly the example of the patient not actually being spoken to and their partner being spoken to, that's just unacceptable and we would look at that.

Valerie Brasse: Can I just follow that up? So if the substantive allegation doesn't hit the threshold, there is an issue around consent that's part and parcel of the

whole, is it the threshold applied to the substantive bit, i.e. the quality of the treatment or whatever and then what happens if you're getting these tagged on bits concerning the consent element? So you throw the baby out with the bathwater, does the whole thing just get pushed out because it didn't meet the substantive threshold?

Anthony Omo: No, the threshold applies across the complaint. So we're a creature of statute. In the *Medical Act* it sets out five bases upon which we can take action. The fitness to practise can only be impaired by reason of misconduct, serious deficient performance, the adverse health, a determination by another body, or language.

Consent will be part of a misconduct or a performance allegation, so the doctor was rude, didn't do proper consent and then prescribed the wrong medication, for example, could come in as a consent. We would look at all of that and consider whether the doctor, as a result of that, is still fit to practise or presents a risk to future patients. So we do look at all elements of the complaint, not a single one.

Cyril Chantler: Could I just turn back to consent for a moment? The essence of good medical practice, I remember it and I was once responsible for it, is that this is guidance and you have to use your judgement. If you choose not to follow the guidance then you have to be able to justify it if you're criticised and that then can become a fitness to practise process, correct?

Anthony Omo: Correct.

Cyril Chantler: Now, we were told last time we met to discuss this, that an issue was that one person said one thing and somebody said another. What happens behind closed doors, you can't determine that specifically, we were told that. So at that point, isn't it perhaps important to ensure by whatever means you use that the process of consent has been documented? Would you be saying that, do you think and do you say that in your guidance, that the process has to be adequately documented so that it's not just a question of what happened behind closed doors of what the doctor said or didn't say?

Colin Melville: Absolutely, so the process should be documented. I think there's always been some confusion about what gets written in what's called the medical notes versus what's on the consent form. The matter is is it appropriately recorded, but I think to the Baroness's point is how then is what has been documented shared with the patient in a way that allows them to say well, is that your recollection of what we discussed? Because I'm assuming that part of this is the recall or different interpretations of what has been said

and what it might have meant. So it's not just that it should be documented good practice would suggest, although I don't think we say that specifically, but actually it should be shared with the patient in a way that allows them to go away...

Cyril Chantler: I think I'm asking whether given where we are now, because it has changed since I was on the medical register and Montgomery, whether you need to be more specific in saying how this needs to be documented so that if a complaint is made it can be properly examined. If that is not properly documented, whether that in itself would be an issue where the practitioner had to justify that they hadn't followed the guidance.

Colin Melville: Yes, so it's back to your point about professional judgement as well, isn't it, about the extent of the detail of what is documented, how it is documented. But the principle is right, that there should be some record of what has been discussed and what was agreed that should be open and shared.

Cyril Chantler: If it's not there, then you'd have to justify the fact that it's not there because it was some immediate urgency that didn't allow that process, or something like that.

Colin Melville: Yes, it's back to the question of if you're looking, absence of evidence is unhelpful in every respect, isn't it?

Cyril Chantler: So you would, when the outcome of the consultation is known, you would consider, if necessary, changing the guidance in good medical practice regarding this?

Colin Melville: More than happy to have a look at that. I don't have that guidance in my head, but I would be reasonably confident that that is covered in the guidance. I would be surprised if it isn't. But we will have a look at precisely where it is.

Cyril Chantler: Yes, that didn't actually come out of our last session, that's why I raise it.

Anthony Omo: Just while you're on that, just to correct something, it is absolutely not the case where there's a dispute of evidence that we don't take action. In fact if there is a dispute, we don't resolve it without a hearing. So those cases are more likely to go to hearing...

Cyril Chantler: Oh, right.

Anthony Omo: ...because we are not allowed to resolve disputes without a hearing. So if that was put forward, I'm sorry about that, but that is not quite correct.

Cyril Chantler: Thank you.

Simon Whale: Can I just clarify or go back to one point that Professor Melville made about the consent and the recording of the process? So yes, there should be a document audit trail, if you like, of the process. Presumably what you're saying also, I think you're saying, is that the patient needs to be a co-owner of that record. It's not just that the doctor writes it down and files it away; the patient has to see that and say yes, that's how I recollect it too.

Colin Melville: Yes, I absolutely agree with that.

Simon Whale: Have you got any indication of how often that doesn't happen?

Colin Melville: I don't, because in the sense that if it doesn't happen, we would only know about it if, having not happened, someone had enough concern to raise it with us. So it's possible that it hasn't happened, but no one's challenged it. Clearly you are hearing examples where that's not the case. Yes, sorry.

Sonia Macleod: Are we talking if you go into surgery, you get a copy of the consent form?

Colin Melville: Yes, but back to the process, so the discussion about what the choices are, so surgery or different types of surgery versus no treatment, delayed treatment, should all be part of that process. The conclusion of that conversation in agreement with the patient would be recorded on the consent form which the patient would sign, but we don't mandate that the only source of information relating to consent is on the form, because there should be a record of the conversation, the clinic appointments, the visit, the discussions, any telephone calls, that should all be in the medical notes as well. So it's the two parts there.

Sonia Macleod: Do patients have those?

Colin Melville: No, I think that's the point that the Baroness was raising. Although many doctors now - and there was a recent activity around this, wasn't there, writing the letter to the patient, not to the GP, I think that's a very interesting perspective. It takes away this shortcutting medical language, which is probably helpful. So any communication should also include the nature of the conversation and some of the risks and opportunities that were discussed in that and give the patient the right to come back and seek further information.

Sonia Macleod: So as part of your guidance and consent, are you looking at producing patient resources like patient decision aids and things like that?

Colin Melville: Yes, we are. We always look at how can we help the patients to understand the advice that was given by doctors.

Simon Whale: Can I just broaden out the discussion more generally? So as I've said, you sent us quite a lot of data about fitness to practise, which has been really helpful. One of the things that struck us was the relatively small proportion of FTP complaints that are investigated every year. Why is it such a small proportion that are investigated?

Anthony Omo: There are a number of reasons why there is a small proportion. So we've received, certainly for the last five years, around about 9000 complaints come through the door. Roughly about 6000 are sometimes not about the doctor; they're about private disputes, parking disputes and things like that, so they're not matters that would ever impact a doctor's practice and not about clinical. So we close those down or refer them to other regulators. We receive complaints about nurses, dentists and that. We then investigate the balance.

A proportion of them are sent onto the responsible officers, so the senior medical persons within organisations who are responsible for local fitness to practise, because they don't hit our thresholds for investigation but we ask them to look at them and take remedial action. Then we investigate something like 2000-plus per year and we have different processes for doing that. So, in answer to your question, the reason why we don't investigate more and don't send more to a tribunal is that they don't reach the various criteria we have, which is set to legislation.

So we look at all cases that raise a question about a doctor's fitness to practise, that's the first test. If it raises a question about fitness to practise, we then need to see if we can get the evidence about does the doctor present a risk. If there are disputes about evidence, as I've just said, that will go to a tribunal to resolve, so those cases end up there. If the doctor doesn't have insight, is not taking steps to remediate, those will go to a tribunal. So we're about future risk and that's again set out in our legislation. The test we apply is whether the doctor is fit to practise, not whether they were fit to practise but are they going forward. So it really depends on what has happened post the actual event.

Simon Whale: So if you take your 2018 numbers, as you've supplied them to us, total enquiries or complaints 8573, 66 per cent of which were from members of the public, 14 per cent got to the stage of being investigated by a case examiner and only three per cent went to FTP tribunal. The main driver for it being only three per cent, is the main driver that it's inappropriate complaints, i.e. car parking or dentists rather than doctors? Or is it...

Anthony Omo: I wouldn't call them inappropriate complaints; there are complaints that don't meet our threshold. So they are concerns perhaps about doctors'

communication with staff, which we think are better dealt with by the employer rather than the regulator, because we have quite blunt instruments we're dealing with doctors. So we're either going to issue a warning, advice, suspend or put restrictions, which may seem disproportionate for a single complaint about communication.

So what we tend to get from patients is a whole vast array of complaints. It could be about care in general, not necessarily about a doctor, but about the treatment they received in hospital. We would refer that on to the CQC or the hospital to deal with. What we do with employers, which is why when you look through the figures we tend to send more of those to a tribunal, is we have an employee liaison service. So senior members of the GMC talking to them about which concerns we need to deal with, which concerns should be dealt with locally. So we're moderating the complaints that come in from employers.

So when we bring them in they are serious complaints, they're about doctors who are a danger to patients. Those tend to go to tribunal and I think what's interesting, if you look at the tribunal figures, you'll see that the hit rate, if you want to call it that or the suspension rate, is quite high. There are very few cases that we send to a tribunal that don't tend to end up in some sort of order. That to me suggests we're getting it mostly right. But what I would say strongly is they're not inappropriate complaints. They're inappropriate for the GMC, but they're absolutely genuine concerns for employers and others to deal with.

Simon Whale: When you refer them to an employer, do you track - collect data on the outcomes?

Anthony Omo: We track them and we have the data. So the employer liaison advisers I've just described have conversations on a daily basis with the senior responsible officers in the Trust across the four countries. They're talking about complaints and managing complaints locally. They're talking about concerns that are arising, those that we're dealing with, those that have been dealt with locally. So those conversations are happening on a daily basis.

Simon Whale: But it's not for you to satisfy yourselves as the GMC that the complaint was held inappropriate by the employer. You just record the outcome but you don't take a view on the outcome, is that right?

Anthony Omo: We do more than record it, because obviously if the doctor - if we think that it's not been handled properly locally and there's still a risk to patients, then we will take action. So it's a bit more than just logging it. The

conversations are real and we're saying you need to deal with this because there's a problem. We don't think we need to step in, but if you fail to deal with it then we will have to step in.

Simon Whale: Looking at GMC referrals and FTP cases as compared with NMC, there is a striking difference in terms of the percentage that result in impairment, sanction or striking off. In the NMC's case, the data we've got most recently is 2014/15. That's over 5000 total referrals of which 26 per cent resulted in impairment, sanction or striking off, compared with in the same year, I think, 2.5 per cent of GMC referrals. Is that surprising to you?

Anthony Omo: Not if you consider some of the factors at play. So we know for a fact that most of the nursing cases are not contested. Nurses walk away, they have no incentive to fight it. Doctors are quite litigious and they do fight everything. So if they're not represented, they might just walk away. They don't contest the hearings, so they will have a higher hit rate in terms of those that are struck off. Also the types of conduct that are brought before the tribunals are slightly different. So we tend to have by the very nature of what doctors do a lot of clinical, technical concerns that patients may have. We go through experts' reports, et cetera.

The nurses don't, there's a lot of conduct style issues, so there's a lot of dishonesty and things like that. So I think when you strip - break down the factors, you'll find that they're dealing with slightly different things. I think the better analogy is if you look at midwives and the rate of strike off of midwives, if you were to get that from the NMC I think you'd see they're slightly different and more akin to what we do, because of course what they do is slightly different to your general nursing practitioner.

Julia Cumberlege: Can I just ask you, do you keep a record of the names that keep coming up of surgeons or doctors who people are complaining against? Do you get an absolute monitoring exercise and then when the same names keep on coming up, can you take action?

Anthony Omo: We keep a record of all doctors who are registered and licensed and one of the records we keep is around their fitness to practise, so how many complaints have reached us. So in a sense yes, we do have a record of concerns that have been raised about every doctor that we've logged, the action we've taken, conversations we've had with employers, et cetera.

So an example, if a particular doctor keeps coming up and they're in the Trust, we would have a conversation with the responsible officer about what's going on, what needs to be done to try and get them on the right track, whether or not we need to be taking more firm action. Some

doctors have restrictions that we've imposed and we monitor those regularly to make sure they're complying with them and they can last for years while we think the doctor's a risk. So long answer, but yes, we do have if not a single record, a database of all doctors within the UK and their fitness to practise history, which we do use to inform action.

Julia Cumberlege: So it takes quite a long time for you to record all that and then to actually take some action?

Anthony Omo: No, it's recorded as they come in. So the database has all the doctors, it has all the registration details.

Julia Cumberlege: I'm thinking about previous complaints, so that you've got a history of an individual whose name keeps coming up. I thought you said it took you some time in order to take some action on that.

Anthony Omo: No, no, forgive me if that was - no, we have a database that has all doctors on it. If we get a complaint, that complaint's logged against the doctor, so you're immediately building a picture. We're of course reliant on information coming in or complaints, but as soon as it comes in we're assessing that complaint, we're looking at previous history and deciding what to do. So it isn't the case that we have to wait for a package to do something.

Julia Cumberlege: I see.

Valerie Brasse: Is that complaint logged, whether or not it goes through to fitness to practise, whether or not it drops off at the investigation stage?

Anthony Omo: Yes.

Valerie Brasse: So the first enquiry that comes in, the first mention of that doctor, that will stay on that doctor's registry, registered entry and stays for a long time?

Anthony Omo: At the moment, although we've recently introduced a policy, it stays forever, but we have a policy now which has different timetables and we can let you have this. So I think if we get an enquiry and it doesn't hit the first stage, I think it stays for 10 years. We keep a brief record of it, so we will know there has been a complaint, but we won't keep all the paperwork. So as soon as we get a complaint in, we log that, assess it.

Simon Whale: On the question of multiple complaints about one individual - and I suppose we should be clear, we've certainly met plenty of people who coincidentally in the same meeting to us have named the same doctor as someone who they've been extremely distressed by or dissatisfied with or both. If there are multiple complaints about a doctor over a reasonable

timeframe, not over many, many years but say months, does that of itself trigger an investigation, the fact that there are multiple complaints rather than just one, even if the statutory threshold doesn't necessarily get hit?

Anthony Omo: It could do but it would depend on what. So if I give you an example, [REDACTED] we received thousands of concerns about the doctors in those cases. We had to look at them and we were not going to open a case just on that basis. We need to see what the complaints are about. We receive complaints about patients who can't access particular drugs that they want, not what they need. So the threshold is quite important, because that's our statutory trigger. But if we got these complaints at the same time, we would open a case if they met that threshold. So I can't say we would disapply the threshold because we have to, because we do unfortunately get lots of little complaints which are not necessarily about doctors' fitness to practise.

The doctor could be doing the right thing, for example, not doling out drugs that shouldn't be doled out and a group of patients would complain about that practice. So we would look at what they were complaining about, not necessarily the number. The number would be a trigger and it might be the trigger to have a conversation with the responsible officer to say you may need to find out what's going on down there. We don't think we need to act just yet because it hasn't hit our threshold. Obviously if it was something more serious and patients had been harmed, a single complaint would trigger our action.

Valerie Brasse: So a group of patients complaining about a doctor's dismissive attitude...

Anthony Omo: Would be something for us to look at because...

Valerie Brasse: ...would be something to look at.

Anthony Omo: ...we do talk about communications as one of the things we look at. So yes, that would be something, because that could lead to other risks to patients.

Julia Cumberlege: I think perhaps, Cyril, do you want to...

Cyril Chantler: Can we move on?

Julia Cumberlege: Yes.

Cyril Chantler: One of the issues that's arisen over the last years is the notion of accrediting on the register for subspecialties. I believe the GMC has or is considering that but it's quite complicated. When the president of the

Royal College of Surgeons came to talk to us, he made an interesting point about the complexity of recording, validating an individual.

Because sometimes even within a speciality, say paediatric neurology, there are issues about which operation and what - and that he felt the current thinking, because no decision has been made, is that it's probably better to accredit the units and then accredit the person who works in that unit as competent to do what that unit is accredited to do. So you may have say two centres in the country doing one particular operation. Do I make myself clear?

Colin Melville: Yes.

Cyril Chantler: Do you have a view?

Colin Melville: It is complicated. We've had conversations with quite a lot of people and Derek Alderson was one of those. It is trying to get the right balance as to how you subdivide doctors and at what level of regularity and how important it is to have that recorded at a regulatory level as opposed to, for example, at an organisation or an employer level. So we have not reached a firm view just yet, we're still contemplating how we might take that forward. Our sense is that going to that level of detail would create an enormous amount of burden in terms of trying to administer, because if you've only got one or two people you've got to have a similar process whether you've got one or two or more.

I know there's potentially - and I don't know if I'm making a link that we're not ready to make, but I was just thinking in terms of the conflicts of interest part of this and how it is that a doctor declares his role in delivering a treatment. So how does an organisation decide when they've got a new treatment technique or device, whether or not they should adopt that and what the evidence for introducing it might be and what conflicts the person proposing it might have. So something around the governance that sits within an organisation around that might be helpful.

Cyril Chantler: Well yes, that's interesting because actually that was the preliminary question to what I now want to move onto, which is actually a big issue that's come up as we've met people across the country. That is potential conflicts of interest of people who may be doing things or using materials or devices with a conflict as to between the person who's provided that device and the best interests of the patient. You understand where I'm going. So it has been suggested - and I know you've carried out a consultation - that the General Medical Council on the medical register should record a register of interest. Not conflicts of interest; a register of

interest, just as parliamentarians have to do so and that is very much for the protection of the public.

Now, in the evidence you gave us you say that doctors are expected to declare a conflict of interest, that's been in good medical practice for many years. But you say you take the breach very seriously and action ranges from warning a doctor to removing a doctor from the medical register for a breach of that. Have you an example of a doctor who has been removed? Because when I looked at the case studies you gave, they seemed to basically more refer to people who weren't registered medical practitioners; they were osteopaths or acupuncturists. So do you have an example of any doctor who has been removed from the register for failing to declare a conflict of interest?

Anthony Omo: Not to hand, but I can get you that information. I'm pretty sure we have data actually. It won't be for a single...

Cyril Chantler: No.

Anthony Omo: ...but I'm pretty sure we can get that information.

Cyril Chantler: Yes, I think that would be helpful to do. So moving on, when you did the consultation, because in the evidence you've given us you support the idea of a register, as I see it, but you say it wouldn't be appropriate necessarily for the GMC to hold it and you would expect it to apply to all healthcare workers. Is that a reasonable summary of where you are?

Colin Melville: I'm going to ask Anthony. The reason I'm slightly batting this to Anthony is that when that consultation was carried out I wasn't in the GMC. So some of those conversations and things I wasn't around for, so I hope you don't mind.

Cyril Chantler: But looking at the evidence you sent us, that seemed to me that what you were saying is that you think it's an interesting thing, you're not against it, but you don't think the GMC should hold it. It perhaps ought to be held by somebody else and it should apply to all healthcare professionals.

Anthony Omo: I think in general terms, yes. I think what we're trying to say is a single register held by the GMC is part of the solution, it will provide transparency, but it won't necessarily solve the problem if you don't have employers monitoring and managing at a local level. So if I take my employer, I have to declare my interests on the website. My employer requests returns from me every time there's a regular process we're doing, they check and monitor that.

So we have no objection to a register, wherever it is held, be that GMC [or others]. I think we say that should be part of a process where employers and others - and if you take the independent sector - those organisations are responsible for maintaining, getting things on, monitoring, managing, reporting to us and then the action. Then you have that package of things and that should all be transparent and available to patients. So I think that's the gloss I would put on that.

Cyril Chantler: So when you look at the outcome of the consultation in 2016, you say the majority of respondents were against it, but the majority of the respondents by a long way were members of the profession. The number of individual members of the public who responded was very small and the majority of them were in favour of it. So it does seem to me that given the main responsibility of the General Medical Council, as set out in the 1983 Act, is the protection of the public, then maybe the views of the public should carry more weight than the views of the profession in this instance.

Anthony Omo: I would not disagree with you. I think that consultation landed at a time when the profession was in a particularly unhappy place. It was more about the register we hold and trying to make that more useful. It wasn't specifically about conflicts or register of conflicts, although it was about [enhancing the] register. As I said, I completely agree with you. I think where we are now is to say we would support the idea of more transparency around interests and conflicts of interest. We would support a mechanism that involved employers and organisations who are first line defence, in a sense, managing and monitoring that with regulatory oversight.

Cyril Chantler: But given that the Act exists right back to the 19th century to tell the public who is a registered - a medical practitioner, given the registry exists, shouldn't that information be available to the public directly? It is and you've said you want to make it more useful.

Anthony Omo: It should, the slight wrinkle is that what goes on the register is in legislation. So if we want to add things on, it can only be done on a voluntary basis, unless there was legislation...

Cyril Chantler: No, it was laid down by secondary legislation, I think.

Anthony Omo: Yes, so if we had legislation we would...

Cyril Chantler: You could do it through secondary legislation.

Anthony Omo: We could but that still requires a department, not...

Cyril Chantler: Yes, but if you asked for it, if you - would you be prepared to ask that there should be a register of the interest? Actually, I put it to you it could be quite positive in not only saying these are my interests which I must declare, as I would on Disclosure UK, but you could also say what the individual's professional clinical interest is, which might be helpful to the doctor as well as very helpful to patients. It would get back to what we were talking about, accreditation, validation and subspecialty interests. Couldn't you bring all those together to produce a register which is more useful to the public?

Anthony Omo: The short answer, yes. I think if the Review were to say to the Department - because we already have several wish lists with the Department that this is a priority - then we would be happily backing that, as I said.

Cyril Chantler: So in principle, I know I'm leading you, I'm sorry, but in principle you wouldn't be opposed to considering that the General Medical Council should enhance its register to record interests?

Anthony Omo: No, absolutely not, we would be behind that.

Julia Cumberlege: So would you consider taking this further and employing lawyers to draw up the secondary legislation so that you could just present it to parliament? Because you could do it through a private members bill, you could do it through various other mechanisms, but people need the information and they need the legal language in order to do it. I presume you employ a lot of lawyers for various reasons, so if you were to do that then we would at least start it rolling, as it were.

Anthony Omo: That may be a step slightly too far for me to commit the GMC to at this stage, but I can take that back, because this is a decision our Council would have to make; I can't make that decision. So I can say where the organisation is is we fully support that idea and principle. How we then try and achieve it, I would need some of my paymasters to agree to that. But I'm more than happy to take that suggestion back.

Julia Cumberlege: Right, because we feel that actually it would maintain an enhanced public confidence, and I just think of the register that I have to update every month, every two months and so on, when the House is not sitting in the House of Lords and we have to declare all our interests. There may not be conflicts of interest and I think Cyril's point is a very good one, that actually it would not only enhance public confidence, but it would actually ensure that the public would have access to a single source that they could interrogate.

I think what you were saying, Mr Omo, on the question that it's about employers as well and I can absolutely understand that, but that is more difficult for people, whereas if you have a general register then they can interrogate that for the particular purpose that they are seeking to find answers to.

Anthony Omo: Okay, I will certainly take that back.

Colin Melville: We have discussed that, so the issue of understanding is really important, I'm not disputing that at all. I was trying to work out in my own mind the extent to which a national register would entirely achieve. So we're not opposed to it as we've said, but - so if I can just use my own personal experience as a clinician employed in the NHS, I have memberships of a number of professional societies. The question would be in a clinical role working for the NHS, they're not conflicts of interest; they're necessary to do the job. I now move into the GMC, I still hold those professional memberships, they are declared on the website and they are now conflicts of interest.

So there is this slight challenge about the contextualisation of the conflicts of interest and how that is overseen, I think, in my mind. If it was a register of interest - and I guess you can choose what you put on it, but does it then mean that if you've not put something - so we make it clear that if you think it's a potential conflict you should declare it. But there are all those questions then about the threshold, I guess, in my mind and the role of the employer and the organisations, whether they're NHS or independent sector, in also knowing what is relevant to the person's employment across all the professions.

Cyril Chantler: There is already guidance in the National Health Service on managing conflicts of interest, which was published recently, which you've seen and indeed the General Medical Council participated in the consultation about it. But we're talking here beyond that to the whole of the healthcare system in this country, private as well as public. We're not suggesting that you should perceive what the conflicts are you register; we want a register of interests.

I would expect the GMC to issue guidance about it, but on this register you would expect it to be, if in doubt, more comprehensive, and the guidance that the parliamentarians have to follow seems to be at first sight relevant for you to consider when you give advice about that.

Julia Cumberlege: Can I just give an example? In my register I always put that I am actually a trustee of a private school. I don't see that as being a problem with the

public or anything like that, but I think if people see oh, she's got an interest in education, then we ought to discuss this with her or whatever. I think it actually enhances the whole debate that you can have and certainly for people who are going to have an operation, they may not want to go to their local area; they may want to go to somewhere quite different.

We feel that - well I feel, we haven't come up with our recommendations yet, but when the medical profession are being supported by the industry in their research and all that sort of thing, we ought to know about that. So I think it's got, as Cyril was saying, actually a much wider remit that would help patients, would help indeed clinicians. I think it is part of the open, transparent honesty that we are trying to establish in all sorts of areas.

Colin Melville: Yes, forgive me, I wasn't challenging whether there should be; I was trying to think through whether it would solve the problem, I guess. So you can have the register of interest but that does then require that other people use it in a way that helps them solve the problem. So that was all I was trying to think through in my own mind and trying to help people to understand what would count seems also quite important. I was just conversationally observing I can't recall to my fairly certain knowledge, at any time during my NHS clinical career, being asked whether I had any conflicts of interest.

When I moved into academia and into the GMC, in both cases a regular recurrent registration of conflicts, declaration of conflicts, mine are all published including things that I think may not be important but are there for people to see. So please understand, I am not disputing the intention; I was trying to just think through whether it would assist at the frontline in helping to...

Cyril Chantler: You've made a very interesting point, Professor Melville, because I've been through exactly the same. It struck me as odd that the requirements for me to declare through my academic life have been more than through my clinical life and that seems to be bizarre.

Colin Melville: But it was your employer, the university, not a national body and that's...

Cyril Chantler: Indeed it was and you can't, as you and I know, stand up and present something without actually being absolutely clear about that. But given the function of the medical register is to protect the public, given that it can be done because it's done in other areas, surely this is something we should really go back and look at again.

Colin Melville: Well as Anthony said, we will certainly take it back to our Council, but unfortunately it's not within our gift...

Cyril Chantler: We understand.

Colin Melville: ...to accede to that here today.

Cyril Chantler: This is a conversation, thank you.

Sonia Macleod: In terms of back on that theme of trust, and trust in the profession, it is very interesting what you said that one of the professions that we regard as certainly one of our most trusted professions has never had anything like that. But there have been some incidents that have certainly dented and damaged trust in our profession recently. What are you as an organisation doing to look at that potential repair?

Colin Melville: I think you've set out it's not the profession as a whole. What we're facing is a number of individuals for whom clearly a number, maybe quite a large number from the way you've been speaking, of patients who've had a very bad experience and that is clearly not satisfactory. The dilemma for us as a regulator - so we can provide guidance that sets out what we think is good practice, but we're not there on the frontline daily, inspecting how that happens.

As Anthony has already referred to, unfortunately we're only in a position to take action if we're alerted to there being a problem. We do work, as Anthony has said, with the employment liaison advisers to try and understand more locally, so to intervene at an earlier stage to try and avoid things becoming serious. Clearly there is always more work to do in the sense of the trust with the public, but as we've already said that is first and foremost our *raison d'être*.

Cyril Chantler: I think it's reasonable for us to put on record in relation to this conversation because it's being recorded, that we do acknowledge the changes that have taken place over the last years in accreditation and revalidation. Every employer has a responsible officer who is in contact with the regulator all the time. So there isn't one single process which can improve the confidence and trust, which of course is so vital because so much of what doctors do is about conscience as well as contract. So how that works together and I think much has taken place since I was on the General Medical Council to actually take that forward. So I think we should acknowledge that.

Anthony Omo: Just a couple of things we are doing with patients is we've made it much easier for complaints to be made, so you may or may not know this. You may know this, but back in 2002 you had to swear an affidavit to make a complaint to the GMC. We now accept complaints by email, phone, anonymously or online. We also have a patient liaison team that helps

complainants through our process. Often what we find, which is probably what you're finding, is patients have been round the system and no one's listened. This is the first time they've actually had someone tell their story.

Now, whether we can take it forward is a different matter, but at least we've given them the opportunity to tell us and we can act on the system, we can push the buttons on the system that they've not been able to push. So there are things we're doing, we're looking at appointing - because we do struggle to engage with patients at large. You have campaign groups and they have their topics. We're looking to appoint a senior person as a patient tsar, somebody who can take that on so we can get better engagement with patients. So we're doing quite a bit to try and engage patients inasmuch as we're engaging the profession in this, because it's got to be a joint effort.

Sonia Macleod: Do you think that patients struggle to find you, or do think they just don't...

Anthony Omo: No, not with the volume of complaints we receive. As I said, when we started, the 6000 we get which are not about us or doctors show us that there's no struggle. If you Google complain about a doctor, we're number 2 or number 3 on the search. Trusts don't come up, others don't come up, but the GMC does come up. That's fine in a sense, but they're coming to the wrong place in a lot of cases. Sorry, I didn't mean to jump in, but there's no way patients are finding it difficult to get hold of us.

Sonia Macleod: But is it navigating the system?

Anthony Omo: But navigating the system and trying to get at the heart of what has happened, why a lot of them have been harmed, that remains quite a challenge.

Julia Cumberlege: Can I say, we've spoken to hundreds and hundreds and hundreds of patients now, and what has come up very clearly is just what you were saying, that they have to fight so hard to be heard. You mentioned your patients' tsar and I presume that is an internal appointment to the GMC. Can you help us in any way to think about how we can ensure in a much wider sense, beyond the GMC, how we can actually ensure that patients are taken seriously, that their comments are responded to and that at least someone is listening? Can you think of beyond your tsar what else we could do as a nation?

Anthony Omo: We think it has to be within the institutions where the concern occurs. So we now have the senior doctors, responsible officers, but their reach is limited to doctors, for example. So one of the things we think - and we've said this in response to the past inquiry - is having a member of the board

who is responsible for seeing that complaints are heard, that complainers are heard. Now, some Trusts do have this, we've seen this in some Trusts, not all, it's not uniform.

So we think a uniform system, where a senior person who has the pull to get things done and heard is responsible for complaint handling, not left to the junior officer who probably has 1000 to deal with and can't get the doctors or the other professions to respond. But a senior member of the board whose role is to say every month, every six months, these are the complaints we've had, this is what we've done, this is what we're dealing with, this is how we're doing it and can push the things that need to be pushed within these very large organisations. So the patients have clarity, patients know if you're unhappy this is where you go.

It's quite difficult in general practice to go back to the practice and complain about the GP who you'll have to see the next week. So again, what is a mechanism outside that where you can complain and have that heard and dealt with. We think responsible officers have a role in that; the commissioners have a role in that. If they set the contract in such a way that - [unclear] obviously Colin will jump in. But if they set the contracts when they commission services that it has a complaints process that is simple and easy to understand, that does not involve you having to talk to the person you're complaining about, that will go some way to helping patients be heard.

But again, I think without that senior person check and balance, looking down the track and saying okay, what are we doing about that, are we taking it seriously. A lot of Trusts, as I said, do this and complaints are escalated up to the board - most don't. So board members are oblivious to what is going on below the financial line and the other pressures they have to deal with. That's not to suggest that they don't have a lot to do, but I think it is so serious, it is so important.

We hear this time and time again and until something like that happens, I think it will continue to happen where patients are being lost in the system and looking for who to complain. We think we get a lot of the complaints because they haven't got anywhere in the system. Unfortunately it's two, three, four years down the line and our ability to take action is quite limited at that stage. So I think certainly having that senior person on the board who is responsible for complaints and complaint handling, having a streamlined process, has got to be a start.

Julia Cumberlege: Well thank you, that's very helpful. I think I'm going to just ask my colleagues if they've got any more questions.

- Sonia Macleod: One final question, on the question of timing and latencies, a lot of the interventions we hear about have very long latencies from the point of treatment to the point of somebody realising there's an issue and complaining. As you've said you get things in quite a long time after the event often. How does your five-year rule work in applying these cases?
- Anthony Omo: The five-year rule, it actually says if it's more than five years old after the event, it shouldn't be investigated unless it's in the public interest. We interpret public interest quite low. So if it's serious harm that's been done and the patient has struggled around the system, then we will look at that.
- Julia Cumberlege: So have you got any questions for us?
- Anthony Omo: No, I don't.
- Colin Melville: No, I wondered if I could just add an addendum to what Anthony said. I was very struck by a paper, actually also by Michael West from the King's Fund, called Caring to Change. It does seem to go largely unnoticed and in that he talked about compassionate leadership. Your question about how can patients be heard is mostly in my mind about trying to understand their perspective. We're very good at defending our position; we're not always very good at understanding the other person's perspective. In his four steps of compassionate leadership, one of those things is actually called understanding, but it is about understanding their perspective.
- I do think we've potentially lost something in the way in which we practise now, that we're not very good at getting inside the mind, inside the shoes of the patient. Since I left clinical practice, I've been approached by several people who've just said can I ask your advice and it's nearly always I don't know what to do. When I ask this person in the hospital, they can't help me. So it's helping to navigate people through those processes and actually one of those resulted in a very productive conversation.
- I said well, it feels to me as if this is what you need to ask. Go and ask those questions, try and get some - and they came back and said that was really helpful. So I think some of this is about trying to understand the patient's perspective. It is a heart issue, not a mind issue and we haven't quite got that right.
- Julia Cumberlege: Well, thank you very much for that. This is what comes of inviting a professor to come and give us information.
- Colin Melville: I'm not going to live that down, am I?
- Julia Cumberlege: It's really very useful, thank you both very much.

END OF TRANSCRIPT

Session 2: UK Epilepsy and Pregnancy Register*

START OF TRANSCRIPT

Julia Cumberlege: Thank you very much indeed. Would you like to just say who you are?

Dr J. Morrow: I'm Dr Jim Morrow. I'm a neurologist - or I was a neurologist based at the Royal Victoria Hospital. I retired a few years ago because of illness, unfortunately. I'm really here because I set up – the founder and principal investigator of the UK Epilepsy and Pregnancy Register.

Julia Cumberlege: Right. Thank you very much. Could you then describe for us what you consider to be the strengths of the registry, the UK Epilepsy and Pregnancy Register? Perhaps you could tell us if you think it could be improved, how it could be improved?

Dr J. Morrow: The first thing to say about the pregnancy registry is it's a research project. It is not affiliated to any professional academic or other bodies, it's simply a research project. The strengths of the project is, and why I set it up was not because of valproate. The reason I set the UK Pregnancy Register up was, because at the time, around the mid-'90s a number of new anti-epileptic drugs were coming on stream. These drugs basically were tested on rats. I thought hm, I'm not sure about that, let's look and see if we can do better than that. Current monitoring systems really don't pick up pregnancy problems, they pick up acute adverse effects.

So at the time carbamazepine and valproate were the two main drugs that were being used. So they are really our comparators or controls. Not, as I say because we were worried about valproate, with the retrospectoscope yes you can go back, oh look that drug's been showing problems since the 1970s when it was first licensed. But actually, yes it was but these were anecdotal very small studies. Often journals that neurologists would typically read, genetic journals or neonatal journals. So carbamazepine valproate in the group of women who had epilepsy but were on no drug. Now, they're a bit of a funny group because if you're not on a drug you probably don't have epilepsy anymore.

But those three were our controls or comparators and we set it up really to look at the new drugs. Now the only way you can really assess trigenicity is to have many hundreds or preferably thousands of subjects. Because of the background risk you basically need about 300 subjects in each group to gain statistical significance. So we thought about how to do this. Basically, it was very simple, and I think registries have shown this. What we did was we asked first of all GPs, neurologists etcetera, to let us know about a

woman if she was taking any kind of anti-epileptic drug in the early stages of pregnancy. We would then contact the woman and get their written informed consent to follow up the pregnancy.

The basic thing was to follow the pregnancy up three months after the baby was born. Now, this was primarily then to look for structural abnormalities. We thought if you've got a structural abnormality you probably still know about it after three months. We go to the GP to get that information because he's the centre of all knowledge, but we have their permission to contact other doctors that were involved in their care. So the strength of the registry is it was very well supported. In fact, our main supporters at the moment are the women themselves.

We get the vast majority of our referrals from the women because they're interested, not just because of their pregnancy but because of other people's pregnancies. We recruit them through our websites and through our freephone. The registry has some 13,000 registrants, so it's really quite powerful. There was a lot of antipathy about it to start with from neurologists etcetera who really didn't think it would work and they were worried that we'd show something that would get them sued. Maybe that's true. But basically, as I said, we set up to try and get as many thousands of hundreds of patients on each drug as possible.

As I said we've kind of achieved that. We needed 300 patients on each drug to show statistical significance. We have that from most of the drugs that are around. So the strength is the numbers, and the strength is that it's got a pretty hard endpoint vis-a-vis structural abnormalities. Now as time went on, we realised the structural abnormalities weren't the end of the story. We teamed up with the University of Liverpool, Professor Gus Baker and Rebecca Bromley who you may have spoken to already, to do the longer-term follow-ups on these. There is a weakness in that group because they tend to follow-up small numbers of patients.

To my mind, we really again need large numbers to be sure of the actual incidence of neuro-developmental delay because that's the thing that's driving a lot of this at the moment because figures of 30 to 40 per cent of patients being affected, is really quite worrying. The structural abnormalities come in about 10 per cent. But again, some of these are minor, some can be corrected. I only look in retrospect, how did we miss this? Well, if you're a neurologist you might see one woman who's pregnant on a drug every year or so and if somebody has spina bifida, that happens. So it wasn't picked up.

It was not like thalidomide where the abnormalities were really unusual and became obvious very early on. This has been going on for 40/50 years with valproate. It's only really been picked up since the registries were founded. We were the first national registry. The Europeans came along and then the North Americans and the Australians and the good thing is we're all very powerful. We've got thousands of pregnancies and we all tend to agree on the outcomes.

Julia Cumberlege Right. Well, thank you very much indeed. I think it's very interesting what the history is that you were really doing a research project.

Dr J. Morrow: Yes.

Julia Cumberlege And it's now become the first national registry, you said, in the UK. But thinking about the parameters of it.

Dr J. Morrow: Yes.

Julia Cumberlege Do you think that it could be improved? Because one of the things that you've told us is about the three months after your baby is...

Dr J. Morrow: Yes, yes.

Julia Cumberlege ...born and clearly some of...

Dr J. Morrow: Yes.

Julia Cumberlege ...especially perhaps neurologically...

Dr J. Morrow: Yes.

Julia Cumberlege ...there are other issues that come. So would you think of changing the registry and perhaps making it more comprehensive?

Dr J. Morrow: Yes.

Julia Cumberlege Because as I understand it, it's voluntary.

Dr J. Morrow: Yes. It's totally voluntary, it is a research project. At its peak we were recruiting about, we reckon, about 30 per cent of all of the pregnancies in epilepsy in the UK. Which is not bad for a voluntary research project. The numbers have tailed off because doctors now think they know it all, and they don't. There are other drugs that are coming along that we have concerns about. The obvious thing is that the Yellow Card System or other marking factors don't work. The registries are very, very simple. I mean we've got one nurse part-time who essentially runs this.

So I mean it really needs to be taken over, I think, by an administrative body who will ask not just about antiepileptic drugs; there are anti-depressants and other drugs that there are suspicions about. Are these drugs safe? And doing it our way with a three-month outcome, it's a solid secure outcome. The structural abnormalities tend to indicate whether a drug is teratogenic or not and if it is then you can look further on. The other studies that are very important are neurodevelopmental ones, and I think that will be something that needs to be extended with the registry.

Vis-a-vis we've got some 1500 valproate outcomes. These kids should be assessed later on. Many of them are at school now, some further on because it's been going since 1995. It wouldn't be rocket science to try and get hold of some of the school assessments and tie it up with the drugs that people were taking. Rather than do full neuropsychological assessments which are, you know, very intense and require up to 1500... I don't know how long that would take. But I think extending it, making it more compulsory, extending it to other drugs in pregnancy and looking at longer-term outcomes, I think would be important.

Julia Cumberlege: One of the things that we've been considering and thinking about is the difference between a database...

Dr J. Morrow: Yes.

Julia Cumberlege: ...and a registry.

Dr J. Morrow: Right.

Julia Cumberlege: One of the reasons on the database is that it is - well actually I'm going to ask the expert...

Dr J. Morrow: Okay.

Julia Cumberlege: ...because he has set one up.

Dr J. Morrow: Okay.

Julia Cumberlege: Cyril, would like to - rather than I read out the definitions...

Cyril Chantler: When were you setting up this - how long ago it's about...

Dr J. Morrow: 1995 I started, yeah.

Cyril Chantler: Yeah. Well in the 1970s I was involved in setting one up for children...

Dr J. Morrow: Yes.

Cyril Chantler: ...with end-stage renal failure which is nowhere near as large as yours, but it was across Europe. Of course, it was entirely voluntary but...

Dr J. Morrow: Yes.

Cyril Chantler: ...basically every unit registered the name of the patient. We asked the patient and it was comprehensive. The world has changed hugely since then and you just said it's got to be compulsory - you just used the word. The trouble is under GDPR...

Dr J. Morrow: Yeah.

Cyril Chantler: ...you can't do that...

Dr J. Morrow: No.

Cyril Chantler: So, leaving to one side whether it should or it shouldn't, what is necessary is to try and make them as comprehensive as you possibly can. For research purposes you're absolutely spot on, but for - once you go beyond that into long term surveillance, then you do need it to be as comprehensive...

Dr J. Morrow: Yes.

Cyril Chantler: ...as it can be and you need personally identifiable information, not anonymised information.

Dr J. Morrow: Yes, yes.

Cyril Chantler: At that point, you do run against, and rightly so, the common law due to confidentiality and now the general data legislation.

Dr J. Morrow: Yes.

Cyril Chantler: So what we've been wrestling with this, and we're still working our way through it, is we are testing whether under GDPR and there are four-way - five ways you can introduce this under GDPR. One is a legitimate interest which can be mandated by a competent authority which might be the Secretary of State. That means you can create a database. That means that you register every event for an operation, the surgeon will raise that, and we've discussed with the president of the Royal College of Surgeons in public... For medicines, there are other ways of doing it through the prescribing system. That would be on the database, but it would not be a register. To create the register...

Dr J. Morrow: Yes.

Cyril Chantler: ...you can use the database, but you've got to get permission from the patient.

Dr J. Morrow: Right.

Cyril Chantler: For their name to go on the database.

Dr J. Morrow: Yes.

Cyril Chantler: But once you've got that, then you can - and you can find out who the patients are

Dr J. Morrow: Yes.

Cyril Chantler: ...by linking to the database.

Dr J. Morrow: Yes.

Cyril Chantler: So we've been distinct between the database and a registry.

Dr J. Morrow: Okay.

Cyril Chantler: So your patients are patient identified?

Dr J. Morrow: Yes, they have to be, yes.

Cyril Chantler: They have to be. So this would be a way of striving A) to make it more comprehensive and B) to be able to keep it going beyond three months. So you get long-term outcomes.

Dr J. Morrow: Mm-hm.

Cyril Chantler: So with that tortuous explanation, how do you react?

Dr J. Morrow: There's one slight difficulty, you've no idea how many women change their names. The child moves around.

Cyril Chantler: I'm going to interrupt you...

Dr J. Morrow: Yeah.

Cyril Chantler: ...it's called the NHS Number.

Dr J. Morrow: Right. Ah, right, okay. That's [unclear] I mean these things are beyond me basically. As I say, this was set up to be a very simple project and patients are identifiable and they gave their written informed consent and we put it all into a database.

Cyril Chantler: Baroness Cumberlege and I were involved. Yeah...

Dr J. Morrow: Yes.

Cyril Chantler: ...ages ago.

Dr J. Morrow: Yes.

Cyril Chantler: In the introduction of the NHS number and that was the purpose of it.

Dr J. Morrow: We haven't got that, that's not on our form you see...

[Over speaking]

Dr J. Morrow: ...that is a very good idea actually to have that because it is sometimes very difficult to trace these kids as far as time goes on.

Sonia Macleod: So how many - because I mean you do three months follow up.

Dr J. Morrow: Yes.

Sonia Macleod: What's your sort of [loss rate of being able to find [unclear]]?

Dr J. Morrow: It's not that high, it about 10 per cent perhaps. We've got pretty good at trying to track people down.

Sonia Macleod: You'll find them.

Dr J. Morrow: But as I said it really runs on a shoestring. I mean it's really one part-time nurse that literally runs the whole thing with us harping on about it and presenting it to anybody that will listen basically. To professional bodies, academic bodies et cetera, et cetera.

Julia Cumberlege: Can I ask you how your register is funded?

Dr J. Morrow: Right. We had huge difficulty getting it funded at the outset. Professional bodies – I think that bodies - grant providers were not interested in this. So we reluctantly went to the pharmaceutical companies. I was very reluctant to get money from one pharmaceutical company...GSK for example (unclear)

[Audio drops out]

Dr J. Morrow: ...were very interested in us because they thought they would [unclear]. I was not going to accept money from them unless I could get equal amounts from essentially all the drug companies, so at least it was fair. We got about £5000 from each of the drug companies.

Julia Cumberlege: Right. So, do you have some sort of governance arrangements to ensure that people respect your integrity?

Dr J. Morrow: I think people do respect our integrity, but I'm not sure we have [unclear] things laid down as to why. I think people just know that we're a group. It's monitored by a group - a multi-disciplinary group that meet every six months. They're all from around the UK obstetrician, GP, other neurologists and so on, on that who oversee it. So I mean we're all professional people and people who understand that we have no interest beyond actually trying to prove whether a drug is safe or not.

Julia Cumberlege So the university doesn't insist on that?

Dr J. Morrow: No. Well I do [unclear] we've got ethical approval to do this and that was a nightmare at the outset as well. Because at that time you had to get ethical approval from every single university in the area that we were recruiting patients from. Happily now it's multicentre ethical approval. So we have that as well.

Simon Whale: What about from clinicians themselves?. Neurologists...

Dr J. Morrow: Yes.

Simon Whale: ...GPs and so on? How willing have they proved over the years to...

Dr J. Morrow: As I said there's initial antipathy to it, but once we started to present results and say look here we are and this is what we're doing. Actually, you know what, the doctor is trying to stand out a wee bit here we need to know this, and they really have bitten into it. But I don't think you'll come across a neurologist or GP who doesn't respect what we do is and is anti it now. They actually think this is a very useful tool. So you know we've never had any problems with...

Valerie Brasse: Why were they hostile to begin with?

Dr J. Morrow: I think they thought that they if we showed something they might get sued. I'm being facetious [unclear] but I think to a degree that's come true. I mean.

[Audio drops out] The FACS charity who you will have interviewed

Dr J. Morrow: ...are quite vocal about this and a lot of their thing is getting people to blame for this, and I think in that - and I don't want to get involved with that, it's not what I'm doing. I'm trying to improve things.

Valerie Brasse: Can I ask you about the feedback arrangements of information.

Dr J. Morrow: Yes.

Valerie Brasse: what you find in the registry and the industry.

Dr J. Morrow: Yes.

Valerie Brasse: Was there any buy in, what did they think they were buying into?

Dr J. Morrow: To who?

Valerie Brasse: Industry, pharmaceutical companies.

Dr J. Morrow: In new drugs they were buying into it because people had a reluctance to prescribe [unclear] because they weren't sure. [Unclear]Happily? we were proving most of them to be safe. Now there is one that's coming out with a trigenicity? [unclear] profile very similar to valproate. The MHRA are not listening to us because we're flagging it - so I flagged this up to them and it's [we're not interested, we're going to use what we are, valproate is our subject]. It's a drug called topiramate

Cyril Chantler: Sorry...

Dr J. Morrow: [Unclear] topiramate [unclear]. This is very bad because topiramate is an anti-epileptic drug. We have about 150 outcomes on it, but it does seem to have a trigene profile at least as bad as valproate. We have just had funding to do the follow up studies, neurodevelopmental studies. Neurologists, however, happily don't use topiramate too often in epilepsy because it causes a lot of psychological effects. We've been saying about it, so its numbers for use in epilepsy are quite low, that's why I've only got 150 outcomes so far.

Where topiramate is being used though is in migraine. It is by far and away the best migraine prophylactic agent. Vis-a-vis if you're getting more than two migraines a month you take this drug on a regular basis, for three to six months. Who gets migraines? Young people, young women. You take away their headaches they get pregnant on this drug. It's worse, this drug interacts with the pill makes the pill less effective.

Valerie Brasse: Is this off-label prescribing or is it...?

Dr J. Morrow: No, it's licenced.

Simon Whale: Are you - sorry, how aware did you say prescribers are of this...?

Dr J. Morrow: Neurologists are aware to a degree because we've been presenting it to them. I've talked to the MRHA when I was there for the pregnancy prevention group about this and they said 'look we're not interested in topiramate, we are where we are valproate is what we are going to try and prevent.' I said to them well I said to them 'you'll be back in 5/10 years' time talking about this other drug.'

Simon Whale: Do you have any data on the overall prescribing volume of...

Dr J. Morrow: No. [Unclear]. I'm sure somebody could get that. But I'm a jobbing neurologist [unclear].

Cyril Chantler: Can I just ask a question about...

Julia Cumberlege: Yes, can I just follow up this - so just one thing. So have there been clinical trials on this drug?

Dr J. Morrow: The only clinical trials are at the outset where you do randomised controlled trials. But what you're interested there is the efficacy of the drug. You're interested in side effects, but you've got to bear in mind randomised controlled trials consist of. 20, 30, 40 patients. They're not allowed to get pregnant, they've got to sign a thing saying they mustn't get pregnant during this trial. So this is only after a drug gets licensed do you run into these pregnancy issues. At the moment the monitoring systems won't pick that up.

Simon Whale: Are there any warnings on the packets?

Dr J. Morrow: Well there are on some of them now I think - I should have looked at the packets before I came but the BNF would tell you whether they've...

Sonia Macleod: I've got the BNF...

Dr J. Morrow: Yes.

Sonia Macleod: ...and it does have increased risk of major congenital malformations following exposure during the first trimester.

Dr J. Morrow: In topiramate?

Sonia Macleod: Yes.

Dr J. Morrow: Well that comes from us. They've got that, you know its...

Sonia Macleod: But how – how strong that warning is to patients as well.

Dr J. Morrow: Yes. Well we can't be too strong because you've only got about 150 outcomes. As I said at the outset, we need 300 to be statistically significant.

Sonia Macleod: That presumably is major physical malformations?

Dr J. Morrow: Yes, yes

Sonia Macleod: Limited data on...

Dr J. Morrow: We've got - Rebecca Bromley has just secured, I believe, some funding to do the neurodevelopmental studies following this.

Cyril Chantler: But at the moment you haven't been able to prove this, but you are strongly...

Dr J. Morrow: Yes. It probably - I think it is statistically significant because it's a 10 per cent rate same as valproate.

Sonia Macleod: Is this - I mean have other registries in other countries...

Dr J. Morrow: Yes...

Sonia Macleod: Found the same?

Dr J. Morrow: Yes.

Sonia Macleod: And there's a consistent...

Dr J. Morrow: Yes, but then I think the numbers are always quite small because the drug hasn't been around that long. It's not it's not now widely prescribed for epilepsy because people are aware of this and they also don't like it because of the side effects.

Cyril Chantler: But as you said it is widely prescribed to people who are of the child-bearing age?

Dr J. Morrow: Yes, for migraine, usually it's a great drug for migraines.

Julia Cumberlege: But presumably it's very effective...

Dr J. Morrow: Yes.

Julia Cumberlege: ...in terms in terms of controlling epilepsy?

Dr J. Morrow: The worry here is that valproate has been around for 50 years. It has side effects, it causes weight gain, it causes hair loss and it caused thrombocytopenia drop in your platelets [unclear] and the trigenicity now is pretty well known. But we still use it. Why do we still use it? Because it's a very effective drug. The problem is it's very effective for idiopathic epilepsies. Epilepsy which has no discernible cause, and this is young people usually. It is by far and away the most effective drug for many of them. For some of them it's the only effective drug. So that's why it continues to be prescribed.

We'll never get rid of it unless we get another effective drug. The second most effective drug for these types of epilepsies is to move to topiramate.

So we could be driving people to use topiramate more often. It will be back.

Sonia Macleod: Have you seen any evidence in terms of changing prescribing practices?

Dr J. Morrow: Yes valproate prescription has gone right down.

Sonia Macleod: Has topiramate sort of kicked back up or not?

Dr J. Morrow: It's hard to tell because we've got so few on it and we don't register migraines. Yeah, and I think if we did that you would see a rise. This is speculation, I don't like to do that but...

Sonia Macleod: Would it be sensible, given there seems to be an overlap between the sorts of products used to treat epilepsy and migraine...

Dr J. Morrow: Yes.

Sonia Macleod: ...the register covered both?

Dr J. Morrow: Yes. I think it should be for all drugs that are going to be used over a period of time women can get pregnant and anti-depressants have always got a bit of suspicion about them and nobody really knows. So I mean it's not really rocket science, and as I say we do that with one part-time nurse. I'm sure the regulatory bodies could do something, make something similar.

Cyril Chantler: Does your register link to any other databases?

Dr J. Morrow: No, not really.

Cyril Chantler: So it doesn't link automatically to the Yellow Card system?

Dr J. Morrow: No. Maybe it should?

Cyril Chantler: Yes.

Dr J. Morrow: Maybe it should. I think that's why I'm saying. Outcomes could include effects of pregnancy but you have to do it slightly differently than how the Yellow Card system works where a doctor just fills it in because someone's got an acute side effect. When somebody comes along with a child who's got educational difficulties six years down the line. You don't necessarily relate to what the woman took during the pregnancy.

Cyril Chantler: No I understand.

Simon Whale: Just on your point the MHRA...

Dr J. Morrow: Yes.

Simon Whale: ...and their reaction when you told them about topiramate.

Dr J. Morrow: Yes.

Simon Whale: Does that mean as far as you're concerned, they're not - the MHRA collectively...

Dr J. Morrow: Yes.

Simon Whale: ...or just the...

Dr J. Morrow: Well it was just a meeting about the pregnancy [unclear].

Simon Whale: [Unclear].

Dr J. Morrow: I have concerns about it to start with okay? But when I said look, you're doing valproate are you thinking about other drugs? No, we're doing this because this is who we are. I went, well hold on [unclear]. I don't know.

Simon Whale: So we don't know whether - to what extent there are yellow card reports relating to topiramate?

Dr J. Morrow: I suspect there's very few if any, regarding the pregnancy outcomes. There will be quite a few about psychological effects, it can cause psychosis and things. So I really don't like it particularly But in migraine we're using it for a short period you see, and it's so good you can still use it.

Simon Whale: But in the context of pregnancy...

Dr J. Morrow: Yes.

Simon Whale: ...given that what your early data is suggesting...

Dr J. Morrow: Yes.

Simon Whale: ...is that it has similar risks to valproate.

Dr J. Morrow: Yes.

Simon Whale: Are you surprised that the MHRA said they don't want to look at it?

Dr J. Morrow: Hm, I was taken aback. I mean valproate has been around for 50 years and we've been presenting this since - we have pretty strong data since the early 2000s. We're in 2019, I mean why are we discussing this? This should have been flagged up a long, long time ago.

Sonia Macleod: Why do you think it hasn't?

- Dr J. Morrow: Well one of the problems is because valproate is such an effective drug. Although I would say - I'm speculating a little bit but the prescriptions for valproate to young women to my mind has dropped. Because neurologists who generally prescribe the drug and paediatricians as well and other people, maybe paediatricians aren't quite as aware, but certainly neurologists are very, very aware of this problem and will be reluctant to prescribe it except to certain epilepsies like juvenile myoclonic epilepsy where it is basically the only drug that will work.
- Valerie Brasse: Okay. Are you picking up in your register the impact of switching from one drug regime to another during pregnancy? Does that give you any information or not?
- Dr J. Morrow: Yeah. We've got limited information that we haven't specifically looked at. It's kind of tricky switching. I mean for structural abnormalities there's no point in switching because that's a first trimester problem. You can't switch, it's bringing down one drug and bringing up another drug that probably takes you about three months. However, neurodevelopmental stuff is probably not just the first trimester, it's all the way through. So there's an argument there to switch the drugs.
- The trouble is of course when you're switching for a period of time maybe up to three months somebody's on two drugs. Polytherapy carries more risk than monotherapy. So you're between the devil and the deep blue sea.
- Simon Whale: In terms of the drop off in valproate.
- Dr J. Morrow: Yes.
- Simon Whale: Can you tie that to the introduction of the tool kit or the pregnancy prevention programme in terms of timelines?
- Dr J. Morrow: The pregnancy prevention programme has not been run for very long. What was the other one, sorry?
- Simon Whale: The tool kit that was introduced in 2014?
- Dr J. Morrow: I think it's been falling before that. I mean we've been jumping up and down about this since the very early 2000s. I think neurologists have bitten into that. I can - you can probably get the data, I can't. I'm saying that there's been a drop off because of our registrations really for valproate. As I say we think we reflect prescription levels but it's [unclear] - it's not all of them it's a percentage of those prescriptions.
- Sonia Macleod: In terms of your registry obviously it's been running since the mid-'80s.

Dr J. Morrow: Yes, oh, mid '90s

Sonia Macleod: So - mid '90s sorry. Do you have the capacity to look at say transgenerational follow up at all?

Dr J. Morrow: How do you mean by that?

Sonia Macleod: In terms of the children who were exposed...

Dr J. Morrow: Yes.

Sonia Macleod: ...are now adults.

Dr J. Morrow: Yes.

Sonia Macleod: Their children?

Dr J. Morrow: No. But you're right, I mean ours is a very, very simple project. We made it as simple as possible. We just took data at the time and all that was, was the patient's name and the GP's name and the drugs that they were taking. Then three months afterwards we contacted the GP and we found out if there's been a problem. Now we have that data, but it's not anonymised, so we have the patient's name and we have the GP's name. So we can - and that's how we did the [unclear]. That's very interesting. That data is all there, and these kids now from 1995 are, you know...

Cyril Chantler: It seems to me you're demonstrating to us a fundamental truth and that is if you are going to do an experiment, you have to design it properly...

Dr J. Morrow: Yes.

Cyril Chantler: ...and carry it through. What you can't then do is take the information and just automatically apply it to another issue...

Dr J. Morrow: Yes.

Cyril Chantler: ...and hope that it will...

Dr J. Morrow: Yes.

Cyril Chantler: ...be valid information.

Dr J. Morrow: Yes, yes. The good thing though when we set it up, when we got the informed consent, we got the consent for long term follow up. There was no time limit. So we can do what you say? [unclear]. But you know I'm a jobbing neurologist, I'm retired now. There is a team but we've got jobs and we've got one part time nurse.

Cyril Chantler: Yes.

Dr J. Morrow: So you guys [unclear].

Cyril Chantler: Pretend you were starting again.

Dr J. Morrow: Yes.

Cyril Chantler: And you have plenipotentiary powers...

Dr J. Morrow: Yes.

Cyril Chantler: What would you say we should do in our country to set up a better system?

Dr J. Morrow: I think it would be useful to set up through the CSM, the Committee for Safety of Medicines, registry type systems to look at drugs taken by young women when they're pregnant and ask for follow up through their GP. You will pick up pretty quickly because as I say you need about 300 patients to [unclear] effect. Whether there is a trigenicity? [unclear] effect with regard to structural malformations. If there is, structural malformations are a good indicator that there may be other issues further down the line and then that drug could be followed.

There's another thing you could do. If a woman has a child on valproate with a problem, you can bet your bottom dollar if she has another child that child will also have a problem. Whereas if they have a normal child, they will probably have another normal child. So you have to ask yourself why are 10 to 20 per cent of children affected and the other 80 per cent aren't. So, to me that it's not just valproate, there's something in the gene that is making that child susceptible. If a study is done to try to identify that, then you could target the women that are going to have a problem and make sure they don't get valproate, but the rest can. Because we haven't at the moment got an alternative.

Cyril Chantler: It may not be in the child's gene it could be in the mother's.

Dr J. Morrow: Yes, yes could be or the father's.

Cyril Chantler: Because we do know that picking a drug which is also occasionally used in migraine, clopidogrel, that some people activate it faster than others do. And that could apply, I guess.

Dr J. Morrow: But genetics has moved on so much you can do a whole gene analysis. My bet would be it's in the child's gene because the child is susceptible. But what do I know about genetics?

Julia Cumberlege: Do you have any questions?

Valerie Brasse: Just one actually because of course you did say that you were looking at the new generations of drugs...

Dr J. Morrow: Yes.

Valerie Brasse: ...that came up in the 1990s. So that would be the Keppra generation?

Dr J. Morrow: Yes, it was the lamotrigine and gabapentin first of all, then it was levetiracetam, Keppra and topiramate. So they've come - yes but it's still there if you look at other drugs [unclear]

Valerie Brasse: Yeah, but those are not causing you concern and have not?

Dr J. Morrow: No. We've got good – lamotrigine is now thousands of patients on lamotrigine are pretty secure in it.

Valerie Brasse: And likewise with Keppra?

Dr J. Morrow: Yes.

Valerie Brasse: That was the one we thought that people were being diverted...

[Overlapping speech]

Dr J. Morrow: Yes [unclear] but it's not as effective against certain types of idiopathic epilepsies that Epilim is used for. That's the big problem we will not get rid of it even with the pregnancy prevention.

Sonia Macleod: Is that structural abnormalities or have those progressed on to neurodevelopmental studies as well?

Dr J. Morrow: We haven't really got the neurodevelopmental studies on those drugs, but as I said we're interested in topiramate and Rebecca's got funding to do topiramate follow up. But I think you could do it differently and probably cheaper if you'd got the kids' school records with what you suggested there.

Cyril Chantler: Well, you really have struck a chord here because and I don't mind this being videoed because I and others have been trying for years to get the schools to register the NHS number...

Dr J. Morrow: Right.

Cyril Chantler: ...for children with chronic illnesses. Particularly epilepsy, asthma and diabetes...

Dr J. Morrow: Yes.

Cyril Chantler: ...so we can do just that and so I'm very grateful to you for giving me that opinion in public, thank you.

Dr J. Morrow: We had we.. in Northern Ireland have the 11 plus. Wouldn't that be great if you could get the kids' 11 plus results? [unclear]. The trouble I have with the neurodevelopmental studies is that they're very small studies. There are only 20 or 30 patients and they're often by the same authors, and they're often recycling the patients. There is some selective bias in those studies. So, they quote these big numbers. I just - and that's driving all of this. I just worry how strong that evidence really is and the way you do it as I say is to do longer [unclear] on bigger numbers. But that's open for debate on how you do it.

I leave that up to you guys...

[Over speaking]

Julia Cumberlege: ...Dr Morrow, I'm sorry I've got to bring this to a close...

Dr J. Morrow: Okay.

Julia Cumberlege: ...because we've got another group coming in in a minute and there may be other questions that perhaps we could put to you in writing...

Dr J. Morrow: Yes, of course.

Julia Cumberlege: ...or whatever and the same for you if there are things that you think we've missed out on you'd like us to know, please let us know. But I do congratulate you, I think it's terrific what you've been doing and certainly with so many barriers in the way in terms of funding and other things. But it really has been a step forward. So thank you very much.

Dr J. Morrow: Thank you very much, thank you.

END OF TRANSCRIPT

Session 3: vCJD Trust

START OF TRANSCRIPT

- Julia Cumberlege: Perhaps then we can formally start, and you could say who you are and what you do, and why you're here.
- Elaine Motion: My name is Elaine Motion, I'm the chairman of Balfour+Manson solicitors in Edinburgh. I am a litigator and I was one of the - and remain one of the original trustees of the vCJD Trust which started - signed off in 2001 and I came on board when everything started in 2002, I think the Trust Deed was signed off. I am sure you're all very much aware of the background to the Trust itself, but it started off with the first...
- Julia Cumberlege: Shall we just introduce your colleague, so that we get it on the...
- Elaine Motion: Oh sorry, I do apologise, this is Jonathan Zimmern of Fieldfisher. Fieldfisher are the secretariat for the Trust and have been absolutely indispensable in the running of the Trust smoothly, and the compensation for victims. I'm sure we'll come on to questions like that later but specialism, certainly is something that I think was key to the Trust running as best as it could.
- Julia Cumberlege: So, Jonathan, could you just say who you are so that we've got it on the record?
- Jonathan Zimmern: Yes, certainly. My name's Jonathan Zimmern and I'm a partner at Fieldfisher solicitors. I primarily do clinical negligence work, but I've been involved as the lawyer for the Trust since I was a paralegal back in 2002 or 2003. I've been working with Elaine and her team pretty much solidly since that time.
- Julia Cumberlege: Thank you very much indeed. I just wonder if you could speak up a little bit.
- Elaine Motion: Certainly, and please let me know. If my accent causes any difficulties, I'm sure you'll let me know as well.
- Cyril Chantler: It's just, we're a bit deaf.
- Elaine Motion: Well, so am I, so I do - I get that. The Trust came about by way of cohesive meetings between representatives of 117 victims and government and a team. So, it was very much a joint project to have the Trust set up, and I think that was, and remains, absolutely key to the success of getting victims' families to actually buy into and trust what we are doing for compensation, so it was a joint effort. The Trust Deed, when it came out was incredibly complicated and, while there are huge benefits to that in giving the trustees the ability to have some discretion in cases, but also to

have the foundation to explain to victims why they could or could not do - or victims' families, more importantly - why they could or could not do things.

It was a very complicated document, but it was what the families wanted and what was agreed with the DoH at the time. As the cases developed, and as the Trust developed, it has been varied three times. It has been simplified right down to make (a) it more cost effective, and probably equally - if not more importantly, easier for the families to actually apply for and get compensation. One of the issues that we found right at the beginning - and I promise you - we spent a few days at Heathrow Airport hotel doing our first tranche of claims, and the room - probably this size - was full of files because of the amount of information that we were having to gather.

Families and - victims and their families were providing a huge amount of information - some of which was relevant to the Trust Deed, and some which was not. It took a huge amount of effort - and emotional stress - to provide that information to the Trust, and frequently we ended up having to go back to get clarification or request additional information. Of course, there were all sorts of different heads of compensation in the Trust Deed that people could qualify for and apply for. So, if you put all of that together you get a combination of emotional stress as well as a lot of cost involved in actually processing the claims.

So, after a number of years we went back to the Department of Health and we got permission to simplify the Trust. Now, going back to the Department of Health was great, but it was time-consuming as well and that brought its own problems in terms of families waiting to hear if we'd managed to vary a Trust to either - to try and give them the compensation or to simplify it. So, whilst it was a good thing in many ways, it brought - it had disadvantages in time and cost involved in actually getting those variations. So, I suppose where our starting point is, is that if there are - if any other Trusts are to be set up in future, they should be as simple as possible - but balancing fairness and making sure that the right people get the right compensation, and that's not an easy task.

Jonathan Zimmern: I think - just to add to that - I think that actually the people who are seeking compensation don't necessarily always know what it is they want. So, when - I understand that when this scheme was first put forward, the suggestion was a simple lump sum, but actually those family members of the first 117 victims fought very hard that the scheme should be more complex with more discretion and more ability to look at the individual circumstances of those who were affected. But of course, as the years ticked by it was

exactly that requirement to delve into the individual circumstances of each family that caused the most upset.

So, I just think that there is an unintended consequence to decisions made very early on that should be thought through very carefully.

Julia Cumberlege: That's very helpful and good advice, thank you very much. Could I just ask you: on your system - because I don't really understand it - you've got obviously claimants, and I do know with CJD it's quite difficult because you really only know when you have a post-mortem which of course is too late. But you have these qualifiers, and I'm not quite sure - it seems the qualifiers - members of the family or spouse or whatever - could you tell us a bit about why they qualify?

Elaine Motion: Again, I think it was part of the negotiation to include as many family members as possible in the scheme and that brought its issues in terms of identifying the qualifiers, and then trying to allocate compensation to them in - under and in terms of the scheme. I'm pretty sure it came about because of the negotiations.

Valerie Brasse: Did it have a precedent? Were you able to look elsewhere and say, oh yes that's how they did it elsewhere?

Elaine Motion: I wouldn't think so. I don't think so - do you?

Jonathan Zimmern: Well, very broadly it was - the whole scheme was based on common law principles and the *Fatal Accident Act*, and the reality was that people who have vCJD don't live for very long. So, actually the people who are most affected by the death - and the horrible, horrible death that it was - are the people who are left behind. So, the obvious example was the children or the spouse who were financially dependent on the person that died. So, very broadly, the qualifiers were designed to be a list of people who might have been impacted by the death.

One of the very difficult jobs that the trustees and we had, was that we - the way the scheme is worded is that you have to identify every qualifier who might be eligible, even if only to disregard them. A very common situation would be, you would have a - say for instance a marriage would have broken down and very acrimoniously - and the wife would tell you that the husband had nothing to do with the child who died of vCJD. But of course, the husband would then appear out of the woodwork a year later and it turned out had in fact been very heavily involved.

So, the scheme was trying to get the balance right between making sure everyone who might have been seriously impacted by the disease had a

voice, but also not - well in fact I don't think it did the balance very well - but trying to make sure that we didn't spend too many hours looking for Great-Aunt Bessie in Australia who had never been around.

Cyril Chantler: I'm just a bit confused, can you just tell me: what proportion of the cases came from children given growth hormone, and how much from bovine encephalopathy?

Elaine Motion: I don't think any...

Jonathan Zimmern: If any, it'd be one or two.

Cyril Chantler: So, one or two from the growth hormones?

Elaine Motion: Yeah, tiny, tiny proportion.

Cyril Chantler: Because that's - I'm a retired paediatrician and I can remember that being a huge issue - but that wasn't - that's not materialised?

Elaine Motion: It's not come to pass. As you know the scheme was set up for the first 250 victims, and we're on number 186 at the moment - 17 years on, which in many ways is fantastic because it's not developed in the way that was feared, but it brings its own challenges in terms of...

Cyril Chantler: So, pretty well all of your cases are from bovine spongiform encephalopathy?

Elaine Motion: Indeed.

Jonathan Zimmern: And some from blood infection from - yeah.

Julia Cumberlege: So, can I ask you - going back to the families - how wide is - in order to qualify for the compensation, does the family have to be a carer or can it be even wider than that? They might not live with the victim, as it were, but they - but how far - how wide do you go? Do you go to the in-laws who live somewhere else, or - you know, where is your - what is your criteria?

Elaine Motion: In some ways I wish I could show you some of the diagrams that we had put together of family relatives that literally - some of them would go two or three A4 pages of the family members. So, sometimes we had to go very wide indeed, so it did go beyond carers themselves because of course in terms of the Deed there was compensation for carers as well, over and above the general compensation itself. So, in fact, I think it just went down to...

Jonathan Zimmern: So, it's set out in the definition of qualifier in the Deed, but it is husband, wife, child - including step-children - siblings, parents, grand-parents,

cousins and all of that by marriage as well. So, it was a very large qualifying group for each victim.

Julia Cumberlege: So, the cousins might not even have much contact with the victims?.

Jonathan Zimmern: Absolutely, but the problem was that we had to contact the cousins in order to ask that question because, of course, some families you had the cousin who'd brought up the boy or whatever.

Simon Whale: Did it - does having that breadth of potential qualifiers give rise to greater potential for disputes and [indeed] litigation? Is that what happened?

Jonathan Zimmern: Definitely.

Elaine Motion: I don't know litigation, but certainly widened the scope for disputes and upset, because if you would - you find that they may have been a second cousin but they have nothing really to do with the victim then they wouldn't be getting any part of the compensation. So, you've contacted them and caused upset for no reason, so yes, it does. Jonathan's quite right: there wasn't a Trust that we referred to by way of - as an example or precedent - but in terms of common law - and Scottish law of course is different to English law on this in terms of fatal accidents and Section Four, but - so you can go very wide and deep in common law.

Julia Cumberlege: So, you could have cousins - say a cousin who had been in the family home for two years or something, and then emigrated to Canada or another country - would you then have to be in contact with them?

Elaine Motion: Yes, yes.

Jonathan Zimmern: So, what we would - we as the secretariat would identify those people, and then at your - the trustees' regular meetings, a decision would be taken based on the information that we had collated as to whether it was sensible to go and contact that person in Canada. But most of the time the decision was: it was appropriate to contact the family members simply because historically we had seen so many unusual and difficult family situations that it was not always appropriate to take what we were being told at face value.

Julia Cumberlege: Right, okay well other people may want to revisit this, but I'd just like to go on to the surveillance unit and how the surveillance unit interacts with the Trust and the trustees.

Elaine Motion: I - and I'm sure Jonathan will add to this - I think the surveillance unit have been absolute key as gatekeepers to the Trust in identifying and signing off individuals who have succumbed to this awful disease because, of course

as we know, there are different types of - different forms of this disease. So, they have been fantastic in terms of their involvement. Right at the beginning, Richard would come down to London and meet with the Trust and discuss and take us through and educate us because as a lawyer I can do law, but I don't know the ins and outs until I'm taught it. So, they were constantly and regularly updating us and coming down to speak to us and are absolutely key to the gatekeeping role.

Julia Cumberlege: So, what is the surveillance unit? Is it composed of academics? Economists? Clinicians? What are they doing, and who are they?

Elaine Motion: I know them as clinicians, again it's a unit at the Western General Hospital in Edinburgh that set this up. I have - to be honest I have not researched everybody who's in that unit, but I know that they are active clinicians and academics as well. I don't know, Jonathan, if you know any more?

Jonathan Zimmern: I think that's right. Researchers, clinicians and academics. They exist completely separately to the Trust, but what - the very first thing that we do when we're contacted by a family is we write to Professor Knight, who sends a very short letter back which confirms - or not - whether the person had the disease on the balance of probabilities, and whether according to their records that person lived in the UK during the requisite period of time. Without fail, by the time we contact them they are already aware of this family through the clinical pathways that the national hospital database operates within.

Julia Cumberlege: So, they have that information - what do they do with it?

Jonathan Zimmern: Well, in terms of - for the scheme they just write us that letter. That letter makes the people eligible to claim, but they have their own role in terms of research and treatment and that sort of thing.

Sonia Macleod: Can I just ask, from looking at your website it seemed that there's a slight discrepancy between the numbers, in that it said that the Trust knows about 184 individuals, but the surveillance unit lists 178. So, why is there this discrepancy, and what are those missing people, as it were?

Jonathan Zimmern: It's because the Trust operates in terms of balance of probabilities, and they operate on the much higher medical standard of - well I can't remember what it is but it's the equivalent of beyond reasonable doubt in the medical world - and as a result there will be a few people within our 186 who probably didn't have Variant CJD. But all we need is a clinical diagnosis from Edinburgh saying, balance of probabilities.

Julia Cumberlege: So, from the information that you're getting now, are there likely to be more Variant CJD cases, or are have we seen the end of it?

Elaine Motion: That's the million-dollar question I think. Before I answer that, can I just go back to the surveillance unit? I think they also link in to the activation of the care package that the families get, and I think they're key to that. So, they're sitting in the middle and everything spreads out from there.

Sonia Macleod: So, with the care package, do you have any role in terms of the care packages at all?

Elaine Motion: No.

Sonia Macleod: No, okay.

Elaine Motion: The only involvement we have now in relation to care pack - care costs, is where we have somebody who is outwith the UK and therefore cannot access the care package but are having to incur care costs. That wasn't envisaged when the Trust was put together, so that was one of the variations that we asked to be put in. So, we have the ability to pay for care outwith the UK if that's appropriate in certain circumstances. Whether there will be any more cases is, I think, the million-and-one dollar question. We know that we've had very few in the past five years.

Jonathan Zimmern: But we are - Richard Knight and the unit believes that there will be another spike, I think. The reason for that, I understand, is that a lot of the research on CJD is based on the research that one of our - your fellow trustees, David Stephens did in relation to the cannibals in Papua New Guinea, and it's the prion disease - and I don't understand the science, but they were able to demonstrate there was the hump, and then it went down, another one. So, I think people believe there may well be another spike of new victims.

Julia Cumberlege: Because you had a spike in 2000? In the year 2000? The number of deaths that occurred then, and then it went back down again. Now according to your figures, it seems very low indeed, and indeed in the last two years there haven't be any [unclear].

Jonathan Zimmern: Very low.

Elaine Motion: There's very low - one or two in that period, so of course one of the - I suspect nobody thought that we would not have been past the 250 mark by now. To be honest that was a concern in the early days when we had a lot of claims was, what was going to happen when we got to the 251st victim. Putting a line in the sand on the number of victims who would be

compensated, I think could have been a problem then. If we hit another spike, then - it's not for the trustees, we are caught by the Trust Deed but it's...

Sonia Macleod: Was there not a commitment from the government to put a second tranche of funding if you reached the 250?

Elaine Motion: There may - I would have to remind myself of that. I'm sure they probably did say that, but there's certainly - nothing has been extended in the Trust Deed to actually do that so there's nothing formal in place that confirms to us that if we have a 251st victim we will be able to run [on with the Trust Deed].

Sonia Macleod: In terms of going back to when the scheme was set up, one of the interesting things is the government position for a long time had been that they weren't going to have a scheme, and then they suddenly changed and - changed over to saying, yes we are. That was also around the same time that there was the legal case on the growth hormone cases. How important was that legal victory in terms of getting this shift towards the scheme being set up do you think?

Elaine Motion: I can't answer that with any certainty, but I know that there was a huge amount of pressure brought to bear by the families - by their lobbying and such like. So, I don't know where the balance lies in terms of it, but you have to say that the families take a huge amount of credit for actually raising the profile and bringing it to the attention of the politicians to result in this. There are many other awful things that happen where trusts and schemes are not set up, so.

Julia Cumberlege: I also think that there was a feeling at that time that there was actually going to be an epidemic - it was going to be enormous - it was going to sweep the country. It's quite interesting how the numbers have been lower than those anticipated in your Trust.

Simon Whale: One of the things I was going to ask about, is the compensation - the aim of the compensation was about psychological impact of knowing that you might be at risk of contracting it, because that's - I think I'm right in saying that's part of the compensation package. That's both interesting, because it's quite a novel thought that - I'm interested in how you identify people who aren't showing symptoms but might be at risk, given that no-one really knew what was - what the total number of affected people might be. But secondly, how important was it to families that that was included in the Trust's arrangements?

Elaine Motion: Again, because I wasn't involved in the negotiation, I can't say how much it was important at the beginning, but certainly dealing with the psychiatric claims it came through time and time again, how the families were very concerned that they get the same thing because they eat the same food as their sibling, or their husband, or their partner or such like. Therefore, recognition of that in the award - and although it wasn't specifically singled out, it would be part of the overall psychiatric award that was made. I think that was very important.

Jonathan Zimmern: It is a truly awful disease, and it happened very, very quickly. You would watch your loved one kind of disintegrate before you, both mentally and physically. Without a doubt the families were very badly affected. In terms of the practicalities, if they - once they were aware that this was part of the scheme, we would arrange for them to see psychiatrists who would prepare reports. There were different types of awards - there was a small gateway award which you got if you had a particular diagnosis, and then there were two further awards if you could demonstrate - to use the words in the Trust Deed - particular emotional or particular financial hardship.

But again, it comes back to what we were saying at the beginning: I think the families fought for it and it resulted in them getting more money as individuals, but it was by far and away the most distressing part of the application process for the families and indeed also, I think for the Trust.

Cyril Chantler: So, you very particularly used the impact earlier on. So, if there was a psychological impact on a member of the family because of the stress within the family, that would be grounds for support?

Jonathan Zimmern: For a claim, yes.

Cyril Chantler: For a claim, and following the claim, grounds for support?

Jonathan Zimmern: Not from the care package, if that's what you meant?

Sonia Macleod: From the Trust?

Elaine Motion: No, all the Trust could do, would be to award compensation and they could then decide if they wished to obtain support from that.

Cyril Chantler: But you would get compensation because of the psychological impact?

Jonathan Zimmern: Yes.

Elaine Motion: Yes, so there were two tranches. First was £5,000. Now, there were 410 applications for the £5,000, and 405 - 404 were actually paid out. When it got on to the particular emotional hardship, that was a very - it was a very

difficult thing for the family members to go through and of course different experts would be used. There wasn't a panel of experts that were identified that people went to, so you got - the trustees and the victims' families got a huge variety of types of report coming through which raised its own issues in terms of that. But there were 217 particular emotional hardship claims, and 146 of those were paid. So, we didn't - because it was particular, it had to be out of the norm and therefore how do you work out what the norm is...

Cyril Chantler: So just because you're a member of a family that's been impacted by this awful disease, you wouldn't necessarily get compensation. You'd have to show that you'd actually suffered because of it?

Elaine Motion: Yes.

Jonathan Zimmern: In 2010, that was - when we petitioned the Department of Health to simplify the scheme - that was one of the things that we wanted to do most of all, which was remove that aspect of the claim process because it was so distressing, so time-consuming.

Cyril Chantler: So, what is the present situation? If I have a relative who - say my sister's been affected - and I've grown up in a family with this thing, then I come along now saying, I'm suffering from stress disorder which has been going on for years. Would I get compensation for that?

Elaine Motion: You wouldn't get compensation for that head by itself. What we have now is a one-off payment of £130,000 and we review it every year to bring it up with inflation - £135,000 I should say. We've also got a payment of £40,000, as experience for the family as well as a £5,000 care...

Cyril Chantler: So, I wouldn't directly have a claim?

Elaine Motion: You wouldn't, no.

Jonathan Zimmern: You would have a claim on a portion of that pot.

Cyril Chantler: But that would have to be sorted out within the family?

Elaine Motion: Yes, and that brings its own challenges.

Jonathan Zimmern: Well, no we would - the trustee - we would hear - we would get the relevant information from the family and then the trustees would make a decision as to how it should be distributed.

Elaine Motion: But sometimes it's agreed, sometimes families come to us and say, we have agreed compensation should be divided up, x, y and z and sometimes it is...

- Cyril Chantler: Thank you very much.
- Sonia Macleod: The initial - if we go back to pre-2010 - the initial £5,000 psychiatric injury for qualifying family - that's more generous than you would normally get in common law.
- Elaine Motion: Yes.
- Sonia Macleod: Was - how did that come about in terms of - usually as you say this scheme is designed looking at the *Fatal Accidents Act*. Why was that provision there in the first place? Was it family pressure or was it...?
- Jonathan Zimmern: So, I think you're right, it is more generous than common law. But the concept of getting psychiatric injury as a result of losing a loved one is still part of common law. So, I think - my understanding was that the heads of damage were broadly based on common law but deliberately more generous because, I think, the horrible nature of the disease.
- Elaine Motion: Also, the right to actually sue still remains down to the families as well, so if you're going to put a scheme together then you want it to be a bit more generous than the common law.
- Valerie Brasse: Can I ask about the care package, and how that worked and how it's funded? What I understood - I don't know if I've got this completely wrong - but health and social services would be doing whatever they do anyway in relation to the treatment of those affected. Now, I appreciate there's a very short time span. Are you saying that if they needed extra, it would be funded by the Department and through the Trust that would call on the local healthcare provider to top-up what they would normally do? How does it work?
- Elaine Motion: The Trust generally didn't have much involvement in the care package at all. The only rare occasions that we would get involved would be if we were getting families making application and highlighting that they - remember we have - we actually had living victims as well which wasn't anticipated by the Trust Deed at all. So, you would sometimes have families coming saying, well, our - the individual is still alive but we're not getting the care package. Then we might write a letter, but that's as much as we would do. The - what was given and what was allocated and the timing of that was outwith the Trust's [unclear].
- Valerie Brasse: So, there was no top-up of care packages?
- Elaine Motion: No.

Jonathan Zimmern: No, and in fact the Trust Deed specifically prohibits any payment in relation to care after March 2001 because it was envisaged that from that date, the care package operating in the background would be fully up and running for every single victim - which of course it wasn't. We often got requests for top-ups which the Trust Deed would not allow the trustees to pay.

Sonia Macleod: So, where there should have been provision there wasn't?

Jonathan Zimmern: Well, not adequate provision according to the families.

Sonia Macleod: In terms of, you said you never expected having living victims - do you have any living victims at the moment?

Elaine Motion: No, no we don't.

Jonathan Zimmern: No. They were quite unusual - the living victims, they - I think two of them - possibly the only two, had got the experimental drug - which I can't remember the name of. It worked insofar as it seemed to fix the disease at a given moment in time, but given how awful the disease was, I'm not sure that was necessarily a good thing.

Elaine Motion: But the trustees actually - two or three of us - went to visit each of the living victims just to try and understand what life on the ground was like. I can tell you it was awful, just awful.

Jonathan Zimmern: [Unclear].

Elaine Motion: Yes, and also one of the other - and I know the Trust Deed wonderfully, actually allowed - gave us the power, but we ended up actually buying a property so that one of the victims could live in it until he passed. So, again, the things we didn't expect to have to do, but fortunately the Trust Deed had been drafted in as wide a way to give the trustees discretion to do that, and we did it. So, I think I was on the name for an insurance policy for a house that I never saw until it was ultimately sold. So, all of these different things - it's the unexpected that actually causes more difficulty than the expected. So, allowing some flexibility in any scheme I think is essential.

Simon Whale: The scheme's quite - it's clearly been quite a complex scheme to administer. Is that why the administrative costs are quite high? Simply the complexity of it compared to say the Thalidomide work?

Jonathan Zimmern: Very much so, and one of the concerns that we all have had for some years now, is that as the numbers of claims reduce, there is still a base level of administrative costs that continue. It's roughly £30,000 to £40,000 a year just to keep it ticking over. Then there are tax payments; annual audits;

there's a very large 10-year tax payment every 10 years because it's a discretionary Trust. All of these things need to be paid, even when people are not making any claims. That, I think, is definitely something to consider when thinking about whether this is an appropriate mechanism.

Julia Cumberlege: As I understand it, the compensation scheme was set up by the Department of Health. So, do you think there is merit at all in having independent charities, or something of that nature that actually would be perhaps a bit more sensitive to costs, and things like that?

Elaine Motion: I think what you need when you're dealing with compensation is expertise in that area. As I probably - I said at the start, Charles Russell, who were the initial solicitors who dealt with everything, have the experience in trusts and administration and accountancy - which again, is essential in terms of advising us of the tax payments - they are huge in terms of the discretionary trust. I think the last one was about £4 million we had to pay in terms of that, but also then Charles Russell and then onto Fieldfisher had the expertise in how to handle compensation, and how to work with individuals; how to have the soft skills.

I know that sometimes lawyers are not perceived in the best of lights, but one of the real skills of a very good personal injury lawyer is - are the soft skills. The ability to actually be more of a social worker than a lawyer to get the information you need. So, I'm very strongly of the view that you need that expertise to actually draw the information. This Trust started off with lots victims either coming themselves or going through solicitors, and we'd get a variety of quality of information coming through. In the latter years, Fieldfisher have been basically funnelling all the information, and have been able to get that much more effectively and with much less distress - and actually reduce costs than doing it any other way.

Julia Cumberlege: So, is this Trust still paying lawyers?

Elaine Motion: Yes, we still pay - and as I say - Jonathan says it costs about £40,000 a year to keep the Trust turning over because of course, in theory, no individual claim will actually close, because you never know when a qualifier might actually come forward. We have claims that opened in 2002 that are still potentially live claims, and that's one of the practical difficulties of not putting our closure date. You'll see in the Trust Deed that the date of the period is 80 years past the date of the first Trust - long after I'll have fled this mortal coil. So, the Trust has to effectively remain open for those potential claimants.

Jonathan Zimmern: The costs have undoubtedly been higher than perhaps envisaged, because the scheme is very complicated. You could of course create a simpler scheme, but this goes back to the very first point we were discussing, that - my understanding was that a very simple scheme was put forward and very, very firmly rejected by the people for whom the scheme was designed. If you want a complex scheme that's tailored to each individual circumstance, you need - it costs money.

Even though there have only been 186 victims - and I'm afraid I don't have the exact numbers - there have been hundreds of qualifiers, 800, 900 plus qualifiers, all of whom have a file; all of whom have - there's been a meeting about; all of whom we've had to collate individual information about in order to make a decision.

Elaine Motion: Many of them of have had their own lawyers who have been able to put their costs to the Trust for payment.

Sonia Macleod: One of the things I'm interested in: you said that, obviously as a discretionary Trust, the Trust pays tax. That sits in contrast to, say the Thalidomide Trust, which the government has always put on a tax-neutral footing. Was there ever any discussion about that - about shifting the Trust onto the tax-neutral footing?

Elaine Motion: I'm sorry, I can't answer that. I can try and find out if you'd like, but it's not something I was involved in.

Jonathan Zimmern: I don't know whether it's the same point, but the Trust is a discretionary Trust that's entirely separate from the government. Over the years, that has actually proved a good thing, because things like *Freedom of Information Act* requests have been made a lot; people have attempted to judicially review the Trust. There's always been these allegations that it's - the Trust's in the government's back pocket, and because it's so separate, they have been very easy to - to say that well, that's not right, it's completely independent. What I don't know, is whether you have to have the discretionary Trust and all of the costs that come with it in order to have that distance.

Julia Cumberlege: So, we've got more - no more questions of you at the moment. We may send you some follow-up questions, possibly. Have you any questions for us?

Elaine Motion: I don't have any questions. If you would like the statistics of the claims made and the numbers, then we're very happy to send you down a little schedule of that, if that would be of any assistance to you.

Valerie Brasse: That's not too [unclear].

Jonathan Zimmern: We can send what we can, and you can always ask if you want more detail.

Julia Cumberlege: Thank you so much.

END OF TRANSCRIPT

19th March 2019

Session 1: Thalidomide Trust

START OF TRANSCRIPT

Julia Cumberlege: I'm Julia Cumberlege and I've been asked to chair this Review by Jeremy Hunt before he left. I didn't know he was going; he didn't know he was going, but there you go. On my left is Sir Cyril Chantler, and Cyril is the Vice Chairman of the three-person panel. Then on my right is Simon Whale who is the third person on the panel. He looks particularly at communications and how we work with patient groups and so on. Then on Simon's right is Doctor Valerie Brasse. She's our Secretary to the Review. On Cyril's left is Doctor Sonia Macleod who is our senior researcher, so that's it. Then we've got other people in the room who are just helping us run the event as it were. So, anything you want to ask me before [unclear]?

Deborah Jack: No.

Julia Cumberlege: No. Right. Okay. So, if you would like to say who you are and why you're here, that would be very helpful. Then perhaps we could ask a few questions.

Deborah Jack: Yes.

Julia Cumberlege: Okay.

Deborah Jack: So, I'm Deborah Jack, and I'm the Executive Director of the Thalidomide Trust. I want to preface whatever I say by saying I don't have a good knowledge of the impact of the particular drugs you're looking at and the effect they have or the needs of the individuals affected, but I'm aware that there are patient groups who have given a lot of evidence on that. I'm here because we were invited to come and give evidence, and I guess to share our experience as the charity supporting a defined group of individuals who were born with birth defects. Hopefully there is some learning that will be useful to you.

Julia Cumberlege: Yes, well, thank you very much. Can I just ask, have you any conflicts of interest? Personal conflicts of interest?.

Deborah Jack: No, none.

Julia Cumberlege: No. Okay, well, thank you for that. So, perhaps you tell us a bit more about the Trust. How it works, and how it's changed over the years because of course it's been going a very long time now.

Deborah Jack: Yes. So, I suppose I'm sure you've probably got some knowledge of Thalidomide and the Thalidomide Trust, but just to say the charity was established in 1973. That was part of the original compensation package that was agreed with the Distillers Company who distributed the drug in the UK. We currently support 463 individuals who are affected by Thalidomide and it's worth saying that they're now - we were originally the Thalidomide Children's Trust back when we were set up, but all our beneficiaries are now aged between 53 and 60. In fact, in January the first of our beneficiaries celebrated their 60th birthday which I think exceeded any expectations anyone had when they were born.

I think an interesting fact about Thalidomide is there isn't one pattern of damage. The way the drug affected the foetus was it damaged the part that was growing when the mother took the drug. So, we've got quite a range of disabilities within our beneficiary group. There are some that are quite common like upper limb damage, which affects 85 per cent of the beneficiaries, but there is a whole range of damage to internal organs, sensory impairment, facial damage, that is really - and cognitive impairment in some cases. So, we're not talking about just one known model and one set of needs. Many of the beneficiaries have got quite complex needs that have actually become more complex as they've become older.

The Trust was originally set up to administer the grants that were given in compensation to the individuals but over time the role of the Trust has evolved and has become more and more focused on non-financial support to beneficiaries. Also, over time there has been an increase in the number of beneficiaries who have actually engaged with the charity. So, often it was just that people would receive their money every year, say thank you very much, and there was very little contact with the Trust. Now we have quite a lot of ongoing contact. So, in the last year 75 per cent of beneficiaries had some contact with the Trust in terms of utilising the support and services that we provide.

So - a bit about the Trust, we've got 16 staff. Around half of them are part time staff. They've got a range of skills and backgrounds. So, we've got doctors, trained nurses, people with a background in social work. So, quite a broad range of skills. We also have a skill base board of trustees who are all volunteers. They come with a range of backgrounds including medical, legal, financial, research, that they bring and very much when we're looking

at what we want from our trustees we're looking ahead to what the needs of the charity will be going forward and therefore trying to recruit trustees who have the skills that can help us with that task. We provide a mixture of - I suppose reactive and proactive support.

So, a lot of beneficiaries come to us with specific needs they want help with, but also increasingly over the last five years we've been more proactive in reaching out to the beneficiaries we may not have had a lot of a contact with in the past. I think the support we provide is very much shaped by the needs of beneficiaries and has changed a lot over time. I think something that's worth bearing in mind is that the beneficiaries were born with original Thalidomide damage but over time there has been consequential damage.

So, if you for example have damage to your upper limbs you might use your bodies in ways that they were never designed for, perhaps using your lower limbs to do things that people would traditionally use their arms for or their teeth, for example. As a result, they then develop consequential health problems from the way they've used their bodies. What we're now seeing going into the mix is the impact of normal health issues involved with ageing and how they interact with both the primary damage and the consequential damage. So, the needs seem to be becoming more and more complex for our beneficiaries. So, that's a bit about the background.

In terms of how we actually support them, we do that in a range of different ways. One of the things we've been doing now for just over two years is what we call holistic needs assessments, or HNAs. What that is, is a trained member of staff will go out and visit every beneficiary in their home and spend some time with them, just really understanding what's going on in their life, what the challenges they're facing are, what their health issues are, how they feel the Trust could support them. What comes out of those HNAs is both an action plan for the individual, which is what we can do to help them, but also we're gathering really useful data on what problems are faced across the community, what their worries are about the future.

That information therefore feeds into us planning what we want to be thinking about for the future. We also have a programme of beneficiary events where we bring beneficiaries together. Those are a combination of just general events, so they may be in a locality where we invite people to get together, and we actually ask them for feedback on what issues they'd like covered. We also have some events that are around specific issues. So, we recently had an event called Fit for the Future, which was born out of beneficiaries telling us that they were worried about their weight, about

their fitness as they got older, and their flexibility. Living with disabilities they found it really hard to exercise, perhaps foods that are healthy are the foods that are more difficult to prepare.

So, what we did was put together events which focused on both diet and fitness and had very practical sessions. Actually, more recently we did an event called Future Money Matters which came out of feedback from beneficiaries that they were worried about their long-term financial planning. Particularly they were worried that as their needs increased that they will struggle financially. So, there were a lot of different sessions there, everything for almost retirement planning to thinking about their long-term costs, but also investments for those that have some money now but are worried about how it will benefit them in the future.

Also, external lending because some of them are now getting to the point where they're no longer able to live in the homes they're in now. They can see that in a few years they may have to move to a single storey building or have their homes adapted. They know that they've either got to save money or borrow money to be able to do that. So, the events we do are very much dictated by what we're hearing they want from us and we just try and tailor the support we give. I think 10 years ago worries about money probably wouldn't have been top of the list but they are now. I guess in time the sort of topics they want to talk about will change. We have a whole team of - so, a health and wellbeing team that provide health and wellbeing support. That's mainly by the phone.

So, we have two practising GPs who work for us part time, but we have a team with a range of knowledge on things like benefits, aids and adaptations, mobility, adapted cars, all the different things that might help. So, our beneficiaries can then come to us and we can give them advice and support on what solutions might be. One of the things we also try and do is share solutions that beneficiaries have found. So, sometimes when you go and visit a beneficiary in their home you find out a piece of equipment that is really useful and easy to use, and sometimes they just come up with their own bespoke solutions. Often, we'll take photos or ask them about it, and then that information can then be shared with other beneficiaries who are facing similar challenges, really.

I think the other thing worth saying is that increasingly we are helping beneficiaries to navigate the NHS. Sometimes they really struggle to provide the services and support that they need when routine help isn't available. So, one of the things we do is provide advice to them on what services are available, and sometimes we'll write letters, say to their GP, encouraging them to make a referral, or letters to a specialist they've been

referred to. Also, with social care there is similar support that we provide in terms of letting people know what sort of services they should be entitled to.

Also, a lot of beneficiaries employ carers. They receive direct payments, so they employ personal assistants. That can be quite a big step, employing someone, knowing how to go about it and what the pitfalls are. So, we provide advice and resources just giving them tips of how to do it, what help is available, that sort of - and always we give case studies of how it's worked for other beneficiaries to try and help them with that. I mentioned financial guidance and advice, and that's something that we do provide on an ongoing basis. So, I think like any group of 460 odd people there are some people who manage their money really well and there are other people who really struggle to manage their money.

Traditionally what the Trust has done is given people annual grants. So, at two points in the year they receive their grant. Then it's up to them to manage that money to meet their needs throughout the year and in the longer term. We've worked with some people who were finding it difficult to manage their money, and for example for some people we provide the money on a monthly basis because they find that's easier to help them manage, or we hold some money back for big one-off costs.

So, it's just been there to not just look at their physical health and their emotional health, which is something I haven't mentioned, but there has been an increased emphasis on - because I think as people lose their independence and functionality, often what comes with that is a decline in their emotional and mental wellbeing. So, we provide emotional support through the staff team but also, we have a peer support service where our beneficiaries are trained to support each other if they're having emotional difficulties. So, there is quite a range of personal support from the staff to the beneficiaries and we also produce a lot of written information, factsheets, advice on different topics.

We have a website which is a central depository for all that information. We do try and encourage beneficiaries to share information via the website as well, because it's a way of enabling them to share communication. It - a lot of the content on the website is generated by the beneficiaries themselves, them sharing their stories or experiences, and providing information they think would be helpful to others. We do advocacy, so we advocate on behalf of beneficiaries and that can be across a range of things, whether it's because they're not receiving the healthcare and support that they need or if benefits assessments don't seem to be coming

out with the right outcome we can often step in if beneficiaries don't feel confident to do that themselves.

As well as advocating for individuals we also do advocacy on community as a whole. So, a couple of examples of where that is a role we've played recently, one was in terms of - we were finding that beneficiaries, when they came to be assessed for social care, the money they received from the Trust was being treated as capital if they hadn't spent it in the year, or income. Therefore, they were losing out on the care they were entitled to and on some means tested benefits as well. So, we got into negotiation with the Department of Health and Social Care and the DWP and got changes to legislation so that the money that the beneficiaries receive from the Trust is not taken into account when assessing their eligibility to other services and support.

So, the discussions with policy makers are always really useful even if you don't get the immediate answer you want, it can be really helpful in thinking about how you can best support your beneficiary group. Other things - sorry, I'm going on quite a lot here. We're developing a network of clinical specialists across the country. Because Thalidomide is quite a rare condition and what people found is if they for example, I don't know, needed a hip replacement or a shoulder replacement and they were just referred to their local orthopaedic hospital, often people were completely fazed by it and often they were advised that surgery wasn't indicated or that they didn't feel confident doing surgery.

What we have now identified is clinicians around the country who have seen a number of beneficiaries who have a good understanding of Thalidomide and who are willing to accept referrals and understand that you have to vary the procedures to take into account their needs. So, we're beginning to build that network up across the UK. I think the final thing in terms of the services and support we provide is just we do a small amount of targeted research. We do research only into issues that are specifically of relevance to our beneficiaries.

So, an example, one of the projects we're working on at the moment is around cardiovascular risk. So, as individuals move into their fifties, often one of their highest risk factors is cardiovascular disease or incidence, so strokes and heart attack. The way most people have their risk assessed is through blood pressure taken in the arm. If you don't have arms, then it can make it very difficult to assess cardiovascular risk. The default position for a lot of people was saying well, just take statins, better to be safe than sorry. I think our group more than any are very reluctant to take drugs when there is no good reason to take them.

So, one of the things that we're looking at is, are there other reliable ways of assessing cardiovascular risk in the absence of upper limbs? Obviously, that's very relevant to a lot of our beneficiaries, but it will have broader benefit because people lose limbs in all sorts of other situations as well. So, that's a project we're doing with the Royal National Orthopaedic Hospital at the moment, just to give you an example. Another couple of points are, I mean, first of all with such a small beneficiary group user involvement is quite critical to the way that we operate as a charity and central to our ethos.

We have what we call the National Advisory Council, and that's a discretionary body which allows our trustees and staff to get advice from beneficiaries. So, there are elections every year and all beneficiaries are able to vote. People - a bit like normal elections, if people want to stand, they put their names forward and have a manifesto, and then there's an election. So, we have at any one time 12 beneficiaries who form our National Advisory Council. They come to all our trustee meetings, when we've got big new projects, we involve them in how we design and develop the project. Their advice on an ongoing basis is really useful.

We also look at ways of involving beneficiaries as volunteers. So, I mentioned for example the peer emotional support service that we provide. They help in all sorts of different ways. So, we've got another role which we call our Connect Volunteers which is where one of the beneficiaries will gather information on local services in any one area so that those are available and can be shared with beneficiaries in that part of the country. So, it can be everything from say, massage, which is really important for pain relief, and pain is one of the biggest issues faced by beneficiaries. Again, a bit like I said with orthopaedic surgeons, people are quite reluctant just to find a masseur in the Yellow Pages and go along if they don't feel they'll understand their bodies and how they're different.

So, recommendations from beneficiaries, pulling together information. So, that's just an example, but because we know our beneficiaries well, because we get out and meet them, we often discover skills they have that they're willing to share. So, we recently rebranded. One of our beneficiaries was a graphic designer and was complaining how old fashioned all the stuff that came from the Trust was. So, we said, great, come up with a new logo and branding. That's what they did. Another beneficiary used to work on benefits appeals and has now taken retirement, so we use him to provide advice to other beneficiaries and he's done some training with the staff on it.

So, it is very much a community. There's a real willingness to support and help each other. We try and harness that wherever we can. A final few points, we do have one dedicated member of staff who looks specifically after our beneficiaries who lack capacity. They're a small group, we only have 14, but they have got incredibly complex needs. The fact they receive quite a lot of money from the Trust, we want to make sure that there's the right support to ensure that those resources are being used to their benefit. They're probably more open to exploitation and abuse than our other beneficiaries, but also they often have quite complex needs. So, we do have someone whose job is specifically to look after them.

We also make it a point to draw on external expertise and services and support that's available. So, we do a lot of signposting to other services rather than trying to recreate services that are already out there. I just - we wouldn't have the resources to meet every single need of all our beneficiaries. So, an important part of our role is keeping in touch with what else is out there. I suppose the final point is, as a charity we have to think in the longer term about how we wind down the charity, however we eventually close the charity when beneficiaries aren't there.

There aren't many charities I think that have that particular challenge. I think one of the issues will be the number of beneficiaries will reduce, but their needs are likely to increase. So, I think that the Trust will just have to keep on developing and reinventing itself to make sure it's meeting the needs of its beneficiaries.

Julia Cumberlege: Well, thank you very much.

Deborah Jack: So, I hope that was helpful.

Julia Cumberlege: Extremely helpful. I must say, I think the way the Trust is so sensitive to the needs of their beneficiaries is really very, very impressive. Congratulations...

Deborah Jack: Thank you.

Julia Cumberlege: ...on all of that, and the fact that you've got 75 per cent of your beneficiaries in constant communication with the Trust, that's really very, very good indeed and I love your events.

[Laughter]

Julia Cumberlege: It's really - can I ask you, in terms of - when I was involved in the department with the beneficiaries, your beneficiaries, one of the things I did do was meet the children...

Deborah Jack: Yes.

Julia Cumberlege: ...of the beneficiaries. I wondered if there's any sort of dynamics, interests, whatever, between the children of beneficiaries and the beneficiary him or herself?

Deborah Jack: So between children across the board, or between the children and the...

Julia Cumberlege: Well, when I met the - your beneficiaries, and I think in those days we called them victims...

Deborah Jack: Yes.

Julia Cumberlege: ...I think your term is much better. They were being pushed by their children. They were in wheelchairs and their children were pushing them. It struck me that I had never thought of this next generation. I wondered if there was anything to do with - that you've come across with the children of the beneficiaries, whether they're interested in the funding systems, whether they have any influence over the beneficiaries. I just wondered if there were any dynamics we ought to be aware of.

Deborah Jack: Yes. I mean, I think that's a really interesting question. I think a lot of children took on elements of a caring role for their parents.

Julia Cumberlege: Yes.

Deborah Jack: I think as the access to electric wheelchairs, mobility scooters, other things have come in, and lots of gadgets and gizmos that mean people can dress themselves and do things for themselves, there has perhaps been less of that dependence. People will often say, I dress in clothes that are easy to wear. If I've got - I want to put a bit of jewellery on or do buttons up, I always need help from a family member or someone to do it. I think the children have supported beneficiaries in lots of different ways, and one of the bits of feedback we've had quite a lot is that as they've grown up and left home.

If you think of the age of our beneficiaries, a lot of them, their children have left home, gone to university, and they suddenly realise all the small things that they did for them just to make their life go a bit more smoothly. That has resulted in them often having to get paid care in to fill some of those gaps. I think there is - it's quite complex family dynamics in some cases. I think some beneficiaries have given quite a lot of financial support to their children, partly maybe in recognition of the help they've had, partly for some feeling guilty that they couldn't be the parent they wanted to be

because they couldn't play football with their child. So, there are some quite complex relationships and financial dependencies there.

Certainly one of the issues that's come through quite strongly from our beneficiaries is worrying about when they're not around, about their families, and feeling that if they hadn't been born with Thalidomide damage and they'd been able to work, perhaps in better jobs, they would have had more financial security to help their children. It really varies across the community. One thing I was going to mention, I don't know if you're aware of the Thalidomide Society. So, the Thalidomide Society was set up actually in advance of the Thalidomide Trust and it was very much an organisation for the parents of thalidomide children. It's kept going to this day.

Its focus is very much on the social element and networking, and also on the history of Thalidomide and they've done some amazing work on capturing oral histories of beneficiaries. They have events every year and some children come along and they then meet each other and there's an element of peer support and networking. So, that does give them an opportunity to get involved.

Julia Cumberlege: Can I just ask you, you are still getting new applications, aren't you...

Deborah Jack: We are.

Julia Cumberlege: ...for the Trust? Presumably they're reducing in numbers, but I understand sometimes you get a spike, because you did in 2010 when the government came in with some funding for it.

Deborah Jack: *Call the Midwife*, when they did the Thalidomide storyline created another mini spike as well.

Julia Cumberlege: Also, I think *Call the Midwife*...

Deborah Jack: Yeah.

Julia Cumberlege: ...had an impact, yes. So, I'm just wondering, how do you assess now people who are coming forward who you would have expected to have come forward in the past? Now they come forward perhaps because maybe they've only just heard about the financial support or something like that. Then you have to assess them, and that must be very difficult.

Deborah Jack: Yeah. We have a very robust evidence-based model for assessing new claimants that come in. I mean, very quickly you can discount some people because they're the wrong age, for example. People in their thirties might approach and say, I think I've got Thalidomide damage, and you know that

can't be the case. What we do is we've got a lot of evidence of what the pattern of Thalidomide damage was. We've worked with other countries in sharing evidence. We had a big event with the WHO in 2014 and from that we pulled together the evidence into an algorithm where you can look at the pattern of damage that someone has and assess the likelihood that it's Thalidomide embryopathy.

In parallel, we look at what evidence there is that their mother ingested the drug. In very rare cases you can actually see the mother's medical records and see that she was prescribed Distaval. What's more likely is it's a witness statement from a mother or a family member telling you that.

Julia Cumberlege: But the parents might be dead by now.

Deborah Jack: Yes, and that - I mean, going back a step to why people are only applying now, I think the two main reasons that people are still coming forward, one is that their Thalidomide damage was quite minor and so for many years they were able to live completely independently, they didn't think they needed support. I mean, an example of someone recently, someone who was born without thumbs, but years of just twisting your arms in different ways, they then developed chronic pain. They had to give up work, and at that point they decided, I've always known I was Thalidomide, I wonder if there's any help available.

The other, perhaps sadder, scenario is where they know that while their parents are alive, they couldn't possibly address the issue because it's such a thorny issue within the family. So, they actually wait for their parents to pass away before coming forward. Of course, that makes it difficult, because it then makes the evidence part of ingestion in particular far more difficult to come by. We have a claims committee. It's very formal, lawyers, doctors, they look at all the evidence and then they have to make a decision on the balance of probability as to whether or not someone was Thalidomide affected.

So, over the last five years we've had between 25 and 45 applications each year. On the whole we accept probably two individuals each year. So, it's a small number that reach the evidential threshold. We have to - those decisions are life changing, to be accepted as a beneficiary. So, our trustees take them very seriously and really ensure that evidence is scrutinised, more evidence is asked for if necessary, so we make the best possible decision.

Julia Cumberlege: So, there is an informal right of appeal?

Deborah Jack: There isn't really, no. I mean, if people apply, they're assessed. Occasionally people have employed lawyers on a no win, no fee basis and come back. I think the view is, because we have quite a structured process for assessing the evidence, unless they've got new evidence, they're only going to have the same conclusion because it is quite a, I suppose, clear process for assessing the damage.

Sonia Macleod: You said about the algorithm. Have there been presumably changes in the way Thalidomide damage has been diagnosed since [first] sixties and seventies to now?

Deborah Jack: Yeah. Not vastly, but there is improved knowledge, particularly of the - I think the non-visible elements of the Thalidomide damage. So, for example one I guess of the most obvious ones is if someone had damage to their reproductive organs, that may not have been obvious when they were assessed as a 10 year old, but actually later when they go to try and start a family and are having problems, they suddenly realise that there has been damage to the reproductive organs. So, that then is taken into account, but that sort of knowledge is built in.

So, the algorithm, we're working with St George's Hospital on that. The idea is that if there is new evidence we will refine and develop the algorithm. There are still cases coming through in the UK and in other European countries. It will also have validity in countries like Brazil where there are contemporary cases in terms of assessing whether or not it is Thalidomide.

Cyril Chantler: Why St George's?

Deborah Jack: I'm not sure, really. The decision was made before I joined the charity. I think there are doctors with an interest in Thalidomide there and they have developed as a centre of expertise. Certainly, when we have someone who is indicated to be probable Thalidomide, we then refer them to St George's and they will do the investigation, any scans, and also genetic tests. One of the issues is that a lot of the damage that you see in Thalidomide does occur either naturally or has a genetic cause.

Cyril Chantler: Who pays for that? Is that commissioned by the CCG?

Deborah Jack: No, the Trust pays for that. The money that comes from that really comes from Diageo who provide funding to the Trust and who look to us to have this robust process in place.

Cyril Chantler: So, the NHS would not provide that service?

Deborah Jack: No.

Cyril Chantler: Why not?

Deborah Jack: I don't know. I mean, some people have had genetic tests by the time they come to us. Generally speaking, if we want the genetic test in order to exclude other genetic conditions that could be causing the damage, then we pay for it. I don't know, it's also the speed thing because often it's taken people years to come forward to come forward to apply to be a beneficiary. What we don't want is that process to be really prolonged. As it is, genetic tests can take four to six months sometimes to come back if they're quite complex ones. That's paying for them privately. So...

Cyril Chantler: Thank you. Just so that we can get our minds to the size of the enterprise, how much money have you distributed over the years?

Deborah Jack: I don't have that figure off the top of my head, I'm afraid, but...

Cyril Chantler: About?

Deborah Jack: I don't know, since - I honestly don't know since 1973.

[Over speaking]

Deborah Jack: I can give you some figures.

Cyril Chantler: How many beneficiaries have there been over the years?

Deborah Jack: Over the years I think there have been around 500, somewhere around 550.

Cyril Chantler: Of whom 463 are still [unclear]?

Deborah Jack: Still alive, yes. Yeah.

Cyril Chantler: Right, thank you. Could you just explain again very - in a very summary way, briefly, how you have approached right from the start the distribution of the funds?

Deborah Jack: Well, as I said earlier the interesting thing about Thalidomide is there's not one established pattern of damage. So, what happened is when individuals were accepted by the Trust, they had medicals which were quite in depth. From that, all of them were allocated a score on a range, which is an indication of the severity of their disability. That's using an established mechanism used in courts in terms of damages. So, everybody - all of our beneficiaries have a number on this scale with a higher number, the greater the level of disability. The money they receive each year in grants

increases with the - it's a multiplier, so the more disabled you are with original Thalidomide damage, the more money you will receive.

Beneficiaries receive from us two grants each year. One is a payment of essentially compensation that comes from funds from Diageo, and then the second payment is what's known as the Health Grant. That's the funding that comes from the four UK Departments of Health and Social Care. Both of them are made on the same formula, which is the greater your level of disability, the greater level of funding you receive.

Valerie Brasse: So, is that the disability at the outset, the initial...

Deborah Jack: Yes.

Valerie Brasse: ...consultation?

Deborah Jack: The original damage.

Valerie Brasse: If subsequently you talked about the consequential damage. That was quite interesting, and that may not [inaudible] overarch the initial. So, it may be that their consequential needs become greater. Is the scoring - does the scoring affect their grants?

Deborah Jack: No.

Valerie Brasse: So, it doesn't change or take account of the consequential?

Deborah Jack: It doesn't. That's one of the things that we've become more aware of, and one of the things we're looking at is having an additional pot of funds for exceptional needs so that if people do develop additional health needs in particular, that there's a way of providing additional funding. It's also really difficult, because you can have two individuals who are born with identical patterns of damage and one of them is functioning at a really, really high level and the other one isn't.

Some of it is down to lifestyle choices, some of it's down to the life they've led and so it is - in some ways it's a very clear, well understood methodology for doing it. In other ways it doesn't necessarily equate with needs. Actually, our beneficiaries are very, very wedded to it. Any time there is any suggestion we might move away from funding say, particularly for the Health Grant, for example, the beneficiaries on the National Advisory...

Cyril Chantler: So, you don't have any funds that you distribute according to needs?

Deborah Jack: Not at the moment, no. That's something we're looking at. At the moment the degree of their original damage is perceived to be a proxy for their needs. We know it isn't that simple and straightforward, really.

Simon Whale: They prefer it that way.

Deborah Jack: They like it that way. How much of that is down - because that's the only way they've known and everyone - no one likes change, I don't know. I suppose the reality is, if we moved to a different methodology there would be winners and losers. I think everyone feels comfortable with the status quo at the moment. I think it is something, and it's one of those tricky decisions that the trustees will ultimately have to make, is how far - we're certainly going to start with looking at these exceptional needs, but over time that pot might get bigger and the other pots will reduce.

Cyril Chantler: What is the most you give out at the moment to an individual in a year? [Unclear].

Deborah Jack: I can provide that information to you, yes. I mean, A) I don't know the figure off the top of my head, and also it is quite sensitive information.

Julia Cumberlege: Can I just ask two questions? You talked about the scale, which I thought was really interesting. Were the beneficiaries involved in the scale so that they understood it? Did they give their agreement to it, or did you - because it was so long ago and you were forming the Trust, you just decided to do it?

Deborah Jack: This is the scale on which their compensation is paid?

Julia Cumberlege: Yes.

Deborah Jack: Yes, no this was in 1973 when they were literally very young and it's not changed. One of the challenges when we have - accept someone new is also slotting them into the scale. Also, focusing on their original damage not their consequential damage, which can be difficult. I think another thing that is a real issue for us is as people get towards 60, they develop health issues. A lot of people think, well, that must be because of my Thalidomide. Actually, who knows? They could have developed a lot of health issues, arthritis or what have you anyway. So, I think that the question of, is this Thalidomide related or not becomes a little bit - you could get really side-tracked into that.

So, I think this issue of saying, if you have needs that cannot be met from the funding you're receiving now, then we will look at if there are ways of providing additional funding but not getting into arguments about well, is -

hearing loss is a good example. Some people say with hearing loss, that must be down to my Thalidomide. Actually, when you get into your fifties a lot of people do experience hearing loss anyway. It's quite hard to be able to say yes or no on that.

Julia Cumberlege: Can I also ask you, thank you for that, but can I also ask you about your relationship with Diageo? Is it - we did have a problem when actually I was a minister, with Diageo running out of the funding. Then there was great concern that this would all come to an end. Now, if they are still continuing to support you and to give the annual grants and all the rest of it, do you see any change in that relationship, or is it still as strong as it was initially when they were involved?

Deborah Jack: I mean, I think the relationship with Diageo now is stronger than the relationship in the early days with Distillers Company. So, Distillers Company was taken over by Guinness, and then Guinness and Grand Met merged and formed Diageo. Diageo are very responsive. We have a legal covenant which sets out that they will pay our beneficiaries an annual grant for as long as they live. So, that's a legal agreement. We have taken legal advice to say that if, for example, someone was to take over Diageo, those liabilities would be part of the package.

So, I think we're very confident that we have as much - I mean, I think because of the size and strength of Diageo it's unlikely the company would go bust and disappear, but as long as the company is operating then they have an obligation legally to provide that funding. Over and above that we have ongoing dialogue with Diageo. We have annual meetings where we share evidence of need and information about claims. Every six years we have basically a renegotiation based on the data we have from actuaries around life expectancy of beneficiaries.

I think unfortunately the two variables in terms of how much money Diageo will have to pay us over the lifetime of the Trust are the life expectancy of beneficiaries, which is really hard to predict because they're a unique group, and secondly, its investment performance. Obviously, the funds we have from Diageo that haven't been distributed are invested, and at the moment both of those are very, very difficult to predict. So, we do do scenario planning with them, but certainly they have to make provision and it's in their annual accounts. They have made a commitment to fund the charity, so we feel quite secure from that point of view. Less so on the Health Grant, which is only agreed until 2022 at the moment.

Julia Cumberlege: So, when Guinness were involved, how did one - how was the negotiation carried out in order to ensure that they had some responsibility for this?

I'm just looking at other issues, obviously, and very interested that here we have a commercial company who feel a sense of responsibility.

Deborah Jack: Responsibility, yes. Well, Distillers accepted responsibility originally, and when they were taken over by Guinness that responsibility moved with the company.

Julia Cumberlege: So, the negotiation was with Distillers?

Deborah Jack: Yes, the original compensation deal was with Distillers in 1973, and that has then been followed through. I've got to be honest and say I don't know how long the covenant has been in place that actually moves it on to an absolutely firm legal basis, that funding. Certainly, that obligation moved from Distillers to Guinness and then from Guinness to Diageo.

Julia Cumberlege: Okay.

Simon Whale: Can I just ask about the status of the charity? Am I right in thinking that you changed from a charity to a charitable company?

Deborah Jack: Yes.

Simon Whale: Can you just explain to us why you did that, what benefit it derived?

Deborah Jack: Yeah. It - there were long debates about whether we should do it or not. We only made the change last year. The key reasons for doing it were really around the liability of individual trustees. So, in our old status as a discretionary trust, the Trust didn't exist in law. So, if anyone were to sue the charity or there was any sort of breach it would be individual trustees who would be liable. Now, obviously there was indemnity insurance to support them, but it was something that I think was of concern to some trustees. Coupled with that came increased scrutiny of charitable trustees by the media and elsewhere, and in terms of insuring that we continued to attract good quality trustees into the future, we felt it was important we modernised.

The other thing was very practical. The agreements weren't between a charity and a company or individual, so often we had to get signatures from all our trustees when we entered into big agreements. That was a logistical nightmare, because you've got trustees all over the country trying to send contracts and agreements with them. So, now having a single corporate trustee, any trustee can sign on behalf of that.

Cyril Chantler: So, you're a company limited by guarantee, is that right?

Deborah Jack: This isn't my strong point, all the legalities, but we are a charitable - yes, a company. I think it must be a company limited by guarantee.

Julia Cumberlege: That's certainly the phrase that's used with a lot of other charities that have just done what you have done.

Deborah Jack: Done, yes.

Julia Cumberlege: There was quite a movement among the charitable sector...

Deborah Jack: Yes.

Julia Cumberlege: ...to become companies limited by guarantee.

Deborah Jack: Yeah. I mean, we were quite a latecomer to it, and I think the feeling was just that if the charity had been set up today it wouldn't have been set up in the way it was, and it was just an opportunity to review the arrangements. I mean, one of the interesting things is, all of the trustees are now directors of the new company but we've been very clear that we continue to refer to them as trustees because for our beneficiaries it's important they see it that way. We do operate as a charity. We're bound by the guidance from the Charity Commission and we don't want to give the impression we're a commercial company that have got some underlying commercial reason for existing. It clearly was around the governance and the structure, and how we operate as a charity.

Cyril Chantler: They actually function like non-executive directors?

Deborah Jack: Yes. Yeah.

Julia Cumberlege: Very interesting. Any other questions?

Valerie Brasse: Can I just ask, when you were previously then a discretionary trust, you still had managed to negotiate this tax neutral position. As I understood it a discretionary trust attracted quite high levels of taxation.

Deborah Jack: Yes.

Valerie Brasse: So, that was something that had been negotiated, the fact you were a discretionary trust, you were still able to negotiate that.

Deborah Jack: Still - yes. So, this is going back a number of years that the beneficiaries had to pay tax on the money they received from the Trust. There was a campaign, and to be fair that was led by our beneficiaries. It wasn't the Trust staff. They - we have some very effective campaigners amongst our beneficiary community. They felt it was really unjust that the money they

received was then taxed, so they led a campaign and that was agreed.
Being a discretionary trust didn't stop that happening.

Julia Cumberlege: How much time as the Vice Chairman of the Trust - how much time do you spend on the Trust?

Deborah Jack: Well, I'm a paid member of staff, so...

Julia Cumberlege: You are?

Deborah Jack: Yeah, yes.

Julia Cumberlege: Oh, right. Presumably not all your trustees are paid members of staff?
[Unclear].

Deborah Jack: None of our trustees are paid. Some of them give a lot of time to the Trust, and that's why, going back to my answer to the previous question, we felt it was really important that we were able to continue to attract trustees who were able to bring their expertise and time to the Trust. We didn't want to have any barriers to that. So, yes, it really does vary by trustee but they do put quite a significant amount of time into it.

Julia Cumberlege: Actually, your administration costs are very low compared to some other trusts.

Deborah Jack: Yes, that's right.

Julia Cumberlege: Right. Any other questions?

Simon Whale: No, I don't think so.

Julia Cumberlege: No. Thank you so much.

Deborah Jack: That's all right.

Julia Cumberlege: It's been...

END OF TRANSCRIPT

Session 2: Mesh Ireland

START OF TRANSCRIPT

Julia Cumberlege: Mary, I don't know how you want to do it, whether you would like Fiona to speak first, or whether you would like to speak first. We're in your hands.

Mary McLaughlin: I'm going to start with an introduction, and then when I've done some introduction, Fiona's going to tell her story. We thought that best.

Julia Cumberlege: So, you're going to speak first?

Mary McLaughlin: I am.

Julia Cumberlege: Yes, lovely, all right. So, if you - both of you could just say who you are, and then perhaps, Mary, you'd like to start.

Mary McLaughlin: I'm Mary McLaughlin, I'm a mesh-injured woman, and I've had a full removal of my mesh. I'm the founder of Mesh Ireland, based in Belfast.

Fiona Bicknell: I'm Fiona Bicknell, and I am mesh-injured times two, and I'm not actually a member of any group, but since meeting up with Mary, I'm an honorary Mesh Ireland member.

Julia Cumberlege: Right, thank you very much, indeed. Mary, some of us of a certain age are slightly deaf, so if you could speak up a bit, it would be very helpful.

Mary McLaughlin: Surely. Yes, so, Mesh Ireland started off as a one-woman campaign in the form of myself. I became injured - I was sick, and realised I was mesh-injured, and I started contacting public bodies in Northern Ireland and politicians, and anybody I thought would listen to me, to try and find out how I could access public services. So, the Mesh Ireland campaign is more about the access to public services for women injured by mesh, and whilst we support the ban of mesh, it isn't the focus of the campaign that I have led.

I am a lady with a transobturator tape. Transobturator tapes have been used more in Northern Ireland than they have in England. I can give you a figure from the recent audit, the ASH audit from 2018, and they said that 55 per cent of women had transobturator tapes in that audit. I'm not endorsing the findings of the audit, but it's an objective figure from a scientific research paper.

So, it started as a one-woman campaign, and I found, my first problem was that I had read from the Scottish campaign, I went on their website and informed myself there, but I discovered that I could have mesh injury from

a YouTube video on Harvard Medical site. I wasn't sure where to take it from there, but I did go to my GP, and I wrote him a one-line letter, dear doctor, I want my mesh implant completely removed. Then I gave an appendix of why. I found that that was the starting point of my difficulty. Because I wanted a full removal of the mesh, because I had read the risk of the implant had gone from low risk to high risk, I didn't see why I should have to keep this implant in my body at all.

So, it progressed from there. I did join - so, I did join nearly every Facebook group there was, and promptly came off them, after a couple of weeks, because I just found it too much information at times. I started to - I wrote to the commissioning public bodies in Northern Ireland and asked why there were no services for full removal commissioned. That was - my understanding was that there is a cohort of patients, and three - the number for a cohort is three, and that when three patients or more present with problems, and there are no existing services in the system, then a sub-commissioning group has to spring up and address those problems.

I couldn't understand why I would be a unicorn, when other countries in the world, America led, I think, the litigation and things like that. I couldn't figure that out, why we didn't have commissioning of services. I did talk to the public health agency, and the bodies in Northern Ireland, and they suggested I go down the extra-contractual route, because it became apparent that the Northern Ireland system did not have surgeons who could remove transobturator tapes. So, that took me - and it took several months and a lot of paperwork, it took me - in mid-2017, I was referred to ██████████ in the University College of London ██████████ had appeared on BBC Northern Ireland and had expressed concern that women in Northern Ireland didn't have good services for mesh-injury, which alarmed me, as well.

I went to London, I had five visits to London for my surgery, and my understanding was that I was going to have a full transobturator mesh removal. In the meantime, I'd started my own Facebook group, mainly because I couldn't talk to a public body if I didn't have a Facebook group. But I - my Facebook group was mainly full of information, and I kept women updated on my journey, in the hope that I could tell them how to get there more quickly, or what to do, who to speak to. So, it was informational.

We had women from the north and the south on our site, with the idea that, if we got services in the north, we have cross-border arrangements, that maybe one side could benefit from the other, or one public health authority could buy something and the other share it. Because a lot of

women were going to England, and I find this journey to England not - I don't think it's desirable, if it doesn't have to be. I couldn't understand why we didn't have full mesh removal services.

So, to get to the point of this, is when I got to the end of my London journey, I did an informed consent procedure, and I was not assured by the conversation that I was going to get a full transobturator mesh removal, because I'd seen a doctor in America, [REDACTED] who put up a video, that you have to do a groin incision to remove the mesh, and that was not being offered in London. I did correspond with London, and I shared some of that correspondence with the panel. In the end, London said that they did a full vaginal mesh removal, that they did not take the pieces out of the transobturator nerve.

So, I was disappointed and frustrated that I'd spent a year repeating invasive diagnostics to then get to the end of the story to find that had I not questioned that informed consent process, that I may have ended up with a partial removal that I thought was a full. So, I went to - I was here in September, the day after that appointment with Mrs Henderson, and we talked to the panel in private. I also put forward to you the offer of [REDACTED] to come to the UK and you expressed your concerns about some issues, and also suggested that maybe a training program for surgeons on pro bono might be a good way to start something like that happening.

So, I went back to [REDACTED] and he was agreeable to that in principle, and I informed the review team of that, I informed the Permanent Secretary for Health in Northern Ireland, I informed the Taoiseach, I informed the Scottish government and the Welsh government. The general line that I find in the correspondence was that after due consideration, the UK, on all those things, felt that they had enough expertise here in the UK to manage without any international help. That became the point where I asked for a transfer to America to the surgeon. It was refused both by London and by Northern Ireland. The suggestion was, I could have an appointment with my mesh clinic in Belfast.

So, I felt as if I'd got to number 99 on the snakes and ladders and I'd just rolled back down to number two. It seemed to be, I had no choice. At that point I was bed-ridden. I didn't see this ending well if I didn't get the entire mesh out. I travelled with Mrs Henderson, we both decided that was our plan B. If we couldn't get the surgeon to the UK, that we would go out and have the surgery. So, we were both operated on, Mrs Henderson has allowed me to talk about her as well. We both went out and were operated on. We both had our meshes taken out.

My mesh was 28 centimetres long. London was promising me - my expectation should be 10-12 centimetres. I had a 28-centimetre mesh taken out. My mesh had been inserted into my bladder when I had it put in, and the surgeon found a hole in my bladder. My bladder had been perforated, despite having two cystoscopies before I went to America, nobody had found the perforation. Mesh was in the urethra wall, and I have had - my mobility has improved enormously, it's beyond all expectation, how well I can walk, and sit. I think I told you, I couldn't sit.

That pain went from the next day - I thought it was the morphine. It's gone. It's gone. I can walk without pain, my muscles are weak, but I can walk without pain, I can drive without pain, I can sit without pain. I bought a Fitbit, I'm sleeping eight hours, four hours deep sleep, four hours normal sleep. I'm not on any pain medication. I haven't had an infection since I came back. I had other repairs which I don't want to talk about, but this transobturator mesh is very, very debilitating, and we'll get to the partial removal now, why women don't want partial removals, and why the women on my group that had partial removals, they are on the scrap heap.

Not a single surgeon wants to offer them the removal of the remainder of their mesh. They're being sent to pain management and told nobody wants to touch them. I fear for every woman - every woman in the world, apart from every woman in Ireland, or Northern Ireland, Scotland, England or Wales that has these partial removals and our surgeons don't want to remove them. So, maybe at that point, Fiona, you could tell your story?

Fiona Bicknell:

I mean, I did submit my story to the Review, so there's obviously a lot more information on there that's - I don't know, it would make good bedtime reading, I suppose. I'm Fiona, and I'm 44, and I've got three children and one granddaughter who was born in the middle of my mesh nightmare. In 2009, I had an anterior prolapse mesh kit fitted for cystocele. At the time, I was told, minimally invasive, it will solve all your problems, really quick, no problem. To be fair, I had a wonderful recovery, it did what it said on the tin, and I was actually very happy, and life went on.

Then in 2014, I had a sling fitted for stress urinary incontinence, which was mild, it was irritating, but it wasn't terrible or anything, and again, I was told this will sort the problem out, it will be fine. So, I went ahead and had that done. Then roll on to September 2017, I had a subtotal hysterectomy done laparoscopically, due to fibroids and heavy bleeding. About eight weeks after recovering from that, I became aware of the horrible sort of heavy, dragging prolapse sensation again. I was experiencing a lot of pain, during intimacy with my husband, I was feeling like I'd been kicked really

hard between the legs. That's the only way I can describe it. I had this intense urethral burning, just really bad burning.

I just thought, gosh, what is going on? So, I went back to the consultant who did my hysterectomy, who is also the same consultant that fitted my bladder sling. Over the next six months or so, I had MRI, I had cystoscopies, I had examinations under anaesthetic, I had pain injections vaginally, I had numerous exams with him, and every single one came back, you're fine. Everything's fine. I don't know what the problem is.

I said to him, look, I'm not a hysterical, irrational person. I'm telling you, there's something significantly wrong with my - with me. I'm not making this up, the pain is really bad. He was amazing. He did listen. He never doubted what I was saying to him. In the end, he suggested that the vaginal pain I was experiencing was a certain area of the prolapse mesh that I'd had fitted. He said, well, I can't help you with that, because that's not - I've never fitted prolapse meshes. So, I'm going to have to refer you to somebody who can help.

With that, we went through - there was a list that they all have for specialist mesh centres, and he recommended that I go to Croydon and see [REDACTED] and see if she could help me with my problems. So, eventually, I got an appointment to go and see her, but in between me going to see her, my pain got progressively worse, to the point where I couldn't walk from one side of my house to the other. I was changing my daughter's bed one day, and I had the most horrific - it was like somebody had got some hot glass and was literally slicing my insides. It was so bad that I actually fell to the floor, terrified my poor children, and when I went to stand up, I couldn't walk. I'd lost all use of my left leg. So, I was absolutely petrified, and I just thought gosh, what's happening to me? I just had no idea what was going on.

So, we called an ambulance. I was taken to my local hospital, where my lovely consultant found me and sort of - they dished out morphine and everything. He said, right, we just need to keep you comfortable and get you to Croydon, so we can find out what's going on. So, I went to Croydon, I had the translabial scan, and it was apparent straight away that the prolapse mesh had basically concertinaed up one side. So, one side had come away from where it should be positioned and was all bunched up like this under my bladder.

She said to me, no wonder you're in so much pain. She said that will be your - that will be the reason why you're suffering. So, we then had a conversation, she said, yes, I can take it out. I said, can you remove it fully,

because obviously by now, I'd done an awful lot of research on mesh, and I understood that this whole partial scenario was not a good outcome for women. She said, yes, it's all going to come out. So, I was just like, oh, thank God.

So, I had my surgery, and it was removed, it went well. I had a horrific experience at hospital which left me with PTSD, but that's another story. It was extremely traumatic - anyway, she came and saw me and said yes, it had gone well, et cetera. So, I went through the very long process of recovery - oh, and I also - I did say to her, is my sling okay? On the translabial scan, it showed that my bladder sling was actually perfectly positioned, and there was no concern. When she'd removed the prolapse mesh, it had slightly eroded vaginally, but she'd over sewn it.

So, straightaway, I'm thinking, this is not good. Because I know the moment they start to erode, you're on a highway to hell, really. Anyway, so I recovered, but as I was recovering, I was still in an awful lot of pain, and I was not right, and I just knew something was wrong. So, at this point, I started following a doctor on Twitter [REDACTED] who was very open about his removal surgeries, how it's done, how big the average mesh is, depending on what kit's used, et cetera. So, I educated myself.

I actually spoke to him privately over Twitter, and I said to him, I had vaginal surgery to remove this mesh. He said, you've had a partial, basically. He said, the only way to fully remove the mesh you had was by vaginal and groin incisions, and I was devastated. Because I honestly thought the whole thing had come out. This is what I'd been told. So, when my husband and I went back to see my consultant [REDACTED] for my follow up, we asked again, and I said, has it all been removed, and she said, yes, it's all been removed. My husband said, what, absolutely all of it? She said, well, as much as we could get.

So, I was just heartbroken, because I knew - I was still in pain. My pain hadn't improved, I was still in a terrible way, I couldn't have intimacy with my husband, and at that point, I just thought, right, well, what do I do now? I've got to do something. I've totally lost trust in the UK surgeons. I mean, this is a specialist mesh centre. I said to her, look, I'm still in pain. She said, well, we can refer you to pain management. I said, that's not really acceptable, because I didn't have pain management before I was fitted with mesh. So, why is it deemed acceptable now? I shouldn't live the rest of my life in pain like this. It's not fair. I said, and also, I'm very worried about my bladder sling. She said, well, are you continent? I said, yes, I am continent. She said, well, what's your problem, then?

At that point, I just thought, well, there's not really a lot of point in me really saying much more. I just knew it was a closed door, and she looked at me and said, I don't know why you're looking at all the hype. She said, you don't need to listen to all the hype, she said, most of it's nonsense. I mean, this was a mesh-injured woman that she had operated on, and she told me to ignore the hype. Bearing in mind that this hype, I've experienced every aspect of it. So, we just kind of - my husband and I, we just thought, well, we'll leave it and walked away. Then I went home and cried, a lot.

My husband said, right, well what are we going to do to get you fixed? So, I spoke to [REDACTED] and I said, I can see, you prove that you fully remove these things, he's got great results. He's done over 2500 operations. He really knows what he's doing, so we flew to America, and that's what happened in January. That's how I met Mary and Iris.

He found - he went in through my groin, and he went in vaginally and he went in abdominally. He removed my entire bladder sling, all 24 centimetres of it, and the remainder of my prolapse mesh, which was a significant chunk. It's all gone, and I received the most amazing care, and he also sorted out the prolapse, and he also said that he was upset for me at the state that I'd been left vaginally. In his words, he took a dirt road and made it into an asphalt road. Which was nice of him, but - so, yes, it was amazing. Great care. I'm now completely and totally mesh-free.

When I came back, I emailed my lovely consultant, the one who fitted my bladder sling, and I explained to him, that despite the translabial scan saying my bladder sling was fine, it was actually embedded in my bladder wall, and it was eroding vaginally. At some point, it would have worked its way into my bladder. He was really, really devastated for me, and said that he was extremely sad. He was more than sad that I'd had to go to America to get the results that I needed. It was him himself, actually, who spoke to me before I went to America, and told me that my best bet was to go and see him. This is a senior urogynaecologist, he's the lead in my local Trust, and he told me, you're better off going to America.

Because he felt terrible, he'd sent me to a specialist mesh centre and they left me worse off. Finding fragments of mesh, or portions of mesh is really difficult. Even [REDACTED] said to me, I can't guarantee that I'll find it. Because once you remove that vaginal section, it's like finding a needle in a haystack. You don't have a line - a point of reference to find where the rest of it sits. But he did find it, and the whole operation was videoed, and I've got all the pictures, I can see exactly what happened to me, what was removed. That's the best thing I ever could have done.

I mean, my life is never going to be the same. I'm not ever going to be able to lift anything, my granddaughter, she only arrived last March. I can't hold her, I can't pick her up, and I can't even begin to tell you how hard that is for me. I'm not going to get emotional. I had for a number of months, moments where I was suicidal. My husband had me on suicide watch, because I had no idea what was happening to me. I just had the most horrific pain, and everything was coming back, you're fine. We can't find what's wrong with you. I'm very fit and active, I horse-ride, I walk my dogs, I'm an outdoor girl, I'm a farmer's daughter, I love all of that. I don't have that. I have lost all of that. I don't know if I'm ever going to be able to go back to that. That's what mesh has done.

I have nothing against my implanting surgeons. I genuinely believe they thought they were helping me, when they fitted me with this stuff. But what I have a problem with, is that you can put this stuff in, but you can't take it out. It's causing catastrophic damage, and there's just more, and more, and more women now that are suffering. It's just not acceptable. This is nine years, and five years, post-implants that this happened to me.

Julia Cumberlege: Fiona, I'm so sorry. I'm so sorry. Are you in any pain now, as a consequence of all this?

Fiona Bicknell: I've had just the usual post-surgery discomfort, and occasionally I get a bit of grumbling from nerves in my thigh, but I had that after my partial, and that did settle down. I think - it's quite invasive surgery, so, it takes a while to recover. I'm only 10 weeks post-op, but I feel great. I flew 2500 miles, nine days post-surgery, with a groin full of stitches, a stomach full of stitches, and sitting on a hedgehog, and it was actually fine. Yes. This is how [REDACTED] the level of care he gives, his expertise at surgery is so good, that I was up and walking to the gift shop the day after my surgery in America. I couldn't have even walked to the toilet when I was in the UK hospital. That's got to tell you something.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Julia Cumberlege: Can I ask, because I understand a lot of your members have gone to America. Who pays for that?

Fiona Bicknell: We did. We haven't carried any debt for about 10 years, and we used our emergency savings and credit cards to pay for my surgery. Yes, we couldn't afford it, but my husband said my health is more important than anything. My children needed their mother back, and I've - I can't be intimate with the man that I've loved for 16 years. He's amazing, he's never given me a hard time over it. But when you really love someone, and you've got a real partnership, that's hard. I'll be swinging from the chandeliers again, hopefully, now.

Julia Cumberlege: Can I then just go back to your organisation. Can I ask you, Mary, how big is it? How many members do you have?

Mary McLaughlin: We have roughly 100 members, about 94, 95, some come, some go. Just under 100 members.

Julia Cumberlege: It covers Northern Ireland and Southern Ireland?

Mary McLaughlin: Northern Ireland and Southern Ireland, yes. The situation at the minute is - I'm conscious of the time - the women going to their consultants need to be clear that partial removals can be named under different names. People need to be aware, if my tape was 28 centimetres (and you have the tape), people are saying they've had a full removal, and there's been eight centimetres of tape taken out, or six centimetres of tape taken out. The doctors, up until very, very recently, were saying this was due to shrinkage. That was what I was being told that I should expect eight to 12 centimetres, because it shrinks.

My tape was 28 centimetres, and I was a slim woman when I had the tape put in. So, if my tape had shrunk down to 28 centimetres, it doesn't make sense - it just doesn't make sense. So, there are people, I watch on Facebook groups, and I hear on Facebook groups, people saying they're going in to get a full removal, and come out and say, I'm great, I'm mesh-free, there was a removal of eight centimetres. Those women are getting partial removals. When I look at the language that's used, it's a full urethral removal, a full vaginal removal. A full removal, vaginal. A full removal of vaginal mesh. When most women talk about their entire product as a vaginal mesh.

So, the surgeons are now creating this - it's trickery. There's no other word for it. It is trickery. They know, as we would say in Northern Ireland, fine rightly, that the women think, when they say they're getting a full removal, that all the mesh is coming out. We keep telling women that it isn't possible to take this transobturator tape out, without doing a groin incision. Surgeons are telling women - myself included - that they can take it out vaginally without doing this groin incision.

Fiona Bicknell: It's just not possible.

Mary McLaughlin: It's not possible. The woman - once the tape is cut, it's cut

[REDACTED]

[REDACTED] When the patients go back to them, they are told that they misunderstood. That was the line I had. I misunderstood nothing. I made a tape recording of that informed consent. I've listened to it again. I did not misunderstand anything.

What chance do our women in the UK have, if they have to tape record every intervention with their surgeons. Where is the trust? Why, at this point of the mesh campaigning - the Scottish people have been campaigning for seven years - why at this stage, when the Review is running, why do I still have women thinking that if they get a tiny section of a transobturator tape out, that they have a full removal? It's because they want to believe their surgeons.

If there's anything I can do here, it's to say that the Review team have a massive responsibility to stop surgeons doing this, now. They have to improve their informed consent forms. They have to have it printed out, and not handwritten, they have to have boxes saying, I intend to do a full vaginal removal, a full urethral removal, a full transobturator removal. I expect to get this length of tape. We know that it's not always possible. But it's happening.

The translabial scan, Northern Ireland, I worked with Órlaithi Flynn from Sinn Fein, she's our - she's the chair of the all-party mesh group in Northern Ireland, and she worked very hard with our permanent secretary, and my inside track is that the mesh appointments for translabial scans start next week. So, we've got this scanner. Originally, we thought it was so the people could see what type of tape they have in, because their records are not complete. That problem remains.

But now, it's all the women with partial removals. They want to come back now to see - because they were told it was nearly all out, or it was all out,

and it shrunk. Now they're seeing people like myself, coming back with 28 centimetres of tape, and they're saying, well, I only got four centimetres or six centimetres. Is this why I'm still in pain?

Fiona Bicknell: Do you mind if I just say, just very quickly. You asked about the costs, but a friend of mine had paid privately in London, with a London consultant to have her tape removed, transobturator, and was told it was a full removal, but then realised that she was still in pain and couldn't understand why. But she was adamant that this surgeon had removed it all. She's just been down to [REDACTED] to see another consultant who went in through the groin and removed another 13.5 centimetres. You've got - another person that I know who's been quoted £27,000.

Cyril Chantler: Sorry, I missed that.

Fiona Bicknell: £27,000 to have a rectopexy mesh removed, but that's only partial surgery, that's only one surgery. Chances are, they'll end up with some kind of bag, or ostomy of some sort. £27,000. I went all the way to America with my husband, and I had surgery for full removal in one hit, with no scans, no tests, no nothing, for a lot less than that. So, that's something else that - in my opinion, it's wrong, it's so wrong.

Julia Cumberlege: I think I'll just ask, because we're having to move on a bit. Any questions?

Sonia Macleod: Just a quick question. You said there was a surgeon that was doing a removal by the groin. Is that surgeon offering a full removal?

Fiona Bicknell: The only surgeon that I could guarantee can remove fully was [REDACTED] But the other surgeon in Bristol, I understand is now doing full removals, yes, with the help of a plastic surgeon.

Mary McLaughlin: May I say something to that? I've clarified this - the plastic surgeons are brought in for after the mesh surgeon goes in. So, the mesh surgeon goes in, and when they cannot find the mesh, they cut through good muscle, okay, and then the plastic surgeons are brought in afterwards to reconnect the muscle. On the mesh grapevine, there is word that this has been unsuccessful in a few women, already, and one of them was in a magazine, she's pretty paralysed from the waist down, because the muscle reconnection was not possible.

[REDACTED] he does a tissue sparing, muscle sparing. So, he does not cut the muscle in the leg. A lot of women are now being told, you can't get that removed, you're going to die, it's too difficult, it's too risky. The question is, is it the surgical technique that's being used, has a high risk,

and is it fair to now frighten women who have got this bit left in their transobturator nerves, to frighten them into becoming bed-ridden?

I was up in Scotland, talking with the Scottish mesh survivors last week, and there were women who said they were like me, that they were bed-ridden. They're now in wheelchairs. They're in wheelchairs. It's unnecessary. It's not fair. I mean, people live to a good ripe age, if you were in your late 40s or early 50s, and already in a wheelchair, because of mesh, and your transobturator groin and the UK has slept on the job. Why should the women not get these surgeries that can bring their life back up to where it should be, or something positive?

Julia Cumberlege: Thank you very much. Simon, have you got any questions?

Simon Whale: Well, again, thank you both for what you've told us. I think it's incredibly powerful, and you said it so eloquently, and it's brave of you both to do that, so thank you. I suppose the one question I've got, which you've sort of touched on maybe, already, is what do you think we need to focus on the most, in terms of trying to help recommend things that will improve the position for women that you've talked about?

Fiona Bicknell: You need to get the UK surgeons up to speed, really, with full removals. I think that should be your main focus, really, because there are hundreds and hundreds of us now that are mesh-injured and there isn't the skill in the UK to safely and fully remove these things. Admittedly, people like [REDACTED] are doing an amazing job in trying to move forward to help people with full removals. But ultimately, he didn't have that skillset, so you're still going to have a number of women that have ultimately been guinea pigs whilst he's honing his skills. That's no criticism of him, because I believe he's doing an amazing job, and he's working really hard to help.

But you've got an awful lot of surgeons that can put this stuff in, but when you have a problem, they're kind of like, well, sorry, haven't got a clue. Wouldn't even know where to start. So, I think that's - you need to get people listening, and you need people to accept that this is a big, big problem, and that partial removals are actually worse than fulls.

Mary McLaughlin: Women are stopping going to their doctors. That's my - women are stopping, because they know the surgeons don't have the skills. They feel like they're being the guinea pigs for have-a-go surgeons, previously. Now, the mesh-injured are going to be the learning curve for people trying to take transobturator mesh out of their bodies, and they can be left paralysed.

Fiona Bicknell: I mean, how would I, in a million years, suggest to another mesh-injured lady to go to a mesh specialist centre, when I received the treatment that I did, that potentially could have left in a really bad way, if [REDACTED] hadn't been able to find the remainder of that mesh. I have no faith in the UK at all. No faith. There's an awful lot of us that don't, and if I ever have to have further surgery, I'm going back to America. I'm not stepping foot in another UK hospital. It's shocking, it really is shocking. They need to step up, big time.

Cyril Chantler: Thank you very much for coming and talking to us. We've met before, and it's very important that we hear this. Mary, can you talk a little bit more about what you think a consent procedure needs to be to create trust. Because you mentioned the importance of trust, which is vitally important. You mentioned the notion of recording the conversation, and that seems to me – and to us generally - to be a very good idea.

Mary McLaughlin: Yes.

Cyril Chantler: Because you can go away and think about it, talk to your relatives, and then go back with some other questions. But what else would you want to see in the consent procedure?

Mary McLaughlin: I think that the consent procedure is slightly problematic, because of the way it's structured. The consent procedure is usually at the end of an appointment, and it's often - it's like at school, when you teach, and you're trying to pack something in the last 10 minutes, and the consent is often rushed. The notion of hand-written consent forms - I brought mine with me, which I'm happy to share with you, and I'm happy to share that tape recording privately with you, so that you can listen to it yourselves.

There has to be some type of control within - some type of regulation of how this type of consent is performed. If we know how long a piece of mesh is, in general, an average length, a surgeon must be able to put his best work in front of us, in front of a patient. A picture. I know there's data issues, but they can be overcome. A mesh, a picture of a mesh is not as intimate as a picture of somebody's body parts. There has to be a picture that the person can visualise what that is.

Despite all the information I put up on my sites, some women still aren't very sure of what it is actually the surgeons are doing. There has to be that picture. There has to be an average length. There has to be a confirmation on the sheet that the doctor has signed, that he has told a patient that he can take it all out, or he or she can take partial out. Then, a percentage of what their best achievement is. Best, average, median - you can get some

statistics that people can say, okay, with this doctor, he has a good track record, I know that it's 75 per cent of the mesh he usually gets out. People understand, everybody's individual.

There also has to be some type of control over what the doctors are stating. I don't understand the process of re-validation. I have checked all the doctors in Northern Ireland, and in Ireland if I can, whether they've been re-validated. I question how a lot of these surgeons have been re-validated, and I've questioned the process of it. They're - are they only doing two surgeries a year, or two surgeries a month? There has to be a quantification. The empirical data has to start, that the patient can see the empirical data. Can see if this is a starter, if it's not a starter.

The consent form has this thing on it, I know this is a training hospital, and therefore I'm happy for somebody else. But even I feel a bit awkward to say, no, score that through. I want that doctor. I was given the team narrative. I was told when I started my journey that [REDACTED] from UCLH would be doing my surgery. I was told that from the manager of the hospital when I phoned up. I said, I'm quite happy to have diagnostics with the team, I understand that, but the surgery is with He said, oh, yes, yes, only operates. That's what I was told.

When I got to the - after a year of all this, I was told we operate as a team. I've read on Facebook, where someone said, oh, Dr S did the right-hand side, and Dr such and such did the left-hand side, and the consultant came in and finished the work. I just think, is that the best we're going to do for the mesh-injured women? Because that is a training exercise. People have been waiting so long on these appointments, when we get to the informed consent, they're so vulnerable and grateful for everything they've got, they just don't want to seem like an awkward customer, and say, no, no, I have to have only that one surgeon doing it.

So, it's too loose. The whole process is too loose, and we need - if we're going to do empirical data from all other things, then the patients need the empirical data, and we need to know adverse events.

[REDACTED]

We have one woman in our group who died. She was operated in 1998 by [REDACTED] She developed squamous cell carcinoma, and she lived when they thought she was going to die, and she lived for almost another 10 years, and she died last January. She developed squamous cell carcinoma, [REDACTED] from the friction of the eroded mesh onto the

flesh, and that's the trigger. I'm not good at medicine, but that is the trigger for that type of cancer.

Julia Cumberlege: I'm afraid I have to draw this to a close now.

Simon Whale: Thank you, that's very helpful.

Julia Cumberlege: But I want to reiterate what my colleagues have said. Thank you both so much for coming, because I know it takes a lot of courage to actually explain all this that's happened. It's such a very personal thing.

Mary McLaughlin: Thank you for what you're doing. Thank you.

Julia Cumberlege: We do appreciate it. Thank you so much.

END OF TRANSCRIPT

26th March 2019

Session 1: Care Quality Commission (CQC)

START OF TRANSCRIPT

Julia Cumberlege: If you would like to say who you are and your responsibilities that would be helpful. And that will now be on the record.

Nigel Acheson: So, I'm Nigel Acheson, I'm one of the Deputy Inspectors at the Care Quality Commission, and my responsibility is around hospitals. And the declarations that I have are two-fold, one represents a payment that I had by Baxter Pharmaceuticals for giving a lecture, which wasn't related to their products but I thought I'd mention that. And the other was some training that I underwent which was in Advanced Laparoscopic Surgery and that course in Belfast was completely funded by Johnson & Johnson.

Julia Cumberlege: Right, thank you very much.

Nigel Sparrow: And I'm Nigel Sparrow, I'm the Senior National GP advisor at the Care Quality Commission, a former GP, and held various roles at the Royal College of GPs in Education.

Julia Cumberlege: All right, thank you very much. So, if I perhaps could start by saying as I understand it, and please put me right, if I haven't got this right, but you're sponsored by the Department of Health and Social Care. I'm not quite sure how that sort of in any way influences you, because I think the CQC is independent and prizes its independence.

But you're also accountable to Parliament through the Health and Social Care Committee, and I'm just wondering how that fits together and does one take precedence over the other, or is it - well you'll tell me how it works.

Nigel Sparrow: So, we are an independent regulator. We act on the side of people, and our focus is on people that use services, and that's where our priorities lie. Although we are funded through Government funds, we are largely now fee-based, in terms of our funding, but we are completely independent of Government.

Julia Cumberlege: Right okay. Okay anything you want to add?

Nigel Acheson: Yeah, no, that's absolutely fine.

Julia Cumberlege: That's fine. All right, well thank you. So you've got this dual accountability in some respects, but also you're presumably having to interact a lot with other arms-length bodies, and I'm thinking particularly of the MHRA and NHS Improvement, and I wonder how that works, if you could tell us?

Nigel Acheson: Certainly, with NHS Improvement we have regular meetings with NHS Improvement now being formalised into meetings where we share intelligence. There's a formal agreement now, which is much wider than just ourselves and which has got a number of stakeholders on it, which again is to share early concerns, and that's a relatively recent development.

In terms of MHRA, NICE, we do meet from time to time with them, but it wouldn't be in the same operational way that we meet with the other members of that responding to concerns group.

Julia Cumberlege: So, we've been on a CQC inspection, so we've sort of had a taste of only one, so - and I appreciate you can't draw conclusions from one visit, but it was very interesting. But what I've really wondered was that you do say on your website, I think, that you're very involved with patients, you want to hear from patients - and how do you do that? Because I think some of us feel it's very much a sort of an organisational body, and I'm just wondering how you get the feedback, because the inspection is very much looking at the organisation and whether it's well-led and all the rest of it, but how do you get the impact from individual users of the service?

Nigel Acheson: So, in a number of different ways. So, we run the - a number of the National Patient Surveys, and on - and we share the results of those surveys - which can be broken down to individual provider level - this is for the hospital side rather than primary care. And encourage the hospitals, as a result of that - for example the recent maternity patient survey, encouraged the individual Trust not just to look at their own information, but then to use that as the basis for reaching out to their local patient groups to involve those. So, we are encouraging that to happen.

In addition, we have a huge number of contacts that members of the public make to our National Contact Centre, which is based up in Newcastle - hundreds of thousands each year. And from those, if there are any concerns about a particular provider, then that information is shared with one of our colleagues who is the responsible - connecting a colleague with the organisation concerned and they will pick those up, either individually or as part of the information that we use to help us decide what our regulatory interaction with providers may be.

Julia Cumberlege: Right. Can I ask on those surveys, because of course we've been taking a great interest in the maternity services survey that you've been running; how do you choose your questions?

Nigel Acheson: So the questions are put together by a panel, and so the panel has patients, experts who are experienced on the panels. So, following the survey this year has just been published, and there was a meeting to review those questions, which included two women who had recently experienced a maternity journey, and they were able to help us consider those questions.

There is a - there is a process around how the questions are then moved on from year to year, in order to make sure that there's - that the questions remain - or the surveys remain comparable. But certainly we test with those experts by experience, the - the form of questions, what they feel are the important topics, if there's anything that's missing from the survey, topics that they feel should be added. So we put great store by the experience and expertise those colleagues give us.

Julia Cumberlege: So if you have people, organisations, individuals, who feel that the questions aren't quite the right questions, or maybe one or two questions, you're happy to take that into consideration...

[Over speaking]

...with the next survey?

Nigel Acheson: Yes, so for the next survey now, I'm not sure whether the questions have been finalised as a result of the process that - because I only took part in one of those meetings two or three months ago, so I'm not sure at what stage next year's questions are finalised. But certainly yes, we welcome feedback obviously on a survey.

Julia Cumberlege: Watch this space [laughs] is all I'm saying. Right - over to you Cyril.

Cyril Chantler: I think maybe the processes have changed since I was an observer on a hospital inspection, but I do remember the briefing that took place before the team went to the hospitals. It included the session from your data analyst about what they knew about the hospital, and they talked about the mortality rates from hospital. To what extent do you take other outcomes into account when you visit, and in particular, specific clinical outcomes or patient-related outcome measure or patient experience; do you get that information and then are you briefed now to go and enquire about those very important, much more detailed questions?

Nigel Acheson: So we get the breakdown of both the patient survey and - pertinent to the provider and also the staff survey - pertinent to the provider, so those are two of the - of the formal bits of information that we have. We also are involved with HQIP clinical audit process and programmes and as you know there are a very large number of those. And in fact what we run at CQC is the outlier process for those.

So where providers were given an audit or an outlier, we then - we'll it's the CQC then makes contact with the provider to enquire about what that might mean, what steps the organisation is taking to both look at and then improve upon the service that has been audited. And so that information also feeds into the data [unclear], the intelligence that we have available to inspectors, as does things like complaints and the way that - and the timeliness of how complaints are being handled within a provider.

And as I said, the information, if members of the public have contacted our Contact Centre nationally in addition to that, then we would get that sort of what one might call potentially soft or intelligence from another route, we also get that.

Cyril Chantler: And the record on serious incidents and inquiries...

Nigel Acheson: Yes...

Cyril Chantler: ...that would be part of that?

Nigel Acheson: ...yes, absolutely, yes it would. Yes. And again, the timeliness of how those have been dealt with. And on our well-led inspection, which is a new part of the hospital inspection process, we will assess the - how those incidents have been then handled.

Cyril Chantler: Because the CQC as a regulator, it seems to me, is a very important component for ensuring safety in our hospitals. We're in the situation where we've met hundreds of women whose lives have been very severely damaged by something that went wrong - I'm particularly talking about the use of surgical mesh for stress related urinary incontinence or pelvic prolapse. And it's taken the women forming groups, and working with politicians, to draw it to the attention of our profession - or our National Health Service. And that doesn't seem right to me.

With your experience, and of course there are many players and we're meeting them all - we've seen the MHRA and seen the General Medical Council, can you think of something that we could - ought to be thinking of to try and make sure this never happens again?

Nigel Acheson: So one of the things that we're very interested in, in the work that we're doing, is looking at processes that are in place. And, for example, if we were talking about a new either treatment or a new piece of technology for example, one of the things that we would be looking at, and we do look at now, is in an organisation what is the process whereby the organisation itself makes sure that those are being implemented in a safe manner.

It would be difficult for us because we inspect for two or three days at intervals - it would be difficult for us to be in all of that detail. So what we do is we're developing ways of checking the processes that are in place. I think one of the other things that we are really keen to explore is to see how we could use other sources of information, for example the GIRFT programme, and the information...

Cyril Chantler: Getting It Right First Time?

Nigel Acheson: Getting It Right First Time, sorry, programme and the information that they have, as a way that we could assess the standard. Because that's what they're doing; they're getting that information and sharing it back to the Departments and to tell me something about the quality of the care that's being provided. So we're looking for ways that we could use that sort of information as one of the lenses through which we would look at a provider.

Cyril Chantler: Do you look at the audit reports that go to Trust Boards?

Nigel Acheson: Again, it's a - you know we sample them rather than see every single one of them.

Cyril Chantler: So if you were inspecting a hospital, you would see the audit reports...

Nigel Acheson: Yes, we'd see them, yes.

Cyril Chantler: ...of that hospital.

Nigel Acheson: We would - that would be part of the information that we would have available to us before we did the well-led part of the inspection, as part of our assessment of governance...

[Over speaking]

Cyril Chantler: And to what extent would you engage with the revalidation process run by the General Medical Council?

Nigel Acheson: So we're at the beginning of that process, and one of the reasons that I was so keen to move - having formerly been one of the higher level Responsible

Officers - was to try and see how we can explore using those two forms of regulation in a more intertwined way. And I mentioned a little while ago, the National Audit programme, it seems to me that that would be an area we look at from a CQC point of view. It was an area that I was beginning with colleagues to look at from an RO regulations point of view, to ask colleagues to have a formal performance review of their practice.

And because National Audits are generally accepted by the profession, the colleagues should be submitting cases to them. And we hope that that would be something that could be built into the annual performance review for a colleague, reflected upon in their appraisal, and that's something that we could then triangulate during a CQC either visit or monitoring phase.

Because the intelligence that you have mentioned at the beginning that we used to use just in our comprehensive inspection programme, we now have a plan to use that intelligence, that data as a much more on-going part of how we regulate [unclear].

Cyril Chantler: So when we're talking about connectivity between the different regulators, and of course we know there are a lot of regulators, and sometimes that is a problem if you're trying to run a hospital. But to what extent do you connect with, say, the National Patient Safety part of NHS Improvement?

Nigel Acheson: I don't know, Nigel, if you want to comment - I mean at the moment with NHSE and I in a position where they are just reforming up and coming together. Although we've had, at the moment, relatively informal discussions with Aidan Fowler who's the lead for Patient Safety, we are planning, once their structure gets more established, to formalise some of that. And as I say, any emerging concerns, a group that's been set up in some of the formal meetings that we have with NHS Improvement currently, hopefully we can build some of those quality areas into these discussions too ...but it's early days.

Cyril Chantler: So there's a lot of conversation clearly taking place now between the different partners in trying to ensure or improve patient safety, and you've been involved before in your previous life with the role of the General Medical Council.

Nigel Acheson: Yeah.

Cyril Acheson: It would be very helpful I think to us, and certainly to me, if you could actually pop down on paper what are the changes that you're taking - that are taking place at the moment...

Nigel Acheson: Yeah.

Cyril Acheson: ...and the background to them - but what you foresee as being a better outcome. Because we've got to do everything, all of us, to make sure this doesn't happen again, and that would be very useful. Finally for me, for the time being, private sector; to what extent does what you said now in relation to National Health Service hospitals, apply to inspections on private hospitals?

Nigel Acheson: So the basic inspection process is the same. One of the reasons why we're so keen to push the idea of the, for example, audits or GIRFT or that sort of data collection and sharing as a standard, is that we think that that could then apply in the independent health sector where it's more difficult for us currently to get that sort of data information.

What I would say though is the - in terms of private practice, the NHS-funded private practice, about 85 per cent of that is provided by five providers. They, through the, primarily, RO regulation type thing, have begun to meet on a very regular basis and are very alert to the fact that they need to get on the front foot in terms of assuring quality of the services that are provided.

And again, with the mesh issue, when the letter went out to all providers, including private providers, those - certainly those big five were very, very keen to get involved in a discussion about how they would put in place a stop to the procedure.

Cyril Chantler: Do you find the relationship is different between the people providing the care to the doctors and the institution, because within the NHS, the institution as the employer has major responsibilities?

Nigel Acheson: So again I think that's changed very - I mean I haven't spoken to many colleagues who are providing private practice in those settings, but talking to the Responsible Officers in those settings, and one or two of the Chief Executives of those organisations, they definitely have taken a very different view...

[Over speaking]

Cyril Chantler: Nigel, just for the record, would you just explain what the Responsible Officer...

[Over speaking]

Nigel Acheson: Sorry, yes. So every doctor who is practising in this country, be they a GP, hospital doctor, or in any sphere, has to be revalidated by the General

Medical Council every five years. And in order to help the GMC make that decision and recommendation to allow a doctor to continue to hold a licence to practise, they have to undertake a process of annual appraisal. And that annual appraisal then goes through to a responsible officer, which every doctor is connected to, bar a small number whose connection is directly to the General Medical Council.

And the Responsible Officer then, every five years, on the basis of the output of those annual appraisals, then will make a recommendation to the GMC that this is a doctor who the Responsible Officer feels should be recommended for revalidation recommendation, or that there isn't enough information, in which case that decision can be deferred.

And then thankfully now in relatively unusual circumstances, there will be a small number of doctors who don't engage with that process in a way that the Responsible Officer can make a recommendation of either a positive recommendation, a deferral, and in fact we've recommended to the General Medical Council that this doctor is not engaging in the process, whereby the General Medical Council then get involved with a process which can lead to a doctor losing their licence.

Cyril Chantler: Thank you very much. Okay.

Julia Cumberlege: Can I just ask you, originally I think the CQC was employed to inspect hospitals; can I ask a bit about primary care - about GP inspections, because I think that's been running not for so long, and I just wonder how that works, because we've had quite a lot of concern expressed from patients about the GPs understanding their issues and the question of referrals.

Nigel Sparrow: So we started inspecting general practices in 2014 and completed our first comprehensive round of inspections last year - or 2017 - the first time that general practice was ever inspected, and we inspected them against the CQC's five key questions, whether they're safe, caring, effective, responsive or well-led, and we rated each general practice. At the end of that process, on the first inspections, about four per cent of practices were rated as inadequate, and about 13 per cent requiring improvement, and the rest were good or outstanding.

Because we re-inspect practices then that are inadequate or requiring improvement quite quickly; so if you're inadequate the inspection is six months later, and requiring improvement one year later. So by the end of the first round of inspections, 95 per cent of practices were good or

outstanding, and only one per cent were inadequate, and about three per cent or four per cent - four per cent I think, were requiring improvement.

So there was an improvement journey, from where we founded our first round of inspections. Because general practice had never been inspected before, it was a learning exercise for all of us and certainly safe was one of the key questions that was more commonly rated as inadequate or requiring improvement. And in particular with this - with the enquiry we're talking about now, in terms of drugs such as sodium valproate, we always ask, for example, how practices react to safety alerts.

And we look for examples, and we've refined our processes much more from when we started, and we're certainly now examining more records to check that those alerts have been acted upon. And in terms of valproate, because this is a - this is the most important safety alert that's happened in general practice for a very long time, our inspectors always ask about valproate on every inspection now, and our specialist advisor, who is on those...an inspection, will look at records of patients who shouldn't be taking valproate basically, and all our GP inspections have a GP - a practising GP on the inspection team, as well as an inspector. So we have professional input at every general practice inspection.

Julia Cumberlege: We were told by one of the patient groups who is very active, very well-informed, and they had run a survey and they were finding that women were still being prescribed sodium valproate when they were epileptics and in the early stages of pregnancy. So I'm just wondering if, is your inspection regime comprehensive enough? Because presumably you're only taking a certain percentage of GPs, because there are so many in the service.

Nigel Sparrow: So now we've finished our first round of inspections, our process of inspection has changed and we do a much more focused and targeted inspection based on intelligence. And so, for practices that have been rated as inadequate or requiring improvement - they will get the same process of a comprehensive inspection in those same time intervals. But for practices that have been rated good, or outstanding, will now be subject to what's called an annual regulatory review, where an inspector with some clinical input will review the data from every general practice - from each general practice, combine that with information which we receive from patients, from NHS England and CCGs, and put that together.

And we ask the practice as well for their input - and put it all together and decide at the end of the annual regulatory review whether a practice will be inspected in that year or not. If it's not inspected, it will get another

annual regulatory review the following year, but all practices that have been rated either good or outstanding will have an inspection within five years. That may not be a comprehensive inspection - it is more likely to be a focused inspection where we look at well-led and effective, but using trigger questions for well-led to get into safe, so that we get a - so that we make sure, as much as we can, that practices are safe.

But as you said, we can't possibly inspect every general practice all the time and it is a snapshot when we go in, at that particular moment in time. So we can be assured when we do the inspection now, that, for example, valproate is being managed appropriately - but we do still see practices, 10 years on after the first alert, that are still being, that people are still being prescribed valproate in child-bearing years. And we found an example only a couple of weeks ago which was completely shocking that at this stage, after all this, we are still finding cases.

Which makes the case for why we're doing this now and why we focus particularly on valproate, and we've only done that in the last six months. So I can give you assurance for the last six months; I can't give you any assurance over the previous year or two that valproate would have been looked at, for example, on every inspection. But we will have asked that, are safety alerts being managed appropriately?

If we find evidence that they're not, they would then be in breach of a regulation, and I think its Regulation 12 for safe care and treatment, if my memory serves me correctly.

Julia Cumberlege: And you would take action then?

Nigel Sparrow: Yes. Yes, that would be a breach of regulation and it would be filed up and managed accordingly.

Julia Cumberlege: Thank you very much.

Simon Whale: So what - just on that question of the action you take, if you take the example that you've just talked about of a practice that is still prescribing valproate to women of child-bearing age, what action can you take to quickly ensure that women are protected from exposure?

Nigel Sparrow: So, they would be in breach of Regulation 12 and therefore they would get probably a warning notice and would be followed up immediately, and the inspector would be liaising with that practice straightaway. We would also inform other regulators; so for example, if it was an individual GP, we would inform the GMC, and certainly through the Responsible Officer, of

what we find, because we do need to share such serious information, but we will follow that up.

What I can't say is whether we - we can never say we will - we can give 100 per cent guarantee because we can't do that with the snapshot inspection programmes that we do.

Simon Whale:

Okay. Can I just ask you something about the fundamental standards of care that I think you set out on your website about what - as to what the patient should be able to expect? So they include things like - and this applies in primary care and in secondary care - being treated with dignity and respect, providing informed consent to treatment, not being put at risk of avoidable harm, and receiving a candid explanation when things go wrong.

As Baroness Cumberlege said, we've been up and down the entire country, and we've met many, many hundreds of people across the three areas that we're looking at, not just in relation to MESH. And I think it's safe to say in all of those areas, the overwhelming majority, if not all of the people we've met, have said that some or all of those standards have failed to have been met - and we're talking about many, many hundreds of people, in addition to the thousands who have contacted us separately by email and by phone. Does that surprise you?

Nigel Acheson:

I mean I think - as Nigel said, when we actually physically are in an environment, we have got a set of supporting questions which we ask and evidence that we look for, for each of those elements, upon which we then make a judgement in each of those domains that you mention and we will say either what we find appears to be outstanding, good, requires improvement, or inadequate.

We also, as part of the short time that we've got to inspect, as we heard we've got some information that we gather which helps us both plan the parts of a - certainly a provider that we will inspect because we currently don't - if we went to a Trust, for example, we wouldn't inspect every single department in that Trust.

Currently we would select on the information we have, but we would also use some of the tests I mentioned earlier on of process. And what we're beginning to learn from the addition to our inspection process of providers that we've added is this well-led inspection which tests the broader tests, the effectiveness of the governance structures, the audit in the organisation. And what we're beginning to find is that that part of our

inspection is a pretty good measure, and it seems to correspond with how good or outstanding we find some of the other services.

But given that we cannot be in every bit of every hospital, what we are really encouraging through the work that we're doing, is that sense of organisations becoming improving organisations, organisations really embracing what - and we look for this evidence that they have an improvement, a quality improvement strategy, that they've got a patient focus.

And in the outstanding, some of the outstanding organisations you can see that and hear that from all the members of staff that we chat to, and we talk to a lot of staff when we're on site. We talk to as many patients and relatives as we can when we're on site, and we report what they tell us. Sometimes - and what they tell us is that things are really good and the staff are very caring, and you'll see some of that in our reports; equally sometimes we will hear some of the comments that you've made.

So am I surprised that these comments are being made? Unfortunately not. But we think that our approach is one that is not only looking for an evidence of good practice and we hold a mirror up if we don't think that it's good, but also that our message to organisations and providers as we go there is really to encourage and share with them what good looks like.

Simon Whale: And in private care and GP practices, how do you factor in - when you do an inspection of a particular GP practice, how do you factor in the experience of patients who are on their list?

Nigel Sparrow: So when we're on the inspection we - or prior to the inspection we give out comment cards, so comment cards are filled in by patients. We talk to the patient partnership group and members of the patient partnership group - we talk to people on the inspection. We do get a lot of information from patients prior to an inspection - that often prompts the inspection.

So through our contacts [and so] - we get lots and lots of information. And certainly the one - the practices that - I shouldn't say the worst practices - almost always there has been information received from patients which has contributed to that inspection. But we do talk to people on the day, we do look at the patient survey, we look at NHS Choices, we look at anywhere where we can get information that the public might be able to tell us about that practice.

In terms of consent, we always look for examples of consent, we check the understanding of the doctors and the nurses - do they understand the consent. We look at complaints. We make sure that there is a complaints

process which has the right standards and people are followed up according to that. So we try as hard as we can to get that information.

Caring is one of the most difficult of the key questions to rate. And when we do find poor - poor caring, it is almost the exception, because even in the - even in the practices that are the most unsafe, ineffective and poorly led, they will often get good reviews from patients, unfortunately - because patients only rate what they've experienced. If they've never experienced anything better, unfortunately, they'll say that's okay - and that isn't okay.

And so we need to raise people's expectations of the care that they're entitled to receive.

Simon Whale: The other thing I wanted to ask about was the regulatory system as a whole. You regulate entities to put it straightforwardly I suppose, others regulate individuals, and others still regulate system-wide. Is there a risk in that kind of approach to regulation of gaps appearing and issues not being detected, and is that a greater issue than overlap and duplication?

Nigel Sparrow: There is a risk, certainly. And because we have good communication between the GMC, NMC and ourselves, we try and close as many of those gaps as we can. But we regulate regulated providers, but those regulated providers contain individuals who are regulated by individual regulators, and we have found examples where doctors have got through the revalidation process but are delivering really poor care.

And therefore we have that conversation straight away then with the Responsible Officer and with the GMC, and similarly the GMC will highlight to us areas of poor practice which then would trigger an inspection of the provider themselves.

Simon Whale: So the solution to the problem of under-lapping, as opposed to overlapping, but in a regulatory system, is what - to make sure you all speak to each other more often - is that...

Nigel Sparrow: Communication and sharing information is really important. The GMC are a little bit stuck because of Section 35 of the *Medical Act*, disclose information until a case has been proven, but the Responsible Officer can share information of concerns, and that's the most valuable conversation we would have, because of the restrictions the GMC have, until a case has been proven.

Simon Whale: Mm. The other thing I was going to ask about if I may was the report you did called Beyond Barriers, which was specifically about elderly people and their interaction with health and social care systems. And that was quite a

concerning report, I think the conclusions were alarming reading. Organisations prioritise their own ends rather than service-users' outcomes, or even system responsibilities, for example.

But we also noticed that nothing's actually happened, as far as we can tell, in relation to that report, and you didn't get a response from the Department of Health and Social Care, is that correct?

Nigel Acheson: So there has been one relatively recently, and the Secretary of State has communicated with our Chief Executive, I think I'm right in saying James, and we're now in discussions about doing some more of that work in the future, and although the shape of that hasn't been absolutely finalised.

One of the other outputs of that - of that work, and you are right that as we are currently constituted, we regulate providers rather than systems and have to be invited by the Secretary of State in order to do that work. But as I say there is a - [but that] looks like unfortunately we won't be able to carry on that work. But in response to the initial report, we are linking up with the first wave of these ICSs, these new organisational forms, and in fact one of - [Sue and the DCI who links] to one of those ICSs, I was there with the...

[Over speaking]

Simon Whale: The Integrated Care Systems?

Nigel Acheson: Integrated Care Systems, sorry, I was there with the leaders in West Berkshire yesterday, trying to explore with them are there things that they think that we, as the regulators, could - are doing that are hindering some of the work they're trying to do to work across their boundaries, are there things that we could do to help? And so we're beginning those discussions, alongside that work and to try and explore how the regulatory system could help improve the transfer across those organisational boundaries.

I think the - one of the things that we do in the well-led inspection now of a provider, accepting the boundary of our current legislative framework, is that we want to understand how a provider is playing his part in this wider system. And on almost every - well in every occasion I can think of, the providers when we did that well-led inspection, are very keen to tell us about some of the work that they're doing as part of, and often a very important part of their local system, and so that is a direction of travel.

And I think our report was a point in time which said actually do you know what, there are real risks for members of the public, the individuals across the...

[Over speaking]

Simon Whale: This is not just elderly people?

Nigel Acheson: Not - well indeed, although that report was...

[Over speaking]

Simon Whale: But the concerns go wider...

[Over speaking]

Nigel Acheson: They do, they absolutely do.

Simon Whale: Can I just ask.. one final question from me for the moment; when you think about patient safety, is there a difference in risked patient safety as between private providers and NHS providers - in your experience and opinion?

Nigel Sparrow: I think in general practice the big risk is certainly the online private providers and that's an area which we've tried to focus on a lot in the last year, because of the lack of sharing of information sometimes, because of the ease of access to medications, and because the GP may not know about that. And we only regulate - when we look at online providers, we only regulate providers that are based in England and employ GMC doctors.

We know that a large amount of online stuff is performed by providers based overseas, providers that may be based in England but using doctors based overseas, and we have no control over that through our current regulatory framework. And that is a major risk, particularly with drugs such as valproate, there is - you know there is conceivably examples that patients may be able to obtain the drugs of their choice, not understanding the risks that they're undertaking.

Simon Whale: And in secondary care?

Nigel Acheson: So in secondary care we are just at the beginning of the process to try and inspect all of the - there are a large number of independent health providers of various sorts and we're in the beginning of that inspection process, so materially to say about the - and those are often quite small. And as I mentioned earlier on, some of the really bigger providers, we had a very useful dialogue over the last - well certainly six months that I've been at CQC and it'd be probably six months before that in my previous role, where those providers are really beginning to understand.

And we're beginning to be able to make better use of and the fact that the individual doctors who work in those providers have to, as part of their annual appraising, include information about their whole scope of practice, wherever that practice occurs. And as Nigel said, some of that information sharing we now have much better ways of insisting that information sharing takes place two-way.

And I think we'll be beginning to see over the next, well it's already starting, but I think it can only increase the safety of the care that's provided because those doctors will not be able to, for example, practise in a private setting in one way, or one set of procedures, and not be able to demonstrate to their Responsible Officer that they're appropriately trained and keeping up to date in order to do that. So that I think is palpably changing.

Simon Whale: Mm, and when you look at the system overall, as we've just discussed it, who - you know that's private sector, public sector, system regulators, you and the individual regulators, who's got ultimate responsibility for patient safety?

Nigel Acheson: Everybody who has anything to do with touching patients. So I would say the primary responsibility is for the clinician who is sitting opposite and recommending and indeed treating patients. I think ultimately that is where the primary responsibility must lie. It's certainly what I felt when I was practising clinically. And I think the regulatory authorities above that are - ways of trying to assure that those individuals, and the facility in which they operate, are providing a safe environment and then the safe treatment for patients in that.

So it's more than just about the individual - it's about the surrounding buildings, it's about the support staff, it's about the advice that they are given in order for them to make a choice about the treatment they may choose to take. So, but ultimately I think - if we take that responsibility away ultimately from the individual, then I think that's an error frankly, and everything else is to try and support and make sure that those individuals are practising in a safe way in the safest environment. And that's certainly part of our role we feel.

Simon Whale: Thank you.

Julia Cumberlege: Valerie, do you want to...

Valerie Brasse: Yes, I do. Can I ask you about your relationship with NICE - in fact when you started you said you didn't have a particularly formal relationship with them and it was different to NHS Improvement. NICE came to give

evidence before us and the Deputy Chief Executive at that point told us that they run an intervention procedural programme which is about looking at safe and effective procedures to be [unclear], performed by clinicians, but they have no way of enforcing those.

They did apparently, once upon a time, they told us that CHAI so your predecessor-predecessor, did inspect against those standards, but it hasn't happened since. And they mentioned that they had been in conversation with you about maybe enforcing that, getting that back as an inspection against the standard, but hadn't got anywhere.

So how can we move that along? I mean here they are, they're coming up with their best estimates - of what good procedures, safe medicine should look like, and they're putting that guidance out there and no-one is inspecting against it.

Nigel Sparrow: So, I have a regular meeting on the general practice side with NICE, and we met just last week, and we continue to talk about how we can ensure that the NICE quality standards are checked, to a regular inspection. Where we're currently asking general practice for example, do you - we ask the question do you practise evidence-based medicine? Do you look at NICE guidance? Do you disseminate NICE guidance? We'd need to see examples of that.

Again it's a bit like the valproate for safety; you know we need to just look in detail to say that quality standards are being adhered to. And so we do have a relationship with NICE to try and ensure that happens.

Valerie Brasse: But is it a standard against which you inspect?

Nigel Sparrow: Yes.

Valerie Brasse: I mean we know that they are going to produce new guidelines very soon for the treatment of stress urinary incontinence, for example. Now those people who have been damaged by that, will place quite a store by that guidance being enforced. Who does that? Who's responsible for making sure that happens, so if it is not a standard against which you inspect - who do they look to for that?

Nigel Sparrow: It'd certainly form part of our effective key question.

Valerie Brasse: So it will - these new guidelines, as they come out, will routinely become part of the inspection proforma?

Nigel Sparrow: So this is work in progress, and as I say, we've been meeting with NICE for quite a long time to try and embed this. And because guidance changes so frequently...

Valerie Brasse: Or not.

Nigel Sparrow: ...well this is their argument - because guidance does change, they are not desperately keen to have particular examples put in place all the time. But we do produce what is called Set Specific Guidance which is guidance for our inspectors to ask questions, and we have agreed that any current and - NICE guidance is actually included. Any new guidance will be included within that, and they will provide us with a list of questions they would like us to ask, and we will put that forward for discussion at our next Set Specific Guidance review.

So that happens every six months, and so this is work in progress and we would like to see more evidence-based medicine being checked up on in our inspections. But again, we don't - for general practice we don't inspect every general practice, except every period of five years. So we will look when we go in and we'll check what we can find when we inspect, but there are big chunks of general practice that will not be inspected for a few years.

Valerie Brasse: I understand that.

[Over speaking]

Nigel Acheson: So in hospitals it's not just the fact that we won't be in every hospital every year, but it's the fact that, as I mentioned, we won't be in every core service and in every hospital. And with the - what we're trying to do is move to - to try and check that - so an organisation, for example, will have an executive who is responsible for ensuring that NICE guidance is - relative NICE guidance is enacted in their organisation, or being taken account of.

What we will do in our well-led inspections is to check that process and, as Nigel said, then what we'll try and do is test - test that against a piece of guidance, for example, recent or other, but it wouldn't be every piece of guidance in every Trust every time we visit it - we simply - we can't do that. So what we are - what we're saying is actually if the responsibility ultimately is for the individual who is advising the patient, or treating a patient, then the governance internally in the provider they work in, is the bit that we would test. Because we're better able to test that governance that it works through an organisation, than trying to test each of the individual bits of guidance.

Valerie Brasse: For sure, but one of the ways you test the governance is by looking at a spot check against the specific guidance.

Nigel Acheson: Indeed. Indeed. But - and so the question of which examples that we use is difficult...

Valerie Brasse: How is that determined?

Nigel Acheson: We, if we're in a core service and it would most be likely be one of the bits of guidance that is pertinent to the core service that we are inspecting. But it may be that, rather as Nigel has said, that with the focus being on valproate in primary care, it may be when this NICE guidance is produced, that that's the bit that we test [unclear].

Valerie Brasse: Okay. Can I just come back on the valproate, sorry, just one more on the valproate. I'm just conscious that with NHSI - Improvement - they have recently issued that alert on sodium valproate, which is requiring a sort of systemic approach to reinforce the advice of MHRA; so is that something that you would be testing, the systemic approach, the advice that the MHRA put out is being enforced? Is that something that CQC would look at across the board?

Nigel Sparrow: Certainly in general practice we ask whether their practices are acting on safety alerts, and we look for examples. We always ask for generic examples and we usually ask for the last three safety alerts, to tell us how you're reacting to that. But we now particularly focus on valproate and we will ask our - we always ask our specialist advisor now to look at records of patients who are on valproate to check that there aren't anybody - any patients who are of child-bearing age, or if there are, then...

[Over speaking]

Valerie Brasse: You're now thinking more of a system-wide approach, but that's really...

[Over speaking].

Nigel Sparrow: Yes, I suppose that's in getting to a new general practice.

Nigel Acheson: Yes, and I mean there is a group now called the National Patient Safety Alert - an alerting committee, which Professor Baker and our Chief Inspector of Hospitals sits on as Vice Chair and they are working with the NHSI colleagues to try and work out the best form of communication and assessing how to do that task.

Valerie Brasse: Thank you.

Julia Cumberlege: Sonia, do you want to ask any questions?

Sonia Macleod: I think they're answered...

Julia Cumberlege: While you're thinking, perhaps I could go back to Cyril - do you want to say something about registries?

Cyril Chantler: Oh, well it's a general comment. You need information in order to act, and if we're going to improve the safety, we need the information. And so I've experienced in my clinical past of being involved with a registry so that you register the activity and then, with patient permission, you can enquire into the outcome. And I just wondered if you have any thoughts about that. Because certainly the systems that were involved when I observed the quality, based on standardised mortality rates which were not very satisfactory, coming from HES data as they do.

We are looking at other alternatives, and I wonder if you've got any observations about that?

Nigel Acheson: So my observation on it, in terms of some of the audit for example that's being performed and - but where some of these new procedures could, I would have thought, become part of an audit, the collection of that data is something that I think that, if it's a national audit, people should be contributing all their data to. What we do find is that that is not always the case, and certainly it's one of the messages when I'm talking to audiences, I flag the national audits and say that for providers, if you are providing services for which there is a national audit, our expectation is that those colleagues are contributing their data to those audits.

Now I accept that's slightly different to a registry, but for me the principle is the same, and certainly if it was a new procedure, one of the things that we would expect, and there is a process for this in providers as you know, where there is a - there is supposed to be a process by which individuals will sign up to anything that they're wanting to introduce a new procedure and they will enter their cases case-by-case.

My sense is that either - we've got two vehicles potentially, and currently one is the national audit where, for example, new guidance comes out and, as we've said, that I would have thought to be built into their audit process, or as I say the other area that's of great interest to me, because they've got such richness of data and seem to have such buy-in, is the Getting It Right First Time group.

Cyril Chantler: Yes, thank you. Could I ask another question? How do you encourage an open culture, both for patients and for staff? The Chief Executive for the

Health Watch two or three years ago talked to the Public Accounts Select Committee, mentioned a fear that patients feel if they complain about their doctor, that in some way that might affect their continuing access to treatment, and I've also heard it in relation to hospitals.

So how can you encourage patients to feel able to comfortably come to you, and how do you protect them if they do? And the same thing applies to whistle-blowers?

Nigel Acheson: So in terms of - so we've just started a campaign which is encouraging people to tell us about their care and we are genuinely interested in people telling us about their care. And one of the things that we say when people contact us is that we can't take up an individual complaint, or follow the individual incident, but the information that people are kind enough to share with us, be it good or poor experience, does form, as Nigel as said, some of the information that we then - that we then use to plan our regulatory activity.

More generally, in terms of the organisations themselves, we do see that the leadership, from boards right the way through organisations, is the thing that sets the values and the behaviours and the expectation that takes that fear away...

[Over speaking]

Cyril Chantler: So very specifically because I don't want to run out of time; if I was very worried about my care in a hospital, and I contacted the Care Quality Commission and said, look this has happened to me and I really don't know quite what to do - what would you do?

Nigel Acheson: So one of the things - so we would respond, thanking the person for sharing that information with us, and we do genuinely use that information. So the contact is something that will - that person can be assured that we will use that information. But what we have to tell the individual is that we can't take up the complaint on their - on the individual's behalf. And what we do is we advise them about the steps that they can take within an organisation, and using the complaints process, the PALS process within the organisation.

But if then they are - they don't feel either able to or and (that's given them the response that they need), we'll also share with them the details of the Parliamentary Health Service Ombudsman, and where individuals can take their case further.

Cyril Chantler: And if I was a young doctor that's similarly contacted [to say] I'm really worried about what's going on, what would you do then?

Nigel Acheson: So one of the things that we check and we - one of the interviews that we do on our well-led inspections is the Freedom to Speak-up Guardians in all of the Trusts. So one of the first things I'd be - we'd obviously respond to the young colleague, but one of the things would be to say you know have they felt able to discuss that with their Freedom to Speak-up Guardian? And we've seen and met with a number of - junior and senior colleagues in our inspections - who have felt able to do that. And have felt able to speak to us on inspection as well.

And so that's - we feel that's a really powerful mechanism within an organisation that clearly, if they didn't feel able to then we would - obviously depending on what the concern is - we would note the concern, but again the same caveat applies, that we can't take up an individual case and certainly - and we do get contact from doctors, for example, who are in a process of one sort or another in an organisation and we cannot - we can't sort of take up that individual case. But we hear and we listen to them, and we will use the information they shared with us.

Cyril Chantler: Okay.

Nigel Sparrow: And the same applies in general practice. We have - but the access to a Freedom to Speak-up Guardian is more complex in general practice, because of the small organisations. And so I was talking to - National Guardian, Henrietta Hughes, a couple of weeks ago, and we were talking about how we can embed that somewhere distant from the practice. So Henrietta's starting to look at general practice from April, and we would like it to be at network level, or at CCG level, but it is really important that everybody working in general practice has access to a Freedom to Speak-up Guardian, the same as in Trusts.

Julia Cumberlege: I'm very interested in that conversation. What I need convincing is really that you ensure that you get as much information of the users of the service as you possibly can. And one of the things I was just wondering about, when you're going to do an inspection, do you notify patient bodies, do you - how do you get them actually involved? And taking up Cyril's point, I can understand that some are very reluctant to actually be open and honest because, as Cyril was saying, it's about their future care. Convince me that you are really, A, ensuring that you get the patient voice, and secondly, that you act on it?

Nigel Acheson: To getting the patient voice, there are - when we announce an inspection - we don't always announce an inspection, and this is one of the debates that we are having internally in the CQC. So if we're going to inspect in a provider more than four of their core services, and on inspection we will announce that inspection. And for those occasions, the providers will put their notices up inviting people to submit comments to us. And for the unannounced visits it's slightly more difficult.

One of - as I said, in terms of the response to the National Patient Surveys, one of the things that I'm - every time I get an opportunity to speak, I'm saying actually we don't want to just hear a patient's experiences, we want to involve them as partners in their care very much in terms of the sort of approach we take in maternity. And we're encouraging providers to reach out and engage with their patient representative groups, any of the groups they can, not just to find their experience but to help plan future service developments.

And we know that there are going to be [unclear] service departments in almost every area of practice in the next number of years, and if those happen without the voice of patients being involved in that planning process, I don't think they'll be successful. And certainly that's one of the things that we are - we are trying to promote.

Julia Cumberlege: And do you keep trends, do you on complaints and things like that?

Nigel Acheson: We do. We do...

Julia Cumberlege: So you know how you're doing?

Nigel Acheson: We do. And our National Customer Contact Centre keeps all of that information and they share it with providers - with the relationship owners for providers, and we genuinely use that in terms of how we respond in a regulatory way. So yeah.

Julia Cumberlege: Sonia, did you want to...

Sonia Macleod: [Unclear] I'm all right thank you.

Julia Cumberlege: She's all right, okay. So I'm just going to ask my colleagues if there are any further questions...

Panel Generally: No.

Julia Cumberlege: All right. Well thank you - any questions you'd like to ask us?

Nigel Sparrow: No thank you.

Julia Cumberlege: When is the report going to be published is often a question that we get asked, and I'm afraid that we can't answer that.

[Laughter]

But thank you so much for coming...

Nigel Acheson: That's okay.

Julia Cumberlege: ...we've learnt a lot and it's been really, really helpful. And if we've got further questions, perhaps we can write to you, because I would actually like to know a bit more about your inspectors and how you induce those and all the rest of it. But I think perhaps we ought to move on, because we've got another session coming up.

Cyril Chantler: And you're going to let us know your forward plan?

Nigel Acheson: Yes. The other thing about - we of course have experts who are experienced and who help us by being members of our inspection teams, and we've looked at that [unclear], because they are generally members of our teams, that the importance that we place upon them...

[Over speaking]

Julia Cumberlege: Right. All right. Thank you so much. Thank you.

Multiple speakers: Thank you.

END OF TRANSCRIPT

Session 2: NHS Improvement

START OF TRANSCRIPT

- Disa Young: I'm Disa Young, Assistant Director of Regulatory Affairs at the Independent Healthcare Providers Network.
- David Hare: My name is David Hare. I'm the Chief Executive of the Independent Healthcare Providers Network. The organisation represents the independent healthcare sector in the UK.
- Howard Freeman: Good afternoon, my name is Dr Howard Freeman. I'm the Clinical Director for the Independent Healthcare Providers Network.
- Karen Prins: Good afternoon, I'm Karen...
- Julia Cumberlege: Sorry, I can't see your - there are too many bottles in the way. Right okay.
- Karen Prins: Good afternoon. I'm Karen Prins. I'm the Chief Executive Officer of BMI Healthcare.
- Julia Cumberlege: Sorry, you're the Chief Executive of?
- Karen Prins: BMI Healthcare.
- Julia Cumberlege: Oh yes.
- Karen Prins: I also have a clinical background.
- Julia Cumberlege: Thank you very much.
- Steven Luttrell: I'm Steven Luttrell...
- Julia Cumberlege: Another bottle in the way. Sorry, bottle...
- [Aside discussion]
- Steven Luttrell: I'm Steven Luttrell, the Group Medical Director for BMI Healthcare.
- JJ de Gorter: Hello, good afternoon. My name is JJ de Gorter. I'm the Chief Medical Officer for Spire Healthcare and I'm responsible for medical standards, governance and oversight.
- Julia Cumberlege: Right, thanks very much.
- Mahmood Shafi: I'm Mahmood Shafi, I'm the Medical Director and Responsible Officer for Nuffield Health. I'm still a practising gynaecologist but specialising in oncology and cancer work in Cambridge.

Julia Cumberlege: Right, thank you very much. That's very helpful. First of all, I ought to ask you if you have any questions of what I've just said. Has anybody got any concerns? No? All right.

If I could first of all ask the Independent Providers Healthcare Network, there are relative differences in the proportions of patients implanted with mesh between the NHS and the private sector. I'm just wondering, could you explain to us just a bit about the differences?

David Hare: In terms of the numbers or in terms of the differences?

Julia Cumberlege: Well both.

David Hare: I think on the numbers, we don't have precise numbers of exactly what was done within both sectors. I think one of the challenges that we're engaging with at the moment in our work is to how we can ensure that there is greater alignment and consistency between both the independent sector and within the NHS, and I think there is - happy to get into the details around that.

Part of it is around data, the importance of the submission of data and we believe there is a real opportunity to have an improved alignment of data information available to the public across both the NHS and the independent sector. Clearly, indemnity is an issue that there is focus on at the moment and where there's the opportunity for greater alignment as well, and within some of the areas of governance as well.

So, our view is that we need to be pushing harder to see whether or not we can bring those two things together, for the end user, for the patient. I know you've spent lot of time talking to patient groups through this enquiry. Ultimately, they want a joined up, seamless health service that is as safe and open and transparent as possible. I think a lot of strides have been made in recent years to improve that. But fundamentally, we see there is more to be done to ensure that that alignment between the NHS and the independent sector is done.

Not saying one is better versus the other, and there may be some areas where differences is put right, but generally speaking we need to be bringing those two things together a little bit more. Howard, I don't know if you want to...

Howard Freeman: Just to endorse that and to say that having been at IHPN's predecessor for about three years now and coming into it with a lot of experience in the NHS in terms of being the Medical Director and governance, it was quite clear to me that there were differences which were both appropriate in as

much as you're not running NHS organisations, and I never believe that everything the NHS does is absolutely correct. But what was important was to get comparability, so that we were clear that we could compare like with like. That's really what we've been spending the last three years trying to do to ensure that if we don't have identical systems, we have comparable systems.

You will know that the independent sector previously was regulated in a totally different way to the NHS - in terms of the regulator, CQC, it has moved to regulate both in the same way, and part of it has been to ensure that that has been comparable in sectors which operate very differently, and see effectively different ranges of things. So, there is the acute work in terms of the emergency acute work in the independent sector that the NHS has. But there is, still, a very significant amount of acute surgical work, and it's about 10 per cent in some specialties are done in the independent sector for the NHS.

Julia Cumberlege: So, if you take an individual patient who actually goes to both parts, or goes privately, goes to the NHS, back to privately, back to the NHS, how does the data then inform you of what's happening?

David Hare: I think the - I should make clear that the IHPN is a membership organisation, we don't necessarily have lots of data fed to us by individual providers about patients. That would go into the regulatory system.

I think a general point of course across the NHS and private sector is you're often talking about the same clinicians who will work across both sectors and that is common. There is a small cadre of consultants and clinicians that will just do private work but most will work across both. Both provider types will submit information whether it be adverse events information to CQC. As Howard described, I think the regulator will assess organisations based on are they well-led, responsive, caring healthcare providers? It doesn't necessarily look at the pay-all types.

So, in terms of the requirement, the regulator requirements across both the CQC, they are - they're exactly the same. I think what Howard was describing was, I think, a push that we've made, supported by others as well to say, well okay, where there are NHS specific systems and the National Reporting and Learning system will be one of those now migrating across to the DPSIMS. We've been looking at the health...

Disa Young: HS...

David Hare: ...yes, the Health Safety Investigation Board making sure that too can investigate major incidents were they to occur in the private sector. So, a

part of what we're having to do is push quite hard to ensure that we can align to those systems where they're right, but actually, there is quite a lot of alignment across both systems, particularly from a regulatory context.

Julia Cumberlege: I just wonder, I mean I think both sections have an important part to play in the health of this nation. But I'm just wondering, if things go wrong in the private sector, what action is taken? How is that resolved?

David Hare: I mean, clearly, fundamental responsibility for what happens within any provider organisation is the same in the NHS and in the independent sector - it's for that provider to ensure that it puts right any identified issues or challenges. Clearly, there is also the reassurance to patients around the CQC inspection regime where the CQC will identify problems and issues and ask providers to tackle that. So, first and foremost and fundamentally, it should be for the provider organisation to deal with issues and deal with concerns that gets raised.

Howard Freeman: Yes, and not only is the regulator of the provider the same, but of course the regulator of the professionals is the same, and the standards that the regulator of the professionals applies is identical. It doesn't matter where you work, the General Medical Council or Nursing and Midwifery Council will apply its code to you.

So, there is that level as well. One of the things that we need to reflect on is that the independent sector, the people that we represent, most of them do both work for the NHS which is regulated by the NHS, and they do work which is paid for by the individual or by insurance. So, there are differences between the patients and the way that's regulated. My colleagues may wish to pick up on that because they have to operate that on a daily basis.

Steven Luttrell: We would, in terms of complaints, have a system that's aligned with the NHS system [unclear] system would be the same. So, if things go wrong from an adverse event perspective, we have a system of escalation and recording those. Similarly, a complaints system which has an escalation to an independent review if necessary. Those are regulated to the same standards as the NHS would be regulated through CQC and the GMC system.

We're keen to contribute to single systems that would give a better overview across the whole, but sometimes it's only possible to spot a trend or an adverse trend early on if you can see the system as a whole. I think with my colleagues we share a desire to contribute to single systems that would enable adverse event trends to be picked up and spotted more quickly than they perhaps have been in the past.

Julia Cumberlege: So, do you as private organisations, you have a responsibility to put things right when they go wrong. If you have an operation, insertion of mesh that is causing a lot of problems, that is then recognised and then you try and put that right?

Steven Luttrell: We would do.

Julia Cumberlege: Then if the individual is actually paying for that, and we've heard quite a lot of stories from women whose parents are the banks of mum and dad who have actually supported, especially when things have gone wrong, because the initial operation was affordable, but then they actually have a problem in terms of putting it right. So, who pays for that second event where you're trying to put it right?

Steven Luttrell: We would discuss that with the patient on an individual case basis. There is, for many operations, a recognised complication rate, but in some circumstances, that complication rate might be over and above what would be regarded as usual or normal or related to perhaps something that's gone wrong in the operation or something that's gone wrong with the device, and in those circumstances, we would look to work with the individual concerned to rectify that.

JJ de Gorter: Could I just add to that? I think there are two duties. There's a statutory duty but there's also the moral duty. So, the statutory duty around duty of candour, we all comply with and we follow. I think in terms of moral duty, it's the duty to do the right thing. So, in the example that you've given, we consider it our duty to put the patient right. We've done therefore metal on metal where we had to communicate with four and a half thousand patients, we did it with the PIP breast implant scandal. I think the financial issues are at the very back-end of it. The first thing is to do the right thing by the patient and to ensure that further harm isn't occurring and then we'll consider all the other duties afterwards, which for us are secondary. Because the first is what's our duty to the wellbeing of the patient who has trusted us?

Mahmood Shafi: As far as Nuffield Health are concerned we have what's called the Nuffield Promise, so that we promise to put right any issues that arise from any surgery where the patient is paying for that surgery. So, if there are unforeseen complications as a result of that surgery, that it's put right at the cost of the provider, i.e. us, rather than the patient. So, it's no additional charges whatsoever for the patient.

Julia Cumberlege: Can I go a bit further, because I'm thinking about mesh now, the insertion of mesh, if the patient is really very anxious to have the mesh removed, do you provide that service, or do they have to go to somebody else?

Mahmood Shafi: With mesh removal, it is a very specialised service. I think one of the important things is to get the diagnosis right.

Julia Cumberlege: Sorry, the important thing...

Mahmood Shafi: The diagnosis right, because all actions follow on from a correct diagnosis. Not everybody presenting with an issue post-procedure will that be related to the actual surgery. It may be something else. So, I think it's really important to clarify what is causing the patient's symptoms. There are accredited centres up and down the country. The mesh, as the committee will know, is designed to be inserted and for it to be incorporated into the body so it is embedded within the tissue, and to remove that is a complex procedure.

We need expertise from gynaecologists, from urology surgeons, from bowel surgeons, from people who specialise in imaging for that particular area, and also people with pain expertise, to try and clarify what the cause of the patient's symptoms are and what the correct course of action is. That is primarily within the NHS because that is where the volume of activity occurs.

Julia Cumberlege: I do understand all that, but I'm just sort of wondering that - and I don't know, and you will tell me, because you're providing the service, how much - if you are equipped to do removals or do you pass it on to somebody else? How do you manage that?

JJ de Gorter: If I may answer, it's a clinical decision. So, we're reliant on a specialist to advise whether our facilities are the appropriate one for the patient to have removal surgery. In many cases, it isn't because it's complex surgery. But ultimately, we're having a three-way discussion between ourselves, the clinician and the patient to determine where's the best place for their care to be delivered. That's an individual discussion. It's difficult to make generalisations.

If we're able to do it at our facility safely and effectively, then of course we'd like the patient to return to us and for us to have the opportunity to put things right. Sometimes, that isn't possible. Sometimes, patients, their best outcomes are to be achieved in a tertiary centre which is usually an NHS centre, in which case what we'll do is look to facilitate their care and the transfer of care to somebody at that centre. We've done that a number of times.

Sonia Macleod: Who funds their care?

JJ de Gorter: So, if they were self-funded and they still wish to be a self-funded, we would take responsibility for that. If they were an insured patient, they may be might be covered by insurance. But ultimately, we're not going to allow a delay to take place while that is decided. We'll try to negotiate. First of all, we'd try to identify the best place for them, for their care to take place. If it's clear that the responsibility is on us to fund the care, we'd agree that quickly. If it's less clear, if it's a question of arriving at funding as quickly as possible to allow care to take place, we'll just arrange that and reclaim it at a later date. Our goal is not to delay care and to continue any undue suffering or harm.

Mahmood Shafi: That's a decision for the multi-disciplinary team to make and advise.

Julia Cumberlege: Sorry...

Mahmood Shafi: It's a decision for the multi-disciplinary team to make and advise the patient as to what the next appropriate steps are.

Julia Cumberlege: Yes, right, okay. Cyril?

Cyril Chantler: Before I start, I must declare a conflict of interest, because I'm a non-executive director of the Private Health Information Network as in fact is David.

Right, I am aware how much closer the NHS and the private sector is working nowadays, and in fact the creation of PHIN, the Private Health Information Network is part of that. David mentioned the need for having a database which is - comes together. You've mentioned that a large proportion, 45 per cent I think it is, activity in the private sector is on NHS patients. So, they come together.

It has been suggested to us that in the private sector, the institutions are less concerned about the governance around clinical care than the individual, that in the NHS, the NHS elects to look after the patient, whereas in the private sector, the customer is also the doctor as well as the patient. You've already said this afternoon that you take your responsibility for caring for patients as institutions just as seriously. I accept that.

So, with that as the background, can we just discuss for a moment, the revalidation procedures of the General Medical Council and the position of the Responsible Officer? Because again it has been suggested to us that maybe in certain parts of the private sector, less so I think in the big

institutions, that the Responsible Officer is not as close to the management and to the GMC as they are in the NHS.

So, would one of you just like to - maybe you can tackle that one.

Howard Freeman: Well, it might be better, Cyril, if one of the Responsible Officers here actually answers that as it really is. I don't, if you want to answer that JJ.

JJ de Gorter: I'm happy to pick - I used to be a Responsible Officer. I'm not now. But the Responsible Officer reports to me. I think quite the converse is true. I've been on the Board of an NHS Trust and I've chaired a Quality and Safety Committee for a number of years. So, we have - I would say the process that we have in place to discharge our accountability in relation to the RO regulations are very strong. Indeed, we had NHS England come and visit and do a higher-level RO visit only just in October. They found - they made no recommendations as a result. We have 330 consultants and doctors who connect to us for the purposes of revalidation. I think our approach is extremely rigorous.

On the other hand, the information we sometimes receive from NHS Trusts, and we must engage with over 200 NHS Trusts across the country, some is very good and has definitely improved, but the outputs are variable. That's the truth. And variable in terms of willingness to share information openly, share information proactively, and in terms of quality outputs of appraisal that we receive. If we're unhappy with them, we're quite clear we'll return those to the individual and we put their practising privileges on suspension until we're happy with it.

Now, that has taken some time to get that position and it's created some friction, not only with consultants - who aren't our customers by the way, they're our partners, patients are our customers, and that's quite clear for us - so our consultants as partners we've upped the bar. We've made clear our requirements for them to work in partnership with us to put patients' interests first and foremost.

But we're there now and, as I say, our systems are very rigorous. I can't speak for everybody, but the Medical Directors and the RO across the independent sector, we communicate very effectively, because we're a relatively small group and most of us are headquartered in London, so we come under the same NHS England region, which helps in terms of communications and forward communications and soft intelligence especially. Because it's not all about the numbers.

But my view, from what I've seen, is that the independent providers discharge their responsibilities under the RO regulations, do so very seriously and very rigorously.

Howard Freeman: I'll come in on that, if I may Cyril, because I deliberately let JJ answer it first. I was an RO of course in the NHS and I still do appraisals in the independent sector. My view, having spoken to the ROs in the independent sector is the rigour is exactly as JJ says. The numbers are smaller. It's often easier for them to do in terms of being rigorous.

The constant issue that's come back to me, and I've taken up both with the former medical director of NHS Improvement and the current national medical director of NHS England, is the inability in many cases, not in all cases, but in many cases, for the independent sector RO to get information from a consultant's NHS RO. I've got email after email. It's often that they're just ignored. The emails are not answered.

So, there is a real issue, and a real takeaway for me is, there is a real issue about the dialogue between the NHS and the independent sector ROs when an independent sector RO asks for information. Now, I'm not saying that everyone in the independent sector is perfect. We know that doesn't happen. But there is clearly an issue and it's been going on now for as long as I've been a clinical director at IHPN. As I say, it is something I have taken up on several occasions with the senior leaders of the NHS.

Cyril Chantler: Thank you, that's very helpful. Can I also then ask a question which is related to the same thing about co-ordination between the NHS and the private sector? When we recommended a pause in the insertion mesh last summer and NHS England effected that, what of course was clear from NHS England is that they've had no jurisdiction over the private sector. So, we've had some concerns about whether or not the private sector would themselves follow the advice that we had given. Can you just explain to us how you reacted to that, JJ?

Mahmood Shafi: That was the safety alert that came through. I think all of us in the independent sector took immediate action. So, there was the exact same pause that was recommended right across the board. Since then, as far as I'm aware, no such procedures have been undertaken within our organisation since then, and in fact, we have reassured NHS England that that is the situation, because it's in all of our interests to be able to do that. We're far more stringent than needs to be in this situation. Patient safety has to come foremost with all of us.

- Steven Luttrell: At that time, there was no immediate collaboration between the medical directors about the implementation of the alert and we all implemented it in line with NHS England's expectations. We implemented it in Scotland as well, the same recommendations using the same system. I know that with - in line with the guidance, authorised two operations since that time through the [unclear] system.
- Julia Cumberlege: Can I ask then, what you're doing for women who come to you suffering very much from incontinence? How are you coping with their troubles?
- Steven Luttrell: Those would be managed by individual consultants within their clinical competence using their skills. I know that they have been supported by their associations in terms of explaining the options that are available to women when mesh is not a desirable option.
- JJ de Gorter: I'll come in, if I may. So, we've complied with the mesh and we shared the approach with NHS England and we had a conference call with them. Women on high vigilance procedures can still have those, but what we require is evidence of the MDT prior to the procedure being booked. We need evidence from the consultant's Responsible Officer that this forms part - scope of their NHS practice and that they're deemed capable and competent to undertake the procedure.
- We ensure the patients have all the information to support informed consent as to the risks and benefits and alternatives to the procedure they're having, and then we require the individual consultant to enter the data onto the relevant registry. Those are the five requirements.
- Now, we've had a handful of those since the pause came into effect at the beginning of July, but we audit that, we monitor it and the consultants who have undertaken this procedure comply with all the guidance from the pause and in relation to the high vigilance procedures.
- Julia Cumberlege: It would be very helpful to us if we could have those figures. Is that possible?
- JJ de Gorter: This year, we've had six patients undertake a high vigilance procedure in line with guidance from NHS England and NHS Improvement.
- Simon Whale: Have those been self-funded or are they NHS referrals?
- JJ de Gorter: I can't tell you that I'm afraid. I can tell you, but I haven't got that information to hand.
- Julia Cumberlege: But six...

JJ de Gorter: I'm happy to provide that afterwards.

Julia Cumberlege: Six from your organisation. How about...

Steven Luttrell: Two.

Julia Cumberlege: Two.

Steven Luttrell: Two from...

Mahmood Shafi: None as far as I'm aware.

David Hare: Chair, happy to co-ordinate that more broadly if that would be useful?

Julia Cumberlege: Yes, that would be helpful, thank you.

David Hare: I'll let you know [unclear].

Mahmood Shafi: I think the thing is with surgery, it has to be - you have to look at all the options available. Surgery is not the only option available. I think with the introduction of these techniques, it quite often became a much earlier option in that pathway than would traditionally have been the case. So, there are things like physiotherapy, weight loss and other medical inputs that can help these patients with these symptoms. So yes, surgery should still be an option. I think it's about training, it's about audit of their practice and it is also about consent, proper consent, informing them of all the options available, all the pros and the cons associated with each of those decisions, allowing the patient to choose what they see is the most appropriate for them.

Valerie Brasse: But it isn't just the mesh procedures that fall into the high vigilance by exception.

Male: Correct.

Valerie Brasse: Of course, it's the others, so I'd be interested to know the numbers of the others that you're doing under high vigilance. But also the point that you were making, if one of the conditions is about assessing the competency of the clinicians who are undertaking these, I think your point was that you're not getting the information you want from the NHS when you're asking for it. So, how are you able to satisfy yourself as to medical competency?

JJ de Gorter: We only approve a consultant once we seek the information. If the information is not forthcoming then they're not entitled to undertake those procedures in our hospitals. It's up to them to make the information available. But we require it from the responsible officer. It's not on a slip of paper.

- Simon Whale: Do you monitor individual surgeons' performance within your own business? Do you know once you've got that surgeon practising privilege, how effective he or she is at what they're doing?
- JJ de Gorter: So, we track their practising privileges, well first of all through appraisal. So, we provide them with a standard data set that's made available for the appraiser to consider their scope of practice with us as part of their overall scope of practice. We also undertake a biennial review of their practising privileges, so complaints, incidents, claims, soft intelligence, volume of practice, type of practice, and that's a formal process. That gets considered by the registered manager but signed off by the Manager Advisory Committee. So, that's a formal process.
- Simon Whale: Is that similar across all three providers?
- Karen Prins: Yes, pretty much.
- Simon Whale: So, if that's a robust system, we shouldn't have expected to see mesh operations being conducted in the private sector that resulted in poor outcomes due to the quality of the surgical intervention.
- JJ de Gorter: I think one of the issues was it wasn't - it's not that clear. It's not that clear that once mesh started being used there were all poor outcomes. So, in terms of complaints, there wasn't a trend of complaints suggesting that mesh resulted in poor outcomes. The rates of readmission for an individual didn't look untoward to the point that you would want to intervene or start asking further questions. We have quite enquiring minds. So, our first response to an incident complaint isn't this is a rare thing, it's only happened once or twice. Ours is, first instinct is, is there a broader issue here and we need to investigate until we've ruled that out.
- So, we do have enquiring minds. We don't take an issue, incident, even if it's isolated, purely at face value. I think that's part of the culture....
- Sonia Macleod: Is the system geared to look for long-term latency issues?
- JJ de Gorter: I don't think that the system captures implanted devices of any sort looking for longer term or longitudinal failures. There's a question about the regulation of medical devices, whether that's adequately strong enough. There's a question there. But on the assumption that it is and it gets approved, my view is that any implant device that isn't absorbed - any implant device that isn't absorbed or to be added onto a registry, it's quite often the adverse outcomes which aren't foreseen, because they're unforeseen because otherwise they wouldn't have been approved, don't become apparent until much later in time. Something like the National

Joint Registry works really well and it has helped in the recall or suspension of specific devices because the longer-term consequences weren't apparent at the foreseeable outset.

I think that any implanted device would be subject to the same principles.

Simon Whale: But there are two issues aren't there? There's the device itself and its short and long-term efficacy and safety inside the human body, and then there's the implanting procedure and how well that was conducted. So, are you confident on both fronts that you as an organisation knew enough about what was being done at the time?

Mahmood Shafi: With devices with surgical procedures, the majority of consultants working in the independent sector will have an NHS contract. Their appraisal will be with the NHS. They will have whole-practice appraisal, i.e. data from the independent sector, whichever organisations they've worked with will feed into that appraisal process.

I think there are two issues that are important. It's not just about the quality of the surgery that's undertaken. Also, surgery has a complication rate and similarly, the alternatives to these devices also have complication rates and significant complication rates. In fact, a lot of the surgeons have become deskilled doing these procedures because they have been brought up with these newer devices.

The other issue is with regard to the mesh types as well. So, it's not just mesh per se; it is the different types of mesh and how they react within the body and the evidence that supports that as well. I think there are major issues in the multiplication of the different mesh types and the mesh procedures that came on stream through the industry that has led to some of these issues.

Valerie Brasse: NHS Digital was able to do a 10-year retrospective audit of mesh procedures, stress urinary incontinences and prolapse. Could the private sector do the same?

JJ de Gorter: In terms of identifying all the patients?

Valerie Brasse: A 10-year retrospective audit. Well, first of all, just looking at the numbers and the complications. Because one of the issues when it came out, when that data came out was we've got no information from the private sector so we can't look at the thing in totality. So, firstly, my question is could the private sector do a 10-year similar retrospective audit? Do you have the data necessary? The second point is that, if there had been a safety alert, a

recall, would you be able to find the women, find the mesh, do anything like that?

David Hare: Can I answer that? There's a linked question around that as well which I think it would be, in the event of NHS Digital or any other national body requiring information from healthcare providers, actually it is critical that they come to all providers, including the private sector.

Valerie Brasse: Sure.

David Hare: But I think...

Valerie Brasse: It was done for that retrospective audit...

David Hare: Yes.

Valerie Brasse: ...and I'm just asking could you actually do it? Do you have the data?

JJ de Gorter: We could identify what patients have received the mesh, yes.

Valerie Brasse: You could do a 10-year retrospective audit of the numbers of procedures that were undertaken...

JJ de Gorter: Yes.

Valerie Brasse: ...and when they came back for problems or complications through outpatients, you could do that?

JJ de Gorter: That's more complicated. Given the amount of time, so we could identify patients with - who've had a mesh and what we'd have to do is go back through our adverse event and complaints processes to try to correlate if any of those went through a complaint, ended up in a complaint or an adverse incident.

The complicating factor is they may not have returned to us with the complication. So, we would only know those people who come through to us. We've been working very closely with PHIN and also with the ADAPt program to try to have a common patient identifier so we can track patients across systems. Somebody mentioned that...

Simon Whale: JJ, just explain the ADAPt program because...

JJ de Gorter: Okay, I'll do my best.

Simon Whale: Perhaps David.

JJ de Gorter: Perhaps David.

David Hare: Happy just to fill on that, absolutely. The Acute Data Alignment Program is an initiative led by PHIN in which Cyril said I should declare I'm a director of that organisation, is an attempt to try and identify what are the data feeds and bits of information that can be consistently applied that are currently held by the Private Healthcare Information Network and potentially held by NHS Digital. There is consistency across both and one of the benefits of that, as JJ was describing, much greater transparency around patients that move between private sector and the NHS. You can see more across the whole of that system. As I said at the outset, the ADAPt program we very much support and we think will have considerable benefits around transparency of information and data.

JJ de Gorter: Just following up on your question, we've got written guidance and a process for undertaking a patient recall which starts off with identifying all the patients and when they're affected, so we would be able to identify people who have had mesh, as we've done people who've had metal on metal hip systems or PIP breast implants, or any implanted devices that requires a largescale recall. The more challenging bit will be reconciling those who had a reported incident or a complaint or a claim for example.

Steven Luttrell: I think in terms of partnership working, our preferred approach would be to work more closely with NHS Digital or any data repository for a number of reasons. Patients move back and forward from one bit of the system to another. So, if I just look down a BMI lens, I wouldn't capture necessarily the totality of patients' journeys. Secondly, to detect adverse events at an earlier stage would be much better served in that aim if we aggregate the data across the whole...

Sonia Macleod: I agree.

Steven Luttrell: ...if each organisation just looks at it's on silo of data, it would take us a long time to get the scale of data that would require us to come to that conclusion on adverse events. If we looked across the private sector, my colleagues have said well, aggregate the private sector data. We would be faster at expecting adverse events, but we still wouldn't be as fast as if we aggregated our data across the whole of the NHS and the private sector. That would give us the ability to spot adverse events at an earlier stage.

I think it's fair to say at the present time that the registry system which is a tool for collecting data that enables adverse event spotting is fragmented and not joined up and not necessarily easy to work with.

Mahmood Shafi: We support a unified system of data collection right across the piece. I think the same rules should apply. Currently, barriers exist to information-

sharing data and I think the barriers should be removed. The other thing with regards to these particular procedures is, as far as I'm aware, most of the surgeons, if not all of the surgeons, were actually entering data on their own databases as well and that the society regulation, it was on a voluntary basis as far as I know, with the British Society of Urogynaecology BSUG database, but a lot of individuals working putting that data.

Sonia Macleod: Quite a few weren't as well. It was voluntary and it certainly doesn't have complete coverage.

Steven Luttrell: That's not necessarily joined up with any systems that we have, both that and things like the yellow card system, I can't tell if a consultant has put in an adverse event through the yellow card system. I wouldn't be aware of that or put into one of their professional databases, I wouldn't be aware of that either.

Cyril Chantler: Thinking about all those issues, I think the line of question is very much to assure ourselves that it's going to be possible to have common systems between the NHS and the private sector so to the benefit of patients across the piece.

Steven Luttrell: Absolutely. I think that would be a completely valuable aim.

Julia Cumberlege: Can I just ask you, because we've got the big players, if I can put it like that, and I'm just wondering, David, thinking about smaller players, how comprehensive is your network? Do you know what's going on with other organisations that perhaps are only doing one, two, three or four operations a year?

David Hare: I think, and as I said at the start, we're not a regulator or standards body, so the extent to which we can intervene is limited. I think what we are able to see is the range of organisations, the single surgeon all the way up to the groups. What we have been doing a lot of in the last year, 18 months, and following on from the Care Quality Commission report into the acute sector, I think one of the things that that concluded was there is some outstanding care in the independent sector and the only two hospitals rated outstanding across all domains are in the independent sector in England. But there was a consistency challenge. Now, that wasn't all about big versus small but there was consistency challenging in governance. We absolutely acknowledge we can play a part in helping to support that.

So, one of the things that we're working on at the moment is what we're calling a consultant oversight framework being led by the former NHS England Medical Director, Sir Bruce Keogh, which will identify excellence, good practice, working with colleagues here today and also outside, who

have got systems and processes on safety. We don't compete on safety. It's a fundamental principle and to help and spread that learning, we're running a number of learning events with CQC which involves the sector.

So, what we're trying to get at is clearly, fundamentally, at the end of the day, the responsibility sits with the provider, but there are things we as IHPN can do to try and improve the overall standards, share learning from providers and ensure that actually everybody is given every possible opportunity to ensure that that standard around safety is good or outstanding.

Howard Freeman: Yes, I think attendance at those workshops has been revealing because it's been across the board. It's been, as you say, big theatres but also people who have just one unit. So, there's been engagement across the whole of the size in the sector. I don't think the issue of safety is something which even the small people, want to be left behind.

David Hare: I certainly wouldn't want to give the impression that we are in any way blasé about that. I think the report last April from the CQC was clear. Some excellence and really good work, but some areas for improvement across the sector in terms of consistency, and we need to move forward with that. We are moving forward with that and taking forward projects and programs that give, as I say, the best opportunity for those organisations who are maybe a little bit behind to catch up with the rest and to deliver the safety systems you've been hearing about.

Disa Young: Also, just to say, it is possible for a single site provider to have - to be outstanding in CQC stages, so it's not just the single sites are less in any way. You do have examples of outstanding single sites, and in terms of preparation for this review we certainly surveyed our members to see what their responses were and that included a lot of single site providers. We would say the same.

Julia Cumberlege: Thank you.

Cyril Chantler: Could I turn to potential conflicts of interest? A number of people up and down the country have expressed anxiety that the rapidity of the uptake of mesh in treatment was - the enthusiasm was in some way stimulated by manufacturers working with individual surgeons and persuading them that this was the right way forward. We have asked the question to other organisations as to should it not be the case that there's a register of interests by clinicians? I know the General Medical Council consulted on that I think in 2016, didn't at that time propose to support themselves doing it, but were interested in another body doing it. What is your view

about the notion by Parliamentarians that clinicians ought to have a register of interest for the purpose of transparency and openness?

JJ de Gorter: So, I'm wholly in support. If a consultant or any doctor has an interest in us as a listed company, we're required to put it on the website and we list that for them. I think if a clinician has a financial interest in any medical device, direct interest in a medical device organisation for which they're receiving financial benefit or support, I think it should be a requirement to list that.

The difficult bit is if you invest in funds or pension funds, that then subsequently invest in medical device organisations, it can be tricky. But I think if an individual is receiving support for research or travel, education, a direct financial return, in return for using a product or advising in relation to a product, I think that should be listed somewhere where patients can see it, where providers can see it, where regulators can see it.

Sonia Macleod: Do you currently do that?

JJ de Gorter: No. That doesn't exist in the UK. If they have a...

Sonia Macleod: No, within your organisation?

JJ de Gorter: No, because we don't know who has a financial interest in any medical device, because that doesn't exist nationally. But we would be very supportive.

We don't. So, if a consultant was to say that I have investment - this is my product and I want to use it, then we want that - we would want that association to be made public. We'd consider it when we're undertaking our health technology assessment, which is undertaken separately to the consultant.

So, if somebody comes with a new product whether it's a supplier or a consultant, we have a two-step process. One is to undertake an independent review of the health technology and we'd go to external sources like the FDA, published research, NICE et cetera, and reach a view as to the efficaciousness of the medical device. But then we also then consider the clinician's competence to use that device. Then the Medical Advisory Committee as a first step decide whether we're the right environment for the clinician to be using that device which the answer may be no, even though the device is a competent device and the clinician is a competent clinician.

Sonia Macleod: Once the device has marketing authorisation...

JJ de Gorter: Yes.

Sonia Macleod: ...then that doesn't apply presumably.

JJ de Gorter: No, if the device is new to us, we always undertake an independent health technology assessment. The fact it's CE marked by itself would not pass the hurdle.

Cyril Chantler: But you all - I saw you nodding. You all approve of what JJ said.

David Hare: To be absolutely clear from an IHPN perspective, we fully endorse that. We believe that that would be the right...

Cyril Chantler: Now, when we put this to other organisations, we've said yes, we think it's a good idea, but it would be nice for somebody to do it. There is the question of whether the General Medical Council might do it as part of the register, and we're discussing that. But the other people said well, the organisation ought to do it, the NHS hospital Trust ought to do it, or the private hospital, they should maintain such a register. What's your view of that?

Mahmood Shafi: We do try and do that. Certainly on our website if you log on and you go to the individual surgeon, you will get a statement with regards to their interests or conflicts of interest. Similarly, as far as I'm aware within the NHS, there is a register within the Trust that individuals should list any funding or any interest that they have had from industry.

Julia Cumberlege: Can I just ask, is that a conflict of interest or is that just interests? You see, in the parliamentary system, we have to put our own interests and we have to update it every month and it is scrutinised once a year, and it is then released to the public, so people know exactly what we're up to.

Mahmood Shafi: It is interest that we try and capture...

Julia Cumberlege: Sorry?

Mahmood Shafi: It is interest that we try and capture.

Julia Cumberlege: Oh right, so it's not a conflict of interest, it's an interest.

Mahmood Shafi: If you go onto my name there will be several interests indicated on my website profile for my organisation.

Howard Freeman: Prior to today, I had a look at some of the organisations who are members who are not here today and all of them, when I looked at the consultants, had that. The consultants had put something on the issues. Of course, one can't be certain that is everything, one can't be certain how it's updated, and coming back to your point, Cyril, at the end of the day, it needs to be

regulated by the regulator. So there needs to be governance over that and in the NHS broadly, there'll be governance through the organisation, but for the individual, I think there does need to be GMC oversight and GMC governance of that, otherwise it's got no teeth.

JJ de Gorter: The GMC has guided us with this in 2013. I think it's about creating a single view of the truth and having a single source that people can be confident in, it's been updated regularly, that multiple providers or interested parties including patients can access.

So, I think it's about the how. I think the principle is agreed. I think it's the execution that's inadequate.

Cyril Chantler: Thank you.

Julia Cumberlege: Anybody else any other questions?

Valerie Brasse: Can I just ask one question about the practising privileges? Is there a sort of understood standard that you wouldn't have a surgeon work, or a consultant operating out of one of your hospitals if they were not operating there or working out of there for at least so many periods in a year? Is there some minimum? Because we understand there are some that have a very large body of consultants that are attached by way of practicing privileges but that may only turn up quite infrequently. So, I just don't know whether there's an accepted standard that operates across the private sector about this.

Howard Freeman: Maybe perhaps colleagues would like to...

Steven Luttrell: Yeah, we have been looking at that. I have concerns about surgeons who are doing very small quantities of work both in terms of their competence in that field of work, but also their engagement with the organisation and the teams...

Valerie Brasse: It's clearly a safety issue.

Steven Luttrell: ...in place that ensure safe care. So, it is an area that we're looking at. I don't think I can easily draw a single line that applies to all consultants because it may be appropriate to have a highly specialist consultant supporting another team for specialist interventions who may not engage with the hospital very frequently but their input in certain circumstances is essential to make the whole work. Whereas for other consultants, it may be clearer that our expectation is minimum input to the organisation per year, or evidence of minimum attainment of numbers of interventions that they undertake across their whole practice.

Valerie Brasse: As you say, there is the issue about working within that particular wider hospital example...

Steven Luttrell: Absolutely.

Valerie Brasse: ...and having familiarity with the procedures, policies there.

Steven Luttrell: It is a process we're working through to define when that minimum has been reached.

Valerie Brasse: Is that sufficiently looked at by the CQC?

Mahmood Shafi: That is sufficiently looked at, the annual PP approval in attendance volume are looked at. Just because somebody is high volume it does not make them [unclear].

Valerie Brasse: It's not about their competency; it's just this particular aspect of being familiar, it's a safety issue about being able to operate under that hospital, to know the teams, to know the policies.

Mahmood Shafi: Absolutely.

Steven Luttrell: I haven't heard the CQC specifically asking a lot of questions about this area, because it's an area that we're specifically asking questions.

Howard Freeman: But also it is of course not just an independent sector issue, it is of course an NHS issue because it relies on the MAC. We frequently agreed honorary consulting contracts for consultants from elsewhere who'd come in perhaps just once to assist in a procedure and come back several years later. I'm aware of no oversight that ever occurred with that and I was never aware of a single honorary consultant contract having been given, being reviewed and taken away unless something catastrophic happened.

So, I think it is an issue for healthcare generally, not just for the independent sector.

Julia Cumberlege: Simon?

Simon Whale: Just one other thing from me. One of the many concerns that patients have raised with us, is not just about the outcome of their treatment but the way they were dealt with by the consultants they saw. Women have talked about dismissiveness, denial and an arrogant attitude that they've encountered every time they tried to raise concerns about their treatment or even just questions about their treatment. That applies in the NHS, their experience in the NHS, not just in the private sector. But I was wondering what knowledge you've got of such experiences, whether that sounds

surprising to you, or whether you're familiar with such concerns and what you're able to do about it as providers.

Steven Luttrell: I have patients complaining about the attitudes of their doctors. We recently revamped our practising privileges policy to make professional behaviour a much more explicit part of our practising privileges agreements with consultants. So, we take that, and I take that attitude, and the professional behaviour of doctors very seriously, and have a number of supportive conversations underway at any one time with the executive directors who are looking at patient complaints about attitudes of doctors. So yes, I think it's terribly important.

Simon Whale: So, you recognise it as an issue, as a problem.

Steven Luttrell: In recognising that it's an issue, in managing the issue with the consultants, in ensuring that the patient is heard in terms of the complaint that they have and that that complaint is addressed with the individual consultant.

JJ de Gorter: There's variations. We have seven and a half thousand surgeons or consultants practise with us. Some are excellent, many are excellent. There are the occasional few who, I don't think, engage in the way they ought to. I take responsibility for that. We as an organisation take responsibility for that. So, if a patient complains, then it's our duty to follow up on their complaint, involve the consultant, meet with the patient, understand the nature, the exact nature of their complaint before we respond, and we take responsibility for that even though it may relate to the consultant's attitude.

If it's a persistent issue, we'll follow that formally with the consultant. If it perseveres, we'll suspend practising privileges, and if it's a probity issue, we investigate that formally, take it to a professional review committee and, if needs be, refer them to the GMC. So, we have to refer four or five people every year to the GMC. Some of it is for probity or behavioural issues either towards patients or to colleagues. But we take responsibility for that. We don't always consider that. That's a consultant's issue. They're our partners, they're not our customers. Patients are the customer.

So, it's incumbent on us to do our best and do the right thing by patients. Sometimes the issues are ours, so we make mistakes. Sometimes the issue is the consultant's, sometimes they make mistakes. But it's our responsibility to try to rectify that for the patient.

Mahmood Shafi: They are covered by good medical practice guidance from the GMC and we would hope that they defer to that as a model way of behaving when they

are faced with a patient or faced with issues. So, that's a given as far as we're concerned.

Julia Cumberlege: Of course, your reputation is everything, as it is actually with other hospitals. But certainly if you're in a competitive environment, your reputation is very, very important. Right, any other questions?

Cyril Chantler: No.

Julia Cumberlege: Have you any question of us?

David Hare: No.

Julia Cumberlege: I think we should congratulate ourselves. We haven't talked about Brexit today, thank goodness. But I do want to thank you so much for coming. Thank you very, very much indeed. It's been a really useful session and we're very grateful to you and for the work that you do. Thank you very much.

Steven Luttrell: Thank you.

David Hare: Thank you.

END OF TRANSCRIPT

Session3: Independent Healthcare Providers Network (IHPN)

START OF TRANSCRIPT

Julia Cumberlege: Well, as I said, I'm Julia Cumberlege. On my left is Sir Cyril Chantler and Cyril is the Vice Chairman of the Review. You probably know each other.

Aidan Fowler: We do.

Julia Cumberlege: You do, great. Then on my right is Simon Whale and it is the three of us who are the panel, but we are very well supported by our Secretary Dr Valerie Brasse who is on Simon's right and Sonia Macleod, Dr Macleod who is our senior researcher. So that's us, and then we've got other people in the room who are just helping us run the session. So, any questions? Anything you'd like to ask at this stage?

Aidan Fowler: No.

Julia Cumberlege: No, all right. Can you just say, have you any conflicts of interest because...

Aidan Fowler: No.

Julia Cumberlege: ...That you want to declare.

Aidan Fowler: No.

Julia Cumberlege: No right. Or you don't want to declare but you haven't any so that's great.

Aidan Fowler: I'm not aware that I have any conflicts of interest.

Julia Cumberlege: Right, so perhaps if you could start by saying who you are and what your position is and your responsibility.

Aidan Fowler: So, my name is Aidan Fowler. I am as of July last year the National Director of Patient Safety. So, my responsibility is for, if you like, policy and approaches to reduction of harm. So, increasing patient safety across the NHS.

Julia Cumberlege: Right so in your role as Patient Safety Officer, do you look beyond monitoring and responding to other immediate clinical harm? Is it always immediate or do you look back or do you look forward or how do you approach your responsibilities?

Aidan Fowler: I think the answer is we look at all of that. So we work - essentially we're describing and we're developing a new strategy as part of the start of my term and again from the previous Secretary of State - when he did know he was going - wanted to make sure the work continued, was aware that to

some extent that would mean handing some of the responsibility that he'd taken on himself back to the NHS. So, it was felt appropriate that we reviewed what we were doing and developed a new strategy.

In that we look at three strands of work. One is insight, so how we obtain information about what's going on in the system and we do that through a variety of means. The next is the sort of infrastructure piece of what skills there are around patient safety. What training there is. What roles there are. The third piece is the initiatives how we drive change. So, all the gathering is of no use if nothing changes as a result of it. So, we need to make sure that there are a prioritised set of changes. By prioritised I mean we cannot work on all the issues at once.

So, we have to look at what resource we have and make sure we use it to have the greatest impact based on a variety of factors. We have ways of assessing that because obviously there's a risk otherwise that we do what is immediate, we react to what's in the news and current, rather than saying we have to work in the longer term across the field of patient safety. Now patient safety culture means that you need to move from being reactive, i.e. waiting for harm to occur and then reacting to prevent it occurring, to a more proactive approach which means you would be looking to see harm coming, see issues coming and work to prevent them before they arrive.

Julia Cumberlege: So, you must learn a lot from what comes across your desk and what you have to investigate, and ensure that in the future you would want to try and avoid these sort of incidents occurring. So how do you pass on the learning of that into the service?

Aidan Fowler: Well, in a variety of ways. So, I suppose what we do to some extent is limited by the - what we have currently in our insights domain and by the resource around it. So, we learn mostly from a thing called the NRLS, the National Recording Learning System which will change. It's going to be modernised. It's 15 years old and it's going to be changed to a new system called PSIMS. But in that incident reports from organisations, mostly currently acute organisations, less so others, but they do report least from primary care which we're working on, increasing the amount of knowledge we get from primary care.

But incidents occurring in the system are reported through that and we do our best to analyse as much as possible what comes in, but currently we get about two million reports a year through that. That is broken down into three quarters no harm data. So, there are incidents where something's gone wrong, but it hasn't caused any harm to anyone. Another 23 per cent

roughly which is low harm. So, it's, something's happened that's inconvenienced somebody or changed the treatment plan or caused a temporary impact that doesn't last - no lasting effect.

Actually, what we mostly are focused on because of the numbers is the half per cent which are severe harm and death. Then we would look - if we spot an issue, we would look back, but we do get other things raised. So, for example, recently we noticed that there was a run of a particular report on an orthopaedic plate that came from one...

Julia Cumberlege: Sorry I missed that.

Aidan Fowler: Sorry, there was a particular orthopaedic plate where they were mixing up two types and using the wrong ones for wrist fractures and our assumption of course was that if they'd had it occur seven times in one organisation, it was highly likely it was happening elsewhere that we hadn't seen it reported. So, we worked with the British Orthopaedic Association to put out an alert saying there is a potential risk of this happening because of the design, there have been harm incidents, rarely, as a result of it and we need to respond to that. So, we will put out alerts where we see issues that could apply across the piece.

Sonia Macleod: So how does that work in terms of [unclear] orthopaedic plate as a device.

Aidan Fowler: Yes.

Sonia Macleod: Presumably therefore MHRA would...

[Over speaking]

Aidan Fowler: So MHRA have responsibility for regulation around devices, if it causes clinical harm then - so we have a sort of shared responsibility. Sometimes that's less clear than others. So, for example, if we look at the example of the Graseby pumps which were infusion pumps used in palliative care, the - if it caught fire, it would be MHRA's responsibility. If there is no fault other than the human interaction with the pump, it becomes our responsibility. So, if people are overdosed by an accidental misuse of it, that would be our responsibility. Whereas if it broke or caught fire or was dangerous because of its design, it would be MHRA's responsibility.

Cyril Chantler: So, if a device was reported to MHRA as causing patient harm, would they immediately tell you...

Aidan Fowler: So, they would want...

Cyril Chantler: ... before they tell the manufacturer...

[Over speaking]

Aidan Fowler: The likely thing is that it would be reported through our incident reporting system which they have access to, but we would see it [unclear].

Cyril Chantler: But if it came the other way around...

Aidan Fowler: They would notify us.

Cyril Chantler: They would notify you automatically.

Aidan Fowler: Yes...

Cyril Chantler: Good okay.

Aidan Fowler: ... and we are working on how we improve that relationship. So, one of the things we don't currently have which they would have in transport safety is a transport safety committee. We do not have a patient safety committee which consists of arm's length bodies and others with responsibility within patient safety. At the moment we have a committee that is working on improving our alerting. That is a task and finish group. When that finishes, my view is that we should morph that into a patient safety committee where we would have MHRA as a sitting part of that and we would then get into the habit of routinely discussing issues that come up because at the moment we're that much more reactive.

Cyril Chantler: Who else would you have on the committee?

Aidan Fowler: Well, for discussion, but clearly you would want to include the likes of CQC. We would want to look at how we get the acute sectors and other regions represented. I don't think we want to overburden it with everybody turning up or it'll become unwieldy and probably not function well. Of course, the other issue is the link to HSIB, the Healthcare Safety Investigation Branch, respecting their independence. I'm not wanting to compromise them seen importantly as an independent investigator.

Julia Cumberlege: Looking back, and I appreciate it was probably before the - your organisation was established - looking back at the insertion of mesh into women for incontinence and that, do you think that now with your organisation, you would have spotted what was going on, which we have discovered by going around the country talking to a lot of women listening to what's been happening and surgeons and others. Do you think your organisation would have acted as a break to what was going on?

Aidan Fowler: Unlikely, because it's a chronic issue so it's not something where - so if somebody had put mesh in and there had been a problem with it, the

insertion, it might be reported as an incident. But chronic pain as a result of mesh wouldn't be reported in all likelihood on our reporting system.

Sonia Macleod: So where would it be reported? Who does pick up the chronic safety incidents?

Aidan Fowler: Well, I suppose it's one of the areas where I think there is some confusion over the system of mapping that because - so NICE I would see as giving advice on use of procedures and the evidence thereof. Clearly there are professional bodies and colleges involved as well. But, if you start using something not as part of a trial and you are seeing a high rate of complications, that would tend to be something that people would start to discuss at professional bodies, organisations and so on, rather than directly labelling it to us.

Cyril Chantler: I mean NICE did actually early on make recommendations, but nobody actually followed them on.

Aidan Fowler: No.

Valerie Brasse: So, you had no remit of the long-term adverse outcomes?

Aidan Fowler: No.

Julia Cumberlege: Can I ask you then as a patient, you know that you're deeply suffering because of the device that's been inserted and you hear that there are other patients who are suffering in the same way. In those sort of instances, where does a patient go? I mean where do they go to register - well it's more than a complaint but the problems that they are suffering. Who do they go to? Because it seems to me that there are so many different organisations who are dealing with complaints and you could go here, or you could go there. You could - but you don't know which is the most effective. You don't know who is really going to take up your case?

Aidan Fowler: No.

Julia Cumberlege: So, you have - you see the whole gamut of all these organisations. Where would somebody go to be really treated well and effective and action taken?

Aidan Fowler: So firstly - so it's likely that they would go first to the provider. So, they would go to where they had had the procedure. If they weren't content with that, they could seek a second opinion, or they could make a complaint through the current complaints process which sits separately from us. If they're not content, then there is the Ombudsman service for going...

- Julia Cumberlege: But the Ombudsman really only deals with administration and those issues. We're talking about something clinical.
- Sonia Macleod: I think the other thing is one of the things that we have heard an awful lot is that people don't want this to happen to someone else. They want the issue to not be repeated again and again and again. Although I absolutely agree, all of the complaints services provide an individual resolution hopefully, where does the system-wide prevention of harm come?
- Aidan Fowler: Well, depends what the harm is. So, there is a system-wide approach to certain things but it's not complete cover. So that's exactly the problem with mesh, is that if a patient is saying we have a problem - and remember that there are also significant numbers of patients who did not have problems with mesh as well.
- Sonia Macleod: Absolutely.
- Aidan Fowler: The system is not perfect in that regard I think currently.
- Sonia Macleod: So how...
- Aidan Fowler: So, we have quite an administrative complaints system. Now do I think that's the right system? No, I don't think it's ideal. You'll potentially be aware of the approach we are taking around mortality with the introduction of the medical examiner system and the medical examiner system is designed to give people the opportunity apart from - well it's designed for a number of purposes but one thing it will do is allow somebody to speak to a senior clinician acting independently - and that's a longer debate - to say I have concerns about this. But it is a system designed for that incident in that moment.
- I would argue we don't have an equivalent system for harm as such and I think the complaints process is somewhat administrative and bureaucratic. It's not a conversation, it's a letter going backwards and forwards. So, I don't think it's perfect. I think it does lead people potentially - and I don't have data to demonstrate this - down the route of litigation because they get frustrated. I talk to patients also about other issues where they say I got so frustrated I went down that approach because there was nowhere else to go.
- Julia Cumberlege: So, looking to the future, can you - have you any idea how we could bone up this issue in terms of ensuring that people know where to go? Do we need a single body? Have you had any sort of thoughts on...

Aidan Fowler: I don't have a developed plan forwards. I would only have a personal view of the fact that I think there comes a point where independent clinical advice is what's needed, and we don't have a system for that for these sorts of situations. So, there are a variety of routes people can go.

Simon Whale: Do you think there should be an entity which has overall responsibility for patient safety, because at the moment, what we're looking at is a fractured system. Different bodies have different elements of responsibility which they share and there's a risk of overlap or worse still underlap.

Aidan Fowler: I'm very reluctant to lead to a new body because we're very good at doing that and then we create another arm's-length body to solve the problem and it's a little bit spider to eat the fly sometimes. I think we have a number of bodies who could work better together and that's what we're aiming to do around safety is start with getting bodies to work better together.

Simon Whale: How do you do that?

Aidan Fowler: Well, to start with by working more closely through a board structure if you like, getting people in the room together.

Simon Whale: Should that include patient voices?

Aidan Fowler: Yes.

Simon Whale: You've had...

Aidan Fowler: So, our aim is to create a group or a cohort of patients with expertise in patient safety with whom we would treat as we would any other member of the group that they would expect to have the training others have and so on. Yes, it's important to have that voice for a variety of reasons.

Simon Whale: You're obviously in the process of forming your views around this. You haven't come to a final view on this but...

Aidan Fowler: Yes. You're asking me for a formed view that doesn't exist because...

Simon Whale: No that's fine.

Aidan Fowler: We are busy doing a variety of things at once and I don't have overall responsibility and of course one of the risks is I try and take on, you know, world peace and achieve nothing rather than trying to focus on bits at a time and do it, you know, there's a big elephant there to eat a burger at a time if you like.

Simon Whale: Have the conversations you've had so far with others in the system encouraged you or not?

Aidan Fowler: Yes. I think there is a recognition of - well a variety of things. One, moving from a culture of regulation towards a culture of improvement but also a recognition that we do things in dispersed ways. At the moment, there's a lot of focus on how we manage mortality because we've got the medical examiner model coming. We're looking at how we handle, learning from deaths. The learning from deaths in people with learning disability. How we've got a variety of processes whether that's child death reviews or maternity reviews, Regulation 28s coming from coroners - and how we make some of that a little bit more cohesive and sensible.

I understand how organically things do grow up just as we were talking about a moment ago. Often, we create a body to do a function and then it sits in glorious isolation and you think perhaps that would be better linked. I think we're at that phase of saying okay we've got various bodies that we've created to do various tasks but actually they could be better joined up.

Julia Cumberlege: Can I just say one of the problems - and I do absolutely understand you saying that you would prefer organisations to work much more closely together - one of the things that has come to light to us is the organisations who always pass on the issue to somebody else. Then it never gets resolved because it's like pass the parcel. It keeps going until the music stops.

Aidan Fowler: It's the hot potato that people say well this is - this looks tricky, I don't quite know what to do with it. Is it our responsibility - which is why I would rather be in the room saying here is a problem which needs to be solved, what part are we all going to play, not who's going to pass to who else. We will look at where we can best input to that. Maybe that's slightly naïve that we'll get to that point, but I don't see why we wouldn't try.

Cyril Chantler: Can I go back? I think history sort of started here in about 1999 with the publication of *To Err is Human* by the Institute of Medicine in Washington, now the National Academy of Medicine. Then that was followed up both in Australia and over here. *A Service with a Memory*, Liam Donaldson, showed that in fact the avoidable mortality rate in hospitals here was no better than it was in the United States. A number of different organisations then occurred and disappeared. You're the latest manifestation of that. What do you think you've learnt from the fact that it keeps changing? I mean why did it keep changing and what was wrong with your predecessors?

Aidan Fowler: What have I learnt about the fact that it keeps changing is that we shouldn't keep changing it, is my suspicion on the basis that I think each time we do that, we lose pace. When you go through - and we are going through organisational [unclear] at the moment as you will know and that

is a distraction. With the best will in the world, if you start getting to the point where people's jobs are at risk and there are reductions in numbers and head counts and so on, that gets people's attention and distracts from the job you're trying to do.

Why does it keep happening? I could speculate but it would be speculation and my speculation would be that we are saving a super tanker and if it appears not to be going in the right direction, we feel the need to change it earlier in case it isn't going in the right direction before we've fully established whether it is. We don't give things time to start having an impact which takes time. We haven't the patience. Part of that is because we are so much in the spotlight.

There's so much press attention on us, and having come from another country to this country it is very striking how I have achieved my not on my bucket list achievement of being in *The Sun* two weeks in a row over incidents. There is a lot of attention which I think creates a lot of pressure. It's a very big system, the NHS, it gets a lot of political attention as you all know and therefore people get nervous is my suspicion and say this isn't working, we must change it, we must do something else, we think we could do better. We're going through this with our own how we create activity around change in patient safety through patient safety collaboratives of well, hang on, they've been around for five years, have they had the impact they should? How will it look if we turned them into something else? Put them in region, and so on.

Well what it would look like is actually we'll probably end up re-employing the same people into a different organisation as we have done repeatedly. So since the times you're talking about we've had the modernisation agency, we've had the NHS Institute, we've had NHSIQ, we've had the patient safety function moved from one place to another place to another place from NHSE back to I, now arguably back again, each time possibly changing the number of staff and so on. It's quite a distraction and if you look at other countries who've been more consistent, they've probably had greater impact as a result of sticking with the plan, holding their nerve and developing...

[Over speaking]

Cyril Chantler: What other country would you particularly draw our attention to?

Aidan Fowler: Well you don't have to look very far. I mean, I'm about to go off to Scotland and they've done a considerable amount of work over the last 10 years. Now I started my patient safety work if you like, I mean as a definite thing

rather than as a normal part of my role back when we were doing a big safety programme in the South West based on exactly where Scotland have started. But then the SHAs were abandoned and everything got churned up and lost and reformed. Scotland have carried on and I think they're in a stronger place than we are currently.

I've just come from working in Wales for three years where - goodness knows there are many issues in health in Wales - but from the point of view of continuity of approach to quality improvement and patient safety, they have had greater continuity, a greater use of single language, greater use of training around it than we've consistently had in [unclear].

Cyril Chantler: I'd like to stick with adverse events just for a bit, but I want to go beyond that in a moment. I think you're responsible overall for the Serious Incident Framework, aren't you?

Aidan Fowler: Yes.

Cyril Chantler: Which isn't universally successful, I think, from the reports and the NHS ideas come in and we'll be looking beyond recourse at context and human factors and so how you relate to them and how they relate to local investigations, seems to me very crucial.

Aidan Fowler: Yes, I agree, and there will be a new patient safety incident framework, but it won't be called that. Because at the moment, the serious - sorry it will be called that. It won't be called a serious incident framework because we are changing the language from something that people find disconcerting and puts them off. So we realise that the world of investigation isn't where it should be and we talk to HSIB as you would expect about the benefit of their experience and approach and improving how incidents are investigated to get the best learning you can and to make sure they're done in a satisfactory way. Because there are problems with them still and we know in the high-profile maternity case at the moment, incident investigation and the actions following them are part of...

Cyril Chantler: I mean as it happened and I can mention his name in public, I had lunch last week with a cardiac [REDACTED] who was much involved in introducing a new way of looking at safety at Great Ormond Street and talking to our organisations who have to have high standards of quality in Formula One and so forth. He has always emphasised the importance of human factors and speaking to James Reason and Charles Vincent and all that sort of stuff. That really needs to be centre doesn't it, in your organisation?

Aidan Fowler: Yes, and so we are developing curricular to train people in patient safety in a way that hasn't been done. That's a very big ask. I mean it's a big task

which we're working with at HEE on. There's huge enthusiasm for it. The Academy of Medical Royal Colleges have already developed a curriculum for medical trainees, but we need it across the system. The question is, before we rush down this route where are we going to have most impact? Because training isn't always of course highest on the list of barriers to a safety incidence. So, we have to be careful of that.

So I could say, as I have done, I can stand up and say well you've all done fire safety training, how many of you have seen a fire and everyone puts their hand up for the fire safety training and very few put their hands up for a fire although some of us have in the system. But we've all seen patient safety incidents and had no training. But we have to understand that if we say everyone must have patient safety training, we've got to have training that is worthwhile and will have an impact. Because if we're going to train a million people in the NHS around patient safety, the opportunity cost of that is a million hours at how much - however much average per hour. We have to be certain that that is an appropriate use of people's time as we ask them increasingly to do more and more training, not all of which is of huge value to them.

Cyril Chantler: It's not just a question of process, it's also a question of culture.

Aidan Fowler: Absolutely.

Cyril Chantler: Because if we don't actually change the culture, to avoidable harm rather than blame, we're not going to make progress.

Aidan Fowler: That's right and so - I mean if you look at the example of quality improvement training in my previous job where they had taken the approach their staff at the bottom up. You train people in something; they're going into a culture that doesn't accept it and then all that is forgotten within a year and waste. So, they would say we've trained 30,000 people and they've done this online training to what end? Until you have the architects in the system who can then use the project managers who can use people with that training and support them in that training, then you're not going to get the value.

So, we also want patient safety expertise within organisations and that is a different level training. So, I would see our training as a sort of multi stepped thing with a core in levels and then individual specialist add-ons, if you like, where - just as you would do training for anything else. I've done diving training where you would do the core training, you would do the higher training and then there are interest points. So as an anaesthetist you

would want to do different specialist training than you might as a general practitioner or a mental health specialist.

Julia Cumberlege: But wouldn't you want to do your training across different professions?

Aidan Fowler: Yes, different and together and make it multi-disciplinary.

Julia Cumberlege: Yeah when we visited Holland, the head of midwifery there said to us that I am a Jack of all trades and the master of one. I thought that was really very profound that she understood exactly what was going on, who did what and all the rest of it, but she had a specialism. It just seems to me that very often the training is done in such sort of narrow remit that it doesn't actually - it's the whole systems that we have to think about.

Aidan Fowler: And that's true of many areas and of course there is multi discipline training. There are multi discipline training programmes for maternity which are very aware of that. So, there are programmes where they very deliberately train teams together, back to your Formula One.

Cyril Chantler: We were onto that from another review we did. [Unclear] Can I just then move on to the question of outcome measurement, because how much do you look at outcomes systematically in order to turn the quality of the service - or should - it's not just you, I mean the whole service seems to me it needs to be passionate about its clinical outcomes but also its functional outcomes. You mentioned pain a few minutes ago as one of the things that it wasn't picked up in any way through the use of mesh. So functional outcomes, PROMs, patient related outcome measures and patient experience.

I mean, part of how the National Health Service works ought to be a passion about outcomes and I can't think of any part of the NHS to lead that. I mean you can't do it yourself, but you can lead it from NHS improvement...

Aidan Fowler: I think we can lead on the safety element of it. I think that there is a tendency - if you look at quality, I see it in three domains. So, there's quality planning, what we aim to achieve, what we know from research best practice et cetera and there's quality improvement which is the process of getting there and there's quality assurance which tells you when you've got there and whether you've stayed there.

I think we're not great at quality assurance by which I mean we try and do far too much of it at too high a level. So we will as an organisation at the top look at - and the current structure of the NHS probably doesn't help us - I think the region development is a potentially very strong and helpful

thing because for us to try and look at hundreds of different providers and lots and lots of measures and you will see these huge RAG-rated charts and I doubt they're of very much value whatsoever. (1) We don't like RAG rating - different discussion and (2) We're trying to look at too much data and very often it's process data.

What we should be interested in is outcome data as you say, and we should only be interested in the process measures underlying it if there is a problem with the outcome measure. Whereas we tend to default to the process measures because they're easier and measuring patient safety is really very difficult. You mention a number of different ways of looking at it. If you want to look at the whole system and how safe it is, you would need to do a piece of work that would involve notes review of probably 20,000 patients which would take an inordinate amount of resource. What we need to get better at in my view is measuring the areas in which we work. So, having some key indicators and you can debate which those are, whether that's pressure ulcers, whether it's healthcare associating infection rates, it will change from area to area.

Each area has its typical safety events. So, in mental health, they will have typical safety features, that being violence and aggression, suicide, absconding et cetera. In community, it's pressure ulcers and falls. In the acute sector, it depends which bit you're in, et cetera. So, you can come up with some measures. The fewer you look at the more you can concentrate on them. Yes, from our point of view, we should be looking at outcome measures, not process measures and then further down the track they should be looking at more measures.

But we've got to devolve out more of that work but also in those - so back to the areas we work in, we should be measuring more than we do, the impact of what we're doing. So, we shouldn't do anything without attempting however difficult to measure the impact we have on it. So, of course...

Cyril Chantler:

So, going on from that, and we've raised this with other people who've come to talk to us like the College of Surgeons, and that is the notion that for medical devices, that we need to have properly organised registers. The way we've been discussing it with them is that there has to be a database that is comprehensive. We know for example in Denmark there is a comprehensive database connected to a register for hernia repairs- about the only one we know of - but the notion is that for new devices - and the College of Surgeons, the Royal College of Surgeons recommended this, that when the surgeon - and you are a surgeon - completes the operation, when they're filling in the operation note, they also have the capacity to

register the device [unclear] scanned for safety onto a central database which creates the database which we think can probably be mandated. That would then be accessible to properly organised registers to measure the complexity of the outcomes with the patient permission.

Aidan Fowler:

Yes. I think there are several functions for - so firstly I don't believe that we should implant things into people without recording that we're doing so properly and being able in case of issues to know exactly who's had a particular implant. I do think scanning technology - which is not new - is the way forward. Whether that's through 1D, 2D RFID, whatever process, we should be scanning more, and you all know of examples where they are doing exactly that.

I think there have been a couple of false starts on that and there has been consideration of a big national programme costing hundreds of millions to centralise it. You need a standardised approach using standardised bar coding which already exists and so that the information is transferable.

First of all, we ought to get to the point where individual providers are recording what's going into patients. So, in Derby they would tell you that if there was a problem with a device, within half an hour, they would be able to tell you everybody who's had that device, whereas others would have to do notes reviews. So, I - the technology already exists, and goodness knows we do it in the supermarket at weekends, scanning everything we buy, and they know what we've bought and can recall it. So, we need to get to the point where we do that across the system. Easy to say at this point, more difficult to achieve but not impossible to achieve.

Then there is the issue of the centralised registries that say we can monitor at scale how many people have this device and what the outcomes are as they would do for the national joint registry but that doesn't work in real time. We need to get to the point where it works in real time because one of the issues as you'll be aware of is if implants are mismatched, we don't see it until three days later when it's put on the national joint registry. So, we are actively working on a fix in the short term for that before we have that fix for everything. Again, the risk here is we do this for that, implant this for that, implant rather than taking the same approach to all implants.

Cyril Chantler:

My final question, for the time being - is we are aware that, as you said, the hot potato. Surely it is your organisation that ought to conduct this orchestra?

Aidan Fowler: Well I think it's conducted in a variety of levels. In fact, last night I had a conversation with a number of colleagues about exactly this point. We're all agreed that we need to move to it, and I think the more people involved in that, in some ways, the more organisations that agree with that and work with that, the better. Exactly where that - I mean from the scanning point of view, you will be aware that there is a scan core safety group who have some expertise in enabling this to happen.

Cyril Chantler: No, I know there are a lot of players...

[Over speaking]

Aidan Fowler: Not clear where they're going to sit...

Cyril Chantler: But somebody has to conduct it...

Aidan Fowler: Yeah.

Cyril Chantler: ... and that presumably ought to be the Patient Safety Organisation.

Aidan Fowler: The Patient Safety Organisation is one potential conductor. We've got a lot of symphonies to conduct all at once. I'm going to kill your analogy sorry about that but it's - but if we say well, we'll do that, and we'll do that, and we'll do the other...

[Over speaking]

Cyril Chantler: But if everyone...

Aidan Fowler: ... we're going to overwhelm ourselves fairly quickly. We are but a band of small numbers. But you know, there is a recognition that this needs to be done. There's no decision of exactly who's going to be holding the ring on it as this point. But it does involve a number of players and there have been conversations with the College of Surgeons for one.

Cyril Chantler: Okay, thank you.

Aidan Fowler: It's clear your view is that it should be us. I don't know. We haven't come up with the answer to that yet.

Cyril Chantler: I see, okay.

Aidan Fowler: I'm not sure that's solely my decision.

Cyril Chantler: No, it's not.

Simon Whale: No, but I think our view is that - that someone needs to - yes everyone needs to gather in a room together and there needs to be a collaborative approach, a proper professional open collaborative approach. But as in any scenario, people dealing with any issue, at some point someone has to say right, so this is what we'll do then. So there has to be - it's almost a dirty word in this context, but someone has to give direction to the assembled group and we're not - I don't think it's our intention to put you on the spot and say yes, it should be me. That's not the point. But the question is almost a question of principle, is that right?

Aidan Fowler: Don't get me wrong, I'm not trying to shy away from this but there is a bit of a history. Somebody says somebody needs to do this and you can do it. No resource follows and you're trying to do it in amongst everything else. This is a big ask. I mean one of the things we were clear on last night is this is no mean undertaking - and that nobody in that room last night, senior clinical people, were shying away from the fact that we need to do this and we need to think about how we do it in a way that's most effective, but it is a big ask.

Sonia Macleod: So, what you're saying is it has to be properly resourced?

Aidan Fowler: Yes.

Simon Whale: And probably recognised throughout the system presumably but it's not...

Aidan Fowler: But you have to know what that resource is, and I don't think I could say to you now, it will require the following. We're not at that stage of planning but there is a recognition it needs to happen and the start of this is we should be doing this already. We have to move on this. So, there is huge potential for a variety of means of tracking and in the safety world, you then move onto how we track the things we use in a way that stops us leaving them in people for a start.

That technology again exists but there are knowledge management issues around that. I was keen to invent swabs with RFID in and they already exist and I'm a surgeon and I didn't know that and they're using them in Mass General in Boston. Nobody in this country has said I'm aware of. So, we're looking at that as well.

Sonia Macleod: So how do you get knowledge transfer through? I mean how do you facilitate that?

Aidan Fowler: That's a very good question. I think you start somewhere and where we're starting is with alerting and getting better at that. Then we need to look at - and again, you know, if you compared us with technology that exists, like

Facebook who are able to target information - what we do know is if you overload people with knowledge they ignore it and it becomes noise and they will miss the important stuff.

So, the question is, how do we target information in a way that is most helpful. So, if we have a problem with eye implants, how do we target ophthalmologists? It's not as straight forward as it sounds. How do we target colorectal surgeons amongst a group who are registered as general surgeons et cetera et cetera? So, there is a huge knowledge piece of how do you get proper up to date records? People move around, people change et cetera, how do you keep up to date records that allow you to target information appropriately? Now my view currently would be the pragmatic way to do that is by having the patient safety specialists and team with a responsibility for disseminating knowledge, to some extent.

Sonia Macleod: What I'm wondering is if you have a central data set or devices that have been implanted, if in addition to the patient and device information you also had the surgeon information, that would give you a resource to be able to do that, wouldn't it?

Aidan Fowler: Yeah.

Julia Cumberlege: Valerie [unclear]?

Valerie Brasse: Yes, I do. Can I ask you specifically about one of our interventions which is sodium valproate and you will be aware this has a very, very long history...

Aidan Fowler: Yes.

Valerie Brasse: ... and quite a long battle really to make sure that women of childbearing age do not end up being prescribed sodium valproate with all the consequences that follow. So, when I look at all the initiatives that you're involved in, it's very difficult to take the abstract and put them into the practical. The practical would be for me to say to you how does NSI - NHSI prevent another sodium valproate? What is it that you're doing that would stop us having another sodium valproate?

Aidan Fowler: Well sodium valproate is a medication and that's licensed by MHRA.

Valerie Brasse: The issue is what happens when people who shouldn't be given it, are being prescribed it within a childbearing age?

Aidan Fowler: So, there are a number of issues with valproate. One is would you now license it at all, the medication, with that sort of risk or would you license it for specific groups? Then, it being on the market and knowing that it is a drug that works for some people better than any other medication, how do

you then manage the situation we're in? There are a number of issues. One is how do you have a pregnancy prevention programme that is more effective? Can you ever get one that is sufficiently effective because at the moment we believe 20 per cent aren't aware of the issues. So those - so we know there are what, 17,000 people on valproate in childbearing age and of those - about 20 per cent don't realise that there is an issue around pregnancy still.

So, we can get better at advising those who prescribe it. We can get better at making sure there is a system where patients have to sign in saying they recognise the risks before they are dispensed the medication. But 40 per cent of pregnancies are unplanned, there is still a risk and there are still, as I understand it, several hundred babies a year born on a medication that has a 40 per cent teratogenicity rate. Ten per cent...

[Over speaking]

Valerie Brasse: So, the issue here is, are these avoidable births...

Aidan Fowler: So, the question is...

Valerie Brasse: ...and what would NHSI in terms of its range of initiatives be doing to drive that proportion down or indeed to make sure that the next generation of antiepileptic drugs does not have that experience where we know there's a teratogenic risk.

Aidan Fowler: Well so, it sits with drugs being licensed in one place which is MRHA - MHRA - let me get that right - NICE approving the use of medications which is a newer approach than was around at the time valproate was initially licensed. Then the monitoring which is done again through MHRA through the Yellow Card System.

Valerie Brasse: So NHSI would have no role in this at all.

Aidan Fowler: Currently has no role in that, no.

Valerie Brasse: Interesting. Because as I say that would be an avoidable harm. It's not - it's different to the meshes and it's very specifically where we know there's a drug that should not be prescribed.

Aidan Fowler: I mean we are involved from the point of view of we were involved with the alert and so on.

Valerie Brasse: You put out I think some guidance or some - who were you expecting to monitor that that guidance would be implemented in practice?

Aidan Fowler: So those prescribing the medication.

Valerie Brasse: So, and that was what your assumption is when you put the guidance out. There was no other way...

[Over speaking]

Aidan Fowler: I mean so the guidance was put out in 2017 I believe.

Valerie Brasse: Yes.

Aidan Fowler: That was the assumption at the time. The question now is what is the right approach, specifically around valproate? You know the easiest thing would be to say don't licence it for use in people of childbearing years. But then you will get patients who will come to you and say I would rather be on that and not have a fit and not be able to drive for six months when I live in a rural location...

Valerie Brasse: We get all that...

Aidan Fowler: ...with four other children and you've seen all that I'm sure.

Valerie Brasse: We have. I suppose as I say I'm just trying - you know it's slotting in all the players and who is responsible for what and finding out whether NHSI has a role in making sure that pregnancy prevention programme is absolutely working as it should do. In your words] being proactive rather than reactive, [unclear] when you're thinking about the next generation of AEDs that it's not going to happen again. Doesn't sound like you...

[Over speaking]

Aidan Fowler: It's not our current remit to do that.

Simon Whale: Can I just ask a question about surgeons? It comes back to your point about training for safety. Many of the women who've had adverse experiences in relation to mesh have talked to us about the treatment - the poor treatment, the often dismissive or arrogant treatment that their surgeon has meted out to them. We've heard really quite disturbing stories. Not just one or two. Not just a few dozen but hundreds - hundreds of such stories. When it comes to thinking about instilling a safety culture, how do you do that amongst people who let's say are at the top of their profession, people who've been practising for decades, people who have reached a certain status, how do you do that effectively?

Aidan Fowler: Not easily but - surgeons like any other breed are variable. I would hate to think that I've ever treated anyone in the way you've described as a

surgeon who was practising in this area and by the way, didn't tend to use mesh. I think it is difficult. We've had to do it with other things. So if you look at - one of the big interventions in safety in surgery was the use of check listing in theatres and a variety of approaches were taken. I took, others took to try and get some of the recidivism if you like on board with using that. Those who felt that it was never going to happen to them. A lot of hubris involved and so on.

At some point, certain measures of trying to get people up to speed, training them, supporting them, don't work. I know in my own experience we have to go the route of this is an accountability issue. You will use this, or you can't work in our organisation and that's about strong leadership at times. That's not your default position to go command and control on it but sometimes that's necessary and certainly we had to do that. There were people and I can remember people who I've worked for as a trainee and having to say, if you don't use this list, you cannot work here.

But behaviours around consent and some of the issues that I saw on the receiving end of patients referred to me with mesh issues, I had significant concerns about how they were consented and the approach taken and some of them - and I would get one story, not two in general, and I will get only get a few so it was difficult to build up a picture at the time. Why did more of us not see that this might be of concern? Because I wasn't using mesh particularly and we'd had experience with a sponge for rectal prolapse previously which had been a significant problem. It was felt that we should have learnt the lesson from that and gone cautiously.

But that's not to say I didn't also see a lot of patients with very significant problems around prolapse, continence, and so on who were very desperate, whose lives were very miserable and asked for any treatment. There is this balance. One of my colleagues said the irony is that I'm being pushed to allow cannabis use without much evidence behind it at the same time as being asked why mesh was used without evidence. Some of the same people who express concerns would be the people giving them a very hard time in clinic saying why can't I have this procedure?

So, it is difficult, but I think there were issues around how consent was obtained. I think there was a tendency to say I've got just the thing for you in some cases and you will have heard that I'm sure. It is very difficult to change that sort of behaviour overnight because as you've seen, it was more widespread than we might have hoped.

Simon Whale:

I think you've hit the nail on the head in terms of influencing behaviour at the point of consent or at other moments where it's in consulting room and

it's the patient and the doctor, as opposed to in theatre or wherever. It's that intimate moment when there's only two people in the room, maybe the patient plus their partner or whatever but it's a very different moment from a more process driven moment like a theatre with a procedure taking place.

Aidan Fowler: Yeah.

Simon Whale: Influencing behaviour in that moment is...

Aidan Fowler: Is difficult.

Simon Whale: ... difficult.

Aidan Fowler: But also learning - you know as a pelvic floor specialist, what we knew of any intervention with pelvic floor is it tended to last for five years and then failed. So, they weren't magic answers that would suddenly transform people for long periods of time. That wasn't our experience and we hadn't always gone down the route of the conservative treatments of physiotherapy and so on first, before we were doing some of these more interventional procedures.

I think having grown up in a world where we were very close to some of these manufacturers without really realising that that was abnormal potentially, there has been a huge amount of influence from manufacturers directly onto individuals which I think is unhealthy.

Simon Whale: How has that manifested itself?

Aidan Fowler: Well, so you would have at conferences our manufacturers promoting what they're selling and having very close relationships with individuals who then were applying those treatments. I think we have to be cautious that there is a conflict here and we have to be very careful that you don't get too close to the suppliers of particular mesh or whether it's staplers in [unclear] practice and so on.

Sonia Macleod: Do you think that...

Aidan Fowler: You used what you thought was best not what was handed to you by somebody with an interest.

Sonia Macleod: Do you think that balance is acceptable now?

Aidan Fowler: I think it's got a lot better. I mean I'm not in practice so I can't tell you [unclear] but these were reps who were in and out of theatre. That is now far more controlled than it used to be. There wasn't the culture that

perhaps you'd have in the States where the chief of surgery would come and say you're using too much of this and it's not the thing you should be using or it's too expensive, whatever, there wasn't that culture. It was a lot of autonomy, and still is to some extent, of I will use what I think is right regardless and no one's telling me 'oh we don't use that here because we don't think it's the right thing.'

Sonia Macleod: I think one of the other things that we've heard is that even when people went back and said 'look, I have issues, I have complications', there was a huge reluctance to recognise that those could have been attributed to the surgery and to the mesh. How do you overcome that?

Aidan Fowler: I mean the trouble is you're talking about changing people's behaviours and personalities essentially, and that's really rather difficult. Again, and I'm speaking as somebody who I - it's difficult for me to compute why you wouldn't take that seriously as somebody who practised as a surgeon. If somebody comes and says 'there is a problem, I think there is pain', I would be looking at why it was occurring and trying to understand it. You know we saw this occasionally with hernias where I did use mesh that they would be painful, and you would have to consider whether it was the best approach to deal with that. Not all of which was re-intervention. Once these things are in, they are quite difficult sometimes to remove. Not always but they can be quite difficult.

Julia Cumberlege: I know it's very easy to look back and say things could have been different.

Aidan Fowler: Of course.

Julia Cumberlege: Very easy to do that, but I'm just sort of wondering, do you think if the patients had had a stronger voice, if they had been listened to in a much more sympathetic way, if they had been taken more seriously, it could have actually influenced the progress that was made - I shouldn't say progress but the number of operations that were made for surgical mesh. When one looks at the *BMJ* article 'How mesh became a four letter word', and you see how the number of different products dealing with mesh came onto the market, huge numbers in a very short space of time and were inserted, there didn't seem to be any sort of - any research done to see whether it was actually a good idea over a period. They just - as you were saying, the marketing was really quite aggressive.

Aidan Fowler: Yes, I mean research is quite difficult...

Julia Cumberlege: I'm just thinking - we're thinking about how could the patient voice have actually influenced that? Because they started realising there was real problems 10 years ago and yet still there's been - till our pause - we

introduced the pause – there's been tremendous growth in the number of operations that have taken place, and as you say, I'm sure lots have been successful. An awful lot haven't. Do you think the patient voice - do you think - does your organisation NHS Improvement, does that listen to what patients are telling you?

Aidan Fowler: Yes, and they don't always tell you what you're expecting to hear and that's the whole point. So, they are able to point out from their experience flaws in process, flaws - differences of experience. Now that should - it should if you're monitoring - if you're using a new treatment, you should be following this up and asking specifically about that. So a new treatment should be properly evaluated so that you enquire about that and I guess there is then the difficulty of, even if you did the right thing, developed and treat them appropriately, did some research, evaluated it, you still need that longer term follow up and...

Julia Cumberlege: That's true.

Aidan Fowler: ... there probably isn't a mechanism for doing that because people tend to be discharged from processes and if there are problems that occur five years down the line, that is more difficult and that will become clear late. Yes of course there is hindsight bias here where we can look back and very clearly say this was not right, we should have done things differently.

Julia Cumberlege: Well, I think I ought to bring this to a close because we've got another session. But before I do that, I'm just going to ask my colleagues if they've any further questions and indeed if you have? Valerie?

Valerie Brasse: No.

Multiple speakers: No.

Sonia Macleod: Just quickly, in terms of the patient reporting into PSIMS that's going to be enabled, will that help in enabling patient voice to be heard or will PSIMS still be very much focused on acute issues?

Aidan Fowler: Well one of the things that is developing is the ability for patients to report, so from that perspective yes. So, we are trying to make it easier to report in general but patient reporting would be easier, but we've then got to work out how we read currently two million bits - and that will increase - of information. We need to automate that process and we've talked about artificial intelligence and machine learning and that's very easy to talk about but of course you have to teach the machine what it's looking for before and you have to know what to look for before you can teach it. So, there are some important steps in that.

Julia Cumberlege: All right. Have you any questions for us?

Aidan Fowler: No, I hope that's been helpful.

Julia Cumberlege: Well, it's been very helpful to us and I want to thank you so much for giving us your time and indeed your thoughts. Thank you very much indeed.

Multiple speakers: Thank you.

END OF TRANSCRIPT

16th April 2019

Session 1: Pelvic Floor Society and British Society of Urogynaecology (BSUG)

START OF TRANSCRIPT

Julia Cumberlege: Thank you for coming again, because of course we had a session in February as well when you came, but quite a lot's happened since, and we're particularly interested today in the new NICE guidelines, and we're just wondering if we could explore that a bit with you. It's of course on the management of urinary incontinence and pelvic organ prolapse in women, and it's generated an awful lot of interest among the patient groups, and it was on the Victoria Derbyshire show and that caused quite a lot of problems. We put out a statement, which we thought was very clear, and it was used quite a lot, and we weren't taking sides on anything. It was just saying where we were at the moment on the Review.

So we're just wondering if you've had any feedback from your members, and whether there's anything that you can help us with it, in the views that your members might have or indeed you personally might have on the new NICE guidelines.

Jonathan Duckett: Our main issue is our members are confused, because we use NICE guidelines to practise medicine, and we are told within NICE guidelines and we're medico-legally held to apply the NICE guidelines, as well, often. So our members are saying that there's a new NICE guideline out and it says there are a number of different treatment options for patients, but we're not allowed to use, for instance, retropubic meshes, so how does that stack up? How does that work? Because we should be able to use it if we've got a body of evidence which suggests that there are different treatment options available, to withhold those options is not scientifically or in any way appropriate. So we've got the NHS England, who commissions and runs itself basically on NICE guidelines, giving treatment options, but at the moment, we're not allowed to use them.

So we've had a lot of queries from our membership saying, we understand the Review is going on, but we're now being told by NICE that we can use different treatment options. Why can't we, or can we, or should we, or when can we?

Simon Whale: What's been your response when they've asked you those questions?

Jonathan Duckett: Well, there's a letter from NHS England which has come out quite clearly saying that the pause is still in place, so that's what we tell our membership and we say we're under negotiation and seeing what's going to happen from this point forward. Obviously, we've had the other issues. We've had the end of March was the point where we were hoping to have some decisions, and we've had patients waiting for a year or more, or been lost within the system or not able to have surgery, so there's a growing feeling from our patients that why is there another delay when the NICE guideline is saying that we should be able to have the treatments which we've chosen to have and we've been explained to have and we've had a good decision-making process, and why can't we self-determine our treatments if they're under the NICE guideline?

So yeah, we've fed that back to our members, but it's an argument which doesn't square.

Valerie Brasse: It's interesting also because of course the NICE guidelines are very clear in their search recommendation, because they've accepted that there's very limited evidence as to the long-term adverse outcomes of treating women with mesh, and actually, they say that the final outcomes long term are actually unknown. So there is a confusion I suspect all around, so when they produce the guidelines, they are themselves admitting that there is a research evidence gap here, because they do not know the long-term outcomes for them.

Jonathan Duckett: That depends on the way that NICE looks at research, so they tend to look at randomised, controlled trials and big meta-analyses, so they won't take into account, say, a case series of 18 years of TVTs, for instance, and look at the complications from that. So they have a different way of looking at the research...

Valerie Brasse: They obviously feel the need to make research recommendations. That's what they've just done.

Andrew Williams: But the same criticism can be applied to everything or bar very few exceptions in medicine, and especially in surgery, in that we don't have robust, randomised, quality data that you might have, say, for a drug trial, because, A, they're exceedingly difficult to set up. B, on many occasions, it's not possible to set up such a robust study, and C, there's not enough funding and the infrastructure to do that. So I would argue that you could apply the same criticism for almost everything we do in surgery.

So I'm not surprised that they've recommended more research, and the sort of research that surgery can provide is often poor-quality scientific

data compared to robust multi-sensor randomised drug trials that they may be used to. So I don't think holding out for more data, whilst we all agree that we want more data, we want to know more information, and we've been striving to set this up, I don't think holding out for that's going to be the answer, either.

Valerie Brasse: Of course, at the meeting you're going to go onto next, you'll be able to capture the data that probably is needed to be able to help assess this.

Andrew Williams: Exactly, but then, we've tried and tried to get funding to capture those data, and everyone wants the answer, but nobody's willing to support it or pay for it, and it comes down to cash.

Julia Cumberlege: So you will be, both of you, going to the meeting this afternoon with NHS...

Jonathan Duckett: Yes.

Andrew Williams: Yeah.

Julia Cumberlege: Digital and all these other bodies? Cyril Chantler's also going, but obviously he'll be going as an observer, and he isn't part of the group, as it were. He's just there to observe. But I'm just going back to what is now - what has been produced by NICE. What are you, as a society and you as your members - what are you going to do about this? Are you going to try and clarify it with NICE? It's an action you're going to take?

Jonathan Duckett: So when the NICE guideline comes out, it comes out in a provisional form, and that stems - we send a mail shot out to our members and say...

Julia Cumberlege: Sorry, can you say what?

Jonathan Duckett: Our members get a mail shot when the provisional NICE guideline came back, and they feed back to us their concerns about the NICE guideline. We then feed them back to NICE, and they have a meeting where they take into account all of the different opinions from interested groups. Then the final NICE guideline is published, and it won't change now for five years, so that is how we practise medicine, or urogynaecology, for the next five years. There's very little flexibility or interpretation within that.

Andrew Williams: But all along, all of the NICE guidelines have been exactly what the different societies have been recommending, and they hinge around adequate maximising nonsurgical treatment, adequate information and open information about the options available and the risks involved, and accurate and hopefully complete data recording of the results of the treatment.

Actually, each of the societies or all three of us, one thing we do agree on is that we all agree with the same things. Those are the good, standard, basic treatments, so there won't be major disagreement with the NICE guidelines. But we can't then say, oh, right, we're going to start doing it, because you're still under the pause. Okay, for the bowel side of things, we're under high vigilance still, and so in a way it's business as usual. Now, don't misconstrue what I say as business as usual as glib disregard. That means continued high vigilance under the scrutiny, applying all of the criteria that I've just mentioned, which we set up prior to this process anyway. The only advantage is where it is under such scrutiny, it does focus the clinician's mind to make sure that they are adhering to all of the different criteria, which is a good thing, because it hopefully hones down those clinicians doing this sort of work.

Jonathan Duckett: I think many of our colleagues who have looked at the final report, which was different from the initial one, so initially TVT was included as one of the three options, and then that was altered to the final report, with some other attributions to that. But people will look at that and will say, we are all about offering patient choice and informed consent with good audit and follow up, and that's all that we would want for us as patients or for our practice.

So it doesn't really do anything other than reaffirm those desires from the clinicians.

Simon Whale: So if and when the pause is lifted, what level of mesh surgery for rescue IM products would you expect to see?

Jonathan Duckett: I would expect to see that the patient will go through a decision-making process where they're given all the options, having exhausted conservative treatments, and then the patient will decide for themselves what suits them for their lifestyle and their circumstances. For some people, there will be one of three or four different options what they may choose. It's not for us to tell the patients what they want. It's for them to tell us what they need.

Valerie Brasse: But that's talking about the differences between the different options. What about the actual level of surgery per se? Because there has been an argument, hasn't there, since the introduction of mesh - in fact, many more people have been treated, certainly for SUI...

Jonathan Duckett: Yeah.

Valerie Brasse: ...than might otherwise have been done. So do you think that there will be some sort of reduction generally in the level? Would you expect to see

that, and can you think where we might end up as a natural rate of surgery out of [unclear]...

Jonathan Duckett: Well, there's been a complete all off the cliff, obviously, since 10 July. The rates were generally reducing from about 2014. I think probably what we were doing is we were getting rid of a backlog of a lot of severely affected patients with devastating stress incontinence who were treated and cured, and some of those patients are now out of the system. So certainly, when I started doing TVTs, we'd see patients being controlled for 15 years, because they couldn't access the services. Then, as the time went on through 2010 and 2014, they would call me after two or three years, but not after 10 or 15.

So there's a natural hump of patients who have now gone through the system, but a lot of people have been frightened off, so we are at a much lower level, whether it be prolapse, for instance, which is largely not mesh - has also fallen off a cliff, as well, in terms of activity.

Andrew Williams: I think it's focussed the mind not just for clinicians but for patients as well. It is human nature for a large number of patients who want a quick fix, they want it sorted out - you're the doctor, make me better - without necessarily investment in their own treatment or conservative measures, so pelvic floor exercises, retraining, other techniques. I think it's good, because it focusses the mind in that whilst we're at pains to explain to every patient that surgery is not without risks and it's all a balance, actually, they now know that yes, there are risks to any operation, and so that will engage them in maximising nonsurgical treatment.

Jonathan Duckett: Yeah, and when we go through the patient decision, for instance, these days, we'll have a proportion of patients who decide they don't want anything done at all, and they will choose not to have any surgery, and for them, they'll say, well, it's not a big problem. I would prefer to put up with this and undergo the risks of surgery. But for others, it'll be different choices, and people will want the biggest, nastiest operation that we do, because they want the maximum chance of a cure, so there's a variation of options chosen.

Julia Cumberlege: Some of the patients we've talked to have actually been doing their exercises since they've been told to do, and they have found that it's made a bit of a difference, but they have gone to see the GP and then to the surgeon, and the surgeon said, oh, you don't really want to bother with those exercises, we've got the answer to you. They have then had mesh inserted, and we've seen the results on that individual. Now, I appreciate this is not evidence in terms of statistical or anything like that, but

obviously we've been listening very closely to what patients have had to say to us, and what I'm really asking you is that clearly some of the patients who we meet have had mesh inserted quite a while ago, and I'm asking you whether you think the practice has really changed in terms of consent and the attitude that some surgeons actually exude when they interview patients.

Do you think really, today, that consent is treated quite differently than, say, five years ago?

Jonathan Duckett: It's hugely different. It's a complete world set away from how it was five years ago. So I look at my consents from the late - from 2005 to 2010, and we didn't really understand all of the risks and consequences of some of the surgery, and they were short, and patients would demand surgery, and we would be willing to offer them surgery with fairly easy things, like I've done my pelvic floor exercises, and it doesn't work for me, doctor. Or I've been away for a few weeks and they came back and they haven't worked. So the whole consent process is a hugely different process now.

It takes a good half an hour of our time and has altered our ability to practise continence surgery because we need so much extra time to consent patients properly, go through four individual sets of information, then go through a patient decision aid, send them away to think about it and bring them back. So yes, the whole process is hugely different.

Andrew Williams: The other thing that's changed as well, and I think you'd agree in your world, is the MDT working process, in that the individual surgeon and patient, just two people making the decision, has now gone from pelvic floor decision-making and treatment in that they're part of an MDT process. The decision for surgery, certainly in the colorectal world, is through an MDT process. So it's not just one person deciding. It's, well, have they done this? Have they done that? Let's hear from the people who were doing the pelvic floor exercise. Do you think they've done well enough? Well, could they have engaged more? So you're less vulnerable to quick decision-making in that way, which I think's an important part in addition to everything that Jon has just said, because it's exactly the same in the bowel world.

Julia Cumberlege: So if a patient feels they could have a bit more help in terms of the exercises and so on, do you ever refer them then to the physiotherapist that actually is expert in this particular part of the body?

Andrew Williams: Yeah.

Jonathan Duckett: It's mandatory to refer everybody to...

Julia Cumberlege: It's mandatory. You have to do it.

[Over speaking]

Jonathan Duckett: ...for physiotherapy. In my practice, it's absolutely mandatory. We would not be able to offer patients surgery unless they have a documented evidence of receiving pelvic floor exercises taught by a specialist.

Julia Cumberlege: Right. Okay. So going back to the NICE guidelines, and the pause, if the pause is lifted, and you will know the five safety measures that we actually have to introduce before the pause is lifted, the second-line treatment after conservative treatment has failed, if that's happened, and if the third-line option after conservative treatment followed by non-mesh surgery has also failed, does the previous non-mesh surgery impact on the risk-benefit profile of using the mesh?

Jonathan Duckett: Say that one again. So they've had previous surgery, non-mesh surgery.

Julia Cumberlege: Yeah.

Jonathan Duckett: Oh, I think we're talking if they've had a periurethral injection, for instance, then if we offered them a TVT afterward it is generally considered that that is an appropriate treatment option, and the previous periurethral injection is unlikely to affect the successes of mesh surgery. But there's a study in Manchester specifically looking at that at the moment.

Sonia Macleod: But would it be if they've had something like an autologous sling?

Jonathan Duckett: You're going to get a lot of scarring, and then you're going to get difficulty doing anything after an autologous fascial sling, so putting a mesh in in that situation, when the mechanism of action, so how it works is the same, might not be an obvious choice. But that would be, again, a decision for an MDT and patient involvement in that.

Valerie Brasse: I guess the question is, does using something like an autologous sling become the final surgical step, or is there then a third line?

Jonathan Duckett: You can always find a third line, so you could use a periurethral injection, for instance, after an autologous fascial sling. These are things for the future that we're going to learn, because the autologous fascial slings and the colposuspension have been done in relatively few numbers over the last few years. So now we're doing them again in larger numbers. Then we'll find what we need to do with the failures, but it'll be easing our way forward as to work out what the next best step is.

You might ask five different surgeons and get five different answers as to what they would do for a failed autologous sling. When we looked at failed TVTs, for instance, we get huge different variation in what we think should be done, and a study is going forward now looking at failure of continence surgery to try and determine the best treatment afterwards, so that's an NIHR study I think which has just opened.

Andrew Williams: But I think one of the key points that this - one of my concerns is that for totally valid concerns over the risks involved with a TVT mesh and synthetic mesh, what we don't want to do is get into the situation where we're not doing a very appropriate, appropriately selected operation and we're doing an alternate operation, which has an equal risk component to it, but then that prejudices success of what was the proper operation in the first place.

Simon Whale: Exactly.

Valerie Brasse: That is exactly the issue.

Andrew Williams: So we don't want to go, okay, maximum pelvic floor exercises, maximum conservative nonsurgical treatment, we're all totally agreed with that, MDT process, consent process. What we don't want to do then is go to autologous injection or injections, which we know won't really work, but we're not allowed to do anything else, then autologous sling, which isn't as good as a TVT, we think, but it avoids using the mesh. But then you've burnt your bridge to do what would have been a really good operation, the TVT. Don't you agree?

Jonathan Duckett: That's where we are - that's where we are, so we're putting in autologous fascial slings, because that's the only option that we have for patients who want a significant chance of being cured of their stress incontinence.

Andrew Williams: Exactly, which doesn't work as well, but it's also meant that when you come to do the TVT, which is the best operation, with problems and with risks and we totally accept that, then actually you've increased your risk profile by already sullyng the waters with an autologous sling.

Jonathan Duckett: So that's the negative aspect to any pause is that patients are getting bigger operations, with significant dangers and complications, and we've forgotten those dangers and complications, and now we're remembering how it was 20 years ago when we used to do them. We haven't forgotten them, but we're now having to manage them on a day-to-day basis, whereas with TVT-type operations, we would have complications, but they would be less frequent.

Valerie Brasse: Because of course that's what the patient groups have been saying, that actually the mesh procedure should be the third and final line that actually you reach...

[Over speaking]

Andrew Williams: I think that's an error.

Valerie Brasse: ...done, and you're saying it's an error.

Andrew Williams: Certainly.

Jonathan Duckett: I'm saying it's for the patient to decide. Some of them are so frightened of mesh, they would never want a mesh near them, and some will say, I had a patient [inaudible] and she wants to get back to her job. She can't afford financially to have two or three months off work with a fascial sling, and so she's waiting for when the TVT...

Andrew Williams: Colposuspension.

Jonathan Duckett: ...option will be the one that she wants, and she's waiting until the pause is reversed.

Valerie Brasse: So have you any sense of the numbers who are sitting on the off side, as it were, waiting for this pause to be lifted?

Jonathan Duckett: There's quite a lot, so different places are addressing those issues differently. We're not allowed to keep them on a waiting list, so they have to be taken off the waiting list, because they're not allowed to be on for more than a year. Otherwise, the trusts get penalised for it. So we'll find that patients - we've been told to remove them, basically, so they will be lost within a system probably.

Valerie Brasse: Not being treated, just taken off.

Jonathan Duckett: Just taken off and not being treated, yeah.

Simon Whale: So these are people where conservative treatments have been exhausted.

Jonathan Duckett: Correct, and they want an operation. They've chosen to have a TVT or synthetic mesh and they are unable to have it. So they can't be on a waiting list, so we have to go - they just come off and they just get discharged back to their GP.

Andrew William: They just come back to the clinic for follow up.

Jonathan Duckett: They can go back to clinic follow up. So different places are addressing what we can do, so quite a lot of people have just stopped and paused everybody until 31 March, when we were hoping the decision would be made. Some people are offering injections for a lot of patients on the basis that it might help a bit, but it's not likely to compromise further surgery and may help a proportion of patients. Then some are having the bigger operations, the fascial slings instead. There's quite a lot of people on waiting or on lists somewhere, which are choosing to defer surgery.

There's a specific patient group. So if you're overweight, your BMI is, say, over 35, the operations such as colposuspension and fascial sling are technically really quite challenging, so your MDT is going to ask you significant questions if you've got patients with a high BMI wanting those operations. So for that group of patients, a TVT type operation would be something which would be technically possible, where the other ones aren't, and have a reasonable effect, whereas for periurethrales, it doesn't work for everybody. So we've got a specific group of patients who are, as I say, slightly raised BMI, who have no option at the moment.

Sonia Macleod: But we've been told that losing weight in itself aids continence.

Jonathan Duckett: Part of the NICE guideline is you should advise all patients to lose weight. Those are challenging discussions with patients and challenging for patients to achieve that weight loss, as well. Some CCGs have criteria as to what sort of BMI you can offer surgery for patients. So there are some guidelines for that.

Julia Cumberlege: Right, well when a woman has had mesh implanted, do you do follow ups? Do you call her back in a year's time, two years' time, four years' time?

Jonathan Duckett: We routinely follow everyone up for usually three months is the commonest data entry point for the BSUG database. Some people up for six months or a year, so most people will see a patient back initially. We haven't got the capacity really within the NHS to follow up everybody for a great deal of time, and we're dependent on the GP sending patients back, for instance, if they have complications.

So if we think, say, 100,000 TVTs have been inserted, if they were coming back every year, that would be several people with jobs in itself just to do follow up of those patients. So we will have an initial assessment, and that can be where we fine-tune the treatment for there may be drug therapy needed or there may be other problems that we need to sort out. But most people don't have long-term follow ups. I personally will follow patients up, so we have an eight or a 10-year follow-up point, where we

see we've sent patients' information and brought them back up and seen how many have pain and how many have problems.

So individuals will - may be able to do that within a healthcare setup if they have done it themselves, but not as a routine.

Sonia Macleod: Do you publish your eight to 10-year follow-up.

Jonathan Duckett: Yes.

Andrew Williams: But this is going to be...

Julia Cumberlege: But, Andrew, you have a registry, don't you?

Andrew Williams: We do.

Julia Cumberlege: That presumably you do have a follow up with that?

Andrew Williams: The follow up is fairly ad hoc, though, on the...

Julia Cumberlege: Sorry, the follow up is?

Andrew Williams: Fairly ad hoc.

Julia Cumberlege: Oh, right.

Andrew Williams: As I've said before, the registry is really a registry of operations and implants, and so we spend a long time - and this predates the explosion of the mesh concern, because we'd felt that it's something that we wanted to keep a track of. So we can tell you who's had which mesh and when and for which indication. To some extent, we can talk about the results, but they're not robust enough to give us the data that we need for complication rates, success rates, failure rates, recurrence of prolapse, which is where the HQIP work is going to be quite crucial.

It also comes back to the longer-term follow up, because if we had an NHS digital-based data collection system, then that would do our preoperative, our postoperative data, and then there's no reason why patients couldn't automatically be approached again at six months, one year, two year, five year, 10 year, to get those long-term data that we can't within the clinical NHS. We don't have the luxury unless we're told there's a problem of routinely following up those patients.

Julia Cumberlege: But you could do the following up through digital means.

Andrew Williams: Exactly, yeah, and that's what we would all want, is that an automated - so you'd get an email that said you had an operation two years ago. Can you

spend five minutes just filling in these questionnaires that you've already done? It can all be done electronically.

Jonathan Duckett: We don't get good patient buy-in to those sort of initiatives, unfortunately.

Andrew Williams: No.

Jonathan Duckett: So we send everybody a self-addressed urinary symptom questionnaire at six months, and we get less than 40 per cent of patients who will be bothered to fill out the questionnaire and send it back to us. So we've looked at how to follow patients up, and you have to get somebody to phone them. It's actually the only or the best way of getting anywhere near good follow up, and so when we're looking at our eight-year data, a very enthusiastic registrar at the firm, and we've got 90-plus per cent follow up, but other than that, you don't get patient follow up.

Andrew Williams: Clearly, that's not...

Jonathan Duckett: Tenable.

Andrew Williams: Tenable, but I would argue that actually we would have a negatively biased results from - because the people who've had problems or aren't quite right are more likely to let us know, and so the ones that can't be bothered to fill it in is that you've given them their life back to such an extent that they're too busy on the trampoline with their grandkids or going for a run to actually fill in the questionnaire, which is what we'd want.

Jonathan Duckett: We've looked at that, and actually we find the patients least likely to fill in the questionnaire are the ones who are cured, and they're [unclear].

Simon Whale: But if you know the number of people who have had a procedure, then you know your percentages, so in a sense, it doesn't necessarily matter, if the only people who report back are the people who've had problems, complications. Because if you know your total database, you know what percentage they represent and therefore what percentage the silent minority or majority...

Andrew Williams: Totally agree with you, but that's not scientifically robust, and so we would just be criticised completely, so we can't assume that, that even though we all know that's probably likely to be true, probably likely isn't good enough. That's our stumbling block.

Simon Whale: In terms of mesh removals and salvage, are there - again, if you think about a situation where the pause is lifted, are there enough surgeons to be able to handle that at the moment?

Jonathan Duckett: It's an interesting question. The patients are tending to move toward some centres which are overwhelmed, so there are some centres with long waits. So I'll see a patient. I'll say, you can go to London to blah-di-blah, or I will do your operation here for you. A proportion of them will choose to go to London, and those centres are being overwhelmed. So I've got loads of space, and there's no problem with seeing patients with mesh complications, but that's not the same for some of the well-known centres.

Sonia Macleod: Why is that, do you think? Why are patients voting with their feet in that way?

Jonathan Duckett: I think patients buy into certain surgeons, to be honest, and if you have a profile on the Internet which is positively received by patient groups and you're well recognised in that area and you're understood just to be a caring, diligent doctor, then the patients will tend to vote with their feet.

Andrew Williams: There's a lot of evangelism, as well, and one of my other concerns and concern of many of us is that whilst there's no doubt that meshes have caused problems, we have to be also very cognisant of the fact that we can do harm by our desires to combat the problems that the meshes have caused, and so we need to be equally as restrictive about who's doing the mesh complication work, and it needs to go through the same rigorous process of what's appropriate. Because at the moment, in the absence of a definite mesh-related problem or evidence thereof, be that clinically or an examination under anaesthetic or imaging, there's no evidence that taking the mesh out is going to actually improve your pain, say.

If you talk to all the major pain experts, you may just have the same amount of pain, but you won't have a mesh. I would argue and many of us would argue that actually, that's not necessarily doing the patients any good, and you're much better off doing a holistic approach to actually improve their symptoms rather than just remove the mesh.

Valerie Brasse: I'm going to stay with this on mesh removal. Women have told us that they've been offered a full removal, a full vaginal removal, but actually that's not what happens, and the question really for them is whether the surgeons know that when they're going in that they're not going to be able to remove it all, or they hope they're going to and actually come up with a partial but are told that it's been removed. They know they still have a pain - they don't know whether they've still got it there or not, and this question about what is in fact feasible about a mesh removal, so they're talking about the TVTs. They're talking about how you take that out. Are we quite clear that we're all talking the same language?

Jonathan Duckett: No, because the language you use, I don't understand. So when you say a full vaginal removal, that's impossible, so you have to take - if you wanted a full mesh removal, you'd have to do a cut or a laparoscopic procedure to take the abdominal part out.

Valerie Brasse: So that's the point. I think what they're saying is we think we're going in. We think we're going to get it fully removed. What actually happens is you take the sling bit out, but the arms are left in, and actually you couldn't do the full removal - and let's be quite clear that I've got this right. You can't do a full vaginal mesh removal without doing the groin incision too? Is that absolutely fair?

Jonathan Duckett: Okay, so there's a retropubic removal, and there's a - sorry, there's a retropubic and there's a transobturator tape.

Valerie Brasse: Let's deal with the retropubic.

Jonathan Duckett: The retropubic, you can remove the whole of the tape usually, but it will involve some sort of abdominal procedure to take out the abdominal aspect to it.

Valerie Brasse: So let's be absolutely clear. If you're going to take out that transpubic one, if you're going to fully remove it, it can't be done unless you're also doing an abdominal incision somewhere. It's not just taking out the bit through the vagina. You can't just do that.

Jonathan Duckett: I wouldn't be able to take the abdominal bit out through the vagina. It's usually stuck to the bones at the back, and you have to remove it from above.

Valerie Brasse: So for the women, they've been quite clear they've been told that's not going to happen. They don't have to have a groin incision. The chances are it's not been taken out fully.

Jonathan Duckett: Okay, so the situation here is I would discuss with the patient how much of her mesh she wanted removed and how invasive we wanted to be. So if she had pain suprapubically, then we'd be more likely to say, well, I think we need to take the upper aspect out. If she had pain vaginally, then we might just take the vaginal aspect out, so usually the surgeon would come to a discussion with the patient as to what her symptoms were and what the best approach to the mesh removal was. The more mesh you take out, the more likely you are to be incontinent again, so sometimes we just do purely abdominal excision of the mesh. Sometimes purely vaginal. Sometimes a combination. Sometimes a bit at the back of the bone. Sometimes just the bit superficial on the sheath.

So there are various different ways of doing mesh removal, and not all suits one person.

Valerie Brasse: But the women should not be misled to believe that they've had a full one when actually or potentially they've...

[Over speaking]

Jonathan Duckett: Misleading patients is a propriety issue which should go to the GMC..

Andrew Williams: Quite...

[Over speaking]

Valerie Brasse: Completely that. Can I ask you this question, because one of the women said, well, surely it's very simple. If there's any doubt about whether you've had it removed or not, if the implanting surgeon were to say, this is how much has been put in, 24 centimetres or whatever, and when it comes to be taken out, actually we've taken out eight, would that be so difficult to record that automatically as part of the surgeon's notes?

Jonathan Duckett: We tend to now, because patients ask for it. So they said, show me all the mesh that you've removed, so we have to take a photo of the mesh that we've removed.

Valerie Brasse: Do you record what you've put in, so that there's a clear measure of how much has been put in?

Jonathan Duckett: We don't record. We've never recorded what we put in.

Valerie Brasse: Why?

Jonathan Duckett: I don't feel it's necessarily valuable. You find one end of the mesh and you go and you get it down until you get to the other end, and that's then the whole of the mesh.

Valerie Brasse: But you can see if the women are saying, well, we don't know, how can we be sure, wouldn't that be just a very simple way of dealing with that problem? Because they know what was put in, they would have seen it. The surgeon will have told them, 24 centimetres went in.

Jonathan Duckett: No, it stretches as well.

Andrew Williams: And shrinks.

Jonathan Duckett: Twenty-two might go to 26

Andrew Williams: Or down to 18.

Valerie Brasse: But it wouldn't go from 24 down to eight or...

Andrew Williams: No, it shrinks. It wouldn't go from 24 to eight, no.

Valerie Brasse: So if eight comes out and 24 went in, that's clearly you haven't taken it all out.

Jonathan Duckett: Yeah. I think these are not different decisions. They should be between the surgeon and the patient, what of mesh have you removed, and the surgeon should then be able to say, I removed the suburethral portion. I removed the retropubic. They will occasionally get the situation where you think you've got it all out and there's a few strands left. That can certainly happen, and then scanning and things may help you with that, but I don't think surgeons are - should not be specifically misleading patients about what's been done.

You will go the patient afterwards and you say, yeah, I've removed it, so the lady on Monday, I said, no. I've left the old mesh in the retropubic space, because it was too difficult to remove, but I've taken the suburethral portion out and I've taken the bit out here. I had a discussion before with that patient as to whether that was acceptable to her.

Julia Cumberlege: I think there's a problem with communication, because a lot of the patients...

Andrew Williams: Exactly.

Jonathan Duckett: I think you're right.

Julia Cumberlege: ...actually believe they've had it all taken out and then they find they haven't.

Jonathan Duckett: Yeah.

Julia Cumberlege: They are then very concerned, because they thought that it had all been removed, and I also understand that mesh gravitates, as well. It goes into other parts of the body, and so I imagine what you're trying to do is actually extremely difficult, because you're not only taking out what was put in, but actually, you don't know where else some of the mesh has gravitated to.

Jonathan Duckett: I don't really buy into some of the thought that it disseminates around the body or spreads. I think some of the non-heat-treated earlier meshes, they could fragment a little bit, but the meshes don't move. Once they've been

in a fortnight, they stay there, and I don't really think they go anywhere else around the body. But a little strand or a little bit here and there, yeah, you could miss that.

I think you say, communication is exactly the most important bit here, and I can only speak for myself when I say I hope I'm communicating well with my patients. Whether they necessarily remember what I told to the patient on Monday about how much mesh she'd have removed in five years' time is also the challenge.

Sonia Macleod: I think one of the other questions we've had raised is that if you take out a central portion of the sling, it is then in subsequent surgeries much more difficult to locate the other bits that were left, and that's what we mean by gravitated.

[Over speaking]

Jonathan Duckett: That's with transobtured meshes, so that's certainly - yeah. It can be difficult to identify them full stop, so you may have to search around in all sorts of ways to try and find the mesh and remove it in its entirety. Yeah, it's not necessarily easy surgery.

Simon Whale: Are you aware of any surgeons internationally who use different methods of mesh removal than we do in this country?

Jonathan Duckett: We've heard from the patients group there's a chap in the States who's been very well regarded within those forums for mesh removal. The transobtured mesh is removing the lateral arms is a big challenge, I must say, and we're learning those challenges now. So yes, it's something that's been new to us a few years ago, to remove the lateral aspects to it, and there's different centres are along that learning process.

Simon Whale: Is there - are there efforts to learn from colleagues internationally who seem to be doing it for longer, or has that not happened?

Jonathan Duckett: Certainly, I think there's a challenge with the lateral aspect of TOTs, and Chris Harding sent a very useful video around about finding the lateral aspect of a TOT, and I found that really interesting to watch, actually, and very informative.

Valerie Brasse: I'm not sure what the opportunities are for importing that sort of learning to practice in this country. Is there any way that the societies think they can do this?

Jonathan Duckett: We have international meetings, so we often will go abroad and talk to other surgeons at those things, and for instance, there'll be video

techniques where this is how I remove a mesh. Obviously, you show your best version on the video, rather than the one that's very difficult and challenging. But we do already have international collaboration, and I think Scotland is also doing that at the moment from what I've heard.

Simon Whale: You mentioned scans just now. Can I just ask about translabial scans, as many of the patients have talked to us about translabial scans as being the most effective way, as they understand it, of imaging mesh.

Jonathan Duckett: Yes.

Simon Whale: They've obviously also talked about the very sparse availability of translabial scans on the NHS and the fact that they have to resort to private scans, which are costly and apparently increasingly costly. What kind of imaging is optimal and what should be available on the NHS?

Jonathan Duckett: So the person from America we've just talked about doesn't believe in scanning at all and never uses it, so that's one interesting thing. I've just written a paper with a group of international experts on the place of imaging for TVT type tapes, which will be published within the next hopefully few months. So translabial ultrasound scanning is best at imaging the suburethral portion, but it doesn't image any bit behind the bone. So to image that, you need an MRI-type scanner. The experience of that is that there's not a lot of published experience. It's one of the areas that does need more research.

For most clinicians, the use for scanning is if you can't find it and you need to know where it is. But if you've decided to remove a painful mesh, a scan may give you relatively little extra information over - if a patient has pain and you want to remove it, you need to remove it. If the scan says X, Y or Z, it doesn't make any difference to your treatment plan. So the translabial scans offer relatively little extra information. The MRI scans, you have to have special techniques and protocols which are not widely available, which we will publish for looking at the bits behind the bone.

You can compare one side to the other, because there's no good data about what they normally look like, so if you can see one's twisted or in the wrong place or close to a nerve, you may get information, but if you've decided you're going to remove it, you're going to remove it, and the extra information you get may not be a significant amount.

The people - there's less people doing translabial scanning now, so some people are moving from the market. They're not offering it, because they find that it's a difficult consultation when they do the scans with patients to give a fair and unbiased information. So you can say that the tape is there

or not there, which can be useful. You can see sometimes when you're on secondary removal, because that's very useful if you think someone's been left behind, but there's a reluctance for people to get into this area.

Simon Whale: Why is that?

Jonathan Duckett: You may be the guinea pig in the middle between the clinician who's referred you for the scan and the patient, and the patient is obviously or may well be anxious and may have a lot of buy-in to what this scan may find, and actually, all you may say is I can see your scan, your tape. It may give you no extra information, so the patients may be putting a lot of weight on that scan, whereas actually as clinicians we don't put as much weight on it.

Valerie Brasse: So is there something about communicating that message out? Because if what's happening is the NHS aren't providing it, private sector thinks, ah, this is something we can move into and the patients seem to want it...

Jonathan Duckett: Yes.

Valerie Brasse: ...and they're charging what the market will bear and making quite a lot of money. Do we not owe some responsibility to the patients to say, hang on. We need to be telling them this message that it's not actually making a difference, or we need to be [unclear] part that...

Jonathan Duckett: Perhaps we're giving different messages. So I would - when a patient has come up and said to me, I need a scan, and I'm going to go and pay for it, I will do the scan hopefully there and then in the clinic and say, there's your tape and give them the information so they don't necessarily go and pay for it. But if we're getting mixed messages - so some surgeons will send all their patients for a scan, so there's mixed messages going to the patients.

Valerie Brasse: So the societies have a job here to try to make sure that message is consistent, do you not?

Jonathan Duckett: We need specialist centres for mesh removal where we can analyse the technology better and find the place of scanning. At the moment, we don't see a huge place for it, but we need to run that study where everybody gets a translabial ultrasound scan and an MRI. We go then to look at the clinical indications and we try and work out whether that scan has been a beneficial effect or not. So rather than using the anecdote, we need more evidence.

- Simon Whale: Can I just ask something about implanting in relation to scanning? So am I right in thinking that when inserted, TVT or TOT is inserted blind, as it were. You're not using a camera or any imaging equipment?
- Jonathan Duckett: The needle goes to the back of the bone in a - I don't like the word blind fashion, if you know what I mean. It is - yes, a blind method of inserting it, I suppose.
- Sonia Macleod: It's not guided, and that's the point. There's no...
- Jonathan Duckett: It is guided. Yeah, it's guided by anatomical landmarks, so we all insert them slightly differently, actually, so I insert them slightly laterally to my colleagues, who insert them more medially, so we use anatomical landmarks to reduce the risk of damage to the bladder or the urethra or other things. Some people will move the urethra out of the way and some people won't, so there are lots of different ways of doing it.
- Simon Whale: Is it unusual compared with other surgical procedures to do it - let's use that word blind advisedly.
- Jonathan Duckett: No, not really. One of the most commonest gynaecologic operations is putting a telescope into your tummy, and that's done blind, and one in 200 cases, it goes into your bowel and you end up with a bag on your tummy because of a major complication. Sometimes it's a bit less than that, but those are the broad statistics. So certainly within - well, I think within many specialties I would think that blind is...
- Andrew Williams: I think blind is the wrong term. The best analogy is you're getting up to use the toilet in your own house in the dark. Do you get up, turn on all the lights in the whole house, wake everyone up and have them guide you to the toilet? You don't. You know where your toilet is. You know the various obstacles you'll have to negotiate, and you'll find your way through, through experience and through knowledge and through knowing the pathway. A lot of surgery is experience and knowledge. You know all of the different landmarks. So you're not blindly going to the toilet and walking into the wardrobe or the wall.
- You go to the toilet well negotiated. Very rarely, one of the children will have left their toys halfway across, and you may trip over, and so rarely in an operation you'll find unexpected aberrations to your anatomy where you may have a problem. But the vast majority, it's all fine.
- Simon Whale: But if you take something like TOT, you're operating very close to some major nerves and blood vessels.

Andrew Williams: That's the same for most of what we do.

Simon Whale: So it's not particularly unusual in that sense is what you're saying...

Andrew Williams: No.

Simon Whale: ...for it to be unguided or blind, and for there to be very significant nerves, blood vessels and other...

[Over speaking]

Jonathan Duckett: The NICE guideline is not recommending we use TOT as a surgical treatment, so we should put that to one side, if you know what I mean. Yeah, when we - it's basically a big knitting needle, and there are some big blood vessels there. One in 400 cases, I will hit a blood vessel and somebody will have a haematoma. Six per cent of patients will have hematomas up to five centimetres, because there's some bleeding where you're passing it through behind the bone. But we - we all have got specific ways of how we thread the needle up.

It's funny, with the newer, the mesh operations, we're now opening up and we move everything around, so we move the bladder out of the way. We still stick it through the bladder unfortunately every so often, but yeah, blind is a coarse word of describing a highly skilled procedure.

Andrew Williams: It's very difficult, because as a patient, a lot of these terms and a lot of the descriptions can be very alarming, because you think, you what? Understandably so. But actually, putting a - I'm not a urogynaecologist, but I've worked very closely for many years with them and we work together, and actually, putting it through the bladder is not a disaster. What is a disaster is not realising you've put it through the bladder and leaving it unrecognised.

So again, a lot of the bleeding is all contained, and so actually it isn't a major problem. It is an accepted percentage risk, and if it happened in 100 per cent of the cases, then clearly the operation is not a good operation and we'd find other ways of doing it. But just because these problems happen doesn't mean to say it's a flaw of the operation or it makes the operation unsafe. I think you'd agree, and I think that where problems occur is when there are problems and people do not recognise them or don't act upon having found them. That's the crux of the matter.

Julia Cumberlege: Can I just ask you, all the time things are changing and the NICE guidelines are an interesting example of that. But we know that in November 2019 this year that the commissioning is going to be done by a specialist

commissioning, and the current estimates I understand are that we will end up with 4-7 mesh removal centres around the country.

There are currently I believe about 50 centres, I think, that you've told us about inserting the mesh across the country. So, just thinking about the framework for the future, to access these 50 centres I'm talking about, do you think that through this specialised commissioning that they will actually reduce the number of mesh inserting centres? Do you think that will happen?

Jonathan Duckett: So I'm a clinical adviser on that, on the specialist committee specialist commissioning board. So some of the things are just a little bit wrong - so they're looking at somewhere between eight and 12 mesh removal centres, so there will be regional mesh removal centres. So there may be two or three in London, which will purely be looking at mesh removal and also mesh insertion for prolapse without...

Julia Cumberlege: That's quite a lot compared with what we have now.

Jonathan Duckett: I think it would be appropriate, so the figures have been looked at, so you see the number of patients that are coming through and that's the numbers that have been recognised as needed. There is a bulge of these patients coming through at the moment I think with the anxiety and fear that's come across. So I think they're going to be very busy, those centres, to start with the mesh removal.

There will be then the 50, as you say - roughly 50 specially commissioned centres, and they would be the sort of centres that you would expect to provide surgery such as an autologous fascial sling and a colposuspension. The TVT before the pause would not be specially commissioned, so it would be performed within normal commissioning, so within the normal DGHs, as they used to be called, hospitals, because say up to 10,000 of those procedures were performed a year. They wouldn't be specially commissioned. They'd be routine care.

So if the levels fall below 2000 procedures a year, then they become part of specialist commissioning. So I would have thought if we restart where we were, that TVT-type procedures wouldn't be specially commissioned. That doesn't mean to say there shouldn't be special governance and requirements, so that we are sure that patients get full conservative therapy. They get the proper consent process, and all patients go on a database.

So there would still be those requirements I would hope wherever the care actually takes place.

Sonia Macleod: So you were saying there are 10,000 paused TVTs. Are you expecting those still to be around that number?

Jonathan Duckett: It went from 14,000 to about 7000 I think before the pause, so it was already falling down. We're seeing the periurethral injection treatments. You would expect those would have gone up massively within the pause. They've actually gone down by about half as well, so we think the general treatment for continence is probably going to be a half of what it was before the pause started.

Sonia Macleod: So if we're talking a half and we're talking increased anxiety and other options, you still don't think they'll fall below the 2000?

Jonathan Duckett: That talks about 3500-type level. If it does fall below the 2000, then yes, it will be a specially commissioned surgical procedure, and then it will go to specialist centres. I wouldn't be too surprised if that didn't happen. But it's a problem then with the provision of service, so the specialist centre will have difficulty doing all of the fascial slings, colposuspensions and TVTs. We're looking at networks to make sure these things work, so perhaps a specialist centre may do all the fascial slings, and then you can commission out to experienced surgeons who've been doing TVTs for 20 years possibly to do those in a different centre. So there needs to be a hub and a spoke, and it needs to work for patients.

Julia Cumberlege: But the thing we don't want is just people to have a go.

Jonathan Duckett: I really believe I don't want people to just have a go. I think that's gone.

Andrew Williams; The secret to that is the MDT working in that that lends itself to a hub and spoke. Each hospital will not have an MDT process for pelvic floor problems, but there's no reason why they can't feed into an MDT, and then that's exactly where the hub can be where the MDT is based. They can do the super-complex, redo surgery, but then not sanction - sanction's the wrong word - support the decision-making for more routine surgery, where TVT will take the place.

I think if it falls below 2000, we're doing too few, so either you are just allowing a large number of patients to go untreated or the threshold is inappropriately low. Again, I'm from the bowel point of view, but that's the feeling looking in.

Jonathan Duckett: Yeah, colposuspension before TVT came in was about 2500 cases a year, so - and that was then only offered in specialist centres often, so patients from Kent where I work had to go to London to have their surgery for the pre - before I was a consultant. So yeah, 2000 would be too less - too few.

Julia Cumberlege: So as a patient, wouldn't you really want to go to a specialist centre? Wouldn't you feel that you were getting more security or a higher standard of care, or a higher standard of surgery?

Jonathan Duckett: I'd want to go to a surgeon who was trained in the operation that he performed, regularly performed the operation, was under proper governance procedures, recorded his information on the registry and had some idea of his outcomes, as well. So wherever that surgeon were would be the place for me to find that care. The NHS is very poor at providing that information, so if I got another problem, say I need a hernia repaired, in my hospital, I don't know who's good or bad. I've got no idea who's the good guy, who's the bad guy. I know who's the fast guy in the theatre, but I don't know what happens six weeks, six months, six years later.

So as a surgeon, I can't find that information for myself and my family. What we're proposing for TVTs and mesh procedures is that we will have that information.

Andrew Williams: The other thing is you may not as a patient want to travel from Kent all the way out to London for your surgery. But if you know that the decision for your surgery has been gone through in the specialist centre, you've got all of the advantage of all the experience, and yet your local surgeon has been doing them for 20 years. They probably taught the person in the London centre anyway to do the operation. It's the crux of the decision-making and the communication, rather than necessarily the surgeon.

Julia Cumberlege: I think it depends - well, of course, it's a patient choice and it depends very often on what age you are, whether you're prepared to travel. It depends where your family are, whether they can - so there are a lot of other reasons, I think, where you want to want to be treated.

Andrew Williams: Absolutely.

Julia Cumberlege: But can I just ask, from the point of view of the Pelvic Floor Society, does the potential for an overlap between mesh insertion centres, which we've been talking about, and the rectal mesh insertion centres, do you think it's right that they should be sited in the same place or do you - how do you see this happening in the future?

Andrew Williams: At the moment, the centres for complex mesh problems are colocated with colorectal, urogynae, urology, and that's we think entirely appropriate, because the skill set and the different clinicians involved - taking out a TVT tape probably will not involve colorectal at all, whereas taking a mesh out of the vagina with involvement of the rectum definitely should involve a

colorectal surgeon but also someone who is experienced in dealing with mesh problems and the bowel.

So it makes total sense, we feel - I don't know what you would say, Jon, but to have all of the key players in the same centre. I think it's going to happen anyway, because that's the way that the commissioning's coming through. It's coming from the women's health and gynaecology side. It's not coming from the bowel point of view.

Jonathan Duckett: The specialist commission is expected to commission specialist women's centres, so there will be colocation of urology, colorectal and gynaecology within the same centres.

Andrew Williams: Rather than reinvent the wheel, we will...

Jonathan Duckett: You couldn't practise without those three collocated specialties, and imaging and pain.

Andrew Williams: Exactly.

Julia Cumberlege: So in the specialist centres, you might have people who are removing mesh, but you might have also people who are inserting mesh. Now, that kind of worries the patient groups. It's something that they've brought up and talked to us about.

Jonathan Duckett: We've seen that right from the start, actually, where some of the patient groups have lost faith in a surgeon because they're actually still putting in TVTs as well as removing them. I think that it's a difficult circle to square, really. It shows that the surgeon has faith in the operations that they perform, whether they're inserting or removing them. For the patient, I can understand it's more difficult, if they've had a very traumatic and difficult time with their mesh, and they are very vehemently against mesh insertions.

But we have to be - well, we are - hopefully, as surgeons, we're pragmatic to offer different surgical options for different problems.

Andrew Williams: Also, if you want - taking the mesh out can be some of the most challenging surgery. What you need is a surgeon who is really comfortable with the operation, with the techniques involved, and is confident and comfortable with putting them in, so you know exactly what the problems are when you want to take it out. What you don't want to do is go to a surgeon who just takes mesh out. I would argue the other way.

Julia Cumberlege: Do you have that now?

- Andrew Williams; Have?
- Julia Cumberlege: Surgeons how just take it out?
- Andrew Williams: I think there's a tendency in some of the mesh centres where they're so busy just taking it out and they're so vehement against mesh that it gets quite polarised. Therein lies a potential problem, I think.
- Simon Whale: But from a patient's perspective, if surgeon A inserted mesh which caused that patient terrible pain, going back to surgeon A, presumably having had various interactions with him or her in the interim as well, which may or may not be satisfactory from the patient's point of view, going back to that surgeon A for the removal operation is quite a difficult, emotional process.
- Andrew Williams: Possibly, but that depends on the level of communication, counselling, information beforehand and how he or she has dealt with the complication thereafter. I have had complications from a surgery that I have done, but to my knowledge, my patients come back to me. I then discuss whether they want to stay with me or whether they want to see somebody else, and I'm more than happy - I just want the best for them - and the vast majority stay with me, because we've had an open dialogue throughout. It's difficult for the surgeon as well as the patient, for sure, in that one feels very responsible if there have been problems with an operation that you have done.
- Equally, you would do your damndest to make them better afterwards, so it cuts both ways, I'd argue, and that comes down to what we were saying earlier about either probity or communication, and that's the underpinning line of all of this. Whatever sanctions we put in, whatever plans we put in, it won't change the fact that at the end of the day, an individual surgeon's practice is between him or her, the patient, the GMC and the Trust with whom they work, and there is no regulation above that.
- Julia Cumberlege: Can I just ask you, you've been inserting mesh and all the rest of it for some years, I gather. So are there different types of materials that mesh - we have a general description. We call it mesh, and I think you called it tape at one point, and that's something that has really concerned patients. They didn't understand what tape was. They do understand what mesh is, and really what I'm asking you is are there certain mesh materials that are better than others?
- Jonathan Duckett: There were in the past, so I've inserted 2648 TVTs since 1999, 12 December 1999 when I inserted my first one. But all of those ones have been a specific type of mesh, so it's a macroporous, so it has big holes in it, so that if you get a problem, the bugs can be eaten, the cells that scavenge and

destroy inflammatory infections can be treated. It was before then, yes, we had some horrible meshes. We had microporous and there's been one used for prolapse which was probably in the early 2000s which was a dreadful mesh. It was a microporous one that the body rejected, and as a trainee, I had the experience of using bad meshes. But almost all of the TVT ones since the late 1990s are the type of mesh which has the least negative aspects to it.

When they introduced the TVT, they trialled four or five different meshes. It's in the original work from 1995. They had problems with the other meshes, and that's why they came to the macroporous TVT-type mesh, but even that's changed a little bit over the years, but it is still a mesh with big holes in it, which allows it to be incorporated into tissue, not to move, and for organisms to be destroyed within its network.

Andrew Williams: That's different for the bowel side of things, in that we have the luxury of being able to use a collagen mesh as well as synthetic meshes, whereas correct me if I'm wrong, using collagen mesh for a TVT doesn't work and it just dissolves and gives way.

Jonathan Duckett: It [does]. Yeah.

Andrew Williams: So we would - we know that polyester mesh is bad and is linked with a higher and unacceptable complication rate with mesh erosions and pain, and so we use polypropylene mesh, or titanised mesh, so titanium-coated or impregnated mesh, again. It's the polyester - well, the polypropylene mesh is the same mesh that's used in urogynaecology and urology world.

Collagen mesh, there are three types, usually porcine in origin. Our data at the moment, we can't say that porcine or collagen is any worse than synthetic, although there's a concern that recurrences may occur after two years or so. The advantage of the collagen mesh is it is resorbed by the body and replaced by the body's own scar tissue. So in two years' time, there'll be no mesh left and only your body's tissue, usually, but that is unpredictable and very variable between patients.

We can say there's no - again, no nice, robust data with randomised trials, but there's a suggestion that the incidence of mesh-related problems are lower with a collagen mesh, but that is anecdotal or case series data. We can say that the significance and the magnitude of the complications are lower with a collagen mesh, is the first thing that happens is the mesh dissolves and is eaten away by the infection, whereas with a plastic or synthetic mesh, it's there and it's there until you take it out.

So we're in a slightly more favourable position in that most or many surgeons in this country would now use collagen meshes predominantly, myself included, because we feel that the risk profile is lower.

Valerie Brasse: The reoperative rates?

Andrew Williams: Reoperative rates? It would appear - the data such as we have it is that it either works or it doesn't. We don't see a whole tranche of prolapses coming back after 18 months or two years when one would envisage the pig's all gone and then it all just falls apart. It either works and supports or it doesn't work, because the reason for failure is not necessarily that the mesh has dissolved. It may well have come undone. It may well have come off of its fixation on the bone, or it may well have been that they've managed to prolapse and continue straining such that it becomes lax below where you've done your repair previously. So it's not quite as binary as mesh failure or mesh success, certainly.

Sonia Macleod: One of the things that's very clear is that there is an evidence gap, but also one of the concerns that we've heard is that a lot of the reported outcomes don't necessarily match up with the patient experience. So going forward, in order to fill this gap that we've seen [happen], what outcome measures should we be using?

Andrew Williams: Specifically for the bowel-related?

Sonia Macleod: Both.

Andrew Williams: Again, this is where the HQIP data set is going to come into its own. Clearly, as a surgeon, we want to know - the indication for surgery for bowel is either constipation and inability to empty or external rectal prolapse. So at the most basic level, we want to know the recurrence of prolapse at two years, five years, whatever metric we include. We want to know what the raw complication rates are, so mesh erosion rates, pain, fistulation rates. Then we want to know some of the more subtle things, which is it's all about quality of life, and so we then want to measure the bowel-related quality of life and see if we've done what we want to do.

So our success rates, as far as we know, having reviewed all of the literature, you have a 65 per cent chance of having significant improvement in your ability to empty the bowel if you have a ventral mesh rectopexy for that indication. You've probably got a 15 per cent chance of it being no better and a 15 per cent chance-ish of it being slightly worse. Those are as good as it gets at the moment.

Whether or not we're ever going to get any more robust data - because it then comes down to how you're measuring quality of life, how you're measuring symptoms. What we will know is we will have a better handle on the risk strategy and the risk complications, which is where I think the disparity of many of the patients who have been harmed by the surgeon would say, well, actually, all of the published data say that a mesh erosion is 2 per cent. I know lots of women here, and this surgeon's done that many operations and the maths doesn't add up.

Clearly, having the data recording, we will have better handle on those data, which is where probably the urogynae and the urology specialties have got a much better head start with your database than the...

Jonathan Duckett: Our data's from 2007, so we've got quite a lot of data on that, but it's obviously done by experienced surgeons who have used the database, as well, so it might be slightly biased in that way.

Julia Cumberlege: Like us, you have a very clear understanding of the difference between a database and a registry, because that's very helpful.

Andrew Williams: We have a registry. They have a database.

Julia Cumberlege: Yes.

Andrew Williams: We need to build on our quality of data and our outcome data, but that's hopefully where this afternoon will come into it.

Jonathan Duckett: It's quite difficult to try and work out what you should be collecting, is the frank and honest answer, because there are various different fields there. So we want to look at success, and we want probably an overall patient assessment of whether they feel the operation has worked for them. Then when we start on questionnaires, then they become very lengthy and more difficult to complete, so if we have a sexual function questionnaire, that's a lengthy 10-page document, and then we add that to a bladder-specific questionnaire and then we have to assess UTIs and pain. It suddenly becomes so unwieldy that nobody completes it.

There's a balancing act. We're meeting with one of the patient groups I think regarding what they think is acceptable data collection, as well, so we're trying to involve the patient groups in that.

Julia Cumberlege: Yes, I think it's quite - wait for our recommendations. I was going to give an opinion, but I don't think I should. Right, anything else?

Sonia Macleod: Yes, in terms of obviously recording under the NICE guidance, they've stated that all procedures have to be recorded. Do your societies have a

view on what would be the most effective mechanism for ensuring that happens?

Jonathan Duckett: We've spoken before about mandating is very difficult. It has to come from the Trusts and within governance structures, and we've looked at our data on the BSUG database recently, and we have a 95 per cent concordance with HES data, which is really good. So the latest data is certainly suggesting from centres that are involved in these difficulties that the data is all going on or largely going on at the moment. But mandating it is the challenge where NHS England purchases care, doesn't mandate this type of activity often. I think we need to get around that.

Sonia Macleod: So you think you're capturing 95 per cent of your operations?

Jonathan Duckett: When we compared in two or three centres, we compared our HES data with what was going on in the BSUG database, and yes, we got 95 per cent concordance.

Sonia Macleod: Which again, you've got voluntary data, so it's [unclear].

Jonathan Duckett: Yes.

Julia Cumberlege: Are you satisfied with HES data?

Jonathan Duckett: I've published extensively on HES data, so I have to say, yes, completely satisfied with that. The HES data is a good enough database to be a robust and reproducible, so the HES data is - I threw my stones at HES data before I started working with it, and there are ways it could be improved and better, and it has been improved and better, but it's generally considered good enough now for research to be done on it. So it is considered sufficiently accurate for research to be done, so it must be considered as being acceptable data. I have my reservations.

Andrew Williams: Working with getting it right the first time in the NCIR, I've recently just looked at my own data, which is their data is based on the HES data, and it's amazingly close.

Jonathan Duckett: Yes.

Andrew Williams: It's not...

Julia Cumberlege: Amazingly what?

Andrew Williams: Close and accurate in what it's doing. Clearly, the weakness is it's down to the clinical coding, but having said that, it's not beyond the realms of

possibility to say, right, these are the codes, and actually as clinicians, we can tighten up what we're declaring as the codes.

Valerie Brasse: But that does seem to have been a problem. Accuracy around coding and especially around mesh removals, partial, full. We asked to have some analysis of the data from a number of the accredited mesh centres, we did get comments back saying, can't provide this because the coding data is inaccurate and we actually don't know.

Jonathan Duckett: So the coding data, I was part of the NHS England group on coding data, and that was only altered two years ago so that there are codes now for mesh removal. I think that was a prolapse mesh removal. So there weren't any codes before then, and they're due for another...

Valerie Brasse: So it's a catch up.

Jonathan Duckett: It's going to be a catch up on the mesh. If you think mesh removal is a relatively newer science, so there weren't any codes for the - 18 years before that.

Andrew Williams: Short of the time issue, we won't get around that. We just have to move forward and make things more robust, so that in five years' time you'll look at the data and you'll look at the codes and you'll say, well yeah, that's 98 per cent case accrual.

Jonathan Duckett: It needs updating again. It's not perfect, but there is data there now, and there was none before.

Sonia Macleod: Can I just go back, and obviously you said you've got a very high reporting rate. Pelvic Floor Society?

Andrew Williams: Probably 40 per cent, something like that, maybe more. This is one of the reasons I'm working with the coding side to see which codes are most likely to capture all of the cases that we're interested in, because again, there isn't a code for a lap ventral mesh rectopexy. It could be coded in any way - any number of six different permutations, and so it's working out the subtleties of those to capture the majority of the cases. Then we'll go back and we'll see exactly how many cases are being done, because quite sensibly, the first question I've been asked is well, how many lap ventral mesh rectopexies are going on in the country? Nobody knows. Nobody knows.

Valerie Brasse: But how long have they been going on for? Then the question is, how long does it take to identify the proper coding so that we can find out?

Andrew Williams: Well, exactly, which is what we're working on. What we're confusing here is we're confusing how the country works with what we really want to get to. Nirvana's over here, and we all know what it looks like, but this is how the NHS is.

Valerie Brasse: But this particular procedure has been going on for how long?

Andrew Williams: For the last, what, 10 years, eight years maybe?

Valerie Brasse: We don't know after 10 years how many?

Andrew Williams: No, absolutely...

[Over speaking]

Jonathan Duckett: I think for TVT, it was 2007 when the codes caught up to date with the clinical practice.

Sonia Macleod: So a decade.

Jonathan Duckett: Yeah, a decade. Yeah, just under. Yeah. So they're where we were in 2007 with no data.

Valerie Brasse: It's not really a healthy way going forward...

[Over speaking]

Andrew Williams: It's the same for everything else in the NHS.

Valerie Brasse: I get that. I'm just talking about new procedures, new device, trying to assess accuracy about data.

[Over speaking]

Andrew Williams: Welcome to the NHS.

Jonathan Duckett: That's why we introduced our database all the way back from those early years, so that we could try and get a handle on the risks and the complications and the negative outcomes. Because we were aware that there may be things that we weren't going to capture.

Sonia Macleod: Should it be the societies to be taking that role, as a voluntary assumption?

Jonathan Duckett: We were anxious that nobody else was going to.

Andrew Williams: Well, no one else is doing it.

Valerie Brasse: That's my point, thank you.

Andrew Williams: That's why. In a way, it's quite analogous to where the cardiac surgeons were 20 years ago, because none of this happened and then a big thing about outcomes, and then the database comes in. It's only when something happens that public demand then decrees that we have to do something about it. Luckily, each one of the three organisations have pre-empted this and started doing things in advance of things...

Sonia Macleod: But should we have to wait for a catastrophe?

Andrew Williams: Of course, we shouldn't. It's a rhetorical question. It's obvious we shouldn't, but at the end of the day, who's going to pay for the information and the informatics to game the data so that we can pre-empt this in everything? Where's the next catastrophe going to come from? So where shall we put all the energy? And nobody knows.

Julia Cumberlege: Well, I think we could continue with HES for some time, and I can remember it being introduced, and it was really for administrative purposes. It really wasn't for clinical purposes, and therefore we need to probably go onto something a bit more refined. Anyhow, final questions?

Valerie Brasse: Final questions. We've been talking history. I'm a student of history, and I'm always interested in what's happened in the past as well as what happens in the future. Changing of attitudes. If we go back and look at some of the documentation that you and BAUS have supplied to us, there was very clearly a concern expressed by clinicians when mesh appeared on the scene, and that concern was registered right at the beginning. It was certainly registered in meetings, documentation of meetings I've seen between your society and BAUS, say in 2004, concern about it coming on too fast and we don't have the evidence base.

I see it again in letters in 2010 written from your societies. So I'm left wondering, at what point do clinicians have a change of heart? So although they had these concerns over a number of years, at some point, the attitude changed, and I've not actually understood why that came about.

Jonathan Duckett: How do you mean attitude changed?

Valerie Brasse: Attitude towards absorbing and taking on mesh as part of their clinical practice rather than we don't have the evidence here, there's inadequate evidence, we don't know the long-term outcomes. I've seen the documentation and it runs right through, and yet at some point clinicians do take this on with quite some force, with quite some force. I'm not clear I understand how that attitude changed or why.

Jonathan Duckett: The older operations were big operations with significant side-effects and complications, and so when you are given a newer operation that seems to be fairly a lot easier to perform and a lot safer, and then people start using it and they report, and then it does snowball of the positive aspects. So we see this in many cases in medicine, there's a sharp, swift lift when operations, and then there's a static state and then they fall down to a normal level when people understand the risks and complications.

So I don't think the TVT operation was any different to any other procedure that has that exuberance to start with and then a realism and then a...

Valerie Brasse: The documentation would suggest there was this underlying concern throughout, and that's the thing that slightly worries me and I'm sure would worry others who may recognise these concerns still exist but people don't feel they're comfortable - they haven't got enough evidence as to the effectiveness of these procedures, and yet, as you say, it rises.

Jonathan Duckett: So the leaders and challengers of our societies were uncomfortable with some of the things that went on, so you've seen those minutes which state that. That was how many of us felt at those stages. Then for TVT, for instance, a randomised, controlled trial was published in I think it was about 2002, which showed good efficacy and limited side-effects and complications within a small patient group. That's probably where the interest in TVT changed, and then it was expanded in an unregulated, uncontrolled way, which is I think we're looking in hindsight was wrong.

Valerie Brasse: Thank you.

Simon Whale: Can I just ask one question, final question? Should there be a mandatory register of interest for clinicians?

Jonathan Duckett: There's already a mandatory registering of interest for clinicians within the individual hospital Trusts, so if I speak to a drug firm, I'm A, not allowed to, and I, B, have to declare any interests. So whether that's done well within all Trusts, I don't know, but it's already there, a process.

Simon Whale: But it's not a national register. It's not...

[Over speaking]

Jonathan Duckett: It's held individually within hospitals.

Sonia Macleod: Is it publicly accessible?

Julia Cumberlege: Like the GMC?

Jonathan Duckett: I think people have asked for that information, haven't they, from various hospital Trusts and been disappointed how un-full it was in some declarations. So a national mandatory register is tricky. Again, you think, who would pay for it, would it be useful, and those sort of things. I'm not necessarily sure. I'd have to have a reasoned, long, lengthy argument for justifying it and its costs and who was going to pay for it, but I wouldn't say no.

Simon Whale: Andy, do you agree?

Andrew Williams: I do. I think the trouble is all of this information is going to be there. It's how easy it is to get hold of and how public it is. Clearly, I don't think any of us or the people who are working with industry in an appropriate way, none of us have any hesitation about declaring what we do, and that's fine. There isn't a general structure to declare interest in that sort of way. Clearly, it's presented if one sticks to published data and a declaration of interest, it's given before lectures. There's a disclosure statement, so all of that stuff's out there. I agree, it's supposed to be on your individual hospital's database, but I probably - I'm fairly cynical about the robust nature of that, if I'm honest.

Simon Whale: Your professional regulator has a register of every doctor. Wouldn't be a massive leap to sit alongside that a register of every doctor's interest.

Jonathan Duckett: As long as you're paying, we're up for it.

Valerie Brasse: Is that your only objection? Is that it?

Jonathan Duckett: It is my only objection. It's quite complicated with conflicts of interest. So I have to have a lecture on all of my slides which shows my conflicts of interest. How far back do I go? What sort of conflicts of interest are they?

Andrew Williams: What interest was it?

Jonathan Duckett: Was it a conflict in terms of this paper, or was it not a conflict? I'm filling these out all the time, and I don't quite know if I'm doing it right or not, so I just declare everything from 1999, and I don't think anyone else does.

Andrew Williams: Exactly. They gave me a pen and bought me a coffee, does that prejudice me?

Jonathan Duckett: But I can't even remember that pen, because we couldn't even remember who bought us those pens in BSUG.

Andrew Williams: I think the interesting thing is how industry regulation has changed, and you're more likely to get things sharpened up through the industry side

than reliant on the clinicians. Clinicians are usually too busy to worry about what they're given or what they've done. By and large, the majority are not interested.

Simon Whale: I think it works for parliamentarians such as the one we've got here, surely it can work for clinicians, can't it?

Andrew Williams: In theory, and none of us are against that.

Valerie Brasse: You'll know in the States, they have the Sunshine Payments Act, and physician groups say, why don't we have that here?

Julia Cumberlege: I think we should draw this to a close, because I could tell you a lot about the parliamentary system.

END OF TRANSCRIPT

Session 2: MESH SPECIALIST CENTRES - South Tees Hospitals NHSFT and Central Manchester University Hospitals NHSFT

START OF TRANSCRIPT

Julia Cumberlege: One of the things we are asking people is that if they've got a conflict of interest and we - perhaps you could fill in a paper after this session to say what your conflicts of interest are. So, as we're a bit short of time, perhaps we could just start off - unless you want to tell us anything particularly about your individual Trusts or anything you want to say, or shall we just start questions.

Simon Fulford: Nothing that [unclear].

Julia Cumberlege: All right. Great, thanks very much indeed. One of the questions that we're putting to everybody now since the new NICE guidelines have been published, we wondered if you had any view of those? If you think that they are clear and precise and whether you think they could have been improved or adapted or whatever?

Karen Ward: I have to declare a conflict because I was...

Julia Cumberlege: Sorry you're going to have to speak...

Karen Ward: Sorry I have to declare a conflict because I was the clinical lead for incontinence on the NICE guideline.

Julia Cumberlege: Oh, right okay. So, you obviously think they're perfect.

Karen Ward: I think with the evidence available, I think it was the best that we could do and using the expertise of the committee that we had, then I think that nothing is perfect and they never will be perfect but I think they're reasonable, We would have liked to have had more evidence particularly about complications. I think that was part of the problem with writing the guidelines, was a lack of...

Julia Cumberlege: [Unclear], right.

Simon Fulford: I don't have a conflict of interest that I'm aware of. I think they're quite reasonable, particularly if you take in mind the mechanism of creating a NICE guideline which is very mechanistic and depends on the literature that's available. That's the issue, I think.

Julia Cumberlege: So, it's about resources, are you saying?

Simon Fulford: Well, it's about publications. Would you agree, Karen?

Karen Ward: It's about what exists, yes and the problem being that there wasn't a lot of evidence of long-term complications of any operations whether they were mesh-related or not mesh-related. I think that was part of the issue.

Valerie Brasse: So, you're saying that's a common problem right across the board and it's not specifically this area that we're looking at?

Simon Fulford: Yeah.

Karen Ward: Yes.

Valerie Brasse: Because of course one of the things that women were telling us over and over again if there isn't the evidence to say this is something that is going to be in our bodies permanently, how can anyone declare that it's safe?

Karen Ward: Yes, and I think that also sutures are in their bodies permanently from other operations so there are long term complications of all surgery. I think we're - I think that one of the concerns is that patients haven't been aware of what's been put in their body and I think that's a really important thing. But also, we're also in danger of then not being able to do any operations at all and not offer people treatment for a quite horrible condition because we don't have evidence for any of the operations in the longer term.

I think that's quite a difficult thing as a doctor to say we want to give some guidance and the important thing is that we are as transparent as possible to patients and that was I think what was aimed to get out in the guidelines, was as much information to people to make their own decisions.

Simon Whale: And to be clear about what we or you as doctors don't know as well as what you do.

Karen Ward: Yes.

Simon Fulford: Yes.

Simon Whale: Do you think the NICE guidelines adequately ensure that is going to come out through a consent process?

Simon Fulford: Well, a consent process is always an individual process between one or several doctors and one patient. So, I hope it does, but it is an individual process.

Simon Whale: But it should, yeah?

Simon Fulford: Yeah.

Sonia Macleod: I think with more standardised things like mesh incision [unclear] should presumably standardise the consent process [unclear]?

Simon Fulford: Yes. I mean as a urologist, I now use all of the BAUS information sheets and there's - I'll literally give the patients a half-inch thick wad of A4 at their first appointment. So, they usually come back and say there was too much information, what would you do?

Julia Cumberlege: Yeah so...

Simon Fulford: Where do you go from there?

Julia Cumberlege: So, can I just ask you, because we've invited you here for lots of reasons but clearly, you're people who are actually having to deliver the service to your populations. I'm very interested what you say about getting the patient's consent. Now it's a big issue that's arisen as you can imagine with patient groups with us.

One of the suggestions we've had made to us is that there would be an opportunity perhaps at that first interview that you have with the patient that you could record it, [audially]. So you could do it on an iPhone or something like that so they could then listen to what you've said, take it away with them, talk to their family or friends or whatever because it is a lot to take in at the first interview they have with you. Then I'm sure there are other questions they might - might be triggered once they've listened again to the initial interview. They could then ask you more questions. Do you think that's a possibility?

Simon Fulford: It's certainly a possibility but it runs up against practicalities in the NHS I'm afraid.

Julia Cumberlege: It runs up against what?

Simon Fulford: Against practicalities in my NHS life, which is extremely busy, overrunning clinics, lack of peace and quiet to actually sit and record an interview.

Julia Cumberlege: But you said that they come back to you anyhow.

Simon Fulford: Yeah.

Julia Cumberlege: So, they could come back to you having listened to this interview and that might have triggered some more questions, which might be helpful to you in order to help them reach a decision.

Simon Fulford: I'm in favour of it, yes.

Julia Cumberlege: Okay. Can I ask you about - again the NICE guidelines and the fact that they're recommending an MDT team. Can you tell us a bit about your teams, your multi-disciplinary teams?

Karen Ward: So, we have a team for our primary surgery it's a sort of core team for our trust. So, we've got a trust that's made of...

Julia Cumberlege: I'm so sorry I'm going to interrupt because I should have said at the very beginning who you are...

Karen Ward: Oh sorry.

Julia Cumberlege: ... and why you're - no it was my fault. So perhaps you could just say...

Karen Ward: So, I'm Consultant Urogynaecologist, Manchester.

Julia Cumberlege: And Manchester is the biggest unit in the country?

Karen Ward: I think it's one of the biggest. Yeah, we have five sub specialist urogynaecologists. We have a couple of urologists. We have colorectal surgeons. We've five colorectal surgeons, three radiologists, a plastic surgeon and pain specialists. So, it's a huge team but we don't always meet at the same time, so it depends on what we're discussing, whether it's mesh or...

Julia Cumberlege: I'm just going to ask then, Mr Fulford...

Simon Fulford: So, I'm Simon Fulford.

Julia Cumberlege: Just say who you are.

Simon Fulford: I'm Simon Fulford. I'm a Consultant Urologist in Middlesbrough.

Julia Cumberlege: Right. Would you like to continue about your MDT?

Karen Ward: Yeah so, we have a huge team, but practicalities because it's expensive to have everybody sitting in the room at the same time. That's one of the problems, is job planning, a huge number of people to all sit in the room. So, we try to take a practical approach to that which is to have the people that need to be there. So, we have the fairly straightforward cases, primary surgery that we deal with every week. So, we have a whole morning a week that we spend an hour MDT.

Then we'll have additional MDTs with whoever needs to be there. So, whether it's a pain specialist, which is usually about once a month or radiology and urology. All of those are about once a month depending on what patients we have. Because it's just not feasible to have an MDT of

everybody sitting there at the same time. It's a very expensive service to run and so we've got to try and make the most of people's time by not having them all sitting there for a whole morning if they don't need to be there.

Julia Cumberlege: So, you use other methods of communication, do you?

Karen Ward: No, we limit it to about once a month with the extra people, so, the more complex things. We are in the process of organising teleconferencing for our outlying Trusts.

Julia Cumberlege: Right, and so that works quite well? Does it work for patients?

Karen Ward: We write to them when we - so they know that they're going to be discussed at the MDT and then at the end of the - when we've discussed it, we dictate a letter back to the patient to let them know what we've decided. So, we'll have had a conversation with them beforehand, assess them and we'll have had a conversation with what the options might be. Then once we've discussed it at the MDT, we write back to them to let them know what we've - what the plan is going to be and when they're going to be seen. We might telephone them if they come from a long way away or we might see them back.

Julia Cumberlege: You don't have the patient present when you're discussing the options that are available?

Karen Ward: No.

Julia Cumberlege: Is there a reason for that?

Karen Ward: Logistics mainly. So, some of our patients come from a long distance. It would be quite difficult to time that and also the availability of different people sometimes it doesn't happen exactly when you think it's going to happen. So, I think it would be difficult to do that, but not impossible.

Julia Cumberlege: So, you could give it as an option. Then if they can't travel or can't get there, that would be their decision.

Karen Ward: I think it would be a challenge to do that because it would take longer because obviously you can't use lots of short cuts in your conversations and so I think it would be a lot more resource intensive to do that, if they were to attend. But there wouldn't be a reason why they couldn't come. But I think it would be difficult to organise that.

Julia Cumberlege: Your MDT.

Simon Fulford: Right our MDT, we have - there's two consultant urologists - myself and a colleague [inaudible]. There's two consultant urogynaecologists, who do nothing but urogynaecology. There's an associate specialist in urogynaecology. There is - we have two interested colorectal surgeons who attend, one of whom does - the majority of his work is functional work. We have a radiologist with a particular interest in pelvic imaging. We have a specialist physiotherapist and a couple of urology nurse practitioners and urogyny nurse practitioner. I'm trying to think who else is in the room - and some trainees.

That - we meet over lunch time once every four weeks and we discuss - we aim to discuss all new stress incontinence cases amongst all the other prolapse cases, urethral diverticulums, a whole variety of things. We do have a liaison with our pain specialist - one of our pain specialists occasionally - well, will attend if we ask him to.

Julia Cumberlege: Right, and again, you would find it difficult to have a patient present, would you?

Simon Fulford: We would I think because of the timing, the nature of the meeting and the number of patients that we're trying to put through. It's possible. It could be arranged. I think just on a practical basis, the room that we use at the moment would probably not be terribly user-friendly for patients sitting outside and so on. But that's - it could be done.

Julia Cumberlege: Right okay.

Simon Whale: Can I just ask something about - so the NICE guidelines have come out but as is recognised in the NICE guidelines, the pause and the high vigilance regime continues. A couple of questions around that. Firstly, are you confident that both within your own trust that more broadly that situation is understood?

Simon Fulford: Yes.

Karen Ward: Yeah.

Simon Fulford: Very confident within urology. I was surprised to see the guidelines. I'm surprised they were published before your enquiry was published. I wasn't expecting that to happen. Within 24, 48 hours later, BAUS sent out an email from Chris Harding saying, hang on guys, the high vigilance is still in place. This isn't the green light.

- Simon Whale: The other question that we'd be interested in your views on in relation to the pause is what - how are you managing patients who, were it not for the pause, you might have been recommending mesh related treatments to?
- Simon Fulford: Well, I wouldn't go as far as I'm recommending mesh related treatments to anybody at the moment, but it is one of the options that we would discuss. If they choose a mesh - if someone, as happened last week that 'I really quite want a TVT please Mr Fulford', I just said 'well that's not currently possible. Why don't you come back and see me in six months'. I also did a rectus fascia sling on a lady yesterday who wanted a TVT just before the pause came in place under a colleague but decided she'd go on holiday instead. Came back and was told that she was longer on the waiting list. Go and see Mr Fulford. So those are the two routes that people are taking.
- Sonia Macleod: What proportion of people are waiting? What proportion of people are having the alternative treatment?
- Simon Fulford: A minority of people are waiting. There's only a few. In fact, there's one group that - a minority of ladies are waiting. I have quite a few men who are waiting for an AdvVance sling who've also been caught up in this.
- Karen Ward: Our experience is similar. So, most of our patients have opted for a different procedure. I think - I don't have anyone waiting myself but my colleagues may do. But it's only one or two and most people - we've brought them back and cancelled them and we wrote to them all to let them know what was happening, last July and then we brought them all back to clinic. They've all been operated on - the majority have had something else.
- Simon Whale: [Unclear] slings or...
- Karen Ward: Yeah so either a colposuspension or a sling, most of them. Then there are the group under the high vigilance procedures that are having prolapse surgery with mesh and we are writing to them when we've discussed their procedure to let them know it's a high vigilance procedure. We're obviously conducting an audit of all of those procedures that we're doing.
- Sonia Macleod: But you wouldn't expect a huge - when the pause permissions are met and it's lifted, you wouldn't expect an influx of people who've been waiting?
- Karen Ward: No, I think our practice may be slightly different from other hospitals around the country, but we always had a higher number of patients having alternative procedures. So - and we'd already seen a big drop in mesh procedures before the pause. So, we were seeing that nationwide TVT was

dropping. So, we'd already started to and seen patients opting for alternative procedures. So, no I don't think there is in our practice.

Simon Whale: So, does that mean that the expertise within the team, both your teams to provide alternatives - alternative surgical options, [unclear] slings, colposuspension. That's already available. It's not like you've had to re-skill yourselves in order to do that.

Karen Ward: No.

Simon Fulford: I've had to train my colleagues to do it because I - my main role is in neuro-urology looking after spinal injury patients and so on in whom I've continued to do rectus fascia slings forever. So, when this occurred, my urogyny colleagues were going, well how do you do a sling and we had conversations, we've operated together and we're now all up to speed.

Julia Cumberlege: Can I just ask you about the high vigilance. What sort of numbers are you having in terms of operating through the window if I can describe it as that, of high vigilance?

Karen Ward: Well, we've - it's difficult because we've increased our number of consultants recently but the high vigilance procedures - so the slings and the colposuspensions, we're doing a few of those every week on our theatre lists. We're doing fewer prolapse - abdominally placed prolapse meshes which come under high vigilance - so they have dropped. So sacrocolpopexies and sacrohysteropexies have dropped. So - but it's predominantly - under high vigilance it's bulking colposuspensions and slings that we're doing.

Julia Cumberlege: Simon?

Simon Fulford: It's difficult for me to comment on how - or what the activity of my urogyny colleagues is in terms of prolapse but they never really did very many meshes at all and they're not doing any. They are doing some sacrocolpopexys, sacrohysteropexys often as joint procedures actually. I've been involved in a couple of those recently. We're all doing more bulking agents and more slings and the occasional colposuspension.

Julia Cumberlege: Thank you very much. When the women that come to you hear about the pause and all the rest of it, do you get any sort of feedback from them about the pause? Do they - are they deeply disappointed or they understand why the pause is being introduced? Do you get any feedback?

Karen Ward: Not really. I think most of them know before they come what's happening. They've heard about the mesh situation so they're coming knowing that

already. So, no I think they don't seem to - I think they seem to value our transparency in telling them what's happening and the reasons for it. So, I haven't really had any negative in the patients I've spoken to.

Simon Fulford: I'd say my - the patients I deal with fall into two groups; one the sort of naïve patient who comes with a problem and you discuss things and they react in exactly that way. But I also get a reasonable number who come along because their friend had a TVT done by me a few years ago and they are quite upset that they are now being blocked from having that option. That's a huge issue in the men as well, with the AdvVance sling. The number of men that I see who come along and say I'd really like a sling. You say well you can't have one at the moment. They ask why, and I explain, and they go well, but I'm a man, I don't have a vagina, what's that got to do with me? So that's a different route. It's not big numbers but they are disappointed about it.

Karen Ward: I think it though depends on your own individual hospital circumstances and referral pattern. So, the patients that tend to come to us are people who have come because they know we can do the other operations, or they've been referred in from other hospitals because they know what we can do. So, we probably see a lot fewer of those kind of patients who've - whose mother had a TVT and now wants one, you know, we just don't see those kind of patients. They've come specifically because they know we can do an alternative.

Simon Fulford: We have - and in terms of certainly the continence side of it, the five people I mentioned in our MDT are the only urologists or gynaecologists on Teesside. Sorry that's not quite right because there are urogynaecologists in peripheral hospitals who actually do feed in to our MDT and occasionally attend that - I forgot to mention them but we - so there's seven of us I think on Teesside which has a population of about a million who do continence surgery and we work within this - our MDT network. So, everybody should be aware that all of the options are available.

Simon Whale: In terms of the surgical alternatives to mesh, what's your view and experience of relative risks and benefits compared to mesh?

Simon Fulford: Do you want to go first?

Karen Ward: That's a good question. Obviously, there's been a 20 year gap of people not doing those previous procedures and there was a reason I suspect that mid-urethral slings became so popular. Not only were they perceived as being quicker and easier and a quicker recovery, but we did know there were complications with the other procedures. So, I think that's the - the

issue really is that those procedures haven't been done for 20 years and the quality of the evidence from 20 years ago looking at complications from those procedures, is not good. But we did recognise that patients having for example a colposuspension had a high risk of getting a prolapse afterwards. That we did recognise.

So, it wasn't a procedure that was necessarily completely straightforward, and I think the technique may well have changed a little bit, but we also saw people had difficulty emptying their bladders. But when you actually look at the comparative studies, there's not a huge difference between the TVT and the colposuspension apart from in prolapse.

Slings I think have gone through changes and I think the other issue here is that - that the operations that were being done 20 years ago have been modified in that time. So, the original sling operations would have been big operations, the Aldridge type sling, big operation and it's now become a lot more similar to a TVT except done without the mesh. So, done with the tissue from the abdominal wall. So, we're not really - the numbers haven't really come - the studies haven't come in to really get to the bottom of whether they are - the safety of those because the longest term data we've got is probably about 10, 15 years data on fairly small numbers done in one trial.

So, my feeling is that we had a lot of complications from doing Aldridge slings. We didn't do big numbers, but we did have patients with hernias. That's the big problem for patients who don't want mesh is if you give them a hernia then they can be quite difficult to repair without using a mesh because they're very low down hernias. So, by changing the technique we hope that the complication rate will go down, but they certainly do take longer to recover, longer to get back to work and there is a question mark about the comparative safety of them.

Valerie Brasse:

If now under the pause you are offering alternative procedures that are surgical, should they fail and then the pause does get lifted say, does the fact that that procedure has failed so compromise the outcome for the mesh procedure further down the line? Because there is this debate, isn't there, and - we've heard from all these groups. We actually want to see mesh as the third and last possible option. Guidelines from NICE didn't say that but there is this question on the other hand is that if you do go down secondary line of surgical procedure which isn't mesh, how might that affect the outcome if that failed, for a subsequent mesh operation they might need and I'm not sure...

Karen Ward: It's a difficult question to answer because there aren't any good studies of surgery for recurrent stress incontinence. We know that mesh procedures or specifically retropubic mesh procedures do work for recurrent stress incontinence, as do slings and they were traditionally the procedures that were done, maybe bulking as well for recurrent stress incontinence but we don't know enough about the prior procedure.

So, we're going to have a huge cohort of women who have had a retropubic or a mesh procedure, having surgery but actually looking at people who have had colposuspensions and slings and then seeing what their outcome is, I'm not sure that we're going to get that. My feeling is that probably - I don't think you can say - I think - we know that when you do recurrent surgery for recurrent stress incontinence the success rate for every operation is lower. So, you might say an 85 per cent chance of success for the first operation. You go down to about 60 per cent if you need more surgery. But I don't think we've got that level of evidence, unless you know it?

Simon Fulford: No.

Julia Cumberlege: Can I ask about removals?

Simon Fulford: Sorry could I answer that question, the previous question.

Julia Cumberlege: Sorry.

Simon Fulford: As someone who actually did my primary research into slings 20 odd years ago, I've always been a proponent of slings rather than colposuspensions. But both are very morbid operations. Both have a high long-term failure rate compared to the TVT which is the standard sling that I was using. The rate of [unclear] infections and as we said prolapse are quite significant with both operations. The lady's recovery from having a TVT compared to having rectus fascia sling is a few days versus six weeks. I mean it really is chalk and cheese and I think it's very important that that's understood by patients and everyone else.

In terms of recurrent stress incontinence, the first chance of resolving something is always the best. I would agree that of the mesh options, the TVT would always be the option for recurrence. But generally, if someone had recurrent stress incontinence, you would be recommending a sling, a rectus fascia sling. I frequently do those for recurrence for all sorts of stress - previous procedures and then they're not easy. They're more difficult, more morbid and I really don't think I would be recommending mesh for re-do procedures if someone had had - which I think your question was a sling before, then trying to do a TVT with all the scarring and so on, I think

would be more difficult. My gut feeling would be there would be more issues with erosions and so on.

So, the patient's wish that it's the third option is not in keeping with what we know about the device, the procedure, in my opinion, based on no particular written down evidence but experience.

Julia Cumberlege: I just wanted to ask about removals. I understand in Manchester you do quite a lot of those removals.

Karen Ward: Yes.

Julia Cumberlege: I don't know about South Tees, do you?

Simon Fulford: We do. I don't know - in my submission we included our data from 924 patients that we'd have operated on ourselves. Our rate of actual problems seems to be an awful lot lower than we hear about from elsewhere. Whether that's because it all seems to be kept inhouse I - amongst the same cohort of surgeons putting them in, I don't know. So, we are removing tapes but very few, relatively speaking.

Julia Cumberlege: Right, and Manchester?

Karen Ward: We have a lot of patients referred in from elsewhere having mesh removal - yes from the North West and the North of England.

Julia Cumberlege: You don't see any sort of concern where you're inserting mesh but also, you're removing mesh, because some of the patients have worried about that?

Karen Ward: Yes. I think there are different types of mesh. Things that we're getting referred in, and I think that is a difficult - I think it is a difficult one to understand but within the pause, we're still inserting mesh for prolapse operations. I think for some of those women coming with really big prolapses, recurrent prolapses, the alternative to offering them mesh is for them not to have surgery often or have their vagina closed, because they've had all the other operations.

So even though I think we need to be as transparent as we can, and patients understand what the options are, the difficulties specifically with prolapse is the options can be really limited and these women have got quite significant symptoms, big prolapses. I mean if we couldn't offer them procedure with mesh or their vagina being closed, then they would have to just live with their prolapse and that's quite difficult.

Julia Cumberlege: You don't see a conflict between your colleagues who are putting in mesh and others who are...

Simon Fulford: Well, my colleagues are no longer putting in vaginal mesh. I mean prolapse mesh, we pretty much abandoned that before the pause happened because our disappointment with the results. We do do, as I said sacrocolpopexys and so on, but again, it's a matter of what is the alternative? If that's not palatable to the lady, then accepting the risk, taking on board the risk, seems reasonable. I think if we're to put it a different way around, if we're prepared to put them in, we should be prepared to take them out, in terms of offering the full skill set and service to the patients.

Valerie Brasse: I was just going to pick up two things, actually. I think there seemed to be a little bit of confusion between what you are both saying because hearing from you, the alternative for somebody who has prolapse, there is none. But you're saying actually my colleagues don't do mesh for prolapse. So, I'm...

Karen Ward: I think they're not doing vaginal meshes. So, there are vaginal meshes for prolapse and the abdominally placed, so the laparoscopic or open. So, I think your colleagues are doing...

Simon Fulford: Yes, they're doing sacrocolpopexy meshes but they're not doing...

Karen Ward: Because nobody's doing those.

Simon Fulford: ... prolapse repair mesh.

Valerie Brasse: Right because that's one of the interesting points about the new NICE guidelines, is it not, that in fact where previously vagina inserted mesh for treatment of prolapse was restricted to research only. That has been lifted from the new NICE guidelines and actually you're the clinical lead for that. You might be able to explain why.

Karen Ward: Not for the prolapse. I was incontinence lead. But I think the very, very few women, if you look at the numbers - if - very, very few women would actually fulfil those criteria that they had a recurrent anterior prolapse and they were wanting to consider mesh and they have the [unclear] support...

Valerie Brasse: [Unclear] complicated.

Karen Ward: ... and all those things that are there. We were looking in our own group of patients in a year - even before the restriction - before the high vigilance and the restriction on vaginal mesh - we hadn't done one and we're a busy centre. We hadn't put a mesh in for - we'd done it under prospect trial, but

we hadn't had someone that we would have considered a mesh for. So, there may be one or two per year that we might discuss it with, someone with recurrent anterior vaginal prolapse but again, this is in the context of really having nothing else to offer somebody and that they may wish to consider that as an option.

In practice, it happens so rarely because often the skin is very thin, the vagina is very scarred, you just really wouldn't want to put a mesh in. But it - there are a very, very small number of women that that might be appropriate and so that's...

Valerie Brasse: Can I just stick with the removals a moment? I mean we have heard from women who say we were going to have a full removal. We've been promised we're having a full removal. They're having a full vaginal removal and they believe that's what's happened to them. Actually, that's not what happens to them. They go into the surgery believing that's what they've been offered, and they come out, it's quite apparent that they haven't had that.

Now one of the issues is, can you actually do a full removal going through the vagina without the incision in the groin. It's not possible. So are surgeons saying...

Simon Fulford: I can't see how you could do that.

Valerie Brasse: Right, so in effect, what you're left with is you're taking out the sort of central sling bit.

Karen Ward: I mean if it's infected, then you could take it out through the vagina because they - essentially they fall out if they're infected and we don't see very many of those at all. Maybe one a year. But generally, if it's a full length - and we're talking about obturator devices - if it's a full length transobturator, then they're about 22 to 24 centimetres long. The vaginal part is maybe eight to 10 centimetres. So, there's a lot in the groin and it's quite fixed in the tissues, which is why it works. So, I can't - I personally can't see how to do that. It may be possible but to - you're kind of going up and around the corner into the groin. I don't understand how you can do that.

Valerie Brasse: So, in fact you can't do it. If you want to take the full thing out...

Karen Ward: I can't.

Valerie Brasse: ... it is impossible.

Simon Fulford: I can't. We can't.

Valerie Brasse: So being told one thing and believing that's what happened and then they're still in pain and actually they discover later on that they've still got mesh in them is not really surprising, this language of communication, whether they understood in fact what they were being told. One of the things they say is, well, if we're to have confidence that what we're being told is actually what happened, wouldn't it be very simple if every surgeon when implanting such a tape, were to say it's 24 centimetres long and recording that on their implanting notes. So, when it comes to the point in which you remove it, you could actually say well I've taken out eight. It's obvious you haven't taken out all of it. Then you'd know because there'd be a difference. I mean they're saying isn't that a very simple transparent way of being able to...

Simon Fulford: Unfortunately, they contract, which is part of the problem.

Valerie Brasse: But wouldn't contract from 24 to eight?

Simon Fulford: Not to eight no.

Karen Ward: Also, you don't know how much - what the length is because the way that the devices are put in, is that you trim the mesh at the level of the skin and then lift the skin up and it drops down at the time. So, whether or not it contracts, you don't have a measurement of how much - I suppose you could subtract it from what was left on the introducers. But actually, we know that - how long a TVT is and when you get to the end of it, you can see when you're dissecting, when you've reached the end of it.

If we're doing a retropubic removal, we would record the procedure, all of our - with permission from the patient - our laparoscopic procedures are recorded, and we'll ask medical photography to come and take a photograph of the explanted mesh. So, we would try and give the - and sometimes you'd take the mesh and show it to the patient if they want to see it.

I think you just need to tell - and sometimes it's not possible to remove even when you go in with the intention of removing an obturator, particular an obturator mesh or a vaginally placed mesh for prolapse, it's not always possible to remove all of it.

Valerie Brasse: So, you might have said to the woman beforehand, this is our intention but actually when it comes to it, you can't do it.

Karen Ward: Yes, and then you have to tell them, that you have - what you have managed to do. Then obviously have a plan in place for what to do next.

Valerie Brasse: So that's one of the issues...

Karen Ward: But it may not be possible.

Valerie Brasse: ... isn't it, if you've left it in and you've taken out the sort of central bit, is it actually then almost impossible to get into the bits that are sort of left?

Karen Ward: Yes, especially if the mesh is a colourless one, you can't see it. You rely on just feeling it...

Valerie Brasse: So, does that mean...

Karen Ward: ... in amongst the groin muscles.

Valerie Brasse: Right. So, there's a sort of compromise for the next step if they need to get the rest out, the chances are you've compromised that.

Karen Ward: But some women would - yes and I think that's - and that's my worry, when obviously we're discussing with patients, is that you almost go along a route where they've ended up with a very big operation for something that may not have required it. But they don't want to take the risk of losing the chance to have it removed from the groin. So, there will be a large number of women who will respond to just having the vaginal part removed and you can touch it, it's tender, if you remove it, they will get better. But the problem is if they don't and you have removed it, then you've lost your chance really to be able to get that groin part out if you need to.

We don't know really the way - how to assess women and we don't have the evidence of how to assess them and how to predict which people are going to get better and which ones aren't. So, we have to just explain these are the options, these are the risks and come to a...

Valerie Brasse: So, the recovery rate and complications would be that much bigger for the full removal with the groin incision?

Karen Ward: Yeah.

Valerie Brasse: That's why you're saying, you wouldn't do it automatically unless the pain or the symptoms presented suggests that's what you need to do?

Simon Fulford: As Karen was saying, if someone's got pain just in the central portion of it, and you go digging and getting the full tape out and they have groin pain after that, you know...

Valeria Brasse: You've lost your opportunity. You made the point about colour of the mesh; somebody did also say that, but maybe what we should have is mesh that is coloured and it's going to make it that much easier.

Karen Ward: That was in the 2013 guidance actually.

[Over speaking]

Valerie Brasse: That's a very simple obvious thing to have done.

Simon Fulford: The original Gynecare TVT has always remained - well, no, it didn't...

Karen Ward: No, it was clear, [unclear] was clear.

Simon Fulford: ... - it went pale for a while, but it went back to being blue, which is one of the many reasons for only using that one.

Simon Whale: Can I touch on another issue that we've been asking about which is the role of scans with MRI and translabial. Lots of women have told us about the importance they attach to translabial scans but at the same time, the difficulty they have in accessing translabial scans on the NHS, and the cost increasing it seems, the cost of doing it privately, and perhaps the unfairness if they've had an NHS insertion and they end up having to have a private scan to find out where this mesh is. It would be interesting to know your views on relative merits of translabial scans versus other scans versus no scans because we understand there are surgeons internationally who don't use scans at all.

Simon Fulford: We routinely would use an MRI scan as a standard looking at a complicated mesh. Our expert radiologist would do a sort of hybrid transvaginal translabial trying to find it sort of ultrasound scan but she herself is not terribly confident that she's - that's terribly useful. So, our experience is mixed.

Karen Ward: I mean I think this is one of the - another problem that we don't have good evidence for any of these investigations and what's useful and what's not. With MR we use that for abdominally placed mesh and where we might be suspecting infections. So, if someone's got abscesses in their groin or something, you can see it on MR scan. An abdominally placed mesh, we do translabial scans. We have two consultants who do them in our mesh clinics and I think they could be useful if someone's had some mesh removed or they've had more than one tape put in which is not uncommon. We can see where they're going and sometimes you can see them going diagonally. If they're in the urethra, you can see that reasonably clearly.

But I'm not sure of the value of it over a thorough vaginal examination. When I examine the patient, I don't look at the scan result, I examine them and then will compare the two and see - and actually a clinical

examination, if you can feel the mesh, you can usually tell where it's going and where it is if you're experienced. So, I'm not sure - and obviously you need to do - have done examination to see how tender they are. So, I don't think we've completely established the use of transperineal scans. I think they are useful but I'm not sure that we've got any standardisation. Certainly, if we're operating on someone I would rather my - one of my colleagues had scanned them than have a scan from someone in the private sector that I don't know the sonographer. I think there is an issue with standardisation of the technique of scanning and that kind of thing. I'm not a sonographer so I trust my colleagues but there are issues about the quality of some scans.

Simon Whale: But should it be a requirement of future mesh removal sectors, you know the newly commissioned ones that are brought out later in the year, that they all carry out or are capable of carrying out translabial scans. Should that be a requirement?

Simon Fulford: Having a dedicated nominated expert radiologist who could do the appropriate imaging which might include a translabial scan, is the way I'd put it rather than putting translabial scan as the answer because my translabial scan is different from someone else's and it's not standardised. That's a big problem...

Karen Ward: And it's part of the whole assessment rather than the most important. So actually, a cystourethroscopy might be far more important for some patients than a translabial scan because you can't see it once it leaves the vagina. You can't see it in the groin for example. So, and retropubically, you're only really seeing it in the vagina. So, I think it's part of a package of what we should have available. I think more importantly is that we actually conduct some research into the usefulness of it.

Julia Cumberlege: Can you - with scanning, can you pick up where the mesh has actually splintered and gone away from the original one? One of the things women have been saying to us is that they feel that the mesh actually, not as a whole, but as pieces, breaks up and then it gravitates into other parts of the body. Have you ever come across that?

Karen Ward: No. So, I've seen it where it's directly attached to the rest of the mesh, can go into the bladder, can go into the urethra, into the [unclear] ...

Julia Cumberlege: But it's still attached?

Karen Ward: But yes, and the ones we've seen that have been detached - are people who have had surgery and you may have a piece of mesh left. But I haven't seen that myself.

Simon Fulford: No.

Julia Cumberlege: But splintering is nothing that you've come across.

Simon Fulford: No.

Karen Ward: No.

Julia Cumberlege: We've heard a bit about that. You're never quite sure with communications what people are saying. Can I just ask you about the medical device industry, because one of the things that we've been listening to women and when we've asked them when they had it inserted, it seems that over the years urologists have told us that actually the product has improved, the mesh has improved, whereas in the early days, it was far less useful in the way that it's been now because it was different products. I was just wondering with your colleagues, your fellow surgeons, do they - have they noticed the difference in the quality of the mesh that's been used, say five, 10 years ago compared to today?

Karen Ward: I mean I think there's a big difference from meshes used in the 1980s and before TVT came along.

Simon Fulford: Yeah.

Karen Ward: I'm - and I think for prolapse, I think we've moved to a lighter weight mesh so that there's not as much mesh in patients. So, they're lighter weight and they're softer. But for continence, I don't think we know which mesh is - has got the right properties. I don't think we know enough about the properties. A lot of the devices have a different weave of mesh and none of that has really been evaluated comparing it to another mesh. So, if you say that the first one was TVT and that would be the standard, we don't know how the modifications have affected the properties of the mesh in the patients.

So, I don't - I'm not seeing anything that I think this is better than a TVT. So, I would have been doing a TVT and never changed from doing a TVT because I knew that's where the evidence was and that's where the majority of the evidence for retropubic tapes was originally with TVT, over long term. So, I haven't changed, and I would need a lot of persuading to know that something was better. There are - all manufacturers will have - they have to because otherwise they wouldn't get a patent, but there will be a difference in their device. But I don't know that one mesh is better than the other because we haven't got any evidence for that at all for incontinence meshes.

Julia Cumberlege: I'm just thinking also about the manufacturers. Do any of your surgeons or colleagues actually have any sort of connection with the manufacturers? I mean we don't have actually a database, do we? You don't know the interests different clinicians have with different organisations even in terms of charity work or whatever. There's no register of their interests and I'm just wondering if that's something that you think would instil further confidence in patients if they actually could see that?

Karen Ward: I think so.

Simon Fulford: I think it would. Could I just make a comment about the mesh? The only work that's really been done on the pore size, the knotting or welding, the size of the fibre, was done by Alfie Onsden before he introduced the TVT to clinical practice. He worked it all out. He looked at different pore sizes, he looked at different mesh diameters, knots and so on in animal experimentation and he chose the material that we use in a TVT because that was the best option in terms of producing fibrosis and not inflammation. He gets onto the market. He does - becomes the market leader.

All the other industry areas look at this and go I want a piece of that, but it's got to be different. So, they produced me-too devices, using different meshes. It's how the TOT arose. It's a complete failure of my profession and the industry to do things in a safe way and I'm ashamed of it. I have never put anything in, other than an original Gynecare TVT. For years, reps would come and see me and say Mr Fulford, you put in lots of tapes, don't you? Yes. Please put ours in. No. Why not? I would like to see five-year, 10 year randomised control data against colposuspension or TVT. They went away.

Valerie Brasse: That's an interesting point because one of the things I was going to ask is what control surgeons have over the supplies that are being used within their Trust. So there is obviously the NHS Central Procurement supply system over there. But I mean, as you say, a rep comes and sees you and you might be persuaded that this is the next best thing. Do you go then to say I'd like to see that on our system, and I want that be used and that's how I'm going to proceed from now on. I mean I don't know if you have the power to do that.

Karen Ward: You could.

Simon Fulford: You could.

Karen Ward: Or you could do what we both have done and said no, we're not doing that because that's not where - that's not where the evidence is. I think that has

happened in other hospitals where there's a significant price difference and they look substantially equivalent and they feel the same and...

Valerie Brasse: But that sort of comes back to the question we were just asking about registry of interest and being...

Simon Fulford: Absolutely.

Valerie Brasse: ... very clear who is providing it or supported a surgeon for example, the training or competence or whatever, yes that's the particular mesh that's being used in their hospital.

Karen Ward: That's a real change in - a surgery, you have the Burch colposuspension, the Aldridge sling and now we've got manufacturers who are running the training and all the operations are named after the - by the manufacturer now and - so that has happened that the manufacturer will come up with a new device and arrange for training for those surgeons.

Valerie Brasse: But for the women, should it be...

Simon Fulford: And the [unclear] ...

Valerie Brasse: ... at random, should it, it shouldn't be well in one hospital, we'll stay with what we know, it's tried and tested but you know [unclear].

Karen Ward: But equally you want to know your surgeon has been trained in it because there was nothing really to stop you taking a box off the shelf and...

Simon Whale: Having a go.

Valerie Brasse: Having a go.

Karen Ward: ... doing it, which sounds horrific but there technically isn't anything to stop you doing that or wasn't anything to stop you doing that.

Sonia Macleod: In terms of different manufactural products, do we have any way of knowing if one product is superior to another or if you've got higher complication rates, things like that?

Karen Ward: I mean there have been - the ones with the higher complication rates have been withdrawn. So, you saw different - at the time of the TVT introduction, there was another tape called an IVS which did have a higher erosion rate or exposure into the vagina and has been withdrawn. So yes, there are differences. But unless there's a head to head comparison - and a lot of the evidence is one group of devices versus another. So, obturators versus retropubics rather than one specific device versus another.

I think that's particularly the case for the mini slings. The ones with the single incision slings with the little hooks or devices to anchor them, is that they are all completely different. If you look at them all they're all different. So, they're very difficult to aggregate the data together and you shouldn't really - to know whether - what the complications are and whether they work.

Simon Fulford: The usual argument was well it's the same as a TVT but it's different and, you know, have five free and see what you think, was the sort of line that you'd get. Try it out.

Valerie Brasse: Can I ask? If there was to be a safety alert call for any of the products, any of the mesh products that you've been using, if there had to be a recall, could you actually do that for the women that have been treated in your hospital?

Simon Fulford: Yes.

Valerie Brasse: So, you would have the means and the [unclear] ...

Simon Fulford: But by device or by operation?

Valerie Brasse: By device so there's something about a recall, National Health...

Simon Fulford: Yeah, I'll have five years' worth of patients' data and the operation...

Valerie Brasse: And you could find the [unclear].

Simon Fulford: We would have to go several steps back to get to what was actually put in, but it would be very simple if my name was on the operation list, it would be a TVT.

Karen Ward: So those of us who have stuck to the same device, it's relatively easy because you just get everyone who's had that procedure.

Simon Whale: If [unclear] have varied the device, the particular brand that they used, then unless they recorded that at the time.

Simon Fulford: Yeah, well, it will be recorded in the operation.

Sonia Macleod: But would you have to go back to the original notes or not though [unclear], are they?

Simon Fulford: Probably.

Sonia Macleod: Paper [unclear].

Karen Ward: Well, going back to - not that I've worked in my Trust for that long, but you would be going back to the early 2000s so they're unlikely to be electronic records for all those.

Sonia Macleod: So, did you [unclear]?

Karen Ward: It would be difficult. It would be difficult but possible.

Simon Fulford: It would be a chore.

Julia Cumberlege: Do you think if we had a comprehensive database that that would actually improve surgical procedures et cetera?

Karen Ward: Yes.

Simon Fulford: Definitely.

Julia Cumberlege: Yes. It's a question of getting it.

Karen Ward: It would have been good if we had it in first place.

Simon Whale: To make it comprehensive, you - do you also need to make it mandatory?

Karen Ward: Yes

Simon Fulford: Yeah.

Simon Whale: So how do you make it mandatory? What mechanism do you use?

Simon Fulford: Same mechanism that the orthopaedic surgeons have used, which is peer pressure. There's not an orthopaedic surgeon in this country that would put a hip replacement in now without putting it on the National Joint Registry. It's not mandatory but they just wouldn't do it because they have such peer pressure and result focus.

Simon Whale: But is - I don't know enough about hip replacement issues but is - does that arise from the problems that have been associated with hip replacements, as opposed to clinical ethical decision?

Simon Fulford: Well, they had a similar spraying about of different prostheses and interestingly when you look back everyone's comparing them back to the original and not actually getting better than the original but inventing new complications, as I understand it, not being an orthopaedic surgeon. But I did get involved in the metal on metal scandal because that - part of that, involved the bladder. So, I think the Joint Registry pre-dated the metal on metal thing but that really ramped up the peer pressure and has become essentially mandatory.

Valerie Brasse: But given that the concerns around mesh go back now quite a way, why didn't it happen with mesh, the peer pressure? People were clearly concerned, and we've seen - all of the documentary evidence going back to professional societies. Why didn't that happen, those databases that have been talked about since 2003, it never got off the ground?

Karen Ward: I think there were issues of funding. So, people wanted a registry and originally, I think the idea was that Gynecare would create a registry which I think would have been unacceptable now perhaps to patients. But I think it is - I think answering your question about how you mandate it, I think it's really difficult to do that because it's - it takes a lot of time and we've been using the [unclear] database in the Trust I'm in now.

I've been using it since I was a consultant but in this Trust, we miss people - and we're real enthusiasts and we use - you sit down after the procedure and we put the patient in, but you get distracted and we audit to see whether we've missed anyone and we put them in. But it is possible to do that and so there has to be some assistance to the process and we need admin support, and actually I think, I don't know but, the patients may actually prefer that we weren't putting our own data in.

So, I think we put it in at the point of doing the operation and we write - we enter the database but actually the outcome data, I'm not sure that patients would be happy that we're entering our outcome data. So, it does need an [unclear] infrastructure and resource to do that within the hospital. I think there are people who are enthusiasts for collecting the data and using the database and there are others who may be - obviously not in this room but they didn't see it as a priority, and they were perhaps not doing very many and they didn't put them in.

I think now that the spotlight is on it, I think it will be easier to make that case as the orthopaedic surgeons have. But equally it may be related to funding that you don't get paid for doing the procedure if you haven't entered it onto the database which I think will be the better way to do it.

Simon Whale: It will provide that assurance to the public.

Simon Fulford: You don't get...

Julia Cumberlege: Well, we've been thinking quite a lot about this and what's been put to us is that you can have a database that actually just has very simply statistics about what's happened, the surgeon, where it's taken place, the - what product was used and so on. It would be anonymised, so you'd actually put in the patient number, the NHS number. So, from that point of view, the patients I think would not be concerned - too concerned but we don't

know, we'd have to ask them. Then we're saying from that you could then lead on to a registry, which would be quite different which is where you do have to have the patient's name and consent. It's essential to have the consent. Then you can follow up the patient as you wish year on year or whatever. Are you still suffering pain, are you, you know, you'd take the views of the patient.

It's been put to us that you could have actually two very different sets of information and one is simply about the data that's been done. I think possibly with new technology, if you've got barcodes and things you can use, you could do it without having to put so much weight on the surgeon's time and all the rest and I do take that [unclear].

So, we're sort of thinking about and seeking views about whether you think that is something that you might support.

Simon Fulford: Absolutely, it's well overdue. The way that the hip replacement and the joint replacement one was funded of course is with a levy on each joint that's sold. So, it's actually funded by industry which is the appropriate place for the funding to come from, in my opinion.

Karen Ward: We've had nowhere really and until recently the database has gone through various modifications, but we've had nowhere really to report complications. So, you report to the MHRA but it's kind of a black hole. It disappears in there and you don't really know - no one makes you do that so that would be useful that it's - that we have somewhere to collect all of that stuff. So we tend to report surgical when we've removed a mesh but I suspect we're less good at reporting the non - the patients who don't end up with surgery and so that - the registry would capture those kind of outcomes that patients could report where they haven't required further surgery but they have had an adverse outcome that could go on registry.

Simon Whale: This would require follow-ups, some considerable time after the original procedure to understand complication rates, long term as well as shorter term.

Karen Ward: You either give - well, there is a few ways of doing it. You can give patients some kind of easy access back in if they think they have a problem and we do quite a lot of telephone reviews. So, I have some patients who are - have anxiety about the mesh or might not have wanted to have it removed and if they have anxiety I offer them a telephone review. I'll say look I'll speak to you in a few months' time, see how you feel. I think that's quite a good way of doing it. It does take time.

Or if it's the whole registry for the country, you could - and you wanted to find the outcomes, then - so we're not talking about my individual patients and how I'm looking after them, but you wanted to know the outcomes, you could take a sample of patients saying we're going to look at these women after five years and we're going to do a sample of the whole database and contact them to get their results. Or you give them a way that they can get their own results into the database and we use an electronic questionnaire that patients can fill in before they come to clinic and we have their information. Now it may be possible to do that to feed into the database.

Sonia Macleod: So, have some kind of a [prong or a prang] that goes in [unclear], not an electronic.

Julia Cumberlege: I think I'm going to have to draw this to a close and I'm sorry that we've been a bit short of time but that's how the world works sometimes. So, I'm just going to ask my colleagues if they've got any final questions, they'd like to put to you, Simon, Sonia. Anything you'd like to ask us?

Karen Ward: No.

Simon Fulford: Don't think so.

Julia Cumberlege: Well, thank you so much for coming. We're really really grateful and thank you for all of the work that you do. It's really, really appreciated, and I think in the NHS perhaps you don't get enough thanks.

END OF TRANSCRIPT

Session 3: Epilepsy Society and Epilepsy Action

START OF TRANSCRIPT

Julia Cumberlege: If I could just say a word about the Review, I'm not sure how much you know but we've been right round the country, talking to a lot of people who have suffered from sodium valproate, Primodos, the two medications that have resulted in - or we believe there might be an association with children who've been disabled. Then with surgical mesh, which is inserted for stress urinary incontinence. So today we're really drawing on the work that you've done and certainly concerned with epilepsy and the problems that that brings.

If I could just introduce my colleagues, on my far right is Valerie Brasse and she's the Secretary to the Review. Next to her is Simon Whale, who is a panel member of the Review, as I am. I'm Julia Cumberlege and I'm chairing the Review. My Vice-Chairman sends his apologies, Sir Cyril Chantler, he's not here today because he's off doing something else for us today. Then on my left is Sonia Macleod, who's our principal researcher. So that's us.

From the point of view of the screening - and I hope this is all right for you, but we were very anxious with the Review that we should be open and honest, transparent, so people really would appreciate that we are saying everything that we're doing so nothing is hidden, there's no secrecy or anything like that which has caused problems in the past. So we are screening it and I hope that's all right. Then in the room also we've got people here who are helping us just run the session.

So I don't know if, first of all, you'd like to say anything about your organisations, Epilepsy Action and Epilepsy Society, that you think that we really ought to know about which you haven't included in the material that you've already sent us, which has been very helpful. But is there anything in particular you'd like to...

Simon Wigglesworth: So if I may, I'll go first. May I also apologise, I've had the worst sore throat for the last few days, so if my throat goes halfway through I do apologise, but I'll try and carry on but if I can't...

Julia Cumberlege: Sorry, I didn't catch that.

Simon Wigglesworth: I've had a really bad sore throat for the last few days...

Julia Cumberlege: Oh, I'm so sorry.

Simon Wigglesworth: ...so my voice isn't quite where it should be. So just shout at me if you can't hear me and I'll try again. Obviously thank you for the opportunity to come and present evidence to the inquiry. We're really grateful for the opportunity and we think it's a really important opportunity. I would say it's well recognised that sodium valproate can harm the unborn child. I think there's 30-40 years of evidence and particularly in the last 10-20 years, I don't think there's any real doubt that that does happen. We would suggest the warnings have been around since actually the introduction of sodium valproate in the early 1970s, 1973, 1974.

They've been strengthened over the years as more knowledge has become available, including I would say probably critically in the early 2000s when the NICE clinical guideline was introduced. As an example, that had as one recommendation that clinicians should discuss with women and girls of childbearing potential and their parents or carers the risk of AEDs causing malformations and possible neurodevelopmental impairments.

Now, NICE's internationally recognised that piece of guidance that they've included is really very strong and should have made a lot of clinicians sit up. The guidance was further strengthened in 2011, when NICE introduced the quality and outcomes framework indicator for preconception counselling. We felt that was a very important marker to try and help improve preconception counselling and so it was doubly disappointing (a) that it took so long to introduce, but even more disappointing that it was retired from the framework in 2014 without any consultation or discussion.

Epilepsy Action has been active over the years in trying to raise awareness of the issues around valproate and have included with our submitted evidence a timeline of some of the activity. But since at least 1987 we have referenced the risks of fetal abnormalities in our patient information and the need for preconception counselling to enable women to make informed choices about their care and treatment. We've run a series of awareness programmes over several years aimed at reducing the risks to mother and baby during pregnancy.

For example, in 2002 we carried out our first Ideal World survey which was specifically focused on women and the challenges that they face. It highlighted that women were not receiving information about the impacts of their treatment. In 2003 we published the first version of our GP epilepsy resource pack that was distributed on request to over 10,000 GP surgeries, which among other things highlighted the issues around teratogenicity. Other public awareness campaigns in 2007/8, 2011, 2013, I could go on.

I think throughout this time what we're trying to suggest is clinicians really should have been aware of the potential impact of sodium valproate on the unborn child. As a minimum they should have been counselling women about the potential risks so that they could take informed choices. It's clear that that has not happened. It has happened in parts, we would agree with that, but it's clearly not happened to the extent that it should, otherwise so many children wouldn't have been born with fetal anticonvulsant syndrome.

We think there is a question to be asked as to why it took the MHRA until 2014 to look at this and to start to take regulatory action. We accept we as an organisation didn't actually ask them to, and perhaps we might have, but actually we think that is their role, to proactively identify these issues in medication and take action. Even having started to take action in 2016 with the valproate toolkit, evidence that both ourselves, Epilepsy Society and Young Epilepsy found from a survey of 2000 women in 2017, almost one in five women at the time did not know of the harm. This was a year after the introduction of the latest toolkit.

More than a quarter of women taking valproate had not been given information about the risks to the unborn child. More than two-thirds of women have not received the MHRA's packs that were developed for women with epilepsy taking valproate at that time. Again, we also have to ask why clinicians were not paying heed to the wealth of evidence and guidance available and undertaking proper preconception counselling. We recognise clinicians are busy, they have many competing demands on their time, but we believe this is, this was important that they should have done better.

If I may just briefly look forwards, Epilepsy Action welcomes the current strength of warnings around sodium valproate and the pregnancy prevention programme. We have been working with the MHRA, clinicians and others as part of the MHRA valproate stakeholders group, and we're particularly pleased that in the last few weeks they've revised the annual risk acknowledgment form, that it's now a better form for use in our judgement.

We also welcome the guidance that's been issued, and I don't know whether you've seen this, it's only come out in the last two weeks, from the Royal Colleges, a guidance document on valproate use in women and girls of childbearing years, which again we think is an excellent support tool for clinicians involved with counselling women about sodium valproate. We have to remember valproate is an excellent drug for epilepsy and can save

lives, and I think that's one of the issues that is very difficult to balance in this issue and I think new guidance does help do that somewhat.

What we do want to know though is whether these measures are actually being implemented, and whether women are receiving the relevant information, are they having the call for annual reviews, are they getting the support they need to make the right decisions. In the light of that, ourselves with Young Epilepsy and Epilepsy Society will be redoing the survey we did in 2017 over the next few months to look at take-up of the new pregnancy prevention programme, to find out whether it is being implemented and indeed how women are finding the implementation of it as well, actually is it working for them.

If the PPP and the associated toolkit is used effectively, I think our view is we would expect to see a significant reduction in the number of children born with fetal anticonvulsant syndrome. It has the merits that it should work, is our initial view, but we do want to see that. I do want to add a however here, and that is that sodium valproate isn't the only teratogen as far as women with epilepsy are concerned. There is increasing evidence that other anti-epileptic drugs including carbamazepine, ethosuximide, fosphenytoin, phenobarbital, primidone and topiramate are all teratogenic.

A recent study using the North American AED pregnancy registry provided estimates of the risks of major malformations among infants exposed to specific AEDs as monotherapy during first trimester of pregnancy. They reported a risk of malformation of 9.3 per cent for valproate, which we know about, but 5.5 per cent for phenobarbital, 4.2 per cent for topiramate, three per cent for carbamazepine, two per cent for phenytoin. Despite this increasing evidence, we've seen no willingness on behalf of the MHRA or others to consider what needs to be done to reduce potential harm to the unborn children of women taking those drugs.

As a lesson learnt from this important review, we would hope that that is highlighted, that it's not just looking back; it is also looking forwards about what needs to be done. One lesson surely that we can learn from the damage caused by valproate and indeed still being caused, is that action needs to be taken and taken now. We can't wait for 40 years before those drugs are critically reviewed and appropriate measures taken.

Drawing to a close, you'll be pleased to know, we also believe that the quality and outcomes framework, if it is to continue, should reintroduce an indicator for preconception counselling. We're aware that there has been a quality improvement activity indicator included in the quality and outcomes framework which is particularly looking at valproate reviews

within GP practices and we welcome that. But preconception counselling for people with epilepsy (a) needs to cover those other drugs that we talked about, but it's also wider than the particular drugs.

There are drug contraceptive interactions that women need to be aware of. There is the impact of pregnancy on seizure rates and the safety and there is also the important factor that maternal deaths in women with epilepsy is 10 times the rate of the general population. Again, another reason why preconception counselling is also important, it's not just valproate from our perspective. We're aware that there is talk of an NHS audit or registry of women with epilepsy and again at the moment we believe it's just looking at valproate.

I'm going to make the point again that we do believe you can't just look at valproate in isolation; we've got to think of those other drugs and the potential impact. So we would hope that that would be widened to all women of childbearing age, or with another hat on, all people with epilepsy quite simply because there are many other issues that we aren't covering in this inquiry that a register would help with.

Finally, just two points. The first is that we obviously all need to pay tribute to the campaigning of the groups who've actually brought this inquiry into being. Their work has been tireless, they have very profound issues that they have to cope with as well as raising awareness and we would pay tribute to them. Finally, Epilepsy Action would also support the call for some sort of support mechanism, including financial support, for those affected by fetal anticonvulsant syndrome. We think this should be above and beyond the standard disability support that ministers seem to trot out every time the question is answered.

We would suggest that it could be linked to the oft-debated idea of NHS no-fault compensation. Potentially avoidable damage to children with epilepsy from sodium valproate is a wide issue. I don't envy your task, it will be a challenge to isolate one or even two factors. I would suggest that this is a prime opportunity for no-fault compensation to be introduced, whereby the children affected by sodium valproate can receive some additional financial support to help them live their lives as well as they can. Thank you very much for your time.

Julia Cumberlege: Thank you very much. Perhaps I ought to make it clear, just on the screening that's going on, that you are Simon Wigglesworth and you're the deputy chief executive officer of Epilepsy Action.

Simon Wigglesworth: I am, sorry, I should have introduced myself.

Julia Cumberlege: Now, moving on to the Epilepsy Society and it's Clare Pelham who's the chief executive officer.

Clare Pelham: Thank you. I was really pleased when I read your guidance notes that what you really wanted to have was a conversation, because I've participated in a fair number of these sorts of events, both sides of the table actually because my background is as a senior civil servant. I think when we're trying to learn and improve, that's the single most important thing we can do, is share our learning and see what we can come up with together. You asked a little bit about the charity, and I'm sure your secretariat have provided you with everything that's on the website. So the only thing that I would want to pull out here and now is our values. The acronym is CAIRO, caring, accountable, improving, respectful and open.

We're here to learn, including on behalf of the charity, because I think the charity has a lot to learn from the way we've behaved over the last 40 years, and we are learning that and we're trying to improve. So we are here not in a spirit of criticism, but in a spirit of shared learning, that's what we're trying to do as a result of this long running episode. I think the only other thing that I ought to say is that - because it may be helpful - my personal perspective is informed by my past as a senior civil servant, but also I think this is relevant because I have been both a sponsor of arm's-length bodies and a chief executive of an arm's-length body.

So I've got some experience of what feels normal in that relationship and that may be relevant as the conversation progresses. So I think what I want to say by way of an opening statement is to highlight two issues that I think are helpful in the diagnosis of what went wrong and why. They are not in order of importance, but the two that we've identified are a failure of listening and a failure of regulation.

Julia Cumberlege: Sorry, a failure of listening and a failure of...

Clare Pelham: A failure of regulation. So just to amplify that a little, I think Jeremy Hunt talked about it, I think you've seen our blogs, our tweets, all the stuff that's in the public domain about listening. Obviously listening is a great skill and it's hard, it's hard for all of us to practise. The particular aspect of listening that bothers me about this is listening to women. The question that I've asked myself repeatedly is would we be here today if sodium valproate was an issue that affected men and I don't think we would be, I really don't.

That's partly informed by my personal experience as a newcomer to the world of medicine and experiencing for myself some of the values and behaviours that I see practised. But it's partly going back and listening to

the people who've participated in various conversations. It's harsh but not, I think, unfair to say that if not today, over the last part of 40 years, that we have been living through, the victims have been living through a patriarchal system, where the phrase that's used is 'white coat syndrome'.

'White coat syndrome' was as pervasive as an epidemic and I'm not sure whether the primary people affected were women, or because they were disabled women, or because they were disabled mothers, or because their disabilities were hidden, but there is something there, I think, that is bothering. I think it continues to bother me actually because - and this may be a point that you want to explore - because I'm not entirely convinced that that problem has been dealt with. I say that advisedly and perhaps I should come on now to talk about regulation. I'm only making these points briefly and perhaps we can explore them later.

As I said, I've been chief executive of an arm's-length body for five years or so. During that period I gave evidence in public dozens of times. I met with ministers, I completed audits, I helped draft answers to PQs, I did KPIs, I was scrutinised to within an inch of my life. There really wasn't a week where we weren't held accountable for something or other. That doesn't seem to me to be the environment at the MHRA. I've tried really hard to look and see what's on the records there in terms of things like appraisals, debates, select committee evidence, published KPIs, public hearings, all of the routine that I would regard as absolutely normal, and I can't find them.

There's something in 2004, you may find a health select committee session, you may have found others, but it bothers me and it bothers me quite a lot because, to coin a phrase, sunlight is the enemy, isn't it, of this shady secrecy that's been practised around this regulatory regime that we've got. You opened this session by saying isn't it good to be open, so that people can see what's happening and I would say yes. I was asked by the MHRA to be a member of their expert working group on sodium valproate. I thought fantastic, isn't that great, we're going to be part of the solution.

The very first thing that happened was I was asked to sign a confidentiality document, so I probably can't tell you too much about what happened in that room. I have been a senior civil servant for more years than I can remember, I am really used to keeping things confidential that need to be kept confidential and believe me, there was nothing in that room that couldn't have been done out in the open. The only thing that happened in that room that couldn't have been done in the open, perhaps to the embarrassment of the MHRA, was that we moved seamlessly from not listening to women saying there was a problem, to not listening to women saying how it could be improved.

I'm speaking personally here because I am respectful of the agreement that I signed, but I have in all my years of public service never participated in a body where the opinion of experts was so roundly ignored by public officials, honestly astonishing, astonishing. I think there's a real question here about why does it need to be in secret when the whole dynamic is that there's been too much secrecy and what's happening to the listening. I think I would just stop there.

Julia Cumberlege: Well thank you, both of you, that's really, really helpful. Can I just ask you, first of all Clare, if I may call you that...

Clare Pelham: Of course.

Julia Cumberlege: ...the failure of listening, can you just explain a bit more about that? Because one of the things that we are very conscious of is that this Review was set up by parliamentarians. It was set up by the Secretary of State, and the issue was that some of these conditions that we were asked to examine have been going on for many years, yet nobody has really listened to what's been happening.

So we've been working with the patient groups and I have to say they are very, very impressive, and I count you as patient groups. The science that they have actually unearthed, the secrecy they've unearthed, as you have also mentioned. I'm just wondering for the future, when our Review has been concluded and we have reported, how can we actually ensure that patients have a voice and that they are really heard? How can we do that? What are the mechanisms? What are the things that we have to instil, that we have to ensure happens in the future?

Clare Pelham: I started, as I often start, to be honest, with our values, because I think it helps just to keep us honest and on the right track. I think there is something about values, and I don't know if this is a matter for medical education or if this is a matter for values-based recruitment bodies such as the MHRA. I think there's something around humility, and I think it's not the same at all levels. So I don't want to talk in black and white because, of course, we're all individuals and we all have done different things at different times in different ways.

But I think there is a tendency, or at least has been a tendency at the senior levels of the medical profession, and perhaps more embedded in those who are now occupying positions of authority, that the doctor knows best, that these are by definition, because they are potential mothers, largely younger women and that perhaps they are women with disabilities and

perhaps that, wrongly, completely wrongly in my view, prompts a certain paternalistic approach and a failure to listen, which is just really depressing.

I think if I were recruiting folk to the MHRA I would have a values-based recruitment system, where I would be very interested, not just in recruiting bright and able young people - young people, older people, I don't want to be ageist about it, people who are able - but people who have a certain humility, what you might call a true academic. People who are willing to learn wherever learning is found, and it is so often found in the patient. One of my - in fact it's the research director at the Epilepsy Society - said to me I always listen to patients because patients are never wrong. I think that's just a wonderful mindset, because if that's where you start, how can you go wrong? I think there has been a lack of humility.

Julia Cumberlege: Do you want to comment?

Simon Wigglesworth: Thank you. Just to add, part of my modus operandi is pragmatics and first of all, I'm not on the stakeholder group, so whilst I have staff that are on it, I don't know the detail of what goes on and I think Clare's right. I've had other interactions with MHRA around anti-epileptic drugs where we made some suggestions and submissions about some guidance they would introduce, and it took a year and a half for anything to come out the other end. In the meantime, we were in the total dark about what was being discussed and considered.

So certainly I would agree that some mechanism of openness, perhaps of their meetings, certainly publishing minutes and documents, papers beforehand, obviously we do need to recognise that some of the work they're doing may be commercially confidential in terms of licensing drugs and that sort of thing. But I can't think of much around valproate, given that the main manufacturer was also involved in those meetings, or the other issues that I was doing that impacted on confidentiality. So certainly I think greater openness is there.

I'm, or we're, also perhaps not as - I'm not saying the MHRA hasn't done things wrong, but I do think you have to go back to doctors as well. It may be this paternalistic attitude, although there are lots of women doctors and maybe they have the same attitudes as well. But in truth, I suspect they don't have time, they didn't know, they didn't think it was important and the question is why do they not think when the word, something like this is teratogenic, should be flashing big headlines in front of them saying hold on a minute, I can do some real damage if I prescribe this. I just wonder maybe they meet now with more technology.

We've heard of alerts in fatigue syndrome and all those sorts of things, but there need to be mechanisms when dangerous drugs - this is what they are, they're dangerous drugs as far as the unborn child is being prescribed. There needs to be a mechanism that makes sure - now we've now got that mechanism for valproate, as I said in my earlier piece, we don't have the same mechanism for all those other teratogens. There will be other drugs elsewhere with other equally devastating impacts and there'll be warnings on PILs and SPCs and so on and so forth, but what mechanism can be introduced to get the doctor to think about that at the time of prescribing, because I think that's incredibly important.

Clare Pelham:

Could I just - a supplement, if that's with your permission. Firstly, I'd just like to say I was referring to the expert working group, not the stakeholder group. But absolutely without any question of a doubt, there was nothing that was commercially confidential in those discussions, nothing. The body I was talking about where we had practised openness did deal with very difficult and sensitive personnel discussions. So I'm absolutely certain that it's possible to have an open arm's-length body within the constraints which MHRA operate in. But I'm trying to respond to your question more precisely about what can be done differently in future.

So you mentioned that the impetus for this review came from parliament, so let's credit where credit is due, that's great. So that shows that something worked, that our democracy functioned, that people were hurt, it took a long time and we have to pay tribute over and over again to the wonderful campaigners who've made this possible, all credit to them, but democracy worked. I think in my dealings with MHRA, I don't want to overstate the point, the link between ministers and the arm's-length body was so remote and ethereal as to be almost invisible.

I've worked in a ministerial private office, we all know how that works, ministers are responsible for their arm's-length bodies. That's not how it feels when you talk to staff at the MHRA. They don't feel that connection, that degree of answerability, so I would posit that the democratic link is broken. So not to give specifics because I've signed this piece of paper, but I did at one point read out something that was said in parliament by the Secretary of State and that was regarded as fairly advisory, a suggestion, not something to be delivered.

So, coming to your question about what could be done differently, I think staff need to ventilate there. I think they need to move in and out more frequently. I think five years is plenty in an arm's-length body actually. It needs to become somewhere that people go, build their career and at least some of them get promoted out of quite quickly so that you break that

slightly fossilised, slightly dusty culture of deference to the senior people there.

So there's no - I don't sense there's a very rigorous intellectual challenge going on. In any Whitehall department you'll have fierce arguments, I didn't feel that. Now that might be because we were outsiders and it was well hidden, but I think it's a good discipline to keep refreshing the cast, that's how you bring in new ideas and new sensitivities and new approaches to problems. The other thing I think I would mention, I was formerly chief exec at Leonard Cheshire and we talked an awful lot there about the social model of disability, so much so that I thought it absolutely ran through the DNA of everybody who dealt with disabled people.

It was quite a surprise to me to find large aspects of the medical profession knew nothing about it. Now that is a real lack of broad education of the subject that they're dealing with. If you're dealing with disabled people every day, to be still thinking in terms of the medical model all of these years afterwards shows a lack of broad understanding of the concept of disability, I would suggest. So when I averted earlier to medical education, I think it has to cover the social model of disability and it needs to be part of refresher training.

Julia Cumberlege: Right, thank you very much indeed, a lot to think about. I'd like to go on now to the NICE guidelines on the management of epilepsies, just to ask you whether you've had any feedback from your members on that. It was about the diagnosis and the management of epilepsy.

Simon Wigglesworth: At the start, can I clarify in terms of feedback whether you think or we think the guidelines are...

Julia Cumberlege: If your members had any view on the recent guidelines that were passed.

Simon Wigglesworth: Certainly we as an organisation, and I suspect I can speak for all the epilepsy organisations, back in 2004 when the NICE epilepsy guidelines first came out we were largely delighted with the content of them. I think the guidelines in terms of what they covered back then was the first time that a fairly comprehensive document covering most of the issues around epilepsy and how it can and should be managed were put together based on evidence largely, some bits based on clinical opinion. I guess naively we thought this is the beginning of transformation of care for people with epilepsy.

I know you've had NICE in here, and the big question around NICE guidance is it's just guidance and clinicians aren't held to account as to whether they deliver it or not. Clearly I quoted from one of the areas where NICE

guidance says you should do an annual review and you should talk about teratogenic effects of AEDs and that's not happening. So, the content of the guidance can be improved and there's another review going on and we're all contributing to that and we can improve it, but the guidance as it stands certainly we think it's fabulous and we had high hopes.

The reality is in areas of best practice it's followed, it's making a difference. In the areas where there are less experts working in epilepsy in particular, it's probably I suspect sitting on the shelf, referred to occasionally but not really understood what it contains. Or the evidence on the ground in terms of how they then look after their patients with epilepsy would suggest that it's not being followed particularly closely.

Clare Pelham: I think the only thing I would say is that we've had feedback and I have no way of understanding whether this is fair or reasonable, but from several medics, that the only things that they pay attention to are things which fill the screen with red and are marked urgent and mandatory. Things which are called guidance just slip to the bottom of the heap. I have no way of knowing if that's fair or reasonable.

The other end of the spectrum is we also know not one, not two, but certainly tens of people with epilepsy who haven't just had a review every year but haven't had a review every decade. This is not an exaggeration, particularly if you live a long way from hospital, or if you have other disabilities which mean that it's difficult for you to travel, or perhaps you live in social care, you may not have a review for 10, 20, 30, 40 years. There are still people who are taking the same medication that they were prescribed as children.

Simon Wigglesworth: Sorry, if I may just have one brief...

Julia Cumberlege: I'm sorry, I just wondered, Valerie, if you'd like to...

Valerie Brasse: Yes, I did and I wonder whether this has been fed back to you, that it was pointed out to me that there is actually an inherent contradiction in the new NICE guidelines and I didn't know whether your members had felt this was the same. So, it's very clear that under the heading women and girls with epilepsy that the guidelines are saying this very thing, must be discussing the risks of taking anti-epileptic drugs, particularly sodium valproate because of the malformations and possible neurodevelopmental delays. That there has to be that assessment and a full discussion between the prescribing doctor and the person.

However, when you go onto the heading pharmacological treatment of juvenile myoclonic epilepsy, it says first-line treatment in children and

young people and adults with JME, offer sodium valproate as first-line treatment and doesn't then go on to spell out all that you should be doing around that. Of course, you've got an MHRA programme that makes it very clear that GPs should not be offering sodium valproate to children and young women of childbearing age. So there's a question in here, have we got an inherent contradiction? Is there a problem about this? If I'm a clinician sitting in a GP surgery, looking at both of these thinking okay, which one trumps...

Simon Wigglesworth: I think I would say two things, if I may, is that certainly with children and girls under the age of 18, they will not have been diagnosed or prescribed by a GP; they will be diagnosed and prescribed in secondary care, under the care of a paediatrician.

Valerie Brasse: Will that neurologist or paediatrician be facing the same dilemma?

Simon Wigglesworth: I think they'll be facing the same dilemma, but I think one of the things which is the extra point I was going to make, things are slightly different in paediatrics at the moment. That's because of something called Epilepsy12, which is a national audit of the care and treatment of young people within epilepsy clinics all over the UK, where they are audited against various standards, including those within the NICE guidelines.

So if you like, they're being measured as to whether they are actually following NICE guidance, because that's the cornerstone of the 12 markers that they use within Epilepsy12. So I think there's an interesting divergence in there and the current review will certainly give us the chance to flag it up. I'm not sure it's a major issue, I think the numbers I've seen that first prescriptions for girls and young women with epilepsy for valproate have been reducing really quite significantly recently. But it is still a damn good drug for things like JME.

Valerie Brasse: That's what you'd expect, but the issue here is it's actually saying offer sodium valproate as first line treatment.

Simon Wigglesworth: Yes and it should, as you suggest, I would agree and will make that point in the meetings with NICE when they're invited, that they should be adding in. The latest guidance from the MHRA's pregnancy prevention programme has been handed in to the NICE guidelines in the last few months, as it were, as almost an addendum. I don't think they've gone through and cross-referenced it line by line, which clearly they need to do. There is a current review going on, so that should make it...

Clare Pelham: Could I offer a slightly different view? Also perhaps if you would permit, talk about the pregnancy prevention programme as a phrase. I observe a

tendency in this area for people who write guidance to fudge questions through slightly obscure drafting. So as you dissect it, as we've been able to in this working group, to say precisely what do you mean by that, the real answer is that the person writing it - and I often have a great deal of sympathy for them, because the person with the pen or the keyboard is often a relatively junior person who's been told two quite different things by quite senior people and has tried to find a way of marrying the two.

So the drafting often reflects an inherent confusion and I think you're right, the confusion is there, you've highlighted it. The observation I would make is that in the discussions we've had about trying to improve communications, there's been a slightly old-fashioned idea prevalent about the way that young women behave, as if there were no sexually active 12 year olds in the country. That if there were, they would be very happy to chat to their doctor about their sexual practices in front of their parents.

There is a certain degree of just otherworldliness in some of this guidance. I think it just needs to be clearer and more specific about all the wide variety of human circumstances that may be present in a doctor's office when they're having this conversation. People with learning disabilities, people from families with multiple challenges and it needs to be very clear and specific and I think it isn't.

While I'm on this theme, if I may, I personally roundly dislike the phrase pregnancy prevention programme. I have done everything I can to ask, persuade, cajole the MHRA into only using it in expert circumstances. We do not have a pregnancy prevention programme, and it is offensive to women, who should make informed choices about these things, to say that we do. Worse than offensive, it is counterproductive, because we know from the dealings we've had with people who have religious beliefs which preclude them from preventing pregnancies, that this deters them from having this conversation with their doctor because they think that the only option is to not have a baby.

They may wish to take an informed choice to have a baby and take sodium valproate. Never has something so straightforward been made so difficult and so obscure by a group of such intelligent people. I honestly despair, I don't know how to be any clearer about it than that, that a nationally recognised body should call a programme something which it isn't. It's just despair making.

Sonia Macleod: What should it be called?

Clare Pelham: Well the terms that have been offered, pregnancy management, pregnancy support, or it could be called a whole variety of other - numerous suggestions have been made.

Valerie Brasse: Does it work?

Clare Pelham: The programme? We are conducting a rerun of our survey in the autumn and I really, really hope so. I really hope so. We know from the last survey that - and I'm not saying that it's the last word in statistical rigour, nobody can say 2000 people is the best statistical practice. But 20 per cent of the people who were currently taking sodium valproate then did not know. I hope it's fewer. I don't think - my guess is it's not going to be many fewer.

We have made numerous suggestions to the MHRA about communications programmes, about looking for further funding from central pots, for getting in central government communications advisers, for making a bid to the Treasury for supplementary funds, for this, that and the other and the answer has been that they have limited funds available. I don't think the amount of communications that have been done, let alone the way that it's been done, will have the effect it's been looking for.

Simon Whale: Can I just ask whether you think the MHRA is the right body to be overseeing this issue, if you want to call it that? Given what you've said, are they the right body? Or does this prompt a question about who should have responsibility, who's better placed to, whether there is anyone who's better placed to?

Clare Pelham: I understand exactly why you ask the question. In theory, clearly not because there is something truly bizarre about the body that regulates being in charge of what is essentially a public education, public health question. There are other people better placed to do that. On the other side of that coin you might say there's also something to be said for the expertise being close to the communications and it doesn't really matter where the lead is, as long as both groups talk to each other, which they don't. But the reason I'm pausing is I really hope that you don't, if I may say so, recommend structural changes. Because structural changes are so often attractive but so rarely resolve the underlying problem.

What we do is shuffle the deckchairs a little bit, we have some new bodies, we have some new people running some new bodies, they take a while to bed in and things go into a bit of a black hole. Then three or four years later they say they've got hold of the issue and they're going to deal with it. So I really hope that we can work with the bodies we've got and not just move the deckchairs around. But they need to work within, if I may call it

this, the health family, drawing upon the expertise that there is within the sponsored and arm's-length bodies that DHSC, as it now is, have within their ambit.

So they ought to be closer and cooperative. I'm not so fussed about where it comes from, as the fact that they liaise properly within the health arena, and much more importantly, they seem to be operating in a vacuum away from the whole of Whitehall. So there are things like the Government Communication Service, there's huge expertise in the public service about how to get messages out there and yet it's not accessed and deployed in what is, after all, a major national scandal.

Simon Wigglesworth: I think if I might add and I don't know who else I might suggest, I think the one advantage of the MHRA that I can think of is they actually have some regulatory clout. Whether they use it effectively or not is perhaps another question. If we were to go to someone like NICE, we'd discuss the problems of their guidance, it being just guidance. They are probably the experts in producing the type of guidance and the issues that Clare's highlighted around religion and people with disabilities and all the rest of it, are real issues.

Actually just to go back, I do think the Royal Colleges have done some quite good work in their latest guidance to address all those issues in a far better way than the original fairly bland directives, for want of a better word, that came in from the MHRA and the valproate toolkit and then the PPP. So I think if there were to be anyone else overseeing it, they need some sort of clout to make it happen and I think that's again the big issue, one of the big problems, NICE guidance isn't compulsory. The other people, I guess, who could issue guidance and make it compulsory are the GMC, because they oversee medical practice. They're about the only two people who can make rules, that I'm aware of, to make these sorts of things happen.

It's clear that it's been talked about, I slightly disagree with Clare's credit maybe to the current political system. I've got a note of a question in 2000 to the Secretary of State asking exactly the same questions as to how many people are being affected by valproate, what are the government doing to reduce the incidences of teratogenic effects and so on and so forth. So they've known about it for years and it has taken an awfully long time, so it does need some sort of clout to make it happen. Maybe the changes to licensing which the MHRA have done are the one thing that will trigger real action now.

Valerie Brasse: Can you come at it a different way and not look at the body that's overseeing the PPP, but ask is the PPP actually delivering? If it isn't, what

then? So I'm not sure, you don't know now what your survey's going to come up with in a couple of months' time or whatever, but let's say it's not showing an improvement, as you fear, suspect. What then?

Clare Pelham: I think, if I may say so, it's an excellent question. The question we often sit around and talk about is if we were the Secretary of State for Health and we wanted to make this work, what would we do? I know exactly what I would do and it wouldn't be what they have done. So I'm not going to call it that set of names, so if you wanted to have a programme that ensured that every woman made an informed choice before she accepted a prescription of sodium valproate, I think it is deliverable, yes. I think we've done many harder things in the medical field and in life generally actually we've implemented many more difficult things.

I think that as a task it's circumscribed by the number of people and we can get our arms around it and make it work. To do that you need to have the right incentives, you need to have the right communications and you need to have the right monitoring and I don't think we've got any aspects of that right. You need to have - it's a classic piece of project management, so one thing you might have done was have a PRINCE2 programme around it, in which you get continuous feedback, so you're continually monitoring and improving as you go along.

That would have been a very straightforward feedback loop to have put in place, but as far as I'm aware it hasn't been done. So yes, I'm certain it is deliverable, I'm not sure the way that it's been tackled in this instance will prove to be effective.

Sonia Macleod: Who delivers it? Who oversees it?

Clare Pelham: Who oversees it now?

Sonia Macleod: No, who should deliver it, who should incentivise - how do you on a practical level...

Clare Pelham: I have a slightly traditional view of these things, which is the democratically responsible person is the Secretary of State. There is a flow of responsibility from there and that's why I started with the importance of arm's-length bodies being held to account via ministers, because that's the democratic link and that's where I think we got into a democratic deficit in this area.

So I don't think I have particularly strong views about naming one person to be responsible as to which person it is, as long as they know they're responsible, they feel responsible, they trot along to the select committee

and start their evidence with yes, I am the person responsible for making this work. They can co-opt and have the mandate to make it work. It's, if you like, a very comparable system to public sector IT projects. If you ask who the single responsible owner is for any IT project in government, there will be a named person. Well this is a project and it ought to have a named person.

Julia Cumberlege: Isn't one of the challenges of the whole programme that children are put onto sodium valproate at quite a young age if they're epileptic and nobody actually makes the break when they become childbearing age? So they continue to have it and they continue to be prescribed and it's dispensed and they take it. So nobody, when they get to perhaps 12, 13 or something, does a break. So who does the break?

Clare Pelham: I think that has to be centrally imposed and I think, if I may say so, it has to come before the young girl is of childbearing age. One of the most bizarre conversations I've had professionally for a long time was we did a bit of a role play about if you're a teenage girl, what time is the right time to have a conversation about becoming pregnant, with some very eminent medical people. I was trying to explain it's before you have sex, not after you have sex.

So exactly on this instance, the doctors need to have the conversation with young girls before they're of childbearing potential so that they're aware that this is among the issues that they need to contend with. So we need to make sure that the alerts are triggered sufficiently early for the girl to absorb the information, for her to think that through, for an opportunity to have a discussion without her parents. There are lots of issues to be worked through and you may not have more than a year or two to do them in.

Simon Wigglesworth: I think I'm going to slightly disagree with Clare, that it might be all well and good for the Secretary of State to be responsible, but the person who has to have that conversation is the doctor. In that instance it's a paediatrician, hopefully with expertise in epilepsy and they have to have the conversation. There has to be a mechanism to ensure that they have that conversation and they have it in sufficient time, so that they have it before they're likely to or be able to get pregnant, or start having sex. So yes, there needs to be a system and it shouldn't be beyond the wit of man now with technology to create the necessary alerts. You can't give this drug out to someone without having gone through that.

There are all sorts of mechanisms within IT nowadays and I know IT and the NHS don't particularly work well together. So where the Secretary of State

can come in is he can make sure the resources are there to enable these sorts of things to happen. But the people who are doing the prescribing, the person who signs, whether with a pen or electronically nowadays, that prescription for sodium valproate in my view is ultimately responsible. They therefore have to take the responsibility for implementing the PPP or whatever you want to call it and for making sure those conversations are happening in sufficient time.

I have someone who is - because this is not just about girls approaching the age when they can have children; it's also about women who've been seizure free for five, 10, 15 years, they're now thinking of wanting to start a family. So they may have been on a very effective form of contraception and they want to change. They need to have conversations, they need to understand the risks, they need to have the time to do that. I go back to ultimately it's the doctor who's got to do that and there have to be mechanisms to make sure that they do.

Simon Whale: One of the things that we've heard in that context is if you're talking about neurologists and women, as opposed to girls, some neurologists will say, they've certainly told us that they feel uncomfortable, ill-equipped or uneasy about having that kind of conversation with a woman. They're a neurologist and they do neurology and they'll write a prescription for sodium valproate, but counselling people on pregnancy is something that they're not currently...

Simon Wigglesworth: So if I can, it would be up to the epilepsy specialist nurse, this is exactly meat and drink, this is what they are expert at, this is what they do now. We can have different arguments about whether there are enough epilepsy specialist nurses, but certainly where there are, the neurologist doesn't necessarily have to, from my view, do the counselling. But they have to make damn well sure it happens before they sign their script.

Valerie Brasse: Are there enough epilepsy specialist nurses?

Simon Wigglesworth: Not enough, but there are more than there have been and the numbers are growing, but no, by no way near enough.

Clare Pelham: Could I possibly build on your point? Because what I think we need to avoid in any new system is a single point of failure. So if everything rests on the conversation with the neurologist, that's what we have and of course it's not just the neurologist who may feel uncomfortable, it may be the patient who feels uncomfortable having that conversation with them. We need to just remember that timelines may be short, so we've spoken so far about a young girl who may become sexually active, or an older woman

who may be looking to start a family, but there are other cases too. There may be, for example, somebody who's mistakenly had unprotected sex and is thinking about the morning after pill.

Now, that's a quick decision and they need to have at top of mind the other risks of a pregnancy. If they can't find somebody sympathetic and expert to contact quickly, that's going to be a badly informed decision. So it needs to be not just one person that can be turned to for advice; we need to have multiple sources of advice. So I would suggest that we don't just need to have a neurologist in the picture; we need to have an epilepsy nurse in the picture, we need to have good public information out there on websites, NHS Direct and so on and so forth.

The people we haven't talked about yet, but who I know are very willing to step up, are pharmacists. Pharmacists are great at this stuff actually.

They're often really good at having really personal discussions, sometimes with people they know, sometimes with people who've driven 15 miles to find a pharmacist who doesn't know them. But they're accessible, they're open all hours and you can have informed discussions with them. I really think we don't want to put all our eggs into the neurology basket when we could have a chain of safety measures, because that's what keeps planes in the air, isn't it? It's not just pilots; it's engineers and so on as well.

Simon Whale: As you say, it's also about everyone knowing, including the woman in this instance, or girl, knowing that those mechanisms, those support mechanisms, those people who can advise and help are available. At the moment there is a lack of understanding.

Clare Pelham: There really is and the other category of people who must know that, we mustn't forget, are the people who support people with disabilities. So some of these people have learning disabilities and may be relying upon advocates or care workers and many of them don't have close family support. That's another chain of difficulty that we just need to be cognisant of when we're dealing with these very sensitive issues. Of course, I hope it goes without saying, that the Epilepsy Society would be so pleased to be asked to be part of that communication network, is really what it needs to be, to support the women concerned.

Julia Cumberlege: I'm very conscious we could go on a lot longer, but unfortunately it's gone four o'clock and we've got another meeting, I'm afraid. So I'll just ask my colleagues, have you got any further questions?

Valerie Brasse: Just one, which you could perhaps write to us afterwards. You talked about the work that you're doing with an international consortium to

identify genetic markers of this during pregnancy. I just wondered whether there are any updates on that which you might want to feed back to us, we'd like to know.

Clare Pelham: We will write to you. We're doing some very exciting work, yes.

Valerie Brasse: There's only one issue, is why does it affect some women and not others and so if you're beginning to identify some of that, we'd be delighted.

Clare Pelham: Yes, no, it's important.

Julia Cumberlege: Simon?

Simon Whale: No, I think...

Sonia Macleod: Same question as Valerie.

Julia Cumberlege: Well thank you so much and if there are other things that you feel we should have asked you and you'd like to give an answer to, please just notify us and all the rest of it. As you've heard, we will ask you certain things. I want to thank you so much, especially coming with a sore throat. To say it's been a really very, very useful session and a great insight into some of these difficult issues. So thank you very much for coming.

Simon Wigglesworth: Thank you.

Clare Pelham: Pleasure.

END OF TRANSCRIPT

23rd April 2019

Session 1: MESH SPECIALIST CENTRES - King's College Hospital NHSFT, Oxford University Hospitals NHSFT and Epsom and St Helier University Hospitals NHS Trust

START OF TRANSCRIPT

Julia Cumberlege: ...but before I introduce ourselves, can I just ask whether you've got any conflicts of interest, because we haven't actually had anything from you yet to say what your conflicts of interest might be? Now, you may want to think about that and to send us by email or whatever, what your conflicts of interest are. Would that be all right?

Linda Cardozo: I can tell you now, I don't regard this as a conflict of interest, but I was one of the participants in the Ward and Hilton trial of TVT which took place from 1997, and the final report was the five-year outcome data to which I contributed.

Julia Cumberlege: Right, but thinking of the pharmaceutical industry or anything like that, are you sponsored by any...

Linda Cardozo: In relation to the mesh review, I don't believe that any of the pharmaceutical industry relations would have any bearing. It's all been to do clinical research or to give lectures and it has no bearing on my involvement with meshes or tapes.

Julia Cumberlege: Right. So you're sponsored for research?

Linda Cardozo: Yeah.

Julia Cumberlege: Well, that would be helpful for us to know that.

Linda Cardozo: I can let you know that.

Julia Cumberlege: Right, thank you, and you?

Natalia Price: Thank you. So I'm Natalia Price, Consultant Urogynaecologist...

Julia Cumberlege: I'm so sorry, I'm a bit deaf. Could you speak up for me?

Natalia Price: Sorry, [laughs] sorry Baroness. I'm Natalia Price, I'm Consultant Urogynaecologist in Oxford. I don't think I have any conflict of interest. I can definitely - nothing to declare. If I have something and think about it, I'll definitely email you, but no conflict of interest.

Julia Cumberlege: Thank you, that would be really helpful.

Simon Jackson: Simon Jackson, Urogynaecologist in Oxford. I don't think really there's any conflict. Oxford was in receipt of an educational grant for about 10 years from Ethicon. They - it came with no strings attached but it was to run an anatomy course where we taught anatomy for various operations, including some mesh operations. So I don't really work with industry in any other way. I've done private surgery over the years, so I have been paid to put mesh in and take mesh out. No other conflict.

Julia Cumberlege: Right, okay. Thank you very much, and if you have further thoughts, just do let us know. As I said to - we've been going around the country, listening to a lot of women and we've been to Wales, to Northern Ireland, to Glasgow last week, and hearing the stories that they have got to tell us because that was part of the remit that we were given when Jeremy Hunt asked us to do this Review. Having done those visits, we are now obviously into our oral hearings and we're hearing from all sorts of people, taking evidence from a great number of people. We started with the patient groups and we will finish with the patient groups. So we're listening, learning a lot and have listened a very great deal.

So if I could start by just introducing the team to you, and then if you would be kind enough to introduce yourselves and say where you're from, and that will be on our screen, so we are videoing this and I hope that's all right. It'll go onto our website so people know what is going on, because one of the things that's come across very strongly to us is that people have been very anxious about secrecy and all the rest of it. So we're being as open and honest as we possibly can.

So I'm Julia Cumberlege and I have been asked to chair this Review by the former Secretary of State, Jeremy Hunt. We have our terms of reference onto our website, so you can see what we're doing and why we're doing it. On my left is Sir Cyril Chantler who is the Vice Chairman of the three-person panel that we've got who are taking the decisions concerning the Review and certain or all the aspects of it. Then, on my right is Simon Whale who's a - the third member of our panel, and Simon particularly deals with communications and lots of other things, as well.

Then, on Simon's right is Dr Valerie Brasse and she's our Secretary to the Review Team. On Cyril's left is Sonia Macleod, Dr Macleod who is our main researcher. Then, in the room, we've got other members of the team who are here just to help us run this session. So perhaps you would like to start by saying who you are and perhaps your special interest, so that would be useful.

Linda Cardozo: Yes, thank you for asking us. I'm Linda Cardozo and I'm Professor of Urogynaecology at King's College Hospital on the other side, at South East London. I was appointed a Consultant Obstetrician and Gynaecologist there in 1984-1985 and I've been Professor of Urogynaecology since 1994. I've got a major interest in women's pelvic floor disorders and I run a 13-person multidisciplinary team at King's providing all forms of treatment for women with prolapse and urinary incontinence, including conservative therapies, pharmacological therapies and surgery.

Julia Cumberlege: Thank you very much, yes.

Natalia Price: Thank you. I'm Natalia Price. I'm a Consultant Urogynaecologist in Oxford, Oxford University Hospitals. So I was appointed as a Consultant in 2010, sorry. Yes, I am a urogynaecologist. I do have a passion and interest helping women with pelvic floor disorders and offering a range of treatments. Over the last nine or 10 years as a Consultant, I've also been helping women with mesh problems and working as part of Oxford multidisciplinary team of clinicians helping me with these mesh complications, but overall it's pelvic floor disorders.

Julia Cumberlege: Thank you very much, yes.

Simon Jackson: I'm Simon Jackson. I work in Oxford too as a urogynaecologist. I've been there since 20 years, so I work with Natalia.

Julia Cumberlege: Right, thank you very much indeed. So perhaps I could ask all of you - as I say, we've been around the country. We've heard a huge amount from women who've had mesh implanted and one of the things that has come across to us is that they are very concerned that they can't get access to the services that they feel they need. For example, translabial ultrasounds, that's something that they feel is very important to them and that it can identify where the mesh is, and so they really feel that without access to this service that they really are not cited about what has happened and where the mesh is at the moment.

So I wonder if you've got any thoughts about the services that women can't access, and particularly translabial ultrasounds.

Linda Cardozo: Well, translabial ultrasound hasn't been proven to show any significant mesh disorders, and usually they're diagnosed clinically. We are able to provide translabial ultrasound but it doesn't necessarily give an answer to a woman's problems. If she has pain, it's not going to tell you why she's got pain. It may show where the tape is if it's a synthetic tape for incontinence, but at the moment there is not a significant body of research evidence to show that it's beneficial in the management of these women.

Julia Cumberlege: So, well, perhaps I'll hear from all of you and then...

Natalia Price: Yeah, sure. So translabial or pelvic ultrasound, which can be translabial or using - and a vaginal probe, can be internal scan, is not really validated imaging modality to specifically treat or assess women with mesh complication. It has its role, but it's not validated, so it can be used as part of the investigations and it does have its role. Out of all other imaging modality, transvaginal scan or pelvic scan or translabial scan helps to locate vaginal portions of the mesh. It's not helpful for abdominal portions of the mesh or groin portions of the mesh. Transvaginal, translabial scan simply doesn't detect those. However, it's not validated modality. It hasn't been.

An interpretation of the scan has to be taken very, very carefully. Any tissue, scar tissue that doesn't belong to the vagina, so which can be formed as a result of previous surgery, and not necessarily mesh surgery, can appear as scar tissue, as artefact. So interpretations of the scan have to be taken into account, clinical history has to be interpreted by a clinician, urogynaecologist knowing the woman's history, knowing this problem. So it has its role definitely as part of the investigation. It does, however it's not the only investigation and we really need to look holistically at those patients.

So simple internal examination will give you often more information about the position of the tape, tenderness. Simple vaginal mesh erosion will be detected on clinical examination and translabial scan doesn't really add much to it. Nevertheless, yes, this scan would have sometimes even the reassuring points. Some even come in upset because the tape is migrating and a performance scan showing them the tape is in a simple place, in the right place, in a single piece, gives them reassurance. So yeah, that's - it plays a role and that's what NICE guidelines reflect, but it's not - I wouldn't focus purely on this. It's about the holistic approach to this patient.

Julia Cumberlege: Thank you.

Simon Jackson: Well, when someone's presenting with a mesh complication, you want to know whether the mesh is in the wrong place and that is, as we've heard, a combination of vaginal examination will tell you whether the mesh is in the vagina. If you want to know whether the mesh is in the lower urinary tract, then the best test for that is a cystoscopy. If you think the mesh may have migrated into the bowel, you'll be looking at a sigmoidoscopy, and then that might be backed up with imaging and the MRI would be the imaging that tends to give the most information.

So a translabial scan is really just looking at the bit between the labia, and it's the bit below the vagina and the urethra. So it's not something that we routinely offer because we don't find it has clinical utility, but I am aware that many patients have been requesting it.

Valerie Brasse: Does it offer anything about the tension of the tape?

Simon Jackson: No.

Valerie Brasse: Nothing at all? There is a communication problem here, isn't there...

Simon Jackson: Yeah.

Valerie Brasse: ...because, of course, it has become a very important feature for so many women?

Simon Jackson: Yeah.

Valerie Brasse: If it's not being offered by the NHS, they are going privately for this and they're being exploited, to some extent.

Simon Jackson: Yeah, I'd agree.

Valerie Brasse: The price of these things are rising. So how are we going to deal with this problem? They're getting a very clear impression, they need this. They feel they're being forced into the private sector because the NHS doesn't offer it routinely, and they're paying a big amount.

Simon Jackson: Some of them are very vulnerable women.

Valerie Brasse: Yes.

Simon Jackson: I think this sort of information-seeking exercise may be useful in that regard.

Linda Cardozo: A lot of it is about expectations, isn't it? The problem is that if women are told that this is an investigation that can see if there's something wrong with a synthetic tape, then obviously they will cling to that, thinking that if they have this investigation, it may help with their management. The problem is that, if you look at the evidence base for the use of translabial ultrasound, it just isn't there. This is something that I looked up recently to see if there was a body of evidence and there isn't.

So it's unfortunate and it's inappropriate advice to women, and I don't really know where they're getting it from, but there must be people who are out there who are profiteering as a result of it and, obviously, that's most unfortunate.

Simon Jackson: We have had patients who come to us having had translabial scans that have shown mesh, and we know they haven't got mesh because we've taken all the mesh out but they've had other operations that have given them scar tissue and that's been misinterpreted.

Linda Cardozo: Or even childbirth injury.

Simon Jackson: If you're using a test clinically, you do have to validate that test in some way.

Natalia Price: I completely agree, and it's actually - it's very worrying because those are very vulnerable patients. They have already been so suffering. They suffered physically and psychologically and it's very important because I came across cases that I do feel that those vulnerable women have been misled and advised to seek a private translabial scan, and actually, the findings of the scans have been very, very poor and interpretational and those patients have been left in - it just added to the suffering of those patients.

So I think tighter regulations would be very welcomed and - because at the moment, it's not well-regulated and we do need to ask for more limitations of the translabial scan and, indeed, stop this practice.

Julia Cumberlege: Mr Jackson, you were mentioning about taking out the mesh, and perhaps I could pass on to Sir Cyril on that one.

Cyril Chantler: You'll be aware that one of the conditions around the pause was the organisation of between four and seven centres across England which will be tested as having all of the resources, including clinical expertise, to undertake mesh removal. That process of identifying what those resources are and testing to the centres is underway at the present time. We've got an operation which sometimes goes wrong and which it's not actually always possible to remove, or so we hear, the mesh that's been put in. So we've got people doing an operation who won't actually be skilled to undo it and put it right if it goes wrong.

So if we're going to have four to seven session - centres across England where they will be skilled at taking it out, should they provide a hub, so their part of the country, to actually work with the people putting it in so that we are sure that those people who are doing the operation to put it in where that is indicated are actually themselves competent. I can tell you from my own experience with [unclear] end stage renal failure that we established a number of centres to make sure that we had the expertise there to do the job, and so it's the same sort of philosophy.

- Simon Jackson: Clearly, the people putting the meshes in also need to have the appropriate expertise. It comes down to numbers, at the end of the day. The vast majority of people who have meshes put in have not had complications, so that's why the numbers being taken out will be much smaller than the numbers being put in. So you will need more centres putting mesh in than taking mesh out.
- Linda Cardozo: Are you talking about tapes for incontinence or meshes for prolapse?
- Cyril Chantler: No, I'm talking for - about stress urinary incontinence.
- Linda Cardozo: Because I think they are two different levels.
- Cyril Chantler: They're completely different, I accept that.
- Linda Cardozo: Yeah. I agree with Simon, because of the number of women who suffer from stress incontinence and who come and request tapes because, relative to other procedures we carry out, the complication rate is relatively small, numerically it's high because so many women have had tapes in the last 20 years, but I don't think that you need to be a mesh removal centre in order to put in a TVT, but you do of course have to know where to access care should that be required in the future. It would be like saying you can't do any form of surgery unless you can undo it, and often surgery requires a much different approach to redoing it or revising it or undoing it than to initiate it.
- Cyril Chantler: I think what I'm suggesting is that the people who are putting it in in different parts of the country, it might be sensible for them to work with the centres who are skilled at taking it out. In other words, we could work as a sort of team.
- Linda Cardozo: I think logistically and geographically, in some parts of the country, that would be difficult. It's not difficult for me in London because everyone is close by.
- Cyril Chantler: If you're going to have seven centres, removal centres across England, then presumably you'll be able to cover the geography reasonably satisfactorily.
- Linda Cardozo: Of course, at the moment, with the British Society of Urogynaecology, there are 18 centres that had registered as appropriate to provide all of the facilities for mesh removal. I, for instance, didn't put us down initially as a mesh removal centre, not that we haven't been removing meshes but because I felt that the workload would be too heavy on the NHS and that I wouldn't have facilities to take on that amount of work. Obviously, in

Oxford, they are a hub and they have their local community that they serve, so they're both putting it in and taking it out.

Cyril Chantler: The process that then NHS England is going through at the moment in specialist commissioning will be designed to establish and commission four-to-seven centres as expert removal centres. That is the process that is going on and it's one of the conditions of the pause.

Linda Cardozo: Well, I think that's very straightforward in London, so from my point of view, it's easy. We all know who is good at what and who provides which services.

Cyril Chantler: This isn't part of our Review. This process is actually going on at the present time.

Linda Cardozo: Oh yes, I know.

Cyril Chantler: Okay.

Julia Cumberlege: Can I ask you then, if you are really saying to us that you've got to have many more places in order to insert the mesh rather than just rely on these centres which they also take the mesh out, as clinicians throughout the country, how are you ensuring that the expertise is there to insert the mesh correctly, because we have had a lot of cases where, actually, the patients themselves are pretty convinced that it didn't have the expertise that was necessary to insert the mesh? If you are people who are not taking out the mesh, how do you know whether it's actually gone wrong or not?

Linda Cardozo: So can I take you back a little way? When I started out, people were doing anterior repairs for stress incontinence and it wasn't a very good operation. Then, with the introduction of the colposuspension which is what most urogynaecologists were employing for stress incontinence surgically prior to the late 1990s, it was a much more difficult operation and so generalists in gynaecology weren't likely to have a go at doing it. Unfortunately, the tapes were seductively easy to introduce, and so women with very mild stress incontinence would say, me too, I want one of those because it's a quick, easy fix and I won't have to do my pelvic floor exercises and I won't have to take any medication.

Therefore, many of the generalists who not only weren't trained to do these procedures but who did not have the facilities to appropriately investigate the patients or to offer them other forms of treatment started doing it. I absolutely agree that this has brought a good procedure into disrepute and it's a terrible shame that it's taken patients suffering to bring

that to light, but I think that you can designate centres as urogynaecology centres without them necessarily being mesh removal centres, because as we use significantly less mesh and women have choices to choose other procedures now, I think you can manage to have mesh centres that are designated for complications.

There are still a lot of women with stress incontinence who will seek a surgical solution, and the NHS in any one hospital is not going to provide those facilities. It just would not be possible.

Cyril Chantler: But would it not be sensible for these specialist urogynaecological centres who don't do mesh to have a relationship with a centre that does mesh removal so they get the feedback and the learning? Because one of the things we've met as we've gone around the country is women who are lost. They - things have gone wrong and they don't know who to go to because there's no connection between the person who put it in and the people who are taking it out.

Linda Cardozo: Well, I think we've become a lot more focused on multidisciplinary teamworking and I think everywhere has their MDTs now, and every surgical procedure - certainly that we do - on women's pelvic floors goes to the MDT before a decision is made. I think most people know where to access a regional MDT if they don't have a good, thorough local one.

Julia Cumberlege: Our real concern is - we have many - but one of our concerns is that we want to be absolutely certain that the people who are inserting the mesh have the expertise to do it so that it is an operation that is successful. We've had many stories where the consent was actually not explored and it was sold to women by their clinicians, surgeons, whoever, that this was the answer. Actually, they weren't given the alternatives. Now, can you assure us that that is not the case now?

Linda Cardozo: I don't think it is the case now. I hope that it hasn't been a very widespread problem because the majority of people that we meet at meetings do provide informed choice for women, and especially following Montgomery, we've all been training our juniors and our nurses to do exactly the same. I think having a patient decision-making guide will help and I think also being able to offer all of the range of procedures would be a very good thing. I've never stopped doing colposuspensions because I was trained to do them, but a lot of my younger colleagues can't because they were only taught to use tapes. Therefore, if you can only offer one operation, it might not be the right choice for all women.

Valerie Brasse: Can I follow that up?

- Linda Cardozo: Of course.
- Valerie Brasse: Because that goes to the heart of what is informed consent. If you can't offer the full choice, you actually haven't offered full consent or you haven't entered that process. I'm not saying that the individual consultant that you see - because obviously, you can pass them on to somewhere else, but when we heard from these sites, it was very clear that with the introduction of the pause that it was certainly time to take stock and reflect on the skills of those who were offering procedures for the treatment of stress incontinence. It was made very clear to us that there needed to be retraining.
- One looks at some of the figures that we've received from the individual mesh centres, the numbers of colposuspensions being done in previous years have been very low if not at all. So you have to ask yourself whether in those centres there was ever full informed consent, and actually that procedures were fully available to all women. I'm not quite sure what your experiences are. Clearly, I hear from you, Professor Cardozo, that you've always been doing it. I'm not sure whether that's necessarily the case everywhere and whether one's had to ramp up the skills base to be able to offer the alternatives.
- Simon Jackson: Can I interject? It isn't just about mesh this, really, in the bigger picture. Colposuspensions are complex operations...
- Valerie Brasse: I know that.
- Simon Jackson: ...and the same arguments apply because if a colposuspension is done badly, there will be...
- Valerie Brasse: Sure.
- Simon Jackson: ...significant complications, as with any operation, really. So it's important that the skills are there, whether it's mesh or whether it's non-mesh. Again, it comes down to numbers. You're right, it should - I don't think you have to be able to offer everything in a particular centre, but you need to be aware what's available and offer to refer patients on if you're not offering that particular procedure yourself. To come back to the, should the mesh removal centres be liaising with the mesh insertion centres, I think yes. It's rather analogous to how cancer was - cancer care was reconfigured years ago. I think the new NICE guidelines which I think are very sensible, actually, the - we're going to have to have a rethink about how we run our MDTs.

The regional MDT is a new development for many of us which is going to be - it's going to require resourcing and it's going to change the way we work. It's certainly going to change the way we work in Oxford and I think probably across the UK - I think a combination of the NICE recommendations and the pause for this Review - and it's going to have some very positive impact on our specialty, actually, because it has allowed time for reflection and I think it's going to mandate proper resourcing of follow-up of patients to see whether they get complications and proper beefed-up MDTs and there's going to be all sorts of positive spin-offs.

Natalia Price: Yes. So I agree with Mr Jackson - this, both high vigilance procedure and NICE guidelines, it's actually - it's been very positive. It gave us time and actually power because we have more resources locally to think, to reflect, but ultimately to give even more choice, to empower patients to make the decision, to give them all the choices, and I also - which is really important this, by a mile. So NICE guidelines is a very comprehensive document, clearly states that any surgery for pelvic floor prolapse or incontinence primarily needs to be very carefully discussed and weighed, pros and cons. Any surgery has complications.

So this high vigilance procedure over a period, and Baroness Cumberlege has really helped and makes us think, so it's a very positive development.

Simon Whale: It's kind of interesting that it's taken us to make you think.

Natalia Price: I think both started before, but you know generally, if you look in medicine and surgery, if you look how training was around 20-30 years ago, even 10 years ago, you're all progressing, you're all - it's all getting better. So it's not new, but actually, it has helped us because it helped us, for example, locally helped us to strengthen our MDT, to have more [medicine] support or co-ordinators to streamline, because you can't run this on goodwill alone. It has been for the British Society of Urogynaecology a charitable organisation run by volunteers. The database was established as volunteering, so the database - so it's - the source process has been there for a long time, but it helped us. It gave us more weight.

Simon Whale: Can I just ask another question about the pause? So how are you managing patients during the pause? So if a woman presents with SUI, you're not able to offer her mesh at the moment. What do you do for and with that woman?

Linda Cardozo: Well, the problem...

Simon Jackson: We...

Linda Cardozo: Sorry, you carry on.

Simon Jackson: We do - I mean, we offer them the operations that we know work for stress incontinence. So we have some patients waiting at the moment for - hoping that the retropubic TVT has reintroduced. We have patients who choose to go ahead with colposuspension. We have patients who go ahead with fascial slings and we have a lot of patients at the moment who are having injectables knowing that the injectables are not terribly effective but have a good safety profile, just waiting to see what's going to happen in the future.

Linda Cardozo: It is very sad to have patients waiting and I don't know how many people you've spoken to who've had successful tapes for stress incontinence, but as you can imagine, over the years, both in the NHS and in my private practice, I've had a number of significantly high-profile women who have had tapes but they don't come forward and talk about it. First of all, they've moved on, they've been treated, they don't want to talk about incontinence, and secondly, now they're trolled on Twitter if they come forward and say something, and so they're frightened to do so.

We have a significant number of patients who were waiting for a tape and continue to wait, incontinent, with pads because they don't want a big operation like a colposuspension which they know has a complication rate. They don't want an injectable because they know that it might not work for long, and if it does, it will have to be repeated, and they think that, if they wait, they will get a retropubic TVT which is what they had signed up to, having read the leaflets and having been counselled about all of the alternatives.

A lot of that is about expectations because if we didn't have the tapes, that wouldn't be their expectation, but at the moment, they still think that they will be able to have one if they wait. That's quite sad for them.

Sonia Macleod: Roughly how many are we talking about?

Linda Cardozo: We brought back all our patients who were on the waiting list for tapes and discussed with them the alternatives. I can't tell you exactly how many it was because we are four consultant urogynaecologists, so they didn't all return to the same clinic, but I saw about a dozen who were on our waiting lists expecting to have their tapes within the foreseeable future. If their mother had had an operation for stress incontinence, they were happy to have a colposuspension and if they knew someone who'd had an injectable, they'd have that, but the rest of them are waiting still and it's nearly a year now that we've suspended their treatment.

- Valerie Brasse: Are they still on the waiting list?
- Linda Cardozo: Well, no, they come back to clinic periodically to see if the tapes have returned. In fact, Thursday before last, I saw a woman who said, but you told me the guidelines would be out in April. I said, well, the guidelines are out, but the pause has not yet been reversed, so I still can't do anything for it.
- Simon Jackson: They're not allowed to be on a waiting list because then they would breach the waiting list, so fair enough.
- Cyril Chantler: Yes, we've heard about that. It's a sort of Catch-22, isn't it?
- Linda Cardozo: Well, it is difficult because the NHS funding is limited, and so you can't just keep people on a waiting list if you don't know when their turn is going to come, because the hospital is fined, as I'm sure you're well aware, if anyone's been waiting over 52 weeks, and it's coming up to that now.
- Julia Cumberlege: Can I just ask you, just thinking about the history and how tapes took off, and we would call them mesh, and that's been a bit of confusion with women because they've thought tapes were something that you might use in dressmaking which is actually something that is made of linen or whatever. The word tapes I think has caused some confusion, so we call them mesh tapes. So in 1998 there were just 214 women in England who had TVT and TOT. By 2009, the annual numbers of operations using polypropylene mesh were at an all-time high of 11,365 in England. That was a huge take-up.
- Can you just say to us, were you convinced at that time that this was the right thing to be doing? What was the role of the pharmaceutical industry in terms of ensuring that surgeons were aware of this operation and that their products could be used? Since then, we have seen a reduction, but not huge, but we have seen a reduction. What impact did that have on colposuspensions which you've been talking about? Because we've seen the numbers decrease hugely on that and I can understand why, because the mesh was understood to be a much simpler - a cheaper operation in terms of bed days and all the rest of it.
- So just - and thinking about what you do, are you now still teaching students how to do those colposuspensions or are you just saying, no, mesh is the answer?
- Linda Cardozo: No, I never stopped doing colposuspensions.

Julia Cumberlege: No, I do understand that. I've got your figures.

Linda Cardozo: Okay, I had always - well, first of all, I didn't introduce tapes into clinical practice until we'd completed the first cohort of patients in the Ward and Hilton trial because I am a slow adopter on any new techniques. So it wasn't until we'd already produced the results from that, which were initially six-month results, and then I was fairly convinced that it was a reasonable process to go through and I train people in both TVTs which I learnt from [unclear] in Sweden.

I train both those and colposuspensions, but one of the reasons for continuing to do colposuspensions is that I believe that, if you have a procedure that fails - and a proportion of TVTs will fail - then it's a little bit illogical to do another one of the same procedure on the same woman because there may be underlying factors that mitigate it being successful under any circumstances. So for redo surgery, I always do colposuspensions and that's why I've continued to train them. I'm now training my ninth subspecialty trainee and all of them have been competent at colposuspensions by the time they've left me.

Julia Cumberlege: Were you surprised, though, when your colleagues, and many of them, came forward and said they were very surprised about the ratings and how the ratings changed from a C rating to an A rating within a year?

Linda Cardozo: I don't recollect that that's something that we discussed in great detail, but it may have been, and I think...

Julia Cumberlege: Well, [inaudible] is quoted as saying he was very surprised because there was no research to actually underline what was happening and why the change was made.

Linda Cardozo: Well, of course, the TVT has been very heavily researched and, in fact, of surgical procedures, there are more publications in relation to it than most other surgical interventions. They do show great efficacy with a relatively low complication rate. So I know that the HES data suggests nine per cent complications, but 50 per cent of those are unclassified, so they may be something as simple as a urinary tract infection.

In our clinical practice, and obviously nowadays because of the pause we've all discussed this - we really don't see a huge number of women coming back. The reason that there are so many women is because so many tapes have been put in over the last 20 years with very little follow-up. The NHS does not allow us to continue to follow up patients year-on-year, so we may see them once post-operatively, but then we might not see them again.

Valerie Brasse: Would that be a good idea? Women have said, we could come back every year, what if that's followed through?

Linda Cardozo: It would be great, but who would resource it? It would be absolutely fantastic, and think of the long-term publications we'd have, but it would be the same as any other intervention and no one is going to fund that in the long-term.

Simon Jackson: Can I interject, Baroness, on your point about the rise, huge rise in TVT surgery? A colposuspension operation, which I was trained to do in the 1990s, was a pretty brutal operation. It was done through an incision, sometimes quite difficult to see what you were doing if the patient was slightly obese. There were significant complications from that operation, in particular a rectocele which is a prolapse on the back wall of the vagina, because it changes the vaginal anatomy.

So when the TVT came along, I too was a later doctor and I think I put my first TVT in at about 2001, but it seemed to be a very appealing operation for both surgeons and patients, in that the trial data was suggesting equivalence to colposuspension but with a considerably quicker recovery. I think the economic side was of secondary importance to the clinicians. I don't think we were really putting them in because it was cheaper for the NHS, but it was certainly a much easier operation for the patients because I remember them sitting around for days afterwards, after colposuspension and suprapubic catheters, being unable to empty their bladders properly.

The TVT, you can adjust it if they are in retention afterwards, you can take them back to theatre and loosen it off. You can't do that with a colposuspension. So there were all sorts of theoretical advantages and, well, real advantages. The mesh erosion issue, although it was always a theoretical risk, in practice didn't seem to be a huge problem. That was borne out in our clinical experience. We published our own mesh erosion data, it was about 2-3 per cent.

These aren't all major mesh complications that you've been hearing about from some of these women who have had terrible adverse events, but the majority of mesh complications were bits of fibre in the vagina which could be trimmed down fairly easily, often without actually comprising the integrity of the sling. So they weren't all major complications that were difficult to deal with. So there was a huge uptake of TVT, just because we felt it was a better operation for the patient.

I think because we felt it was such a good procedure, it was, as Professor Cardozo said, it was embraced very enthusiastically, I think, by both

clinicians and patients, and hence there were people being treated who perhaps wouldn't have come forward for an old-style colposuspension because it was a bigger operation.

Simon Whale: Did it almost by default become an alternative to conservative therapy?

Simon Jackson: I think that would be a fair comment. No, we always offered or should always have offered physiotherapy. I know there were some cases where that wasn't done, but it was never seen as a replacement to physiotherapy. I think the threshold for surgery dropped.

Linda Cardozo: I think one of the problems is that women's health physiotherapists are a fairly rare breed and if women are on the waiting list to see the physiotherapist for a long period of time and they know there's a small operation available that maybe their friend or someone they know has had, they will opt for the quick fix rather than wait a long period of time to see a women's health physiotherapist. In our own experience, we've now got 300 women waiting to see one of our physiotherapists. One's on maternity leave, one's just left and we can't provide those services for all women all of the time.

Julia Cumberlege: Can I ask you about the products now, because we've obviously just had this news from the FDA that they have banned two of the products that are being produced? In 2014 there were 29 different products had appeared on the market. By 2005-2013, there were 170,000 devices. Can I ask you about the devices and what your role, you think, might have been in the - by the pharmaceutical industry?

Simon Jackson: There are a lot of me-too products. The one that was researched was the Johnson & Johnson, the trial of colposuspension versus TVT which is a type 1 polypropylene mesh. I know that there were some other meshes that I didn't quite understand which came on the market. I think [inaudible] was one which was a different product and there was no evidence for it and it should never have been introduced without evidence, but there were other companies, I think, producing other type 1 polypropylene meshes that were copies of the Johnson & Johnson product.

There was definitely inducements. There were - companies wanted you to use their products. We always stuck with the [inaudible] because that had the data, but I think it was reasonable to switch to another, perhaps if it was cheaper for the NHS, another type 1 polypropylene product that should have been equipment, I think.

Sonia Macleod: When you say inducements...

Simon Jackson: What were - yes, sorry.

Sonia Macleod: ...could you be a bit more specific about the inducements?

Simon Jackson: I guess meals out, taken to conferences, that sort of thing, the normal commercial...

Linda Cardozo: It is interesting because I have always chosen to use [inaudible] retropubic TVT on the basis that they publish the data, and I am very evidence-convinced and evidence-based, but in about 2005 our Trust unilaterally took the decision to provide us with the [inaudible] product because it was sold to them for half the price. One of my colleagues went into our day surgery unit and all the TVTs had been removed and replaced with a different product.

At that stage, we said, no, we're not prepared to do this because we don't have published evidence that they are the same, they are a me-too product. So I think that there are people around the country who are taken in by cheaper, seductively marketed products, but I think that you'd have to speak to those people to find out what it was that made them switch.

Simon Jackson: It's not just a mesh issue.

Julia Cumberlege: So was there any post-marketing surveillance done?

Linda Cardozo: Was adequate post-marketing surveillance done?

Julia Cumberlege: Yes.

Linda Cardozo: Not on all the products, I don't think so. I didn't use them but I don't believe they did. The FDA initially was at fault because they were registering products on the basis that they were similar to another one.

Simon Jackson: Can I just say, it's just - that's not just a mesh issue? We've had in our Trust sutures. Sutures are - some of the sutures are implants, aren't they? They don't dissolve. We've had our sutures changed from ones that we've been using for many years and are familiar with to other, cheaper products. So this isn't just a mesh issue we're talking about.

Linda Cardozo: Trocars for laparoscopies, you go in and they've got new ones.

Valerie Brasse: So that's a supply procurement issue for the Trust, and the clinicians you've been saying have no role although you've just said you refuse to use the ones that they did bring in and that was effective.

Linda Cardozo: I was effective in 2005. I wouldn't be as effective now. We are completely differently managed within the NHS. I don't even choose what goes onto my operating lists anymore. They're chosen for me.

Simon Whale: Is there clinical input into the decision?

Linda Cardozo: There's clinical input into the decision that a patient will undergo a certain procedure. There's no clinician input into which day that operation will be done...

Simon Whale: Or what - which products would get used and...

Linda Cardozo: ...or what the case mix will be on an individual operating list or, necessarily, what product will be used.

Simon Whale: Does that compromise safety?

Linda Cardozo: For what I do, in general, no, but there are people who are using far more devices and products and it may represent a safety issue.

Cyril Chantler: There must be patients that you see, because of your experience and expertise, where you're the right person to do the operation with King's, and you're saying that you can't actually guarantee that you will do that operation?

Linda Cardozo: You - under most circumstances, I am able to stipulate, but if that patient is breaching the waiting times, then one of my colleagues who is trained in urogynaecology will be asked instead. I think that's how it is in most Trusts now. You cannot guarantee an individual. It even says on the consent form that no one specific individual will do your surgery.

Sonia Macleod: There are some operations that are undertaken only by...

Linda Cardozo: There are, there are.

Sonia Macleod: [Unclear].

Linda Cardozo: It's one of the things that makes a nonsense of saying that you need to do 20 of a procedure a year to maintain your competence at it. There are some things that I only do once every five years because they only occur that frequently. Playing the numbers game is dangerous, but it is much more difficult now than it was even a decade ago to provide the care for patients on an individual basis because we are very thoroughly managed within the NHS.

I'll give you an example. We used to book our own patients. We had a gynaecology admissions officer. Our patients are now booked by someone

who works in the dental school. They are pre-assessed by an orthopaedic nurse, so when they say, how long will I bleed for after my vaginal hysterectomy, they're told, you should be able to walk on your knee in six weeks' time. They are completely segmented into the places that they go to and are seen, and the lists are booked by administrative staff who decide, based purely on how long a patient's been waiting for unless they're a two-week wait cancer patient. So we don't have the same degree of input as we used to.

Julia Cumberlege: Is that true of Oxford, too?

Simon Jackson: It is, and it's not quite as bad as that sounds, but we would try and keep all the urogynaecology - well, we would keep all urogynaecology within the urogynaecology team, and we work very well as a team. So no, I think urogynaecology would be - our patients would get an entirely appropriate surgeon.

Julia Cumberlege: Natalia, you would agree with that, would you?

Natalia Price: Yeah. You have to work as a team. You can't rely on individuals on the team who could get run over by the bus tomorrow. So it's a team approach, but yeah, so we do - so all urogynaecology procedures are done by urogynaecologists that are trained to do so in Oxford.

Simon Jackson: One of the things that was happening some years ago, Trusts were managing waiting lists by taking a block of patients and passing it across to a private provider and that private provider may be very good, but it may not be. That block would have included things like TVTs which were seen, as Professor Cardozo said, as seductively easy, but actually, it can go very wrong in the wrong hands, but any operation can go very wrong in the wrong hands.

So it's difficult for the people running the Trust, isn't it? They've got to manage their waiting list somehow. You can't have patients being able to choose their surgeon every time, I guess, if some surgeons are more popular than others because waiting lists have to be managed and it's difficult.

Julia Cumberlege: You can if you go privately.

Simon Jackson: Yes, you can. The difference between private care and NHS care is you choose your surgeon and you're then not kept waiting.

Linda Cardozo: Your timing of your operation.

Simon Jackson: You're not kept waiting. It's a different service.

Valerie Brasse: Can I assume that no one under the pause should be receiving a TVT? It's been parcelled off to the private sector?

Simon Jackson: No, well, I can speak for Oxford. The Medical Director at the private hospital will take his lead or her lead from the NHS, so the same clinical governance would apply.

Valerie Brasse: That's what we would expect.

Simon Jackson: I don't know whether that's the same across the country, but certainly, within the Nuffield Group which is the group we do our private work through, that would be the case.

Linda Cardozo: We all four of us have decided right at the beginning that we would observe the pause for as long as we had to, and we explained that to our nurses, physiotherapists, patients alike. To my knowledge, none of us have put in any tapes in the NHS or the private sector.

Simon Whale: Can I just return to the subject of removal? So, a lot of women have talked to us about being offered full removal or full vaginal removal, but it's subsequently become apparent to them that not all the mesh has been removed in their removal surgery. Can you help us understand what you would define as full removal?

Simon Jackson: Okay, before we talk about that, we need to just understand the different tapes because there are transobturator - you'll know all this.

Simon Whale: Yes.

Simon Jackson: There's transobturator tapes, there's retropubic tapes. Now, the problem with the transobturator tapes is that part of the mesh is in the groin, which isn't an area that gynaecologists have ever been trained to operate in. So taking mesh out of the groin - and this is one of the things we were looking at on the anatomy course when I was talking at the beginning of our declaration of interests, dissection of the groin is frightening. There are all sorts of adductor tendons and nerves, the obturator there.

So there are very few, if any, gynaecologists that would be confident to go and dissect out of the groin. So if a transobturator tape is to be taken out completely, by and large that would need to be done in conjunction with a plastic surgeon who perhaps has been trained to operate on the groin. That is different to a retropubic tape where we are fully familiar with all of the anatomy of the pelvis and can take out a retropubic tape completely if it is appropriate to do so.

- Linda Cardozo: It isn't always appropriate to remove the whole of the tape. If a small portion of tape under the urethra is exposed, it's perfectly reasonable to remove that small portion of tape. If it has been inside you for more than about six months, it's quite likely that continence will be retained which was the purpose of putting the tape in in the first place. So I think, once again, it's about expectations, but leading women to believe that having the whole tape removed is going to solve their problems is often inappropriate.
- Simon Whale: So most of the women that we've met where that has been the issue, it's been about pain, pain in the groin, pain down the legs, pain across the back of the...
- Linda Cardozo: I would agree, though, that removing a retropubic tape is not that difficult and not necessarily necessary. Removing an obturator tape is much more of a problem.
- Simon Jackson: I think the morbidity profile with the transobturator tapes is very different to the morbidity profile with the retropubic tapes, and I was very pleased to see, actually, the NICE guideline has just been published, that actually, transobturator tapes are effectively not going to be put in anymore.
- Linda Cardozo: Then, the only reason...
- Simon Jackson: There was never any - sorry, Linda.
- Linda Cardozo: Sorry. The only reason, in my opinion, for putting in a transobturator tape, and I've used them a handful of - well, maybe two handfuls, but not that many times over the years, but for women who have a real problem retropubically, if they've got a plated pelvis from a previous pelvic fracture or there is some reason why you cannot or it would be dangerous to enter the retropubic space, for those women, when appropriately counselled regarding the complications, risks and benefits of the procedure, if they can't have a colposuspension or a retropubic tape because it would be dangerous to go in the retropubic space, then for those very limited women, I would offer it, but not for others.
- Cyril Chantler: Presumably, in the specialist mesh removal centres that are being commissioned, they will need to be aware of the need for a surgeon able to dissect through the groin and familiar with the obturator frame.
- Linda Cardozo: Usually a vascular surgeon.
- Simon Jackson: Yeah. We need some more research in the area because it's by no means clear that, if you've got groin pain, taking out the mesh is going to cure the

groin pain, because if the pain is due to nerve damage, then an operation isn't going to rectify the nerve damage. Indeed, it may cause more nerve damage. So we're still quite a long way to go before we really...

Cyril Chantler: We've met women who have gone abroad to have it removed and they said to us that it's - they've been told that it's important to make sure that you know how much went in, in terms of centimetres, so that you know how much you've taken out.

Simon Jackson: I'm not sure I agree with that. Once you find the mesh, you follow it to its entirety.

Cyril Chantler: You can't follow it through the obturator frame.

Simon Jackson: Well, you would be doing it from two...

Cyril Chantler: Yes, quite, but that's what...

Natalia Price: You can't remove it entirely vaginally [unclear].

Cyril Chantler: That's what I - my point is, that they've said - said one of the reasons you follow it is you've got to then follow the whole thing, so - because otherwise, you - I don't know how to do these operations. I'm reporting what we've been told.

Linda Cardozo: You can't measure how much you put in, but you can measure how much you lop off. So, yes, you can't...

Cyril Chantler: You can measure how much you put in because you can record that when you put it in.

Linda Cardozo: Well, we don't record it.

Cyril Chantler: No, but you could.

Natalia Price: We need to know what type of transobturator tapes. Removing them, there are so many types that I never knew about until - so before you go for surgery, make the decision to remove, you need to know what transobturator tape was put in, because there are huge variations, and then make a decision. Where - it's such a broad topic, Sir Chantler, and to start with mesh removal surgery, counselling patients making decisions is more difficult than surgery itself, and that's why I'm - particularly for chronic pain.

So when there is an obvious problem with the mesh such as erosion or sepsis around the mesh, decision-making is easier. When you get a patient with chronic pain, there's no erosion and no findings on imaging to say

there's a problem, decision-making is a lot more difficult than even doing the surgery itself. There's one particularly beneficial road I can see in the NICE guidelines, the decisions are [regional] and that you're going to make those decisions because the outcome data for mesh removal for chronic pain, they still don't have robust outcome data. We need to make sure that patients are not worse off after this surgery.

So that's very important because those patients will have further continence surgery after removal or further prolapse surgery and it's a cascade of operations with this risk of morbidity. So, to start with, yeah, counselling before surgery. Going back to obturator tapes - you can't remove transobturator tape vaginally entirely. You need a groin dissection, either traditional transperineal, or an alternative would be laparoscopic, but also with laparoscopic technique, you in some cases can remove entire mesh or you would need a groin dissection in combination. Yes, it's a multidisciplinary approach, and I would think plastic surgeons would be the best people to support us in what they do.

Julia Cumberlege: Have you had occasions where the mesh has gravitated at all? Have you had occasions where it's shrunk, where it's stretched, where it splinters? I just want to understand the product because these are the sum of things that we have heard.

Natalia Price: Yeah. I think mesh doesn't break in pieces and splinter and travel somewhere. I think that's a myth. I think that's what probably mesh erosion - mesh can erode into surrounding structures such as the vagina, urethra or bladder or bowel. I think that's what probably splintering of the mesh is perceived by [unclear]. Yeah, so regarding shrinkage, there are conflicting data about shrinkage and there is some evidence it shrinks when it's in place and, at the same time, we don't know to what degree. So - but mesh can definitely - yeah, there is a risk of mesh eroding into surrounding structures, this type of surgery and everyone - we see cases when that happened 10, 15 years ago, as well.

Linda Cardozo: Of course, women change shape over the years sometimes, as well, so if you put a tape in a very slim woman and then she becomes grossly obese, it's quite likely that the tape will not perform in the same way as it would have. Similarly, when a woman becomes post-menopausal and her vaginal tissues and her urethra become more atrophic as a result of lack of oestrogen, then similarly, the tape can cause problems, not because of the tape but because of the aging process or the changes in a woman's body.

Simon Whale: We...

Julia Cumberlege: Mr Walker, can I welcome you? I'm sure you got lost in this building.

Roger Walker: Thank you. No, my apologies. I got caught up last week. This week, I was asked to come at two o'clock and there was, I think, a miscommunication as to the start time, so I was...

Julia Cumberlege: Oh, I'm sorry about that.

Roger Walker: ...patiently waiting at quarter to two to two, so my apologies on both counts.

Julia Cumberlege: Nevertheless, you're very welcome.

Roger Walker: Yes, thank you.

Julia Cumberlege: Thank you very much for coming. Perhaps you could just say for the benefit of the camera who you are and where you're from and your specialty?

Roger Walker: Okay, yes. My name's Roger Walker. I'm a Consultant Urologist at Epsom and St Helier and a Clinical Lead for our regional MDT and Specialist Mesh Team.

Julia Cumberlege: Thank you very much. We were just talking about the removal of mesh and the difficulties that occur. We have been through several other conversations, but I won't bore you with recapping them all.

Simon Jackson: Baroness, can I just follow on from what Natalia was saying? So we haven't in Oxford seen any cases of mesh migrating to distant places in the body and we haven't seen any cases of mesh spontaneously breaking up. So we have had a number of women who have, I think, probably been misinformed by - some of the media reports have not been entirely accurate. Mesh is an extremely complex area and we've had some patients who've had a variety of symptoms that they have attributed to mesh which we've felt, on balance, have not been due to mesh.

The erosion into the adjacent viscous is a very genuine problem which we see, happily not too often, but it is - that would be the commonest complication we've seen with the mesh implants that we've been doing.

Linda Cardozo: I would have to concur. We haven't seen distant mesh migration in the same way that we know that Teflon migrated to distant areas in the body when it was used as an injectable. So I think it is completely different. When we have - collectively, I'm sure - been called upon to remove bits of mesh or tape many years after it's been inserted because it's eroded, it is configured in the same way that it was when it went in.

Simon Jackson: The other, I think, bit of misinformation is, when the mesh is removed and it's sent for histology, it almost invariably shows a giant cell foreign body reaction, which some patients are understandably interpreting as a sort of toxic reaction to the mesh. It's not. That is a normal host response to an implant.

Sonia Macleod: How long would you expect that to continue for? For as long as the implant is in place?

Simon Jackson: We - one would have to ask that question to a histopathologist, I think, but I suspect indefinitely.

Simon Whale: So, do you think we have enough knowledge and data about the long-term effects of having mesh inside the pelvis?

Simon Jackson: Well, I don't think you can ever have enough knowledge, can you?

Simon Whale: Do we have enough to carry on using the product?

Simon Jackson: Any operation is a learning process. Medicine is a technology that moves on and we're doing things now that we probably won't be doing in 20 years' time. That's just the - so one can only have a certain amount of follow-up, but we do have a lot of - we've got 20-year data now with mesh. Linda's been putting mesh in for more than 20 years. I've been putting mesh in for 20 years. We're not seeing a huge number of people coming back with complications.

That's not to diminish the complications that - there are some very sad stories and there are things that we have done wrong as a profession that one needs to understand why mesh has been put in in the first place, because the operations that we had before these mesh operations came along were not good operations. Vaginal prolapse, you just end up repeating the surgery and taking more and more vaginal tissue out, and you completely lose vaginal function. It's not your remit to discuss the abdominal meshes, I know, but the abdominal meshes have a very good safety profile.

I think the transvaginal meshes for prolapse have not had a good safety profile and I don't think those are going to be - and then, they haven't been put in for some years in most centres now. The - mesh is very important for any reconstructive urogynaecologist. If we haven't got access to mesh, there are problems that we cannot help patients with because the tissue, the connective tissue is weak, and you've got to do something to strengthen the tissue. The ideal would be to be able to grow body parts, but we can't do that yet. So, I think...

Linda Cardozo: Polypropylene mesh is used in hernia repair and has for a long time, and if we look just at the published data, six per cent pain with polypropylene mesh for hernia, four per cent mesh complication for TVT, retropubic traditional. They're not that much different. If you look at the British Society of Urogynaecology Database, there are now 40,000 TVTs on it. I appreciate that there will not be a lot of long-term follow-up, but there has not been a huge amount of complication reporting.

Certainly, from many, many years' experience, I have not seen a high complication rate with retropubic TVTs, not in the same way that we did when mesh was being put in transvaginally for prolapse repair, where a much larger piece of mesh is employed.

Julia Cumberlege: Can I change the subject a bit, because you all know of the five safety measures that we said must be introduced before any further surgery is taken for urinary incontinence, et cetera? Can I just ask you your views about a database and whether you think that the information we gather now is sufficient in order to ensure that we can see the trends that are happening, and that it could certainly help in the future to see exactly what is happening with this particular operation? So perhaps I could ask you because - to bring you into the conversation.

Roger Walker: Yes, of course, an opportunity, yes.

Julia Cumberlege: Any views on a database?

Roger Walker: I think without a doubt, a database should be mandatory for incontinence and prolapse surgery. To what extent you take that database in terms of what information you collect at the outset and for the length of time you maintain follow-up data is the nub and the crux of it, really, but there's no doubt that to have a database in the first place would be a very important step in the right direction. There are...

Julia Cumberlege: What are the sort of things you would want to see on a database?

Roger Walker: The obvious demographic data about daytime surgery, what surgeries were performed, what mesh or sutures were used, some early follow-up data and a recording of complications as they arose down the line. What I'm sure has been touched on as part of this Review is what complications are attributed specifically to mesh or product complications and what complications are related to the general complications you would see as a result of an operation. So that indication is difficult to disentangle, but certainly having a complication recorded is important.

- Linda Cardozo: I think it's very important to have some quality of life outcome data because quality of life is what the patient measures. It isn't purely a matter of success or complications. It's how a quality of life for a non-life-threatening condition has been changed. I think the British Society of Urogynaecology Database does a good job. I think what's bad is that people who are doing the surgery don't always input their data and the Trusts don't always allow follow-up of patients, so you don't get the outcome data in some Trusts.
- Sonia Macleod: When you said they don't allow follow-up, could you elaborate a little on that?
- Linda Cardozo: Do we allow follow-up?
- Sonia Macleod: When you said the Trusts don't allow follow-up.
- Linda Cardozo: There are a number of Trusts throughout the country who will not have a physical visit for a patient to the outpatients' clinic after a procedure, but will have virtual clinics where the patients can ring in or the nurse can ring out and the patients will be followed up verbally. Then, if they say they've got no complications, they may not be seen postoperatively.
- Roger Walker: There's a lot of pressure from the NHS to move follow-up back into the community, back with the GP or with the patient themselves, so to create a database or a follow-up process that involves patients being more closely monitored is at odds with some of the pressures within the Health Service.
- Julia Cumberlege: Have you any views on the MHRA, the regulator?
- Linda Cardozo: Do I have views on it? I think we've been very inefficient in reporting to the MHRA, and I've just been to do a visit to a gynaecology department in difficulty in the UK and noticed their appalling reporting of complications to the MHRA, so I suspect it's a widespread problem. On the British Society of Urogynaecology Database, there is now immediate access to report complications to the MHRA which is a great advance, I think.
- Simon Jackson: That's been one of the positives of the high vigilance mesh restriction because the medical directors are now ensuring that anyone putting mesh in in their Trust is reporting to MHRA and that will be part of their annual appraisal and revalidation and everything else. So I think one has to have a robust method for reporting complications. The problem will be, of course, if we're not following patients up at - I would have thought probably one year and five years would be a reasonable minimum - you're not necessarily going to know about all your complications.

One can argue if the patient's asymptomatic, then perhaps you don't need to know about the complication, but I'm not sure that's the case. So ideally, you'd be reviewing and examining your patients at one year and five years and reporting any mesh complications to the MHRA.

Sonia Macleod: Do you think that you see patients with complications? Do you think they are referred back to you or do you think they're possibly referred to other services?

Simon Jackson: They could be either. If you're working in a - in the tertiary unit, you're probably the only unit around who's dealing with the mesh complications, so we would expect to see most of our complications back plus complications from other units around, but clearly there's...

Linda Cardozo: That will be different in Oxford from London...

Simon Jackson: Yes.

Linda Cardozo: ...because in London, the GPs will refer to the department with the shortest waiting time and patients' interests, rather than necessarily referring them back to the place where they had the index surgery.

Simon Jackson: There is geographical mobility then, so we won't certainly be seeing all our complications back.

Roger Walker: Going back to the MHRA, I think a thing that has changed and improved is actually the ease with which you can report complications. It used to be quite a lengthy process, but I think in recent years, it has become a lot more straightforward.

Valerie Brasse: A clinician last week said to us reporting to the MHRA is like reporting to a black hole, black holes being quite topical these days. I'm not quite sure what they were expecting back from the MHRA, but what would you want to see back from the MHRA?

Roger Walker: It would be nice to see some sort of annual output of data complications. They do report back what was reported to them, so you could get a response in the sense that you feel you've reported, and it should form part of your individual service, your unit's appraisal and data involved for your assessment process. So it's valid in that respect. I'm not sure outside of big reports, reviews, that the MHRA has really any obligation or anything I would expect to get back from them, to be perfectly honest.

Simon Jackson: It's more of a national trigger, I would have thought. On an individual basis, you're perhaps not going to pick up on things very quickly, but if you're getting data from the whole of the country, if there's a faulty product...

- Sonia Macleod: That does rely on people reporting to them.
- Simon Jackson: Well, but that's going to - well, that is now mandatory, isn't it?
- Simon Whale: It also depends on recognising complications as complications, so as you - I think you just mentioned, if - there's a case for saying, well, if the patient is asymptomatic, then job done, there is no need to investigate.
- Linda Cardozo: We can cite an example for that. If a patient is not sexually active, she could very easily have a small erosion of mesh into the vagina and no one would know about it because it wouldn't cause any problems to her. Now, should that be reported? I don't know. If she's not coming forward, you don't know that it's there.
- Simon Jackson: We telephone follow-ups of our patients. It's a terrible problem for some of them getting into the hospital. The parking's dreadful. It's very convenient for them to have a telephone consultation with one of our urogynaecology specialist nurses. They're clearly not getting an examination as part of that. If they're reporting symptoms, they'd be brought back for a review and clinical examination, but if they're symptom free and they're happy, they wouldn't be examined.
- Julia Cumberlege: With great reluctance, I'm afraid I'm going to have to bring this to a close because we've got another meeting we've got to go to, and I'm so sorry, I don't feel that, Mr Walker, you've really had a chance to come in.
- Roger Walker: No, no.
- Julia Cumberlege: Any further thoughts you have, we - you are very welcome and perhaps you could send by email or whatever. We welcome that. I'm sorry about the timing. I know it was changed and I'm sorry about that. So I'm just going to ask my colleagues, first of all, have you got any other questions?
- Valerie Brasse: Just a very quick one. It has been mentioned to us that where there has been a mesh removal, one of the complications is hernia repair needing to be done. How common is that, and for a woman who's had mesh taken out who doesn't want to have mesh hernia repair, does she have much option?
- Natalia Price: Well, that comes to the question of decision-making, how far you go if you do mesh removal, and it leads to - the patient needs to be counselled about it. This is why I'm coming back to this. Decision-making...
- Valerie Brasse: I don't know how common it is that happens.
- Natalia Price: Yeah, well, that would be like this - any surgeries will be a risk of incisional hernia following any surgery, laparoscopic, open, tunnel... There's a point

we have to make. So decision-making about mesh removal, particularly when it needs to be weighed very carefully against benefits, risks. The outcome of this type of surgery can be unpredictable. It cannot guarantee complete resolution of the pain, and we need to balance this against the risks such as incisional hernia.

Valerie Brasse: Does that happen reasonably commonly? I have no idea of the scale of that.

Roger Walker: I have to say, I haven't commonly seen a huge recurrence in...

Natalia Price: I think it's fairly rare.

Valerie Brasse: Yeah.

Roger Walker: ...prolapse or hernia after mesh removal, and there are non-mesh related options for surgical repair.

Natalia Price: Correct, yeah. It's relatively rare but it's still morbidity, and one case in 100 is bad enough for this individual. So yeah, the risk/benefits need to be weighted very carefully.

Simon Jackson: The main problem is recurrent stress incontinence and how you then manage that.

Valerie Brasse: Fine.

Cyril Chantler: It's merely an observation, I think it's terribly important to make sure that, as a doctor, you actually have a lot of influence over the doctoring. One advantage of having a proper database connected to a register is it could empower the doctor-patient relationship so that you can actually then find measured ways of following up your patients and they have measured ways of contacting you when things go wrong. Do you think that's a reasonable observation?

Linda Cardozo: I think a lot of our doctoring skills and abilities have been taken away from us and I think it's much harder to do that now than if you'd asked me 20 years ago.

Cyril Chantler: I agree with you because some of the scenarios you describe would not have happened to me...

Linda Cardozo: So I think...

Cyril Chantler: ...but I understand where the tensions arise, but one advantage of having a properly constructed register - and we did have that for kidney transplants,

I'm sure, but the numbers were much, much smaller - is it does give you the capacity to maintain a relationship both ways into the future.

Linda Cardozo: We can all take our own data off the British Society of Urogynaecology Database, either for our Trust or for us as individuals, and we can all report those data to our patients over the last 10 years. So I don't think - I think it's going in the right direction.

Cyril Chantler: Yes.

Simon Jackson: So a database the patients could access, too...

Cyril Chantler: You've got - yes.

Simon Jackson: ...would be great, wouldn't it?

Cyril Chantler: Yes.

Simon Jackson: Because you'd have a much richer database.

Cyril Chantler: That's it, yeah. That's it.

Simon Jackson: A sort of TripAdvisor for - it's - that would be fantastic, but it would require significant IT support from somewhere.

Linda Cardozo: Funding, and funding.

Cyril Chantler: We get that.

Natalia Price: So as the societies have - the British Society of Endometriosis Surgeons that I also belong to, they have a database which is open access, so a patient can enter the database. The only thing they have to have - patients have to have access and IT skills and emails, and some of our elderly patients who do suffer [unclear] skills.

Cyril Chantler: We're keeping - we elderly patients are getting there [laughs].

Linda Cardozo: Yeah, elderly patients have more time to access it [laughs].

Natalia Price: Yes.

Simon Jackson: You don't understand elderly.

[Laughter]

Cyril Chantler: Thank you.

Julia Cumberlege: Sonia, any questions?

- Sonia Macleod: Just a question, once the conditions of the pause are lifted, what level of mesh surgery do you expect to see?
- Linda Cardozo: Well, women are frightened now, aren't they? They've read the media. They've looked at the press. They see social media and they think, 'do I really want to have that surgery carried out on me?' To an extent, that's a good thing because as I said at the beginning, people became very enchanted by a seductively easy procedure, both for the patient, the clinician and the NHS. So I think being circumspect to the future is a good thing, but there will be a proportion of women, certainly, who will be very much relieved to see the reintroduction of retropubic TVTS.
- I think - I don't know how many of us you've spoken to, clinicians in female urology or urogynaecology, but I think that most of us will welcome being able to offer retropubic TVTS as one of a range of options for women with urinary incontinence who require a surgical solution.
- Roger Walker: I think, certainly in my practice, in our unit, there are a number of ladies who are still coming through the door saying, 'my mum, my aunt, my sister had this procedure, can I have it? I've heard the adverse media reports, but they're delighted and have had a wonderful life'. You give them the option, they say, I'll wait until this Review has ended and it's reinstated. So there are patients out there who are the other end of the spectrum from the unhappy patient who...
- Linda Cardozo: To put it in perspective, any prosthetic device has a complication rate. Look at what happened with hips when they were introduced and how awful and terrible press they got, and now we take it for granted that people will have a prosthetic hip, prosthetic heart valves. They're all widely used and they all have a significant complication rate.
- Cyril Chantler: I have one.
- [Laughter]
- Linda Cardozo: Which, the valve or the hip?
- Cyril Chantler: The valve.
- Julia Cumberlege: Oh right. Any questions from us? I'm sure you...
- Linda Cardozo: No. I'm very grateful to you for seeing us and I hope that we've given you views that will be helpful in drawing your conclusions. I think we would all very much welcome the pause coming to an end, or at least knowing when it's going to come to an end so that we can give patients realistic expectations.

Julia Cumberlege: Especially when the five conditions to increase safety are met, because we all share the view that we want as safe an NHS as we can possibly get.
Right, any...

Simon Jackson: Just a quick - is it within your remit to also talk to women who've had good outcomes from mesh? Is that part of the picture you're getting?

Julia Cumberlege: We haven't certainly set out any sort of communication to attract them, but in the course of one's ordinary life, I've certainly heard a number at conferences and things like that.

Simon Jackson: Clearly you know this, but it will be skewing your view significantly, I think, if you are only speaking to the women who've had a poor outcome.

Julia Cumberlege: Well, we certainly believe in the cautionary principle, first do no harm.
Thank you very much indeed. Thank you for coming.

END OF TRANSCRIPT

2nd May 2019

Session 1: Department of Health and Social Care (DHSC)

START OF TRANSCRIPT

[Part 1]

Julia Cumberlege: Perhaps I could just start by introducing ourselves. Because as you are aware this is going to be screened and its - I hope you're happy with that.

Sir Chris Wormald: Yes. Of course.

William Vineall: Yeah.

Julia Cumberlege: Okay. So, I'm Julia Cumberlege and I was invited by the previous Secretary of State - Jeremy Hunt - to chair this Review into three different areas. First of all, of course we're looking at HPTs - hormone pregnancy tests - we're looking at sodium valproate and other medications involved with that - and then with surgical mesh. They are very different areas and perhaps later on you would agree that we could start with some general questions and then we could have the HPTs - the hormone pregnancy tests - and then we'll have a break.

Then we'll have sodium valproate and then mesh and then wrap up questions.

Sir Chris Wormald: Yes.

Julia Cumberlege: Does that sound alright?

Sir Chris Wormald: Yes of course, I mean clearly, we're touching on clinical matters. You will be better informed if...

Julia Cumberlege: Yes of course.

Sir Chris Wormald: ...the Chief Medical Officer was with us rather than just William and I remembering what she has said to us on the subject, so. So, we may at times say that question...

Julia Cumberlege: Yes.

Sir Chris Wormald: ...will be better addressed by Sally.

Julia Cumberlege: Fair enough. So, I'm not sure if you've met Valerie Brasse who is our Secretary and she's on my far right and Simon Whale who's the third

member of this panel, with Sir Cyril Chantler who is the deputy to the review team. Sonia Macleod - Dr Macleod - who is our senior researcher.

Sir Chris Wormald: Yep.

Julia Cumberlege: So that's us.

Sir Chris Wormald: Yep.

Julia Cumberlege: So perhaps if I could just start. You are very aware of the activities that we've been carrying out - going around the country...

Sir Chris Wormald: Yes.

Julia Cumberlege: ...talking to a lot of patients, hearing their stories and also, we've been filming oral evidence and that is on our website for those people who want to have a look at it and see what we're doing.

One of the things that's come across very strongly to us is that there has been a bit of a breakdown of trust between patients, doctors, surgeons, some of the organisations and so on. So, we've been very, very careful to be as open, honest, transparent as we possibly can be so that people know what we're saying. Nothing is secret.

Sir Chris Wormald: Yeah.

Julia Cumberlege: We're just really - as I say - being as transparent as we possibly can. So, for the sake of the screening that we're doing today, it would be very helpful - but if perhaps you could just say who you are so that it's on there and people know who they're listening to.

Sir Chris Wormald: Of course. I'm Chris Wormald. I'm the Permanent Secretary of the Department of Health and Social Care, which I have been for almost exactly three years. May 2016 I started in this role - and just for completeness and to state the obvious - we're in a slightly different position than many of the witnesses that you've talked to because it was of course our Secretary of State - via us - and particularly via William - who will introduce himself in a moment - who sought to establish the - convene the panel in the first place to address exactly the issues you have just...

Julia Cumberlege: Thank you.

Sir Chris Wormald: Just described. So, to that extent we are of course conflicted but to the extent that - you know, our purpose here - is simply to assist the panel in any way we can on the facts of your deliberations. We come with no agenda other than to seek to assist the panel that we set up in search for

the truth. As I say, by - almost by definition that the Secretary of State wished to establish an independent panel to look at this - is a statement that there was truth to be found that was not found previously, if you see what I mean.

Julia Cumberlege: Yes.

Sir Chris Wormald: So, in terms of what you've said you have been doing, that is of course exactly what we expected. My colleague...

Julia Cumberlege: Can I state of course we value our independence.

Sir Chris Wormald: Yes, well.

Julia Cumberlege: [Unclear].

Sir Chris Wormald: That is the whole point.

Julia Cumberlege: Yes, thank you.

Sir Chris Wormald: Yes.

William Vineall: So, I'm William Vineall. I'm the Director of Acute Care and Quality at the Department of Health and Social Care. I've been in this post for just over three years and I've worked in the Department since 1998 and before that I worked in the NHS. Obviously - as Chris has said - we are the part of the Department that commissioned the inquiry from yourself - as you know, Julia - and obviously the role I'm in here today is - along with Chris - to give answers to questions and policy positions and all of those other things.

Clearly just for the purpose of the audience, it's then for you to return the report at a future stage and for us to take it forward from there. So, I am playing a slightly different role today from the sponsorship role from when we set up the inquiry. As you know - for the record - the person in my team who is the day to day contact for the inquiry is Jason Yiannikou who is one of my deputy directors.

Julia Cumberlege: Right, well thank you very much indeed. So, if perhaps I could just start by some general questions really. You will be very much aware because - if you've had a chance at all to look at the website and seen some of the interviews that we've had with patients. Certainly, we've had a huge amount from them. They have campaigned and they have lobbied in parliament in order to bring this thing to a head, to get the Review established and clearly they've been talking to ministers and indeed the Secretary of State.

So, my question to you really is why has it taken so long for these issues to be taken so seriously and for the Review to be set up?

Sir Chris Wormald: Right well I'll start on that question and then I'll ask William to add. As I was suggesting before, the very existence of a panel is a statement that things were not in the position that we wanted them to be. It is obviously - I was about to say - I'm not quite sure what the right word is. It is not an unusual step to set up a panel. Indeed, we currently have different types of inquiry - I think there are four currently running - in health. So, it is an established part of the health landscape.

But it doesn't happen when - as a statement of the obvious - when the standard systems for ensuring the right response to patients and safety have done their job. It's almost a statement - it's almost a circular statement isn't it? You only establish an independent inquiry when you believe that new light is to be thrown on a subject.

Therefore, it is always a question of why was this not spotted before and why is the panel needed, as it were. So, to that extent it's slightly unanswerable. On the specifics - however - of this, I think in all three cases - but William will...

William Vineall: Yeah.

Sir Chris Wormald: ...give further detail. There was action being taken. From our reading of the evidence - and I should say - whenever we say our reading of the evidence, we set up the panel because we wanted somebody else's reading of the evidence. So, it is not - to that extent the Department doesn't have a view other than we want the panel to do its work properly.

But from our reading of the evidence, there were actions in the system - sometimes disputed - but actions in the system on all three of these issues and therefore the question is more not why was action not taken, because it was. But was that action sufficient. Crucially - as you have already pointed to in your question - did it take sufficient account of the voices of patients?

Julia Cumberlege: Could you just tell us then what sort of actions that you think were taken?

Sir Chris Wormald: William - do you want to...

William Vineall: Yeah.

Julia Cumberlege: Or ask William perhaps.

William Vineall: In terms of the actions...

Sir Chris Wormald: Actually, we'll do this on two levels.

William Vineall: Okay.

Sir Chris Wormald: If you want to do it on the individual cases and then I will say something about patient safety overall is probably the most helpful.

William Vineall: So I mean obviously on mesh we took a range of action after it first came to light in 2012 - realistically through Bruce Keogh - to try and address some of the issues that were being raised in terms of there was a mesh working group, there was an interim report in 2015. There was a final report two years later that the clinical quality improved, data improved, patient information in terms of leaflets. Then there has since then - in a sense - your involvement, further data has been published.

The NICE Guideline pulling together all the various guidelines on different kinds of mesh has been published and a number of decision aids for aiding and abetting public individual debate with clinicians on these issues.

So, we have taken action but as Chris says, clearly there was a head of concern amongst patients that - and with all of those activities - probably wasn't being sufficiently recognised. There were various systems in place to capture it - which I won't go through now - but at the same time, there needed to be a more effective way of listening to that side of the equation - if you like.

There is clearly the evidence, there is the advice, there are the processes. But then there are the patient voices as well. Obviously, the Secretary of State felt at the end of 2017 that - notwithstanding the other things that have been done - there needed to be a way of hearing those in a much more systematic way than we had done before - which is why we called the inquiry.

Similarly with valproate, I mean as you know there have been sort of growing warnings since it was a popular anti-epileptic in the '70s and '80s about doing further work. There was a review led by the MHRA in 2014. But following that there was still concern that the advice that they'd done to - I mean effectively start to restrict the use of valproate - had not gone far enough.

So obviously last year there was a further more rigorous review that led to the pregnancy prevention programme that says beyond knowing the risk and there being a clear and obvious clinical indication to provide that - I'm not a scientist - we should try and wind down the use of that particular intervention.

There were also questions - at that time - about the MHRA looking at the question of packaging and leaflets and making sure that that was sufficiently thorough. So, I think in both of those cases, there has been progress made. But again, the question of how adept the various systems we have were at taking on board the patient voice - at an appropriate time, not retrospectively - was clearly the issue that motivated the previous Secretary of State to announce this inquiry.

So, I think - I suppose in summary I'd say there's been progress but there is clearly the issue outstanding about how you bring the patient voice into those other activities at the same time and not necessarily retrospectively or after having to have a further push.

Julia Cumberlege: I mean part of the Review of course is going to be looking forward.

William Vineall: Yes.

Julia Cumberlege: To see how we can do things better...

William Vineall: Exactly.

Julia Cumberlege: ...than the past but just looking at the past, I mean with mesh the campaign groups have been going for over 10 years. I just wonder how we can pick up some of those issues much earlier and listen to what patients are telling us. Because clearly, they weren't picked up over all that period. If you look at valproate - valproate was known to be teratogenic and it was - that was when it was licensed in '73 - but it's actually taken until 2015 for real action to be taken by the EMA.

Now that's 40 years. Forty years is a long time when babies are being harmed and that parents are having to look after very disabled children. Again, if you look at - certainly Primodos and the HPTs - they were put on the market a long, long time ago and it took from '78 to '14 for a government review of the evidence. That was by the MHRA.

So, certainly everything has taken far too long, and we would welcome any thoughts that you have about how things like this could be speeded up and that really in the future these sort of tragedies won't happen.

Sir Chris Wormald: Yeah, well shall I say something about patient safety overall on this. I should again state the obvious. I will describe what I have observed since 2016 and then what I have been told about the previous period - most of which are the ones you describe.

Now, at the top level - again to state the obvious - in something as complex as a health system - making a billion prescriptions a year and you know all the numbers - there will be mistakes and there will be accidents.

So, our starting point is we need a set of functions that minimise the chances of those happening and then - exactly as you say - respond quickly when they do so. It is a battle never won. New patient safety issues come up all the time, partly because - of course - we invent new treatments which have new side effects and new responsibilities on clinicians to deal with.

I think it is fair to say that it is reasonably widely acknowledged that Jeremy Hunt brought a focus to patient safety in terms of national policy in a way that was - again - it's slightly difficult to find the right word. Because it is not - and I do not mean to give the implication that the previous minister did not take patient safety seriously - as I suspect - well you would know - that every minister who serves in health takes these issues seriously.

But I think it is reasonably widely acknowledged that Jeremy brought a new policy focus to patient safety, particularly post - the Mid-Staffordshire question which brought these to light very quickly and has some of the same characteristics of who was listened to and when were they listened to and how did the system then respond. Certainly, what we have seen over the last seven years has been a lot - actually - of new policy and new initiatives around patient safety which have done various things.

A lot of those initiatives have done big things in their own right.

Julia Cumberlege: Sir Chris I think we absolutely agree with you.

Sir Chris Wormald: Yes.

Julia Cumberlege: It is a very complex area.

Sir Chris Wormald: Oh, yeah.

Julia Cumberlege: One of the very difficulties that we've had - and I'm sure that you do in your department...

Sir Chris Wormald: Yeah.

Julia Cumberlege: ...is actually finding some of the facts out. For instance, we just don't know how many women took hormone pregnancy tests. We don't know how many people are affected by foetal valproate syndrome and we don't know how many women have had mesh.

Sir Chris Wormald: Yeah.

Julia Cumberlege: Now, the system really - I think you would agree - needs to be quicker and more thorough...

Sir Chris Wormald: Oh yeah. No, so this is...

Julia Cumberlege: ...and we really do need the facts and for us in the Review, that makes it very difficult.

Sir Chris Wormald: Oh yeah.

Julia Cumberlege: ...when we're trying to think of the future because we don't know how many people have been involved.

Sir Chris Wormald: No, I think that's - I think that's absolutely correct and this is what I was coming on to. Now, clearly we can't reinvent the past - some of those things - if the facts don't exist, they don't exist and that is an issue that we all have to deal with (a) in terms of making the best of what we do have for right now and (b) ensuring that we have the right systems going forward.

The other thing I was going to say about our initiatives and focus on patient safety - and I know this has come up in other hearings - is it has created a lot of action - a lot of focus - but actually a very complicated landscape. Which I think you were pointed to before. We are very conscious - in the Department that - as I say - the work on this area is never done. There will not be a day when we say, now we have the right system for patient safety and it's all fine. We have been doing it as an evolutionary thing.

So, the most recent thing - the appointment of - it was one of the last things that Jeremy Hunt did actually. The appointment of a Joint National Patient Safety Director across - who is both an employee of NHSE, NHSI and a Deputy Chief Medical Officer in the Department - was a - I think the intention - as I say we're only a year into it so we will see if it works - the intention was to create much more of a single point of focus for patient safety work. Which while recognising that we do actually want lots of bodies that look at patient safety from a different angle, that has to come together somewhere.

As I think you know, his intention is to produce a national patient safety strategy in the summer.

William Vineall: Yeah.

Sir Chris Wormald: Which he's working on at the moment. Where we do need to address exactly the questions you are raising. So, where we need to improve our

data systems, that needs to be in the strategy going forward. Where we need to improve the training and development of clinicians, have some of the conversations you've been talking about - that needs to be in the strategy. So, we do need to look across this thing and we are conscious - and what we would expect - is that the recommendations you will eventually make become part of that strategy.

But there is a lot more to do in these areas to ensure that the problems of the past you are pointing to are not also the problems of the future. So, I don't think there is anything between us and you on that sort of diagnosis of the overall problem.

Julia Cumberlege: No - well...

Sir Chris Wormald: What we would say is there has been sort of long evolution of this over the last six years - which is not necessarily to say we've got it right.

Sir Cyril Chantler: Can I come in at this point.

Julia Cumberlege: Sir Cyril, yes.

Sir Cyril Chantler: William, excuse me. Because I think the answer you will give me will be better informed if I actually have the chance to ask you this question. We are aware of a large number of organisations that either directly or indirectly report into the Department of Health, all of which have interests in the care of patients and the safety of the National Health Service. I mean there are I don't know how many people who have regulatory responsibility in the NHS - but we think there are over 100 of them. I mean there are an enormous amount.

When you look at the landscape of NHS Improvement, NICE, NHS Digital, Health Education England, NHS Resolution, NHS Business Authority, Blood and Transplant - Blood and Transplant Organisation. I mean we can see a hierarchy where they report in and - but what I can't see is the cross connection.

So, as well as the risk of vertical disconnection amidst the terms, you have the risk of horizontal disconnection and how much is that a policy problem - and if it is what do you think should be done to...

Sir Chris Wormald: I'll say - I'll say two things.

Sir Cyril Chantler: ...ameliorate it?

Sir Chris Wormald: I'll say two things and then I think - I mean the issue you point to is a real one - you will be unsurprised to hear me say. It of course arises across a

range of policies - not just safety - and we have of course been doing things across the board to try and bring greater co-ordination to those things. Particularly the current proposals - in implementation - to bring together the work of NHSE and NHSI into a single thing. To then integrate - particularly Health Education England - much more into the same thing. Which is a recognition - not particularly of the safety issue concern - but the general issue. Because - as I say - it applies across policy.

What I've just mentioned - having a national director of patient safety who works across organisations and a single strategy - is also a reflection of exactly what you say, now...

Sir Cyril Chantler: Do you think patients are properly represented within those structures and in your solution?

Sir Chris Wormald: I think that's a - I think that's a good question. It again needs to be reflected in a proper, national patient safety strategy - you will be unsurprised. The only thing I would add - before William comes in - is of course that - what you've just described is quite a recent structure - it's a since 2012 structure brought in by the 2012 Act. Which as a deliberate act of policy - as you all know - took the view that you should disaggregate the health system and not have single pinnacles of power was the philosophy of the legislation. Now...

Sir Cyril Chantler: Mind you, some of what we're dealing with goes back, well back...

Sir Chris Wormald: This is exactly what I was going to say.

Sir Cyril Chantler: In fact, it may not have made it any better.

Sir Chris Wormald: Well this is exactly what I was going to say. So if you're looking for causes of the issues that the Baroness was describing, it's difficult to - as it were - apportion them to a system that has only existed since really 2013 when - as you say - many of the causes and issues go much further back into history at a time when the NHS wasn't - as you know much better than I - much more hierarchical and strategic health authorities and et cetera, et cetera - and brought in to one place.

So, while - so sorry this is a slightly complicated answer - I completely recognise and agree with the issues you raise about the structure - and as I say, this is one of the things we want to deal with. But just as a piece of causation, it cannot be the root cause of some of the issues you have been describing because it hasn't existed long enough - if you see what I mean. Does that answer your question?

Sir Cyril Chantler: Yes, it does. Very helpful, thank you.

William Vineall: I mean on the post 2012 part of your question - Sir Cyril - I mean, obviously one of the things that the new patient safety strategy is looking at is to formalise the involvement of patients and indeed it was one of the issues - one of the criteria that is in Aidan's job description. So, we are trying to put that centre stage. I mean obviously the Healthcare Safety Investigation Branch was established partly to do investigations based on impact on people and impact on services both.

One of the reasons why we established that branch - which effectively reports into NHS Improvement - was because we had a run of investigations and inquiries - Morecambe Bay and Mid-Staffs and things that I worked on - and we were trying to put a piece of infrastructure in place - going back to your previous question, Julia - about actually trying to have more real time investigations.

Similarly, MHRA has now done some things to appoint a patient engagement lead and other things like that. So, I think - as Chris said - there are some things that we've done since 2012 to try and simplify the infrastructure that you described - Sir Cyril. There are things that we are doing to try and run alongside the experience of patients in the structures that we have. Obviously, some of the things pre-existed 2012 when we weren't as aware of those issues.

One of my roles in the Department is to oversee various investigations and inquiries as Chris said. I was at the Gosport panel on Tuesday - in my function there for the Department - where people - for a very historic inquiry - not to do with devices but to do with other aspects of care - were saying that what you needed at the time was an explanation in real time that allowed you either to put your mind at rest, or to be able to move on with some further activity.

Now the system of medical examiners - which I know was announced some years ago - but the National Medical Examiner was announced last month - Alan Fletcher - is trying to - will get to a position where once all the medical examiners are appointed - for non-coronial deaths - it is possible to have a small i... investigation and an explanation...

Sir Cyril Chantler: Can I interrupt you...

William Vineall: ...to the families at the time.

Sir Cyril Chantler: ... because we don't have a huge amount of time and I want to return to the patient voice - if we have time - in a minute.

William Vineall: Yes.

Sir Cyril Chantler: But there seems to be a tendency - you're as familiar as anybody with the line of things that have gone wrong. I mean, it's a whole litany. You mention Gosport, you've mentioned [unclear] blood inquiry that's going on at the moment. The answer has been to say, well we better put in something else to deal with it. HSIB is very welcome and it - but it - I think it's an excellent initiative - but they value - rightly - their independence.

The medical examiners are by their nature independent. [Unclear]. So the underlying question which I ask of Chris is how do you make sure that they link together so that if we take something you and I are familiar with - maternity - how do we make sure the investigation links to the support for families and links then to the learning? Because it's all about the cross-links.

Sir Chris Wormald: Absolutely.

Sir Cyril Chantler: Not about the verticals.

Sir Chris Wormald: Yeah, I think there were two things - and again William will - sorry three things. The first - and just to say it on record - the answer to your question is with intense difficulty. When you are dealing with an organisation of 1.4 million people, and all those treatments and all those different specialisms and all those different health settings. Exactly as you say - and rightly in my view - an awful lot of independence in the system. We would add to your list the General Medical Council - the division we have always had between the regulation of individual doctors being entirely separate from the State. I think rightly.

The regulation of institutions being largely within the State - be it NHSI or CQC or whatever - which is an historic division not changed by 2012. I think most people think that is right but creates exactly the environment that you do.

So, I don't personally - and so I don't think that's quite how it sounds. I'm not inviting the panel to disagree with me, but obviously it's one of the things we want from you as well - as you want my personal view. I do think creating things which are not the executive manager of the system but whose job it is to scan the whole horizon - in the way that we want the National Patient Safety Director to do - is very important. I don't actually think a giant hierarchy that all reports to one person [unclear] you don't have those measures of independence. I do think that.

Then the second thing - I think we may come on to this - I do think a lot of the issues we have seen are locked in how do we train clinicians? So I'm sure this is a point that Sally will make - she has made it to me before - is we have - we have already seen a complete revolution in how we train clinicians and people who work in the health system about how they relate to patients and duties of candour and all those sorts of things.

But an awful lot of the issues we're discussing come down to what was the quality of the original conversation and the informed consent between a clinician you have never met and a patient you have never met. You are never going to have a national system that guarantees that success. What will guarantee it is the professionalism of those clinicians based on how they're trained and how they're developed. I don't need to tell you this. But - so one of our questions going forward - we've made a lot of changes in that area. What further changes do we need in the light of the types of incident that you're - that we're - that you're referring to.

I don't know if you share this view - so while I do think that - certainly from what I have been told - the world has moved on considerably in that area in clinical education and those things - but there is still further to go. Is that a...

Julia Cumberlege: Yeah.

Sir Chris Wormald: ...fair summary?

Julia Cumberlege: Yes. We might want to go in with Sally.

Sir Chris Wormald: Yes.

Julia Cumberlege: When she comes in about the individual rapport, the trust, the whatever, between the clinician and the patient. I think what we're talking about here is something much wider.

Sir Chris Wormald: Yep.

Julia Cumberlege: We're talking about where you really have a campaign running.

Sir Chris Wormald: Yes.

Julia Cumberlege: With people who have been seriously injured and nobody has really listened to them. We're trying to sort of think how we can ensure that the patient voice really is heard.

Sir Chris Wormald: Yep.

Julia Cumberlege: Heard at an early stage.

Sir Chris Wormald: Yes.

Julia Cumberlege: Because at the moment, we know people are still being injured.

Sir Chris Wormald: Yes.

Julia Cumberlege: That is really unacceptable in the NHS, but I am going to pass on now.

Simon Whale: Yes, I mean can I pick up on exactly that point. So, I mean we've talked a lot about structure but there's more to this than just structure.

Sir Chris Wormald: Yes.

Simon Whale: So the - a lot of what people have told us - the many, many hundreds of people we've met - is that the system gives the impression of wanting to defend itself, or even deny that there's a problem when patients present concerns about a medication or device that's been used in their procedures.

Sir Chris Wormald: Yep.

Simon Whale: So, it's starting - the starting point - the sort of cultural or attitudinal starting point - as they would say, is one of defensiveness or denial. Would you agree with that?

Sir Chris Wormald: Um, well - the arrival of...

Julia Cumberlege: Shall we just welcome Sally.

Sir Chris Wormald: Yes.

Julia Cumberlege: Thank you very much indeed for coming. If you could just tell the camera who you are?

Dame Sally Davies: Right. Yes. So, I'm Sally Davies. I'm the Chief Medical Officer for England and most senior medical advisor to the UK Government. As Chief Medical Officer, I am an independent advisor, medical - particularly focusing on public health and emergencies.

Julia Cumberlege: Thank you. Yes, that's lovely. Thank you very much, so [unclear].

Sir Chris Wormald: So back to your question.

Julia Cumberlege: [Laughs] Yes.

Sir Chris Wormald: I'll answer your question strictly. Does what you describe happen in the NHS and has it historically happened? Yes, it has. Quite clearly, and we have a number of reports and reviews that have made that point about

institutional reaction and quite clearly when that does happen, it is wrong. Clearly the first thought of anyone who works in a health system has to be the benefit of the patient not the reputation of the institution or individual reputations or whatever.

So - and as I say - there are a number of incidents on which there have been reviews and whatever when exactly what you have described has happened. My understanding is that's true of pretty much every health service - health system - in the world and of course a lot of other institutions that are not health systems.

What I don't think I have ever seen the evidence to say - which is not to say it's not true - but I've never seen any evidence - is that that is the overriding culture of the health system. I don't think - unless...

Dame Sally Davies: I've not seen any evidence.

Sir Chris Wormald: I don't think we have seen evidence that that is the dominant culture and - as I say - I've only been doing this three years and that was well into a change of culture. The people I meet - both clinical and other staff - are dedicated to patient safety. That doesn't mean they don't always get it right. It doesn't always mean they have the skills to do it properly. But I never feel personally that I'm meeting people who do not have patient welfare and patient safety at the top of their agenda.

Now that is slightly different of course from the issues you've been raising about do people listen to patient voices well. Because - as I say - I don't tend to meet people where I'm not thinking they don't put the - they are not seeking to put the patient first. It's why I think - actually the - how do we train people as a system - so that they do have the skills to do that well - is one of the most important features.

So, I can't strictly answer your question on do we think that's the overriding culture because I don't think I have seen evidence either way. But as I said, I wouldn't deny that that has happened and happened historically. Quite clearly things like - in particular the duty of candour - that we introduced. After we - I saw we - before my time - I can't take any credit at all. That was a clear indication that we wished the culture of how clinicians related to patients to change, backed by a legal duty.

So, to the extent that clearly parliament and others would not have thought that needed to be a change unless there was a problem. There was clearly a problem in the system - I continue to - I like to think on the basis of people I've met - that most excellent doctors and nurses and et

cetera - that's how they wanted to relate to patients anyway. But it was clearly a thing on which we needed to take action.

Sir Cyril Chantler: Can I just come in because I absolutely agree with everything you've said. Probably - pretty well everybody in the NHS is in it because they want to help patients. I was for many years the Chairman of the Standards Committee of the General Medical Council who was involved in the introduction of good medical practice.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: Which has at its centre the need for truth...

Sir Chris Wormald: Yes.

Sir Cyril Chantler: ...and transparency in the treatment - in the relationship of doctors and patients.

Sir Chris Wormald: Yep.

Sir Cyril Chantler: So, personally I regret the need for the duty of candour because I thought we already had it.

Dame Sally Davies: Yes, I agree.

Sir Cyril Chantler: But - putting that to one side - what I - we've said to the very large number of people that have come to see us - and institutions - is that it's been at the back of - now the forefront of our minds - that we're looking at three things that have gone wrong.

But there have been quite a lot of other things that have gone wrong over the last decades. William, you mentioned some others today. It's taken the patients to bring it to our attention. It's groups of patients - and who were then working with politicians - that has made the system - and I have to say my profession - pay attention. Somehow, that doesn't seem quite right to me. I just wonder...

Sir Chris Wormald: Well.

Sir Cyril Chantler: ...whether - I haven't quite finished my point.

Sir Chris Wormald: Sorry.

Sir Cyril Chantler: I just wonder whether it's because patients are simply one of the stakeholders in the National Health Service and we don't particularly recognise they're the reason for it. Whether we need [to find a different way of engaging the service with its purpose.

Sir Chris Wormald: Well, my first answer is you have far more experience of these issues over time than I do though not necessarily than Sally. So, I think...

Dame Sally Davies: No, he has more than me.

Sir Chris Wormald: So, I think there is a serious...

Sir Cyril Chantler: But your view of it.

Sir Chris Wormald: ...no sorry, I was going to come on to my view.

Sir Cyril Chantler: In policy terms [unclear].

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: I don't have that.

Sir Chris Wormald: Now. Yes. Now as I say, an awful lot of the patient safety initiatives and policies over the last five or six years have been predicated on exactly the type of analysis that you have just given. So, in terms of do we take these things seriously enough, I would say - as I say this has nothing to do with me, it predates me by several years - that thinking is coming much more to the forefront.

Are we at the end of the process of having a system which we think works properly? No, we're not, and we have more to do. The one thing I would add, however. When I look at quality systems in all sectors - and pretty much in all countries - there is a whistle-blowing and campaigning element to all of them. It would obviously be perfect if there never had to be a whistle-blower and never had to be people who raised concerns in the way that you've been describing. But I'm not aware of a single quality system that does not have in it a big role for how do we actually promote whistleblowing and people raising concerns in that way.

Then having systems within organisations and systems that deal with them. We have of course - as you know - and I repeat - done a lot on how we deal with whistleblowing. Still more to do. So that does have to be part of the system. The question that we all need to address is, is there too much reliance on that for people who are not in the system itself to be raising concerns. As Simon's question was pointing towards, has the system been too reluctant to listen to it when it happens which was certainly the case in Mid-Staffordshire.

As Robert Francis and others found was clearly in the system. We think we've made quite a lot of progress on those things, but I would not dispute

with you that there is considerably - considerably more to do. Then can I just take it back to the...

Simon Whale: Just - sorry to interrupt. Just an observation on what you've just said. I think we'd all agree that there is obviously an important role for whistle-blowers - whether that's from inside the system.

Sir Chris Wormald: Yeah.

Simon Whale: Or people outside the system. What characterises the three things that we're looking at - different as they all are - is that people have had to fight for years and years.

Sir Chris Wormald: Yes, exactly.

Simon Whale: In one case, for decades and decades to get listened to.

Sir Chris Wormald: Yes.

Simon Whale: So, it's not just someone raising a hand.

Sir Chris Wormald: No absolutely. No.

Simon Whale: This is...

Sir Chris Wormald: Sorry...

Simon Whale: This is a chronic problem.

Sir Chris Wormald: Exactly. If I did not make myself clear, that is exactly it and quite clearly the system over time has not done that, as is shown by things like Robert's report.

William Vineall: Can I just add two points on the duty of candour - one of my teams was responsible for the introduction of it - led by me. Obviously as Chris has said, it's meant to be a [formal] break point in discussion in order that people are open. As you say, Cyril, it is a thing that would be expected anyway but it clearly wasn't happening.

Now, when it was introduced - which was the end of 2014 - so nearly five years ago - the expectation was that there would be a flurry of claims and a flurry of activity around the actual duty itself.

Now there have been some of those but there have been less than expected. I think that's partly because actually we have a piece of research ongoing about it so I can't give you the evidence yet. But actually, the system has taken onboard the point of the duty of candour which is how -

as organisations and systems - are we more open. Not do we tick the box every time we have a conversation with a patient. Or do we try and minimise the number of times it comes in to play.

So, I think the way the duty of candour has actually come through has been quite promising. My observation on that - because that came out of Mid-Staffs - so when I was on the other side of the table and I was the Secretary of the first Mid-Staffs Inquiry 10 years ago. This is an observation. It was clear that there are - there were elements within the arrangements there that when patients were saying a consistent message about something being wrong, it wasn't sufficiently acknowledged.

As Sir Chris said, we don't have the evidence - I don't think that is a carte blanche position - but in the instances where it is clearly people making a point - and regularly - there needs to be a better responsiveness. Now the duty of candour was saying no. Don't let it all build up and then have an inquiry. Something else. Actually, try and do it at the base point.

So, coming back to your point about the interactions of the system, I mean there are proposals that I think Aidan was starting to talk about. About being able to look at the various alerts that you have across the system horizontally to see what the problems are. But then there is the more fundamental thing - and probably the thing that does take longer inevitably - which is how do you change the attitudes in the one to one interactions where that is not ideal. Duty of candour is a contribution to that.

So, in a sense, the issues we're talking about are always going to operate at both the individual medical patient interaction and where things have got difficult at the organisation...

Sir Chris Wormald: I suppose the evidence we do have - because it does of course come up in CQC inspections. So, we would be able to tell, and certainly my understanding is outstanding Trusts tend to be the ones that do these sorts of things exceptionally well and at the other end of the scale do not. So, I suppose at an individual institution level we are [unclear].

I mean the other point I was going to make on your point was I was at a medical school a few weeks ago watching future clinicians be trained with actors on how to deal with patients. As it was explained to me, that was not what was happening even 10 years ago and certainly not 20, 30 years ago.

Sir Cyril Chantler: It happens within a few yards of where you are at the moment.

Sir Chris Wormald: Yes. Sitting right now, yeah. That - those changes in medical training to focus on - you know that - is the patient at the centre of it in the way that you describe - as I understand it, that is a very different way of training future clinicians than would have happened for the clinicians who were dealing with the situations [unclear]. Is that fair?

Dame Sally Davies: I think you were responsible weren't you - from the GMC - for pushing for this? I have to say, my younger daughter has just passed her finals and she is much better prepared to be a good doctor than I ever was. The way that she has been trained to communicate with patients is around engagement and listening. She did get 97 per cent in her communication skills which she proudly told me.

But also, our understanding of prescribing and the impacts of interventions. Because as I think about all these issues, I think we've got a number of different things at play. One is something about the culture of - locally - whether it's in a hospital or a practice - and we know that they can fail, or we know with good leadership they can have a really good culture.

To be open and transparent takes not only culture - which means attitude - but time. Because to respect a patient and give them time, you can't be pushing them through. You have to actually spend time with them. It is also about understanding where they're coming from. If they come from a different culture - I mean I had a wonderful - and my subject's sickle cell disease as Cyril knows - I had a wonderful set of nurses who would say, you didn't get that right because you didn't know this about our culture.

They'd pull the patient back in and I'd start again and have to say, I'm really sorry my nurse says I didn't know that bit, so can we talk about this in a different way. But you need - we all need it - help in that. I think that for doctors to be that open, respectful and everything needs managers to be on their side. I come from a hospital that was famous - Central Middlesex - for working effectively with managers. Guys - thanks to Cyril - was effective. Many are. But not all of them.

Again, the ones where that works well are the successful hospitals. The ones where they don't work well are the ones we all worry about. So, we're talking about pressure, and the pressures that are put on managers that they may transmit which then gets in the way. How do you know when to stop the clock and say, look we need to mediate? Whether it's starting again.

I mean I have been known to say to patients, I don't think this works. Why don't we transfer you to a different doctor because I'm not managing to

work effectively? Only one ever did transfer, because if you're that honest they think it's worth pursuing it I found. But getting in someone else to help mediate or open it up. Opioids is one of the issues of the moment. I had a sickle cell disease - there's a big issue about opioid use...

Julia Cumberlege: Dame Sally, I mean we don't disagree with anything you're saying. I absolutely take that on board. But before you arrived, we did say that to begin with we wanted to talk about general questions and we've more or less covered the areas that we wanted to discuss with colleagues across the table.

But we now really want to go into specific areas. We're looking much, more broadly now. We're looking at hormone pregnancy tests. This is one of the three areas that we've been asked to consider by the previous Secretary of State. You were talking about time and I absolutely appreciate that time is of the essence, whether it's with the individual or whether it is on a much broader scale.

But if we look at hormone pregnancy tests - and perhaps we've been concentrating quite a lot on Primodos as one of them. It's interesting that the families have lived with the uncertainty - and the guilt and the hardship - for at least 40 years over the use of these tests.

Now we've heard a lot from the families - both with hormone pregnancy tests - with Primodos - and also with sodium valproate - that they feel really guilty that they took this medication, and the result has been children which they are now having to look after.

So really, we are very concerned that it has taken so long - 40 years - for these things to come to light and for action to be taken. So, we really would like to explore with you the science and the regulatory decision-making which takes place - or doesn't take place. Because obviously one of the most important things within this Review is to try and stop these things happening again.

So, how - what are the mechanisms? How can we ensure that things are seen at a much earlier stage, that action is taken? We've been talking before you came in - Sally - about the structures within the NHS and how they are very vertical and there's hardly any horizontal links. Now, clearly if we're going to make real progress in these three areas - with sodium valproate and with mesh - we've got to think differently. We've got to see what we can do in order to anticipate some of the things that could happen and also the things that are in very early stages that are causing so much grief and suffering.

So, we'd love your ideas.

Dame Sally Davies: So, I'd like to make two general points. First - as not only an apology that I couldn't get here earlier - but actually clearly, I find these stories very distressing. It is terrifically sad that these women and their families have suffered and that it has taken so long. So, I too abhor this.

But the other general thing I was going to say is I don't think we have explained to the public - and I don't think doctors are very good at it - that effective medicines and interventions usually have a side effect profile. Even now, it's very difficult to do an effective consent. I think consent has failed in most of these women - so I'm talking at a general level. I actually agree with [inaudible] who believes that you never truly have informed consent because you can never know everything.

Having been a patient - as most of us have at some point - I think she has a point. But we are not good at explaining that effective medicines usually have a side-effect profile. Discussing that risk balance so the patient takes an informed choice and discussing the difference between the possible side effects of the intervention and the doing of the intervention. So, you know it's one thing discussing side-effects of statins. They very rarely kill, though having started with the Stevens-Johnson Syndrome clearly, they can - they border on that.

But when you're talking about an implanted device, it's not only the safety of that particular device, it's also the practice of the person itself - I'll go back to sickle cell. Because I think these are germane to these discussions. When we started with pre-natal diagnosis, it was first done by amniotic fluid, then we moved to chorionic villus biopsy. The miscarriage rate was 20 per cent until the obstetricians learnt, we got it down to two per cent.

If you were in that learning curve, that was awful. But at least what we did - as haematologists would say - you know, you can have an early one but here's the risk profile, or you can have a bit later and it's much safer. As the risk profile came down, we changed it. but I think we have to be much more up front about all of that.

So, you're talking about Primodos in particular. Of course, this is - there are two big issues here. One that it's historical. So, it ante-dates Thalidomide and we brought in a whole new regulation system post-Thalidomide. I think it's helpful to look at what we do now, but looking back at that, you then have this disputed area about the science of if you did not miscarry and you went to term, did it cause foetal malformations? Having had a look at the literature, there's clearly an association. But is

there a causation? The Zebrafish work showed an association, but it was reversible when the author was quizzed.

The chicken data is not hard data and I looked last night at Carl Heneghan's work and even he said it's important to recognise that observational studies can demonstrate associations of harm. We've got an association. Concern about observational studies in assessing harm is due to the introduction of bias from the uncontrolled confounding and even after careful matching and adjustment for known risk factors, residual confounding may persist.

So, the group of experts who have been looking at this data - and looked at his paper - say, yes there's an association but actually there's no evidence of causation. So, what that suggests to me - and we would have expected if we had - prescribing to 1 million women - that with 1.9 per cent of births anyway having a malformation - 19,000 women would have had a child with a birth defect anyway.

So, what that suggests to me is that we haven't managed to have the transparent conversation at a point where they could have heard that and made them feel heard. As doctors we've all been party to discussions with patients when you think, if only my colleague had done this at the beginning, this poor patient and family would not have had all that distress.

I think there are two things. One is about the data and did Primodos harm, and there's an association, but we haven't found causation.

Julia Cumberlege: Yes, I think we're really well aware of that.

Dame Sally Davies: The other is, how was it handled and communication and then the third is how do we regulate now, and is it satisfactory now?

Julia Cumberlege: What is your view of that?

Dame Sally Davies: I think it's a pretty safe system. I feel that we need to always do more to make sure we are communicating better with patients. I'm perpetually surprised that since we've been putting in packet inserts since '99, patients don't generally read them. I always do, but clearly, I would. So, how do we make it that patients are better informed. I think that is about training. We know we have a number of consultants who are not trainable any longer.

Julia Cumberlege: When we look at the historic evidence, we've looked - what the MHRA said in 2014 and then the second - the expert working group. Now, both those reports have been severely criticised by the patient groups. There is a feeling that they were conducted by - or in collaboration with - interested

parties. So why do you think that those affected parties should have confidence in such investigations?

Dame Sally Davies: Well, I meet with the chief exec and the chair of MHRA on - generally about every six months - and I do discuss some of these issues. I have to say I saw no reason not to have confidence in those reports. I mean, if the patients have a problem then we must explore it. But it seemed to me that they...

Julia Cumberlege: Well they said that very clearly. Very, very clearly to the expert working group, to the MHRA.

Dame Sally Davies: Well, when I looked to the CMO, the panel looked to have the appropriate skills and backgrounds to make the judgments they did. I don't think it's for a CMO to second guess their outcome and their reports.

Julia Cumberlege: But you are ultimately responsible.

Dame Sally Davies: No. I'm an independent advisor. They are responsible and I think they are doing a good job.

Julia Cumberlege: But the MHRA are then accountable to the Permanent Secretary.

Sir Chris Wormald: Yeah and the way [unclear]. I'll make a reflection on Sally's points in a moment. The way we do it - as I say, it is an executive agency of the Department which we delegate the technical responsibilities. The Department does not second guess the technical work of our agencies. That's why they exist to be technically expert. We take a view on the overall effectiveness and accountability of those agencies. But we do not - and are not either - staffed or competent to look at individual products and decisions beyond what the CMO and her deputies do - who of course are medically qualified.

If I reflect on - and as I say, this is a reflection on what Sally has said - and goes to your question. We see a lot of evidence - starting with the respect that the rest of the world has for our system - in the technical competence of our regulatory system. It's regularly held up in other countries as being something to aspire to and of course the MHRA does an awful lot of work - or has done - for the European Medicines Agency, because it is seen as a leader in the field.

I mean, the question that the Chief Medical Officer is raising - and indeed your questions raise - which we think is a fair question, is is that technical competence matched by the ability to communicate and build the trust of patients to the same level as the technical competence. Which is almost the institutional version of what we were describing - or what we were

talking about - before. The relationship between an individual patient and a doctor. The doctor may be astonishingly technically competent but falls down on that conversation.

That can of course happen at an institutional level. That is one of the questions that I'm sure the panel will want to advise us on. So, we certainly have confidence on everything we have seen and [unclear] do the MHRA and indeed a lot of the other bodies that you have mentioned do the science and the technicals of this well.

The question that the issues and your questions raise - and indeed the whole existence of this raises - is has that technical expertise translated into a conversation - the correct conversation - with patients that has built trust, reacted quickly, done all of the things you describe as should have happened.

So - and this is simply my opinion - as I say, with no medical background and three years' experience of this - that that is probably - that's probably the area that as a system we need to improve on. Is that fair Sally?

Dame Sally Davies: I think that's well put.

Simon Whale: Can I just go back to what was happening at the time when Primodos was still on the market. So, in 1967, there was published prima facie evidence of an association - some association as opposed to direct causation. Nothing seems to have happened in terms of regulatory decision-making that that point. In 1970 the MacGregor Committee advised that the product should no longer be used for pregnancy testing and yet the product continued to be used.

As far as we can tell it continued to be used for pregnancy testing and at no point during that period - up until '75 - did women have the risks - or the potential risks - explained to them. Whilst it was a different era - I think we all accept that - would you now - looking back - say that things could and should have been done differently?

Dame Sally Davies: When I look back at that period - and I graduated in '72 - we had a very different system. I'm on record on television talking about being brutalised by it. By how my consultant colleagues behaved to patients which was in a paternalistic way and how I as a woman felt. We don't have a system like that. I mean it can be pretty brutal when you're young and you're faced with people that are sick and dying, but it is very different. I thought it was wrong then. I still think it's wrong.

But we have moved on. It was history, hierarchical systems and serious rationing.

Simon Whale: Do you think women should have been given more information about the risks?

Dame Sally Davies: Well of course I do. I think women should be - patients...

Simon Whale: But back then, I mean, sorry not now?

Dame Sally Davies: Well there were many things I thought patients should be given much more information about, so I join this with it.

Simon Whale: Right.

Sir Cyril Chantler: Sally, can I just go into the details of it because it's really important for thinking about the future. We now know - because we've been researching it - that there are records of concern by both the manufacturer and the system - it was the Committee on Safety of Drugs at the time. That's all changed. About the potential risk of Primodos in causing congenital abnormalities. Certainly - from my view - that by 1970 there was enough information there - in this modern world - for - on the precautionary principle - which maybe it didn't apply in those days. For patients to actually - women to be warned of the concern.

Even though it wasn't removed from the market. It was removed from the market in 1978 and we don't actually know why. It was - but those eight years a lot of women took the medicine and a number of them - whether it was causal or not - had damaged babies.

Now, I think what we would wish to think about is whether - given the concerns which were expressed within the system at that time - nowadays the present regulatory system would either at least warn people about the risk directly or maybe remove it from the market. We can't say, but I just want - are you confident now that the system wouldn't have allowed those eight years to happen without the women at least being warned about the anxiety that was felt within the regulatory authorities.

Dame Sally Davies: Yes, I have faith in the MHRA. I do think we've changed.

Sir Cyril Chantler: The Committee of Human - yeah.

Dame Sally Davies: Yeah.

Sir Chris Wormald: Yeah. I mean, I repeat my [unclear].

Sir Cyril Chantler: It's about openness you see.

Sir Chris Wormald: Yes. I completely...

Sir Cyril Chantler: It's about trusting the patients, not just condescending to them.

Sir Chris Wormald: Yeah.

Dame Sally Davies: I agree.

William Vineall: I mean I think if you look at - I mean you will probably know this - but if you look at the chronology of the 1970s there were some first indications in 1970 [unclear] remove the indication diagnosis of pregnancy from the data sheet following a recommendation from the MacGregor Committee. There was a Committee on Safety of Medicines review - which reported in 1975 - which advised prescribers not to use hormone tests for diagnosing pregnancy because of hazards. They published various letters in the BMJ, other places. Sent letters to GPs, family planning doctors, put it in the professional journals.

Now of course, that was in an era where it wasn't the norm at that time to have the open conversations about risks that are now much more prevalent. It was only in 1999 that the patient leaflets had to be published for all cases. It was eventually removed in 1978 by Schering - reportedly for commercial reasons - because in a sense medicine and the way you did pregnancy testing had moved on.

So - I mean - there was some progress made in the 1970s to start to look at the risks. The way those things were communicated -going back to the earlier discussion - but it's relevant - was through in a sense professional routes. It didn't particularly get out to the patient route.

That would be a different situation now.

Sir Chris Wormald: The only thing I'd add to my colleague - who I agree with entirely - I'm merely repeating what I've said in public lots of times at the Public Accounts Committee - [unclear] I never use the word confident. The word confident is a difficult and potentially complacent word. Our attitude needs to be ever vigilant. I say this about all issues in health and social care and I'm of course challenged to say I'm confident in X or Y all the time. That is always my answer.

But with that proviso that I always give - I agree entirely with my two colleagues.

Julia Cumberlege: Certainly, in his statement the previous Secretary of State - when he was launching the review in parliament - was saying that we didn't have to go into the science again. The science was ambivalent in terms of causation as

opposed to an association. But, so the MHRA - as I said earlier - in 2014 and also the second expert working group in 2017 - were looking at the evidence again and trying to make the assessments.

Now we were hoping that we would get some real clarification on this and it's good that the expert working groups were set up et cetera. But we still have a problem in that even what the expert working groups have come out with have been so criticised by the patient groups. So, if you're trying to build confidence, how do you do that if these very important groups - who are trying to decide on the science - how do you actually ensure that the patient groups have some confidence in what they have come out with?

Because at the moment they certainly do not have and I'm not sure where we go from here. Because we were looking to some resolution on both the MHRA and the expert working group.

Sir Chris Wormald: Well, I think in terms of - well I mean as you say we're not here to particularly replay the science and it's not the right set of people to do so - but what we're really talking about is that - is the thing about how science meets public communication. As you say, many of the areas - and we deal with this the entire time - the science only has value if it has public trust. I mean we have to have more than trust.

The advice we give - based on the science. So, what you're describing is one facet of a general problem. In terms of where we go, we just have to keep going and do better to be honest. If there was a magic bullet to how we...

Sir Cyril Chantler: One point we put to the MHRA - when they came to see us.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: Both Simon and I are members of the National Academy of Medicine in Washington. When they do reports, they put in place a peer review group to review the report independently...

Sir Chris Wormald: Yep.

Sir Cyril Chantler: ...before it's released, and we suggested to the MHRA that would have been the better way to deal with this.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: I think they - well I don't know whether they accepted...

Dame Sally Davies: I think that's worth looking at. The other one I think - I was going to suggest - that you looked at was what we've done with NIHR. Because we are the world beacon for patient and public involvement. We have a programme called INVOLVE. We train patients and the public in how to sit on committees. We train chairs how to involve them and listen and bring them in. They are part of every decision we take through NIHR. I just wondered whether it would be worth thinking about whether our scientific committees on the MHRA should learn from that experience.

Sir Chris Wormald: Yes, I mean certainly from my experience - which as I say is largely not in medicine - on these things. It is never one thing. It goes back to some of the questions that the panel was asking earlier. It is about having that whole culture of we have to do better each time. So, it will be exactly what you've described and then exactly what you've described and then it will be 15 other things and it will be every year challenging ourselves on the question of how are we making the science accessible and et cetera, et cetera.

Recognising that as we see - nothing to do with the three areas you're looking at - but we see this across - at the moment - science and public opinion as well - is that they won't always agree. The science will not always say what people want and give them the answers. All the [unclear] you say in some of these areas, the science simply won't be able to answer the question when what the public wants is a clear answer.

So, we have to recognise there will be those tensions but be sort of ever restless on the - what do they do in other countries that - where they do this better and what can we steal and borrow and go further and further. So, I do think - I don't think there is a single answer to your question but nor am I pessimistic that it can improve every year - that we have these problems is an incentive to try harder in my view. Where I have seen these things work it has been that culture of you are never in a position where we now listen to patient voice as well as we conceivably can. That's not an achievable state.

It has to be the culture that you've been describing of let us continually challenge and look for the next thing that will help build that public trust and that confidence. Which is partly about the communication skills of people from science and partly about - as you say - the systems that we use that bring people in but recognising that not everyone will always agree.

Simon Whale: I think that one thing that would help...

[Over speaking]

William Vineall: I was only going to say that one of the planks in the Primodos working group was about communicating to patients and the public with a number of actions for the MHRA specifically. Obviously although the working group was looking at Primodos, it was looking at the forward issues of - about how do you communicate risk, which I mean is true to Primodos and other things. So, although it was historic - Primodos was - stopped being given in 1978 - it was trying to say, okay so how don't we replicate those things that may have gone wrong in this particular instance in more general circumstances.

Sir Chris Wormald: Yes. The - and of course - oh sorry.

Simon Whale: Yeah I was going to touch on a similar point that - and it touches on what Sir Chris has said as well - that if you take the EWGs in relation to Primodos as the relevant point here - in order to give the patient group confidence in the process, it's not just in the science, it's in the process that leads to the science.

Sir Chris Wormald: Yes.

Simon Whale: I think their concern is - at least in part if not mainly - around process as much as it is about science.

Sir Chris Wormald: Yeah.

Simon Whale: So, involving the patient group more closely in how to do this.

Sir Chris Wormald: Yep.

Simon Whale: Not necessarily in the doing of it - because they're not equipped perhaps to do it - but in the how are we going to do this in such a way as to get everyone involved - including you as the patients...

Sir Chris Wormald: Yep.

Simon Whale: ...people who've suffered, confidence would have perhaps led to less criticism when the EWGs produce the work.

Sir Chris Wormald: Yeah.

Simon Whale: Would that make sense?

Sir Chris Wormald: That makes a lot of sense and in particular greater transparency is always part of the answer. But obviously - as I say - nothing to do with these three cases - but that feeling across public policy where you treat the public as grown up adults unable to understand difficult messages and have the

conversation bluntly and transparently, almost always makes the world better.

I mean the culture that Sally was describing from the 1970s was the sort of much more extreme end of - you know we're the experts, we know best. Your job as the patient is to believe the grand expert. That culture needs to go completely. Of course, you want your experts and of course you want people who are highly trained who know the answer. But acting in a way of - again it goes back to the sort of duty of candour - is our job is to be transparent about our expertise and have a grown-up conversation with people.

As I say, recognising that you may not agree and actually not agreeing is an okay thing as long as the conversation has been done properly and transparently. So, I wouldn't disagree with anything you've said.

Julia Cumberlege: We're always learning, aren't we?

Sir Chris Wormald: Yes, and as I say, battle never won is a very important phrase to me on this.

Julia Cumberlege: One of the things that we thought we might have a break now. I don't know if you would welcome that.

[Part 2]

Julia Cumberlege: So, we're now going to discuss the issues concerning sodium valproate and we just would like to ask you some questions on that. It's always been stated that valproate should not be used as a first line of therapy in pregnancies. I'm just wondering when the Department first became aware that this was being ignored and what action has been taken. We're talking about the - particularly the pregnancy prevention programme which we really - all of us - I think have tried to make sure that that's a foolproof programme.

But unfortunately, it isn't, and we know even now that some women are still taking sodium valproate when they are of childbearing age and obviously it's to fight epilepsy. We know all that. But we just sort of wondered how we can instil it in a much, much stronger way and ensure that it's not being ignored.

William Vineall: Look, shall I run through the broad chronology to start with, Julia? So, I mean - as you said - it's an anti-epileptic that's been available since 1972. In terms of harm, it may cause birth defects and they were first apparent in 1974 and the advice then was it should only be used in severe cases.

Obviously - as we touched on earlier - that was for doctors via the Committee of Safety of Medicines at the time. It wasn't necessarily communicated to the individual patient because that wasn't the way those information systems operated at the time. It was a popular anti-epileptic throughout the '70s and '80s. There were a number of warnings from the '80s onwards roughly about once every five or 10 years - about half a dozen - that continued to raise more seriously the issue of congenital malformations and birth defects and latterly autism.

These warnings led in 2014 to the EU wide review led by the MHRA which we touched on earlier which said the balance of benefits and risks remained favourable - caveated by the fact where other drugs were not indicated and new risk and [unclear] measures were put in place. As we said, the view by 2016 - when the MHRA did a communications exercise on the back of the review in 2015 - and published a toolkit in 2016 - was the fact that those warnings from 2014 had - probably hadn't had the desired effect.

That led to the review in 2018 which strengthened regulation with the aim to reduce and eliminate pregnancies exposed to valproate and I think in 2016 the figures - the calculated figures as best you could from the number of people - the number of pregnant women who were given sodium valproate - was between 240 and 550. So about 0.05 per cent of 28,000 people of birth giving age who had valproate at that time.

That led to the pregnancy prevention programme that said you could only be prescribed valproate if the patient knew of the risks, the patient was on contraception - if appropriate - and perhaps most importantly they were reviewed by a specialist prescriber annually. As I said earlier, there was some addressing of the fact that the messages on the packaging and leaflets hadn't been properly publicised.

The General Pharmaceutical Council put out a note last autumn trying to restate that information for its professionals. There were various articles that followed up in the autumn, and the MHRA and CQC I think at the moment are speaking about how the CQC - through its routes - can put out the messages of reinforcement. So, we're trying - so I suppose to summarise - it was a typical treatment in the '70s and '80s but concerns became aware in the '90s and the '00s.

In the last five to six years we've taken various regulatory actions. 2014 - probably not strong enough, 2018 further - to leave a de minimis number of people who are prescribed sodium valproate, but with an end point of eliminating that as a drug of choice for people who are pregnant.

Julia Cumberlege: Yes, I think you are right to use the word 'choice' because some of the patients we've talked to, they have said that if they were fully informed - if they had been able to give proper consent - they may well have actually made a different choice that was being recommended to them. It depended on the severity of the epilepsy and the impact that sodium valproate had on them and their lives.

I don't know if you want to pursue that, Cyril.

Sir Cyril Chantler: Because this is different from Primodos in the sense that it is...

William Vineall: Yes.

Sir Cyril Chantler: ...a generation later.

William Vineall: Yes.

Sir Cyril Chantler: I accept your timeline, but put it another way. It's 32 years since valproate was shown to be teratogenic and to cause congenital abnormalities. It's 12 years - up to 2014 - since it was shown to cause developmental delay. That is a long time before putting out very clear, specific warnings to potential mothers about the risks and pregnancy prevention programme. It's a long time to take to get to that position.

As we've listened to people, we've become worried about whether or not the present situation - which is now fully in train for valproate - is actually there to deal with other potential damage - drugs which might cause damage during pregnancy. One we've heard of is topiramate which is another anti-epileptic drug. We've been told that that - it may also cause teratogenic effects. Whether that is true or not I do not know.

But are you - are we happy that we have in place now a system for spotting early drugs that might cause damage to foetuses and to warn mothers accordingly?

Dame Sally Davies: So, there were some health warnings actually to professionals in '83, '93, 2003 and 2013. So, every 10 years. But that wasn't to mothers. Packet inserts went in in '99 and a pictogram in '17 - before this. But I think what you're getting at is something much deeper. I asked - and was told - that only five drugs are actually licensed for use during pregnancy.

Sir Chris Wormald: Sorry, is that five epileptic...

Dame Sally Davies: No, five drugs.

Sir Chris Wormald: No, five drugs. Right.

Dame Sally Davies: What we have done in research - as you will know - is we have limited research subjects to being in the middle of a – well, young or middle aged - but never children, never old. We've not used people who are feeble in any way, you know. We are excluded unless we are the objects of study, and we've excluded pregnant women. Until they are licensed and then people - the companies - can go and do more RCTs. So, we've relied on teratogenic evidence - and I think we should take that very seriously.

But it does raise a question as to whether - as a global community - because this isn't a British issue. This - remember that we work as part of one of the best regulatory systems in the world - the European one and the FDA have the same issues. But what are we going to do to try and get a pharmacopeia that works for pregnant women?

So, I think there's something about information and transparency but there's something much deeper about who's involved in research and all of that.

Sir Cyril Chantler: Also, it's not just about - I know you accept - it's not just a question of warning the profession, it's the mother that needs to be warned.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: I mean, we're not even completely sure we've got an effective system now - it's a darn sight better than it was since 2014 - but we are - and the patient groups have been fantastic in bringing this to our attention. Even the failure of the present system to our attention and raised with us the notion of whether there shouldn't be a register of women so we can contact the women directly through the system.

So, these are issues which have wider importance than valproate - important though that this - so we need to consider how we identify early drugs that might cause damage and how can we warn the mother not just the doctors. Because of course there are a lot - patients have lots of doctors these days, not just one.

Dame Sally Davies: I do think pharmacists have - could play a much bigger role.

Sir Cyril Chantler: They are doing in the valproate prevention programme.

Dame Sally Davies: Yeah.

Sir Cyril Chantler: But again, you're back to the person who really needs to know is the mother.

Dame Sally Davies: The pharmacists usually...

Sir Cyril Chantler: Yes.

Dame Sally Davies: ...have that dispensing role, so I think there's a role there. Sorry I've forgotten. I thought there was a role for someone else who could help too. When it comes back, I'll tell you.

Simon Whale: Just to go back to the point Sir Cyril raised about topiramate. So, we asked the MHRA about topiramate and it has similar - or it has teratogenic effects. There's no dispute about that. You'd expect a degree of consistency. So, if you're talking about two teratogenic drugs - valproate and topiramate - you would hope and expect that the approach to safety is consistent - similar or identical.

I think what we've heard in relation to topiramate is that it's not exactly the same. What the MHRA has told us is that they have put in place elements - as they described it - of a pregnancy prevention programme - but not all of them.

So, educational materials around the risks associated with topiramate don't exist. The risk profile is not articulated in the same way. So, the concern we'd have is that - I think you've touched on a major point about how do we make sure that women in pregnancy are able to take medicines they need to take to treat conditions not related to their pregnancy safely. That's a major and significant point but on the - in terms of where we are today - consistency between these drugs that have that effect ought to be something that women can take for granted. It doesn't seem that they can.

Sir Chris Wormald: I don't think we can - [unclear] I don't think we can comment on the second drug because none of us have come [proofed] on that.

Simon Whale: But in principle I mean...

Sir Chris Wormald: Well I mean in principle what you say is self-evidently true. Obviously, you would need to know the details of the effects of the individual drug and you would want whatever the rules and regulations around them to be specific to the concerns around that drug and proportionate to the balance of benefit and risks. I mean this case - I mean it is completely different from what we were talking about before because the science in this one is not in doubt at all.

It's obviously a drug that is only taken by people who've got some extremely serious medical condition anyway and it is one - therefore - one of those classic challenges that our medical friends face about how do you weigh up the benefits and the risks of a particular drug which - as it has

always been explained to me - there's a sort of general 'what is the approach to this drug' and then there's a very patient specific - that patient with that doctor having - as you started this a proper informed consent conversation. It's the interaction of those two levels that leads you to a safe system.

I mean I assume the MHRA is follow up the concerns you raised already if you have raised them with them. We will of course check that. But I don't think we can comment on that particular drug.

Dame Sally Davies: I think the other thing I'd say is we need a system - and I think the pregnancy prevention programme is one - where you have both the discussion, but you go away with something in your hand. Because my experience - both as a doctor and a patient - is you can have a good discussion, but you don't always remember - because it's so anxious - all the details. So, the bit in the hand is also very important. So, we need to design something that includes both.

Julia Cumberlege: We've been thinking about the mobile phone in the hand rather than something written. So that actually the consultation with the GP - in this case - or whoever - is recorded and then people can take that home and they can discuss it with their family and their friends and everybody else. Oh, we should have asked that question. What a shame. Go back again and then you've got a much better-informed understanding of the issue and the consultation that took place.

Sir Chris Wormald: Yeah.

Julia Cumberlege: Now, with modern technology that is actually very easy.

Sir Chris Wormald: Yes.

Julia Cumberlege: It seems to me that that is something we could be thinking about.

The other thing I just want to say, Dame Sally, I mean you're right that the pharmacist has a very important part to play. But in a way they're the fallback from the GP who prescribes it. We've been told that one of the problems with the GPs is they have so many alerts on their system that they can't take into account all the alerts. But they have a wonderful database in terms of the number of women who are registered with them who are of childbearing age.

I just don't know how we can actually ratchet this thing up so that it becomes more important.

Sir Chris Wormald: Yeah.

Julia Cumberlege: Because we cannot have women now still taking the drug and delivering babies that are disabled.

Dame Sally Davies: We all share your concerns and view. I also personally share your view about too many alerts. I'm frequently asked to sign off an alert in my name or someone else's. I basically say, no. Because I think when we send an alert - and I did send one on valproate - it's very important that it truly matters. Because then it will come through and people will see it. That's why we're reviewing the alert system because there were too many and too much going on. So, I hope that we will end up with a better system.

Because if you're pervaded by bureaucracy, another alert is yet more work and does it percolate, but...

Sir Chris Wormald: Yes. I mean this is well researched both in medicine and well beyond the sort of overload alert systems are [unclear] out by everybody. So, the warning light is always on therefore you ignore it. We've seen that in lots of transport as well as in health.

I mean again, there's no mathematically right answer. Because of course you have - as a public policy person - you have pressures in both directions. You have - as Simon says - lots of individual cases where a lot of people want you to issue an alert for perfectly good reasons. You know, from their individual perspective. Then you have effectively a pressure to say, well actually if it's more than 10 a year people stop reading them or whatever it is.

Now, as you can't solve those questions mathematically, it does in the end come down to a judgment.

Dame Sally Davies: Judgment. So, I have never given away the right to decide on [unclear] alerts.

Sir Chris Wormald: I mean the other thing we've been looking at...

Dame Sally Davies: I see it as my responsibility.

Sir Chris Wormald: ...again this comes with the patient safety directories, is of course there are rightly a number of people in the system who are entitled to issue alerts.

Dame Sally Davies: Yes.

Sir Chris Wormald: That's of course right. You want a diversity. You don't want it to be all the same person. But we do need to look at then how are they received. If you're getting an alert from a CMO and an alert from NICE and a - you know et cetera.

So, how you coordinate that whole system. I don't think the answer is to try and centralise everything in a single person because - you know - we're relying on a single person's judgment rather than a - it's not a market but you know what I mean. It's a - you know, having a diversity of people who are looking. But then you then have to make it understandable to your GP who is receiving things from different people on slightly different basis. Which is why it's right to look at all these things.

Julia Cumberlege: Are there lessons - do you think - that we have learnt from this in terms of are there other actions we should be taking to prevent this sort of thing happening in the future?

Sir Chris Wormald: Well, I think some of the biggest ones - I'll let William comment [unclear] on this in much more detail. I mean some of the biggest ones have been mentioned already. The - 'who are you actually communicating with' question - I think is a very big one for us. As you've already described - the traditional view of - well not just our system - but all health systems - is the communication route is solely down the professional channel. You are essentially trusting each doctor to pass on the relevant communication to the patients.

I think - for the reasons we've described - clearly the professional route is vital, but it can't be the only one. Partly for the reason you say around you don't always see the same doctor but also by definition that will build variability into the message - as any disaggregated system of communication would.

So, I think there's a big learning point from the story you tell about the direct communication which comes back to what we were talking about before. About treating people like adults who can take all these messages so that's a big lesson. What would you...

William Vineall: The other two things I was going to add to was going back on to the horizontal point. There's a question of having put out an alert, is the impact of the alert actually measured. Do you actually know that it's been received and complied with. It might sound like an incredibly obvious thing, but I mean it was certainly one of the challenges that Jeremy Hunt put back to us, was if you put things out, what's the follow up about the impact afterwards?

I think the committee that Chris was describing is thinking about whether it has those mechanisms built into its activity.

Sir Chris Wormald: Sorry, can I just butt in a moment because it's a very important point. It goes with the small numbers. Of course, if you have a small number of

alerts it is perfectly possible to track, did everyone do those 10. If you have a very wide system of alerts it becomes close to impossible without overwhelming people. People then not only have to implement the report but also have to then validate that they have done so. So, there is a balance in there.

Dame Sally Davies: So, I've sent out 102 since May 2010. When I look at what they are, they cover really important things. The use of antivirals every year. Turning them on and turning them off for flu, valproate, safe transfusion, shortage of adult hepatitis B, pseudomonas infections associated with cartilage ear piercing, deaths due to consumption of DNP. You know, fentanyl contaminated heroin, polio outbreak in Tajikistan.

So, they are quite selective but for - I think...

Sir Cyril Chantler: Antibiotic resistance?

Dame Sally Davies: I haven't found an excuse to send one.

Sir Chris Wormald: Various other things.

Julia Cumberlege: I think William...

Sir Chris Wormald: Sorry William, you want to say something.

William Vineall: Yeah, the only other thing I was going to say was obviously - I mean going back to the earlier theme - if you had each of the individual organisations who is contributing to these alerts - that they do have a patient and public involvement read into that at the outset - then you'd probably get a better-balanced message in the alert. I know one of the things that the MHRA is looking at is appointing a director to do just that. So that then becomes integral to their day to day activity and then gets reflected in how the messages get put out.

Because clearly - as you were all saying before - if you have that as a tag on afterwards, you've missed the point. Whereas if you have it integral at the start, it's more likely to have a resonance with the public and it then it may well affect some of the things the public have been saying along the way.

Simon Whale: Can I just raise a slightly different issue in relation to valproate which is that a lot of the families that we've met have spoken to us about the difficulty they have in accessing the support they need from - not just the healthcare system but also the social care system. Given they've got a child who's - and in some cases - many cases - more than one child who's affected by foetal valproate spectrum disorder.

One of the problems that they have is that the disorder is not formally recognised by the system. It's not seen as a condition by many - within the system - many practitioners and others within the system. Even in the case of applying for benefits - for example - they bump into a problem - a very significant problem - because it's not recognised as a condition. Has - well two points, (a) is the Department aware of that problem and (b) if so, have you been able to do anything to try and tackle it?

Dame Sally Davies: So, I became aware by reading this rather complex thing. So, there are two issues. One, of course the system basically runs on the International Classification of Diseases. I think we're on ICD 11 but I can't remember - which is set up by the WHO and having tried to get them to listen to something else on behalf of patients, I failed. They have a system, they work it and they throw it at us. So that then means we can't get a formal ICD 11 classification - in all likelihood - but how do we put it in to our system?

I hadn't known that until I read this, and I think it is a discussion we would have to take away. But actually, the more the families can talk about [unclear] the media, the more people hear it and then it becomes common parlance then the easier it is to do it.

William Vineall: I mean the other thing that is available - and I know this is obviously after the event - but people can go through the Special Educational Needs process to get support from local authorities to help with educational needs deriving from these cases. So, there is that as well.

Sir Chris Wormald: Which is of course now combined.

William Vineall: Yes.

Sir Chris Wormald: With health.

William Vineall: Yes. Which is now something that's come into our Department.

Simon Whale: Yes. I mean we've - obviously families have spoken to us about that pathway that they have to go through and it's challenging for all of them.

William Vineall: Yeah.

Simon Whale: Because it is not - for the reasons we've discussed - it's not a recognised condition, there are different elements to - different symptoms if you like of the condition. For example, autism. So, a child may well get considered in the context of autism rather than foetal valproate spectrum disorder - of which autism can be and often is a part of it.

William Vineall: Yes.

Simon Whale: So, they - so the system - and this applies in education as much as in health and social care - the system will look at that aspect without seeing a bigger picture that the family sees.

Sir Chris Wormald: Yeah, I mean having run both the education department and the health department - this is a challenging system for everybody and I mean we do think we have made a lot of progress about bringing together educational - special educational needs assessments - with health assessments into a single system. But I don't think anyone would say that that progress is finished.

Or that the system is user-friendly, as it were. So many people find navigating that system very challenging regardless of the condition. What you're bringing to the table is that there are some additional challenges in this particular thing which we will take away. So, I mean again we do think we are better than we were but we are in no way suffering under the belief that the system works to the benefit of everybody, yet.

Sir Cyril Chantler: So, Sir Chris can I finally ask you to take away something that I didn't think I'd have the opportunity to raise today. But suddenly a gap has opened up where I can't stop myself going through it.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: These families have to work under huge stress. Some of that stress is about the benefit system. That's not what we're going to talk about today.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: They've had problems about getting the specialist help they need - and we're talking to NHS England about that. But getting education linked to health is a real problem...

Sir Chris Wormald: Yep.

Sir Cyril Chantler: ...for children with long term conditions.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: Now, we were involved - Baroness Cumberlege and I - on the policy board when the NHS number was introduced.

Sir Chris Wormald: Yep. Which is different from the education number.

Sir Cyril Chantler: I know. You know better than I do. But we finally persuaded local authorities and social services to use it for child protection purposes.

Sir Chris Wormald: Yep.

Sir Cyril Chantler: But we've completely failed. I and others - and there's a group of us - and it's nothing to do with this - to get the Department for Education to record the NHS number in schools. So, with permission - under proper circumstances - we can link the health and education needs of children with asthma, epilepsy, valproate and other long-term conditions.

Dame Sally Davies: Sickle cell disease.

Sir Cyril Chantler: So, it would be such a help. Now I don't expect...

Sir Chris Wormald: I will take - I will take that up...

Sir Cyril Chantler: ...for you to respond.

Sir Chris Wormald: With my former colleagues.

Sir Cyril Chantler: Indeed.

Sir Chris Wormald: Now, okay yes, I mean - I was about to say, in defence of my former department but. I think this is one of those situations. As you cross from education to health you find this both sides - and they shouldn't be sides - but, they are - find the other very frustrating to deal with.

Sir Cyril Chantler: Yes, well I've spoken...

Sir Chris Wormald: Yes.

Sir Cyril Chantler: ...to your successor.

Sir Chris Wormald: Yes, however...

Sir Cyril Chantler: If, between the two of you...

Sir Chris Wormald: The issue you raise is exactly the right one.

Sir Cyril Chantler: [Unclear] There would be lots of clapping.

Sir Chris Wormald: Yeah. Yes, I mean, and we made quite a lot of progress in the aggregate but not in the individual. So, we are much better at linking up anonymised data sets and being able to see trends.

Sir Cyril Chantler: That is not the problem.

Sir Chris Wormald: Yeah, exactly. Do it to the individual level. I mean you know all the...

Sir Cyril Chantler: There is a review which I think maybe was commissioned when you were there [unclear].

Sir Chris Wormald: I will take it up with my successor because as you say it would make everyone's life easier.

Julia Cumberlege: Sir Cyril never misses an opportunity...

Sir Chris Wormald: No.

Julia Cumberlege: ...to take up an opportunity.

Sir Chris Wormald: That's what we're here for.

Julia Cumberlege: Good. Can we move on now to surgical mesh?

Sir Chris Wormald: Yes.

Julia Cumberlege: Which again we have met a huge number of women who suffer from this. In Scotland, in Wales and in Northern Ireland, but particularly - of course - throughout England. One of the things that really has concerned us has been the enormous amount of suffering that we have heard. The way that women are in such, such difficult situations in terms of their health and the agony that they are suffering at the moment and the fact that later on they have to give up their work.

Having given up their work they then find it hard to pay the mortgage, having possibly great dangers of losing their accommodation. They then have problems in terms of people get very interested in their children and whether they are able to bring up their children. So, this is an issue that has horrific consequences. We have heard - as I said - from hundreds and hundreds of women around the country and through emails, and the office has been extremely busy responding to concerns.

Now, it's already had a 20-year history and the interesting thing about the history is how it really had such a rapid rise, and then there has been fewer surgical operations made - partly through the pause. But anyhow, we know that the numbers were beginning to go down. But just thinking about the history of this great tragedy that's happened - I'm just wondering if you've got any advice for us. How could we avoid something like that happening in the future?

Sir Chris Wormald: Yes, well I mean I'll leave my colleagues to comment on your direct question. I mean obviously we've seen many of the same testimony as you.

As so often with these inquiries it's impossible not to find them both intensely moving and deeply harrowing. We've seen this in other inquiries on the national television and obviously no one in the system wants to see those kind of stories as a result of things that were supposed to help.

That's not what we're all for. I think everyone who has seen the things that you have described has been - I'm not quite sure what the one word is - touched in the same way that you describe. Obviously when people are harmed, we have to do everything we can to put that right.

On the what can we learn - I come to the Chief Medical Officer first but also William.

Dame Sally Davies: This is absolutely horrible.

Julia Cumberlege: Sorry.

Dame Sally Davies: This is absolutely horrible. Those poor women. The impact on their relationships and families. We all feel unhappy and saddened. I think we have a number of issues at play. First of all - as I enquired about this - I learnt that there are women who get to the end of their tether with their incompetence or prolapse who can benefit from an appropriate operation by an experienced operator.

So, clearly - and if you look at the Scottish review - there are equivalent numbers of women who had good outcomes and think it's a good thing. Clearly therefore it is something we want to keep on the books. So, what is the issue? The issue seems to me to come back to two things. Transparency, information consent - that block of things - and trust between the patients and doctors and whether the doctor is properly trained and up to it and what were the side-effects.

One of the driving reasons that I persuaded government to set up NIHR - why I wanted to do it - was because I felt strongly - as I've already said - that the public don't understand the balance between an intervention and the risks. But that actually we needed to get much more into surgery and the interventional things. I found it quite [inaudible] now temporarily lost but there was [inaudible] saying the ones who are worst at looking at the outcomes are the obstetricians and gynaecologists and we still haven't learnt.

What - so I - what I'm frankly horrified by is the lack of understanding by the operators of the general outcomes of the operations - and they're not evaluating, monitoring and evaluation. I mean I used to audit the outcomes of my own practice and get other people to check I was doing it

properly. You know, they weren't doing that, let alone applying for the trials when we had the money.

So, they weren't able to tell how they were doing, let alone putting it together as a specialist group or something. Then being able to say to patients - so I mean I'm sure this is another one where there would be a learning curve - were they going - at the beginning of laparoscopic surgery - to centres to learn it from the best and practicing with an experienced operator. It doesn't sound like it.

I think that it spread because it seemed to be a quick fix and for a number of women it gave them relief. But for too many - without expecting it - they have ended up with a disastrous outcome.

Julia Cumberlege: Has the manufacturing industry - has that had an impact in terms of the very sharp rise in the use of mesh? Have there been issues that you have come across on persuasion or marketing?

Dame Sally Davies: I haven't, and I think things have changed a lot. The ABPI set the standards by - you know not - agreeing not to sponsor a lot of educational meetings and trips and things like that. The devices industry usually follow them. I'd have to go and check what their advice is. But there's much less of that been going on over the last 10 years. Maybe I'm not the one to ask. But there is much less.

But there's peer pressure. You know they meet at meetings. We meet at meetings. I am a doctor. I'm part of the tribe. Having a tribe [unclear] seems to work and I think what seems to have happened is they didn't check up and that brings in the value of PROMs - Patient Recorded Outcome Measures. Because if they'd been doing that, they would have known that the outcome for some of the women wasn't good enough. They'd - I'm just gobsmacked at the lack of looking at their own practice.

Julia Cumberlege: Who should have done that post-marketing surveillance?

Dame Sally Davies: Who is within the system to do it? In drugs of course the pharmaceutical companies have to - we have a Yellow Card system and MHRA keeps an eye on it. Is it the same for devices? Sorry I should know.

William Vineall: Well devices is slightly different because they come from a...

Dame Sally Davies: Notified body.

William Vineall: ...European starting point and they move in and out of the market much more often. So, it is basically the MHRA through the Yellow Card and the

reports it gets back from manufacturers which is the way of picking up some of these problems.

Can I add two other things to what your original question was. Obviously - as the others have said - you know, I've watched some of the patient testimonies here at the hearings and it's very harrowing and you wouldn't want anybody to suffer in that way. The two things that I think probably haven't happened quickly enough is first of all the question of data which was first raised as an issue in 2003. In 2018 we got the first cut of data looking at the previous 10 years' practice. Just an analysis of the figures, nothing more.

So clearly that is a sort of unacceptably long lag. The second thing which came out of the thing - of the earlier discussions - is the whole question about understanding the patient experience and hearing from the position of those who have had the treatment. I say those who have had the treatment because obviously if you look at the Scottish report from last year - which is small scale - but is probably the best we've got at the moment - there's lots of people expressing things that don't hold as truths together.

Some patients saying - as we know - that it caused difficulties in terms of personal relationships and in terms of sense of self-esteem. A feeling that that wasn't always recognised in the interaction with the clinician. Another group of people saying that they had positive outcomes in similar numbers to the people who haven't. That doesn't belittle the people who haven't, but it shows the complexity of the issue.

Probably more importantly than either is that most people - even in that survey - didn't share a particular opinion. So, there may be a question about how - as well as getting the medical side of the debate to listen carefully - that we encourage people to be able to speak out about what their experiences of these treatments are. Because obviously with something like mesh it is a surgical procedure, but it has - it can have fundamental personal and social impacts as well.

Allowing people to speak about both of those is probably a way of better informing the system - those systemic things we were talking about earlier actually have a richer inflow of information over time. So, data...

Dame Sally Davies: Can I pick up on that one?

Sir Chris Wormald: I was going to add to - you go first and then I'll...

Dame Sally Davies: I mean, I absolutely agree. Of course, I agree. But we are in an area where none of us like talking about it. I did an annual report on women's health which was published in December 2015 and I actually did focus on incontinence and as I talked about it on the *Today* programme, I mean, the *Today* presenters were quite horrified - they were even more horrified when I moved on to sex - but that's not today's issue.

But I was just gobsmacked by how prevalent incontinence is in older women - particularly those post-partum - and how women don't talk about it. Then I thought, yes, but I don't talk about the problems I had after childbirth. So, I did talk about it - as you know - publicly on a Facebook live and got some quite unpleasant letters as a result. So, I think we want people to talk about it, but we need to give them a safe space to talk about these very personal issues.

Julia Cumberlege: Yes, I do agree with that.

Sir Chris Wormald: The things that I was going to add - a completely different flavour of comment - and I think many of the things I'm going to say, I think the MHRA has said to you already [unclear].

We do have - as a system - a much greater challenge regulating devices than medicines. Partly because we have a much longer track record but particularly the point that the Chief Medical Officer raised earlier - that obviously - clearly - the interaction of the product and the skill of the person using the product is much more fundamental to whether it is safe than in most prescriptions.

Obviously, we do have issues with prescriptions and medicines. But that question of when you have a problem, is it the product that needs better regulation, the people who are using the product incorrectly for better regulation - or potentially both - is a much more complex system and of course runs directly into the issues Cyril and I were talking about right at the beginning. Of - we have always split the regulation of products from the regulation of individuals. Most people think that is the right thing. In these areas, you have to have a way of doing the two simultaneously which simply is more challenging.

Which is not an attempt at an excuse of the things that have happened but to recognise we have a much bigger journey to go around that than you do on sort of classic medicines.

Sir Cyril Chantler: I mean our thinking is getting quite a long way along the line over this.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: But it does represent an example of something we discussed right at the start of this session. That is the cross-linkage difficulties.

Sir Chris Wormald: Yes, exactly.

Sir Cyril Chantler: Because it was in 2003 - or 2004 - that NICE recommended that there should be a register. Now, in other areas I was - looked after children with kidney failure - we had a register to make sure we could follow up the outcomes. NICE recommended it but NICE doesn't effect it.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: So, when we've spoken to people about this - each part has been able to do it, but it's not actually linked. So, they make the recommendation, but they don't do.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: The people who do don't necessarily take the recommendation. So, that is an issue that obviously has to be addressed.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: But what we do know - and we've made progress on this - is that one way to do this is to have proper registers. Not for everything but for particularly interventions which are new - and the College of Surgeons have given advice about this recently. In the conversation we've had outside this meeting, we seem to be making good progress on the notion of what is a database, what is a registry.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: How do you do that with GDPR and all the rest of it.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: That I think is going to be crucial because we've got to have registries which are just not anonymised but with proper safeguards - are patient identifiable - so that we can deal with the issues which relate to the things which aren't expected. It's not just about clinical success, it's about the patient related outcomes, the patient experience. Up and down the country we have met women who said, 'actually my operation was a success in the sense that I'm now continent, but my life is destroyed. I'm in pain. I have dyspareunia. My relationships have gone'.

All that sort of thing. So, we've got to be able to interrogate databases with proper permission so that we can learn before it's too late.

Sir Chris Wormald: Yes. Well I have one more thing to say on the Baroness' question, but I'll let William - we recognise there are some vital issues. William can do that and then I'll come back if that's okay.

William Vineall: I mean, registries - as you say - is a complicated issue. We made some money available last year which has now gone to NHS England.

Sir Cyril Chantler: 1.1 million.

William Vineall: 1.1 million to start the development of a registry. The question is how many registries do you have, to what extent and how can you organise them in a way that you quickly collect the data and you're trading that off against the overall infrastructure you're establishing.

Now, I know that that is work that is ongoing. Obviously as the review reports, we will be very interested to hear about where you land in terms of making registries effective and in a sense - I suppose - moving - if I'm summarising in broad terms - from the position where they're professionally led with the best of intentions, they quite often don't have the infrastructure around them to enable them to make an impact in the system.

Sir Cyril Chantler: Indeed.

William Vineall: Thirdly the way that the data is effectively translated into the other bodies.

Sir Cyril Chantler: Fortunately, there are international examples which we can learn from. I think it's very important to the National Health Service that we do try to learn from people elsewhere who do things better.

William Vineall: Yes.

Dame Sally Davies: The Swedes are clearly people we should learn from.

Sir Cyril Chantler: The Danes.

Dame Sally Davies: I've been on the edge of the registry debate for most of my professional life. I think we've got to find the right balance between collecting enough that we can reasonably go back to patients if we have a concern. One of the first emergencies I had to deal with was the PIP breast implants. We didn't know who had had what. Then there's what data do you collect? So, the more we can do through the electronic patient record and knowing what's implanted and then you say, right well this is new. Let's survey those patients and get some data to find out if it's alright.

Or, hey we're concerned about this, we can let these patients know through their doctors...

Sir Cyril Chantler: We will have recommendations to make in this area.

Dame Sally Davies: Yeah the better.

Simon Whale: One of the problems here is that - again this is reflecting what women have told us - that they feel like they're the guinea pigs in a trial. Because...

Dame Sally Davies: But they weren't in a trial. I mean, that's part of my concern. If they'd only been in a trial, we'd have the answer.

Simon Whale: There was no formal trial - exactly - but the product was introduced into the market as Baroness Cumberlege has said - there was sharp uptake in the use of that product. It was introduced into the market with minimal awareness of what its long-term effects - or even short-term effects - would be on women. The way we - the system - has found out, is through those women's experience. Is there something fundamentally wrong with that?

Julia Cumberlege: Yes, because I think leading on from that, I just wonder how the Department satisfied itself that mesh was safe for use?

[Over speaking]

Dame Sally Davies: Through the routine notified bodies system.

Julia Cumberlege: But it didn't work.

Dame Sally Davies: Well it does work for some women. There are nasty side-effects and it's been misused - or mis-put-in by some surgeons. That - I mean I think that's why we have to distinguish what it - all the different issues.

Simon Whale: We - sorry just to interrupt you - that's true. But we also don't know what the long-term effects of this product in the human body are. Is that right?

Dame Sally Davies: I agree though I suppose I'd say that there are meshes that have been used for long-term - I mean aortic...

Simon Whale: But in the pelvic.

Dame Sally Davies: ...bifurcation grafts. Yes - no. I absolutely accept, but that then argues for much more discussion and transparency doesn't it? Because there will be some people who say, well if it - if that sort of mesh has been used for years or it's been put into rats for hundreds of days - well until they die - with no side effects, then I'm going to take that - that hope.

[Over speaking]

Simon Whale: That point you made about consent actually, that...

Dame Sally Davies: Yeah.

Simon Whale: ...consent should be about making sure that the patient - or the woman in this situation - knows what the system knows.

Sir Chris Wormald: Yes.

Simon Whale: But also knows what the system doesn't know.

Sir Chris Wormald: What the system doesn't know.

Dame Sally Davies: Yeah.

Sir Chris Wormald: Sorry...

Simon Whale: That hasn't happened.

Sir Chris Wormald: Yes. I mean this was exactly the point I was going to make. As I said, we recognise - and MHRA recognise that in devices - that system has got a lot further to travel than medicines - whereas you say there are lots of history.

We of course face the dual pressure. We have rightly the questions that you're raising about should there have been more trials.

Dame Sally Davies: I'd have liked a trial.

Sir Chris Wormald: Yes - exactly.

Dame Sally Davies: As a start.

Sir Chris Wormald: We also - in real time - have intense pressure on why has X - which could help people who are in very difficult - not been implemented yet? To which our answers are the ones you've just given us. Very frequently - as you will know - yes this does look promising, but it hasn't been properly tested and it hasn't had the [unclear] et cetera. We have an example of that right now. They are of course very, very difficult balances when you have a patient who's - who could be helped by something you've got in your hand, but you do not yet have the confidence to use generally.

That is the kind of thing - unfortunately - we have to balance up. But as I say, we are not defensive at all about this question of - we and indeed the world - need to learn a lot more about how do you best regulate that sort of combination of medical devices and said people.

Sir Cyril Chantler: Are you content with the new EU medical device regulations which are coming in?

Sir Chris Wormald: We think they are a step forward.

Sir Cyril Chantler: Is there anything more you think should be done in addition to that?

Sir Chris Wormald: What would you say William?

William Vineall: I don't know the answer to that, I'm going to be perfectly honest.

Sir Chris Wormald: Our focus has been on implementing the regulations we've got.

Sir Cyril Chantler: If you think of things - William - would you let us know.

William Vineall: Yes.

Dame Sally Davies: But you're looking only at the regulatory bit. You have to look at the professional bit.

William Vineall: If I could go back to your - the point you made about...

[Over speaking]

Sir Cyril Chantler: Just to pick up the - the CMO's point. We are absolutely looking at that. Which is, we are talking about making sure that when people undertake a procedure, they're competent to do it and they are competent to know what to do if it goes wrong. Because the person who puts the mesh in may not be skilled at taking it out. Therefore, they need to work within teams which are properly - I don't want to use words that have too many exact meanings because there are issues to be discussed here.

But certainly, we want to have specialist centres where you know that your - the centre itself is competent, it's safe and it's working with people as part of multidisciplinary teams. We're absolutely on to that.

Sir Chris Wormald: Yeah.

Sir Cyril Chantler: Because we've heard up and down the country from women where frankly they have been poorly informed and poorly treated.

Sir Chris Wormald: Yeah.

Dame Sally Davies: Communication.

Sir Chris Wormald: Yes, I think we'd agree with all that. The only thing - the point I was going to make - to your previous question Baroness - there is also a theme about not losing what is wonderful about the medical profession. So, when I was

not in health, we used to look with envy about how ideas spread in the medical profession so fast on your uptake question. We always looked at how something like keyhole surgery spreads across the world to the benefit - without any government doing anything.

That's the huge strength of the medical professional culture. The question you're raising is what happens when you get that kind of spread on something which is really hard to use and raises...

Sir Cyril Chantler: I'm well aware of it. I have an artificial heart valve. So, I'm really...

Sir Chris Wormald: Yes.

Sir Cyril Chantler: ...in favour of new devices being properly used.

Sir Chris Wormald: No, exactly. The way the medical professions are able to pick up ideas and spread them and use them and - as I say - without governments doing anything...

Sir Cyril Chantler: First do no harm.

Sir Chris Wormald: But first do no harm - is the exact culture you want to protect while dealing with all the questions that you're raising.

Dame Sally Davies: But we do handle drugs differently. So, if you look at the debate about warfarin versus the new anticoagulants, we all thought the new anticoagulants were more expensive but would be much safer. The latest studies show that they're not universally safer.

Julia Cumberlege: Yes. Sally, I absolutely accept that. The thing is with drugs, you can change it. You can alter the dose or the type of drug or whatever.

Dame Sally Davies: No, we agree.

Julia Cumberlege: The trouble with surgical mesh has been that it was inserted with the intention it would be in the body for life, and one of the issues that have come up very strongly for us is that the women who want it taken out are finding it very difficult to get surgeons who will do that with the skills that are necessary. We know the terrible, terrible issues when the mesh gravitates, and it goes around other organs and all the rest of it.

So, in some ways it is so different. That is why we have to be really careful about future devices. I accept William's point. They are very different. But the Department was advised to create a statutory body that was very similar to the Committee for the Safety of Medicines. That was for new

interventional procedures. But instead, it created the voluntary SERNIP and you know that really has been a failure.

The way that the SERNIP acted was to change even the rating of the manufacturers for the different mesh devices, and we were told that some of that change was because of [inaudible] who's [inaudible] subsidiary put pressure on SERNIP. Now, I just wonder why did the Department do that?

Because they had an opportunity to have something that was statutory and yet they had a voluntary system that was very much guided by the Royal Colleges et cetera who don't have the statutory authority to actually bring in certain measures that are necessary. So, it seemed to me a very odd decision.

William Vineall: Can I pick up on that and a couple of points of information that you were asking us earlier. So - I mean - SERNIP as you say - was something a bit like the discussion we've been having on registries a moment ago - was something that was voluntary and was set up by the Royal Colleges who didn't have too much data or money attached. That function was transferred over to NICE to try and put it on a more consistent footing and led to the interventional procedures guidance that NICE now produces.

So, the aim of that was to make those advices more mainstream to the health service rather than less that they might have been under SERNIP. In terms of how we monitor devices once they have been produced onto the market - it is the MHRA who do the post-market surveillance alongside the manufacturers. In terms of the new processes that are coming in for medical devices regulations from the EU - which come in between now and 2020 - they're trying to do a number of things that we've been touching on.

Raising the threshold of clinical evidence required for the device, the point you were making about mesh. The requirements and scrutiny placed on notified bodies to look at how they're performing. The traceability of devices and the information that is available to patients and clinicians. So, I think that is - we will clearly have to see how it pans out and we'll clearly have to see what you say in response to your analysis of the issues.

But I think that is starting to pick up some of the major issues that presently distinguish the devices approach from the medicines approach and will bring a greater degree of commonality.

Julia Cumberlege: But NICE doesn't have statutory powers.

William Vineall: No.

Julia Cumberlege: It only offers guidance.

William Vineall: No, NICE - so that is a fair point. Why doesn't NICE do that? It is advice. It is fairly strong advice. But clearly it gets you back to the conundrum that we've all been discussing which it is still advice to give to a doctor - and hopefully their patient - about what is going to be best in the individual instance.

So, it necessarily leaves discretion for that discussion. That's fine. The question then goes on to - for example the interventional procedures. How can you make sure the right level of known information is then injected into that conversation to give it a consistency? That's the whole reason why NICE was established 20 years ago - was to try and give some consistency of clinical and cost-effectiveness.

At the time it was introduced there were lots of arguments about it would be the death of professionalism and all the rest of it and people wouldn't have any discretion. Actually, it's given a much greater consistency to anybody who is - say - giving mesh out if it is available to them and hopefully gives a basis for a better conversation with the individual concerned.

So I think there are quite good reasons why NICE guidance is voluntary but that is no reason to say that people can't be better informed about the guidance and it can't be more firmly put out so that people have the best knowledge at both levels in the conversation.

Simon Whale: If their 2003 recommendations on mesh had been followed - which were uncannily similar to the recommendations that Sir Bruce Keogh made in his letter of 2012 - there are probably hundreds - certainly hundreds - possibly many thousands of women who wouldn't have suffered the way they have. So, something - there's something structurally wrong there that NICE identified, a practice that should be adhered to and they weren't listened to.

William Vineall: I think that is a challenge. We need to take that away. We need to hear what you've got to say and clearly the question about how you translate the advice and the best position on an issue and how you take that out in to practice is something that we're going to have to go away and do more work on, I agree.

Sir Chris Wormald: Yeah, I think what I'd add. I mean I think your question is very fair. Clearly that course of events is not what anyone wanted and led to the effects that you had. We have had however many instances where what you might call the NICE approach has been highly effective, and it is generally seen as a

world leading body and lots of people copy it and there is a lot of power to that sort of professional guidance approach.

Likewise, we've seen situations where you have a set of statutory rules - well exactly the same happens because the real problem is in the implementation - not in the statutory force or otherwise behind the literature.

Sir Cyril Chantler: Can I interrupt you? If it's an advisory arm.

Sir Chris Wormald: Yes.

Sir Cyril Chantler: Then there needs to be an affecter arm.

Sir Chris Wormald: Oh yeah. No, sorry this is...

Sir Cyril Chantler: Doesn't there?

Sir Chris Wormald: This is exactly what I was getting to.

Sir Cyril Chantler: You know the SERNIP decision - I'd like to think wouldn't happen today.

Sir Chris Wormald: Yes. Yeah, no sorry, this is exactly where I was going. You can make a case in these occasions - and it's an arguable thing - so I'm not attempting to pre-judge the answer - either for the guidance approach or the statutory approach. But what Cyril has just described is more important than both of them. Which is regardless of which it is, how does it actually, practically affect what an individual...

Sir Cyril Chantler: How do you know if it's worked?

Sir Chris Wormald: Now, this comes...

Sir Cyril Chantler: [Unclear] make it work, how do you know it works?

Sir Chris Wormald: Exactly. Now this comes both to the list of things that William was describing. Both, do you know if it was done and then do you know the effect and - I won't repeat the discussions we were having before - is there actually a person - and this is what we're trying to create with the National Patient Safety Director - who believes it is their job to be constantly scanning the horizon for what's going right, what's going wrong. What are the things where NICE has made a recommendation, but it's not happened et cetera?

So, there is an awful lot of processes - things you can do - that will improve the situation. But it does all come back to the point you first raised about having data to actually track what is happening and therefore to...

Julia Cumberlege: Okay, we're just running...

Sir Chris Wormald: ...intervene. So, constantly on these things - sorry am I delaying the CMO? Whether statutory is better or guidance is better is a debatable thing and it is fair to debate. But it should not distract us from that set of questions...

Julia Cumberlege: Can I just finally ask - very quickly - because I know other people have got commitments they've got to get to. Is it now appropriate - do you think - to consider a statement of regret?

Sir Chris Wormald: I think whether - in all these cases - I think what ministers will want to do is receive your report and recommendations and decide what to do in that and many other areas, based on what you say. It's an obvious truism that if you are going to set up an inquiry and have people such as yourself devoting their time to doing it, you should listen to what they say before you take those decisions.

Julia Cumberlege: Sally, what's your view?

Dame Sally Davies: There but for the grace of God, go I. I feel intensely sad about all of this.

Julia Cumberlege: Sorry?

Dame Sally Davies: I feel intensely sad about this.

Julia Cumberlege: So, you do feel that there should be a statement of regret?

Dame Sally Davies: I think that is for ministers to decide, it's not my...

Sir Chris Wormald: As I say, I think ministers will want to be advised by the inquiry about it.

Julia Cumberlege: William, can I ask you?

William Vineall: I would say the same thing. I mean particularly - serious point - I'm the commissioner of the review on behalf of the Department - would clearly need to hear the totality of what people have to say and then the ministers will respond accordingly.

Julia Cumberlege: Right. Well I absolutely understand what you're saying - Sir Chris - you know, it's up to ministers and secretaries.

Sir Chris Wormald: No, no sorry I'm not - and that is not an attempt to...

Julia Cumberlege: I just thought you might have some advice for us.

Sir Chris Wormald: Sorry, I'm just saying that it's more - yes well as I say - as the commissioners it's quite difficult for us to answer that question. I think as a general

principle - as I say - if you are going to ask people such as yourself to review something, it's very important to listen to your final word and then decide. I think that is what our ministers will want to do.

As I hope you've gathered - our interest here is to get to the best conceivable outcome on behalf of patients. While we do think - particularly a lot of William's work over the last five or six years - we have made huge progress across a whole range of safety issues. We are - and I hope this has come over - completely open to - you not only can always go further but should always go further and indeed my executive committee were discussing this earlier today.

So, I mean I hope that is the impression that we have given of you because we are proud of many of the things we have done over the last few years. But that is not the same as saying we think we have a perfect system. Or that there aren't big issues that continue to be - need to be addressed and that history is a great guide to that.

So, we are very much looking forward to receiving both your recommendations and the work we described on the national safety directive with the aim of hopefully being able to crack these issues and - as you said right at the beginning - ensure that they don't happen again. So, I hope that is the impression you get.

Julia Cumberlege: Sir Chris, thank you so much. Thank you for coming and with your colleagues here today. I'm sure we'll be in contact, especially when we come to implementation.

Sir Chris Wormald: Yes.

Julia Cumberlege: But clearly you will want to see the report before...

Sir Chris Wormald: We will.

Julia Cumberlege: ...you make any decisions on that...

Sir Chris Wormald: For further...

Julia Cumberlege: But thank you.

Sir Chris Wormald: ...if you have further questions we remain at your service.

Julia Cumberlege: Thank you so much.

END OF TRANSCRIPT

14th May 2019

Session 1: APPG on Surgical Mesh Implants – Took place on 28th May

START OF TRANSCRIPT

Julia Cumberlege: Mr Smith, thank you very much indeed for coming today. It is a recess period and we're very grateful to you for giving up your time when you probably would rather be in your constituency, but as the Chair of the All-Party Surgical Mesh Implants Group, we welcome you today and we look forward to what you've got to tell us. So it's really over to you now.

Owen Smith: Great, thank you ever so much, Julia. Thank you to everybody for inviting me to address you today, and thanks in particular for arranging this so that I could do - because as you know, you had to rearrange this for me to attend a funeral at an earlier stage, so I'm very grateful to the Review Committee for allowing me to come and speak to you today. As you say, I am the Chair of the All-Party Group. That's a group we formed several years ago, I think now five years ago.

I formed it, having first encountered the problem of surgical mesh when one of my constituents, a very brave woman called [REDACTED] came to see me. It wasn't an issue that I knew anything about prior to that. [REDACTED] explained her experience which I think is a very typical experience of a woman injured by mesh, which was essentially in her middle age, late 40s - no, younger than that. I'm doing her a disservice. I think early 40s, she had a problem with stress-related urinary incontinence, went to see her doctor. He recommended that she have a tape inserted in order to deal with this.

She had the tape inserted. She had problems from the first moment, really, after not recovering from the surgery in terms of infection, in terms of what she subsequently believes to have been an immune system response, but in particular with the mesh eroding and extruding as is so often the case for women. When she came to see me, she was a woman who - someone whom you looked at instantly and knew that they were unwell. She was grey, she looked 20 years older, truthfully, than she was, and she was clearly someone who is in constant chronic pain.

I subsequently helped her have that mesh removed through a surgeon in South Wales - this is several years ago - and she's had it removed. She is a transformed woman. She still has some pain, but the degree of discomfort she lived with has been dramatically reduced. She looks dramatically different, her colour, her demeanour, her posture, they're all improved.

She's been saved, as it were, and made younger by going through the removal. I give you that full anecdote because I think that is an absolute classic case of someone living with this problem.

The other thing that was totally classic about her case was that, when she went back to her original surgeon and GP, the GP understood nothing about mesh, didn't really understand the procedure, certainly didn't think there were any problems associated with it, couldn't imagine the sorts of pain in groin and legs and abdomen that she was experiencing might be related to surgical mesh, and when she went to see her surgeon, initially was told that there was absolutely no way this could be anything to do with it, that the complication rates were extraordinarily low, that the NHS and others reckoned that there was only maybe 1 to 3 per cent of people who might suffer these sorts of adverse reactions.

She went through various other tests until, eventually, a different surgeon agreed to remove it and we've seen the results. Her example I think is but one example of thousands of women in our country and millions of women all over the world who've had surgical mesh inserted and found complications like these. I think this is a medical scandal and I think there has to be, and I'm so delighted the review is looking at some acknowledgement and exposure of the scandal and acknowledgement of the fact that this has come about.

The reason it's come about, again, I think is actually quite straightforward. Stress-related incontinence for many women can be very problematic and make lives very difficult, and therefore, there have been operations that have been provided for women, autologous sling, colposuspension, over many years in order to try and deal with the problem of SUI, in particular in women after childbirth in middle age. Mesh came along in the mid-'90s, effectively, and was perceived as being a very quick, very straightforward process. It was day surgery as opposed to the four-day inpatient surgery which obviously required much greater recovery time, et cetera, for women to undergo.

Therefore, there was both demand from women to have this surgery undertaken because it was so much easier and because it was being described by the doctors as so much easier, and there was a big push from the device manufacturers through the GPs and, in particular, through the surgeons, obviously, to undertake procedures using mesh. I think, consequently, what happened is there was a very wide take-up dissemination of this particular technique for prolapse, but in particular for SUI, and in our country, but also in France and Italy and Germany and

other, you see a similar take-up curve in a similar period of time in the 1990s and, in particular, early 2000s.

Frankly, far too many women with - at far too young an age, and often with quite limited conditions, certainly conditions that didn't really require this degree of intervention had this intervention. I think for - and therefore, what subsequently happened is significant numbers of those women found that they experienced problems, chronic pain in legs, abdomen, elsewhere, a debilitating condition that left many of them with absolute changed lives, unable to work, unable to pick up their children, unable to have sex. These are dramatic, life-changing shifts in their lives.

I think the most scandalous thing, other than the overselling and, indeed, mis-selling, in my view, of the procedure was the extent to which the medical fraternity in our country but around the world then essentially denied that there was any evidence that there was a significant problem emerging, stuck to the line that there was only a very small number of women who experienced any serious complications, and essentially defended and denied all of the anecdotal evidence that was emerging not just in our country, but around the world.

By illustration of that, when I first sat down to meet with health ministers and representatives of the NHS and the MHRA in our country - I think four-and-a-half years ago now - a meeting with ministers in the current Government who I think would be excellent at pursuing the truth in respect of mesh and trying to get to a better clinical position in respect of it, and in those first meetings, the MHRA in particular - but the NHS to a lesser extent - were completely defensive and totally stuck to the line that only between one and three per cent of patients in the NHS in Britain experience significant problems after having mesh implanted.

Now, this was in the teeth of emerging evidence, so the Keltie Report in nature, but other evidence too that was emerging from around the world. Indeed, there was evidence that the NHS was starting to shift its position both in terms of the volume of mesh being implanted by surgeons, I suspect in direct consequence of the volume of anecdotal evidence that was emerging from around the world, and then progressively, you saw on some of the literature being produced by the NHS a shift in the degree of risk they were admitting, so at first, it started saying 1 to 3 per cent, then it became 3 to 5 per cent.

Now, of course, we understand from subsequent pieces of analysis that have been done that it's significantly higher than that. I suspect it is higher than the 10 per cent revealed by Keltie. I think if you look at some of the

other studies, notably the analysis done by Keith Willett's team of the HES data and the volume of women going for outpatients for a variety of different problems post mesh surgery, that indicates to me that this is a significantly higher number than we previously recognised.

So, what does this leave us with now, as it were? Well, I think it leaves us with a number of unresolved issues. One is that the status of mesh in the NHS is still, I think, disputed and debated, and the way in which this review has been announced and the pause that I think you so excellently introduced so rapidly after you first started looking at this problem was announced, both good things, but the lack of grip to get that aligned, I think, with the NICE review and the subsequent NICE guidance that came out recently is, I think, problematic and has left surgeons to whom I talk slightly betwixt and between as to what they ought to be thinking about mesh.

So they know that they oughtn't to be deploying it in women now, but they wonder whether the pause will be lifted and whether it will be lifted so as mesh might be used in line with the NICE guidance. Of the NICE guidance, I will say a couple of things. One is that I think the opacity of the NICE process, as far as patients are concerned - and, indeed, other interested parties such as parliamentarians - is something that needs to be thought through. Frankly, we need a greater degree of transparency as to how they arrive at their decisions.

The best illustration of that in respect of this is the reversal of the decision to deploy NICE in prolapse, because in the previous NICE guidance, it was recommended that mesh oughtn't to be used for pelvic organ prolapse, other than in research-only, which is code in the NICE world for don't use it, because there is no research being done in our country or, indeed, anywhere in the world in the use of mesh in pelvic organ prolapse and everybody knows that. So, don't use it other than in research is doctors' code for 'don't use it.'

In the latest piece of guidelines, they reversed that decision, changing it to it being okay to deploy mesh for pelvic organ prolapse. Now, it may be that they've got new evidence to show that, but the reality is, they don't. There has been no big study or, indeed, small study undertaken in the intervening period and there is no attempt in the NICE guideline to illustrate why it is they reversed that decision. Equally, in respect of mesh's use for SUI, stress-related urinary incontinence, there is effectively a change, certainly in the language around its deployment.

Effectively, what they recommend in the new guideline is that it is deployed third-line after more conservative treatments, i.e. physiotherapy in the first instance to try and strengthen pelvic floor muscles, secondly looking at alternative surgical interventions that might be undertaken, colposuspension, autologous sling being the two most commonly practised, although we have a big problem there because the number of surgeons able to undertake those interventions now are very few.

So again, I have to retrain people if we're going to see more of those interventions, and then third-line, effectively, it suggests that mesh could and should be used, but there is, I think, to some extent, a denial of responsibility by NICE to say something more definitive about the risks and benefits associated with mesh, and their argument, I know, would be to say, well, look, we can only work with the evidence and our job is to review the evidence and then make recommendations, but in reality, they are looked to as more than just that. They are looked to to be the arbiter of what is good and safe and sensible for the surgeons to undertake.

When you have an incident such as this where there is controversy, then I think we've got to think about a way in which better, clearer advice is provided both to patients but critically, in this instance, the clinical community. My point is that you've got your review and there is NICE's guidelines, not ideal. There does need at the end of this to be a full stop and a more definitive perspective put forward by effectively arm's-length government bodies to the clinical community as to what they should do.

One of the other things that this issue illustrates is that, although we've made huge strides in data gathering and data analytics in the NHS in the last 20 years, immeasurable strides, and we now have HES data and coding which allow us to see what sort of interventions have been made, et cetera, this case illustrates just how imperfect those systems are and how poor they are, actually, at recording problems, at picking up problems where we don't initially know they exist.

So the vagueness of some of the codings around mesh, where initially there weren't different codes for vaginal insertion versus abdominal insertion and there weren't codes for different types of tape, et cetera, et cetera, and especially where you've got vernacular which is different, so is it a tape, is it a mesh, is it a sling, is it a TVT? There are different words deployed both by the surgeons themselves and, frankly, different understandings, I think, even on the part of the surgeons as to what they're implanting. I don't think it's always the case that the surgeon says, 'oh it's not mesh, it's a sling', or 'it's not mesh, it's a tape', and they don't understand that they are being misleading, but they are misleading.

In some incidents, I think they are deliberately misleading because their assumption is that the evidence doesn't show that there is a problem with mesh, and therefore they are overriding what they believe are misguided or misplaced concerns on the parts of their patients, and I think they need to treat the patients sometimes with a little more respect and assume that they understand and can understand and interpret risk far more efficiently than the surgeons sometimes allow, in my opinion.

So the data gathering is hugely important. I'm very pleased that your reviewers already insisted on better data gathering in respect of registry prospectively. I think there needs still to be a really detailed audit done, a retrospective audit in order to try and get to the bottom of what's happened to people to date, and I think in some respects, that is as important as a prospective registry and I'll tell you why. The surgeons and the patients are already voting with their feet.

There will be fewer and fewer women undergoing this procedure in our country and elsewhere, but there's a big bolus of women who've been injured by this and they deserve both for there to be clarity and truth about the scale of the risk they underwent and for women who've had mesh implanted and for whom it's not posed a problem to date. They too, I think, deserve clarity as to the risk that they ran and might still run in the future.

The reason I say that is, although the evidence we can all agree is that the significant majority of women who undergo this procedure do not have a problem. Maybe 80 per cent, maybe more do not have that problem. That's certainly what the evidence shows at the moment. It also shows, if you look at, in particular, the data set that Keith Willett undertook for the NHS review, the problems emerge at five and seven years and sometimes at 10 years, and therefore there will be women out there who've not had problems to date for whom this may eventually pose a problem. So, a retrospective audit for them is required.

The third reason I think it needs to be undertaken is I do think some of these women will absolutely deserve compensation of some sort. I think they have been injured by this procedure, and I do think that this procedure was significantly oversold and deployed in far too many women when it wasn't necessary. Ultimately, what this is about is women bearing a risk that wasn't justified in terms of the condition they were suffering from.

By illustration of that, I spoke to a very senior surgeon in this field last week who illustrated what he thinks is a change in attitude on the part of the surgeons in terms of the degree of risk they perceive with this intervention when he asked a roomful of male and female surgeons as to whether the

women in the room would undergo this procedure using mesh if they were suffering from SUI, and not a single one of them - I don't know how many women, but not a single one of them, he said, put their hands up to say that they would. So I think you'd probably get the same answer from the men, if you asked them in respect of their wives and partners or mothers or sisters, and I think that it is borne out by the dramatic downturn in the number of pieces of mesh being put into women for SUI in our country and elsewhere.

A couple of other things that I think we do need to think about in future. One is what this says about the licensing regime for medical devices. Clearly, it cannot be the same as the regime in respect of molecules medicines. You can't undergo randomised controlled double-blinded trials in the same way for obvious reasons for a device, but the licensing system, I think, for devices is still far too rudimentary. In some instances, I think it's like the Wild West.

There are, of course, famous examples such as testing the extent to which a piece of orange, the fabric from a bag of oranges might pass the test to be perceived for mesh. Now, that's an anecdote but the reality is that system of equivalence and not having to really go through the same degree of rigorous tests if you are a follow-on producer of a second or third generation mesh, all one needs to do is to demonstrate that your mesh has similar properties and similar efficacies to the original device.

That cannot make sense in the 21st century. We do need to come up with a better means of testing and verifying that devices are safe and efficacious, and given that this is such a big, growing area of medicine and given that we can see that there are going to be many more devices for many more sorts of conditions, this is a moment for us to put our foot on the ball and think about getting a system ready for the next 50 years of development of devices, because the current one just isn't fit for purpose in my view.

I think the last thing I would say is that the - it is wrong that it has taken women to rightly kick and scream and make a fuss about the harm that they've been done for this to have become an issue of national salience, because the medical/clinical fraternity should have realised at an earlier date that this was an emerging problem, that the anecdotal evidence in our country and elsewhere, that was becoming ever more clear, ought to have triggered an earlier review as to the safety of these devices and it took political pressure and, in particular, pressure from individuals like Kath Sansom and all of the other campaigners with the different campaign groups to get this onto the Government's radar, onto MPs' radar and,

frankly, to force the colleges and the individual clinicians to think much harder about the scale of the risk.

There is still a gross reluctance, I think, to acknowledge the scale of risk. There is still pushback. There is still a sense, well, the evidence says it's only 4 or 5 per cent and it's really small. Frankly, if it is 4 or 5 per cent, that's too many, but if it is 10 per cent of women, of the thousands of women, or if it is 20 per cent, as I suspect it may well be over time revealed to be, then that is an enormous, scandalous volume of harm that's been done by these devices, and unnecessarily so in so many instances.

So the system, I think, needs to take a look at itself as a result of the mesh scandal, and I think the women who have very bravely, quite often through the pain and discomfort that they have to endure on a daily basis, whether that's coming to Parliament to take part in meetings or giving evidence to this review or making known their issues, their problems in other means, they've been very brave, many of them. [REDACTED] one example. There are thousands of them and many thousands who I suspect have not been able to take part because their lives have been damaged by it, and I think we need to make sure parliamentarians and clinicians and all of us that it doesn't happen again in respect of other women for some other reason with some other device.

It's a very easy thing, I think, to say to a mother, this really simple procedure will only take 20 minutes, in and out, and you'll be able to carry on doing the things you were doing before you had kids and you had what so many women experience in terms of the changing nature of their bodies. It's just not good enough for women to have to run this degree of risk.

Julia Cumberlege: Right. Well, thank you so much. That was an amazing exposition of what has gone on and your hopes for the future. I thought it was very interesting you started off with [REDACTED] and we've heard so many similar stories, but everyone is unique, everyone's experience is different, but clearly, there are some overall themes, but we will never lose sight of the individual cases and the tremendous suffering that they and their families have suffered. So, talking with great authority, I think it's very interesting, what you were saying about the controversy with the NICE guidelines.

That's something I think we need to address. The data analysis. We share a view that HES is imperfect. It's not the most perfect system. Coding needs to be much more accurate, and the misleading language that has been used in the past, we have also heard that. Your wish for a retrospective audit, we need to think very carefully about that. It's clearly an extremely

difficult thing to achieve, but it's something that is on our radar.
Compensation, clearly other people have raised that.

Just looking to the future medical devices and the licensing system, you said it was rudimentary, and again, that's an issue that we're thinking about and the equivalence assessment, and I think your words were, it's not fit for purpose. That's something that needs to be looked at. Also, of course, your view, very much shared by us, that it's not right that campaigners have had to get this a national issue, an issue of huge importance, but it is really their energy, their determination, their courage in bringing forward individual cases of the experience that they have given to us and, indeed, as Karen did to you, that is so important.

So, clearly, we need to think about the future - the future's hugely important - and share your view that we would not want this sort of thing to happen again. How we prevent it is going to be a great challenge because devices will be coming on stream.

Owen Smith: Yeah.

Julia Cumberlege: Pharmaceutical companies and other device companies will want to promote what they believe will help people, but it needs to be properly assessed before it's put on general release and is used. So that's been extremely helpful, thank you very much indeed.

Owen Smith: Well, if I can briefly raise two other things that have...

Julia Cumberlege: Yes, please do.

Owen Smith: ...occurred to me while we were talking, and they're about the present day, as it were. I think there are a significant number of women who've clearly been injured. I know that this is something the review has already addressed in terms of the conditions that you've put on record as needing to be met before the pause can be lifted, but the lack of a clear set of signposts to where women go if they have been injured, where devices might be removed, who are the right people to remove those devices, and what sort of care women might need physically and psychologically in some case, is I think absolutely essential at the moment.

After the initial review that Keith Willett undertook - and I would also like to place on record that I think he's been hugely important and instrumental in getting this onto the political radar, in fact, I think more so than anybody behind the scenes - in taking seriously and putting in place the evidence that was necessary to get this taken seriously by the Government and institutions. I think it's a shame for me that he's not involved any longer,

but I know he's gone on to bigger and better things. When that initial review suggested, I think that there were 13 or so mesh removal centres or mesh centres of excellence across the country, I think what it disguised were the very different levels of expertise, volumes of patients between those different centres.

We actually have big, black holes across the country where there aren't real experts and there isn't an adequate care pathway for women and there aren't the sorts of multidisciplinary teams that are required to assess women properly, and there aren't the requisite surgeons with the skillsets and the experience to remove the mesh. So I think we've got to come up with maybe - and maybe one suggestion is that we do need to think about some sort of specially commissioned pathway to deal with the bolus of women who've been injured, because I don't think it's so enormously great that it wouldn't be possible to come up with a special pathway as we do for rare diseases and rare cancers, et cetera. I'd centralise that to some greater extent.

The second thing I'd say about that is I'm a devolver and believe in devolution, but I think this reveals one of the weaknesses of devolution which is you don't have always the same degree of expertise in Wales and Scotland or Northern Ireland that you have certainly in London and other big metropolitan cities in England, and we don't always have, I think, the seamless working between the administrations and institutions in all of the different jurisdictions across the UK.

That is - we have got to get better at that because, frankly, devolution cannot allow different citizens in different parts of the UK to be getting radically different services from their NHS. They all pay the same taxes and they all should expect to be able to get a reasonably similar experience, in my view, across the UK. When you've got specialist conditions such as this, it isn't going to be possible financially or in terms of human capacity to replicate the services in all part do the UK, so we've got to get better in joining up ministers and their officials to make sure that people can cross borders and be treated more efficiently elsewhere.

I know they will tell you quite often they do do that, but there are myriad instances I've come across where there are just so many impediments to treating people across borders. Quite often, one part of the system doesn't know what the other part of the system has or does, and equally quite often doesn't know the individuals involved who are becoming rather more isolated, I think, between different health communities in different parts of the UK, so getting that right in future - frankly, not in future, getting it right

PDQ because these women are getting older and are experiencing problems and they deserve to have the system responding rapidly.

Julia Cumberlege: Yes. Can I say, we had a very interesting visit to Cardiff, and also to Belfast. We've also heard a lot from the mesh survivors, the Welsh ones...

Owen Smith: Yep.

Julia Cumberlege: ...and also those from Northern Ireland, and I think what you've just said is of huge interest. I want to ask you a question...

Owen Smith: Sure.

Julia Cumberlege: ...about regulators, but before do, I think Sir Cyril, did you want to come in here?

Cyril Chantler: It was just on your last point, because women have told us about their anxiety about getting specialised services when they live in South Wales, where those services may only be available in England-adjacent - well, I guess in North Wales, too, though we haven't heard so much from there, but that's also been in the newspapers recently.

Owen Smith: Yeah.

Cyril Chantler: I'm not sure whether that's within our unit or not, but there are, I think, essentially political questions there that have to be addressed, and I don't know how those would be addressed because that's beyond my pay grade, but maybe you'd like to explain that to me.

Owen Smith: Well, look, I'm a former Shadow Secretary of State for Wales and a former Shadow Secretary of State for Northern Ireland, and I was a special advisor to the last Labour Government in Northern Ireland, where we were dealing with some also thorny health problems. The system is devolved and, therefore, there are Chinese walls and segregation between the differing health systems. However, there have always been instances where there have been specialist commissioning pathways recognising the fact that you won't have always all of the top machines or surgeons or capacities in all parts of the country, and therefore, there has to be a way to signpost and get women to be seen in the right places and by the right people.

Translabial scanners is a good example in this instance. I don't think there's one in Wales. I know a lot of surgeons now have the view that that is one of the most effective ways that we might determine whether mesh is the cause of a problem that a woman is experiencing. I don't think there's one in Northern Ireland but there are several in England. Now, I know that

women are finding it hard to get referred to be scanned using a translabial scanner in England.

Now, that is a political decision at one level, but ultimately, it's about different bits of the NHS working together because there are memorandums of understanding that have long since been signed that should, in theory, not make that a problem between Health Ministers, but quite often, it's at the operational level that people run into the brick wall. Sometimes, it is because the surgeon in Country A won't know the systems in respect of Country B. If you've been a surgeon in Wales for the last 25 years during a period of devolution, you may not know where it is you might refer someone to have a translabial scan in England. Ultimately, there has to be some centralised system...

Cyril Chantler: So the administrative systems necessary to refer to - enable smooth running of that referral system are in place, I believe?

Owen Smith: Well, the political system certainly is there, inasmuch as there is a memorandum of understanding signed between all of the health ministers across different parts of the UK that is meant to facilitate cross-border treatment where appropriate and where necessary. I think what is probably required in this instance is there needs to be, by NHS England, some thought given to what the optimal care pathway is for women who've been injured and that then, there needs to be dissemination of that and opening up of that to women in other parts of the country where they won't be able to develop a similar and perhaps similarly excellent care pathway, because they simply will not have some of the requisite individuals or kit.

NHS England has to take the lead, and in reality, that is what's been happening. NHS England has been in the lead in respect of thinking through what the care pathway looks like, although Wales and Scotland and Northern Ireland were perhaps a bit quicker to spot some of the problems and quicker to respond, I think, to the women's concerns, which may say something about the benefits of a smaller scale of health provision, but equally, there are risk benefits which are about capacity.

So I don't think it is in your remit to fix that, obviously, Sir Cyril, but I think it might be something, given that you've taken evidence from all around the UK, that you might reflect that, effectively, the sorts of specialist care pathway provision that is undertaken for specialist drugs or specialist interventions, people coming for certain cancers to London, for example, might be undertaken in respect of mesh removal for women so that they

know exactly where they're going to go and to whom they're - that they're going to see somebody who really knows what they're doing.

Because the other problem - and I know this'll be blunt - in some of the centres of excellence that have been listed, the surgeons or the experts are the one who put the mesh in in the first instance. So it's not inexplicable that the women then don't feel terribly comfortable about going back to go under the knife with the same person. So, getting that right, I think, would make sense. Thank you.

Julia Cumberlege: Now, we have been to Scotland on two occasions...

Owen Smith: Of course.

Julia Cumberlege: ...but, of course, they have a stronger devolution aspect in terms of their parliamentary system. Can I just ask you about the regulators? Have you any views on the regulators?

Owen Smith: Yes. I worked in the pharmaceutical industry before I was an MP for a period, and I think the reality is that medicines regulation in our country has largely been - I wouldn't say a rubber stamping exercise, but we have been part of a very centralised European system for a long period now, and the role of the MHRA therefore has been very often - not always, but in most instances - to say yes to things that the European Medicines Agency has approved.

So I wonder whether our MHRA has been as robust as it might have been if it were undertaking these things without external guidance and a European level of scrutiny and approval prior to medicines being marketed or available for marketing in the UK. So I think post-Brexit, if we do Brexit, one of the things that ministers have got to get right is strengthening the MHRA in order to reflect a greater degree of independence, but on the issue of devices, I think the MHRA is reflective of regulatory authorities all over the world, which is that they are behind the curve in respect of medicines.

I think there has been a bit of a - I think there's been complacency, and on the basis that there is kind of a widespread, not unreasonable initial assumption that you can't have the same degree of pre-marketing scrutiny for devices as you have medicines, for the reasons I described earlier, and an assumption that the degree of risk and the level of harm that might be inflicted on patients through devices is that much lesser than medicines, which again is not traditionally an unreasonable thing to think, but when devices are becoming more and more invasive and more and more important in respect of preserving life and bigger interventions.

I'm not just talking about pacemakers, but other ways in which the brain and the heart might be stimulated electrically or by other means, or implanted medicines that are hybrid medicine and devices, we're seeing developed all the time now for diabetes and other things. The truth is, the medicine that is being implanted will have been subject to dramatically more rigorous testing than the piece of plastic that's stuck in the arm for these diabetes, for example, interventions. That can't be right.

Therefore, there has to be a better, I think, set of standards and regulations that apply more computer-based testing, more in silico testing, as they put it, a greater onus on the companies to undertake as rigorous a set of clinical trials as they can. You can't obviously replicate it, but as rigorous a set of clinical trials as they can. Crucially, and I think this is the really key part, a much bigger onus on the companies bearing the cost and implementing proper post-marketing surveillance. So they are monitoring exactly what their devices do, not just initially but over time.

The truth is that the devices companies have essentially deployed what is quite called fire and forget. They market their product, they get their product developed, they get it on the market and then they market it to people. After that, not their problem. After that, it's the clinician's problem. That has to change. There has to be a greater emphasis, I think, on their maintaining databases and registries. Now, some of that stuff is being resolved for them centrally by the introduction of kitemarks and data which will be able to identify RFID systems, et cetera, identify whose device is in which patient, but frankly they will, I think, need to do more in future to take greater responsibility for these devices if they are going to market them as widely as we anticipate they will in the years to come.

Julia Cumberlege: Thank you very much. Simon?

Simon Whale: Well, I was going to raise a linked point. So, these devices such as mesh are designed to be implanted in the body for life. That's the purpose of them. As you quite rightly pointed out, it's very difficult to provide pre- authorisation, pre-licensing R&D that demonstrates safety. So, my thinking is around the consent process. When a woman or, okay, person in the future, not just necessarily mesh-related, but someone who's considering such advice is being consented for that, how do you achieve informed consent?

Because does the system, does the clinician or the regulator or both need to in some ways be clear about what they don't know about the long-term, lifetime impact of having this device inside of you, as well as what they do know from pre-market testing and the post-marketing surveillance, as you

rightly pointed out? So does there need to be that what we don't know consideration, and if so, what impact does that have on the individual patient?

Owen Smith:

I think that's a really good point and speaks at some level to the heart of the problem that we have had with mesh and the acknowledging recognition by the clinical community of the problem and the scale of the problem, because the system is predicated on the evidence and the surgeons, not unreasonably, say, well, the evidence shows that this is safe and efficacious. Indeed, the evidence shows that there's only a 1 to 3 per cent complication rate.

What the evidence doesn't show quite often is what the complications are and, more importantly, when there is no real financial incentive to undertake intensive or, indeed, arguably any R&D or clinical studies in respect of devices once they've been licensed and are on the market. Then you've got always a dearth of evidence, so part of the problem with mesh then and now is we haven't really got enough evidence about its effects. We are all still making some assumptions about its efficacy and, critically, what proportion of women undergo problems and how serious those problems are.

There is no real financial incentive for any of the device companies or, indeed, the NHS, arguably, because they are potentially disincentivised themselves from undertaking research that would prove that there had been problems as a result of the insertion of mesh. So you've got a fundamental issue there about evidence. In respect of - so I think the point you make that, should people be told what we don't know as opposed to simply being reassured that the evidence shows that things will be well, is a really good point because, in this instance, I think a more appropriate and respectful consenting process would have said to women, look, you've got this problem. Only you know how serious it is.

There are two or three ways in which we can try to resolve it if you - but the first instance, physiotherapy is clearly the way in which they would recommend you undertake it, but there are then two or three different ways in which you might undergo a further, more invasive process, and these are the sorts of benefits and disbenefits of each of these individual processes. Crucially, as you say, long-term effect, mesh would be a good example, wouldn't it? You'd have to admit that colposuspension, autologous sling quite often don't work and may stop working after a period and are more difficult to recover from and do lead to greater pain post-surgery for a greater proportion of women.

So you need to be honest about that, but equally, you need to be honest that there have clearly been very many instances - and we don't know precisely how many - where women have encountered significant problems with mesh, too. So yes, in principles terms, I think the key thing is doctors need to treat women and men, but women in this instance, as able to assess risk more efficiently than they allow. Again, this is a debate that's been had in the medical fraternity for ever and ever and ever, how do patients, individuals without medical knowledge have an adequate sense of what risk is? I think my observation is that people actually, in common sense terms, are pretty good at assessing risk.

The common-sense way to describe this is, if you said to a lot of women, look, you've got a problem with incontinence when you're engaging in an exercise class or going jogging or dancing or whatever because your pelvic floor is weakened post-childbirth, and that's probably going to go on for a long period. You could have this intervention, but as a result of it, there's a risk - let's call it one in 10, let's call it one in 100 - that you are going to have chronic pain for the rest of your life and not be able to have sex, then how many women do you think, if it were put to them like that, will say, well, I'm going to go ahead with that? I suspect very few, and I suspect that isn't how it was ever put to women, which is why we've got this problem.

Julia Cumberlege: Thank you very much. Valerie, you had something you wanted to ask.

Valerie Brasse: Well, it was just really to go back to a point that you raised earlier about the opacity of NICE guidance and guidelines. Indeed, I think it is a problem and one that we are actually in a conversation with them now to try to resolve, because you raised the particular point about the research restriction for women who will be treated with mesh for anterior or posterior vaginal wall prolapse. I think we have all been under the understanding that that had been lifted as a result of the new guidelines which don't make any mention of that.

I am in conversation with NICE and my understanding is that the old guidelines still exist. They have not changed. They have not been withdrawn, which is slightly confusing to say the least for all the women because, clearly, people have been under the impression that it was lifted.

Owen Smith: Yeah.

Valerie Brasse: The, I suppose - so as I say, I'm in conversation with NICE to just tell me chapter and verse as to whether it still stands, because that does make a huge difference.

Owen Smith: Yeah, look, one of the things we argued as an APPG from the first moment we were formed - and that is because we respect NICE greatly and they do, I think, excellent work most of the time, and they are hugely respected all over the world for the quality of the work they do. I think they are a vital arm of the state in terms of giving doctors a sense of not just the cost-efficiency of medicines, but the efficacy and safety of medicines, too, but they are opaque, the way in which they go about things.

The thing that was initially deeply irritating is that they refused to bring forward the timeframe, or they refused point blank until they eventually did for this review, even though this controversy was on fire all over the world. NICE's attitude to it is, we've got our schedule and the schedule says, I'm afraid we're not looking at until March in two years' time because the computer says no, there's nothing we can do about it. That struck me as completely bonkers, frankly. Then, when they do produce this, they produce it alongside your review, and as I said earlier, I think it was very confusing as to what it was, they were saying.

I also think they play a bit of politics in this because, if you look at the press releases that they put out about this, I think that there was a bit of politics played with that, as well, as to what they were saying. Were they suggesting that they were in line with you and this was being paused or was there no change at all and it was exactly the same as the previous set of guidelines on SUI, though that always said, effectively, it was third-line? I just think they need to be a bit clearer.

I'm sure that clinicians and Royal Colleges that had been hitherto incredibly defensive of the way in which mesh had been deployed and of the safety and efficacy of mesh, they were no doubt lobbying NICE during this process, informally and formally, with those views, and those views did seem to me to be better reflected in the NICE guideline than the views of millions of women all over the world. It's not forgetting other countries. The Australian Health Minister has formally apologised to women for the harm done to them by mesh. This isn't a small thing. Other countries have banned mesh, too.

So this is happening all over the place, and I think the slightly opaque language that NICE uses doesn't help, in particular where you've got something where it isn't just the clinicians who are looking at what they've written, but patient groups and patients, some of whom are understandably deeply, deeply interested and concerned to find out what the guidelines say. I think we've got to think about their responsibility in that regard.

Julia Cumberlege: Simon, have you got - no? Can I just go back briefly to the issue of the industries, where you said they should take responsibility? Are you suggesting - what are you suggesting?

Owen Smith: Well, I'm suggesting quite straightforwardly that they need to keep a track of to whom the devices - bluntly, whose devices they've - to whom they've sold their devices, they need - part of the problem we've had with the registry is that every everybody's saying, well, who's going to keep it? Is it going to be one of the Royal Colleges? Well, there are two registries have been set up, should we have a specific central NHS England registry as we've got in respect of other conditions? Who's going to own the data and who's going to be responsible for it?

I think, ultimately, it has to be an NHS England or NHS UK centrally-held official registry in respect of mesh, but you're not going to have that for all other devices, are you? Lots of other devices, when they come onto the market, whether it's whatever, if they're uncontroversial in the first instance, there will be no demand for a register or, indeed, sometimes there may not be specific enough coding in respect of those things. So one extra way in which we guard against problems not being picked up over time is that the device companies themselves are under a greater obligation to track and record the people in whom the devices have been implanted and to keep some sort of further registry.

A simple thing to address, it would be that there is some sort of financial responsibility on their part to support device registries that are centrally held, that there is a contribution that they make to the state in order to market their devices in that state, such that that state can then retain a registry. I don't think that's an unreasonable request, and I think it is something I know that's being thought about elsewhere. There are other instances where similar contributions have been sought from pharma companies to engage in support for the dissemination of their product in a country. This would be a similar mechanism.

Julia Cumberlege: I can understand all that very clearly, but it has been put to us that maybe there is some responsibility to those people who have been injured by the insertion of mesh, and people have said to us maybe there should be a levy.

Owen Smith: A retrospective levy, you mean?

Julia Cumberlege: Well, no, it would have to be for the future, I think, because it would be a levy for the future, for when damages are...

Owen Smith: I think that's a very interesting idea. Look, I think there are...

Julia Cumberlege: Would it not be practical?

Owen Smith: Look, there are clearly instances that I've read about in court cases in other jurisdictions which indicate that they were on the part of some companies a greater degree of understanding of the emerging evidence of problems with mesh. Now, I don't know the full extent of that, and I think that's being tested in courts all over the world, but my gut instinct is that some of those problems were probably better understood by the companies than they let on, and I would be extremely surprised if those companies weren't monitoring very closely, even if they didn't know exactly whether it was their device or somebody else's, the volume of problems that were emerging in health systems in different parts of the world.

Now, that indicates to me that they have a degree of culpability and responsibility - as corporate citizens, if nothing else - to engage in this process, and not just in respect of the individuals who are bringing court cases, but in respect of the wider group of women who may have been impacted, a levy might be one way in which they acknowledge that and one way in which they contributed to recompense for women. How that would work, exactly, I don't know. I don't know of any other instances of where that's been undertaken, but I certainly think that's something that ought to be put to the companies for them to think about, yes.

Julia Cumberlege: All right, thank you very much indeed. I think that's all that we would like to cover, but can I thank you so much?

Owen Smith: You're welcome.

Julia Cumberlege: It's been a very, very interesting session and you've brought a lot of ideas to us, and thank you for that. Of course, you speak with huge authority, not only in your work in the past before you became an MP, but having researched this so clearly as the Chair of the All-Party Group, so thank you very much indeed.

Owen Smith: Thank you very much for inviting me to speak to you.

Julia Cumberlege: Thank you.

Cyril Chantler: Thank you.

END OF TRANSCRIPT

Session 2: Hormone Pregnancy Tests APPG*

START OF TRANSCRIPT

Julia Cumberlege: Good afternoon everybody. It's very good to see you here. Thank you very much for coming. It's not the first time we've met, but I thought for, perhaps, Jacob, if we just introduce ourselves, because I don't think you've met us before. I'm Julia Cumberlege and I've been asked to Chair this review. On my right is Simon Whale, and he has been very involved in the communications, he's the communications expert and has been very helpful, and Sir Cyril Chantler is my Vice Chairman. So we are the three members of the panel. We are very ably supported by our Secretary, Dr Valerie Brasse, who is on my right over there, and also Sonia Macleod, Dr Macleod, who is our Senior Researcher, and then other people in the room are here just to support the session, as it were.

So, Yasmin, thank you so much for coming and bringing your colleagues with you. I really want to say how much I think you've achieved as an All-Party Group and I think without all of the PQs, without all of the debates and everything that you've put forward in Parliament, this subject would not have the high profile it does now and indeed, I think would not have been included in the Review. But it was seen to be a very important area that in the past has been neglected to some extent, despite all the efforts that you and your colleagues have made.

So I know it's not just the Parliamentarians you've worked with, but it's also working with the patient group. I would like to pay a tribute to Marie Lyon and to her husband, Mike, who has come here. Together they have researched so much of this area, both nationally and internationally, and of course, have spoken in Parliament and held sessions there as well. All the questions that they've raised that has affected families, we've heard those and that's been really, really helpful to us and, of course, the evidence that they've given both in writing and verbally.

Marie Lyon and her husband here today are observers, although I'm sure she will be itching to talk, but I'm afraid this time, no. And Jason Farrell, very good to see you here also as an observer. Thank you very much.

So just to set it briefly in some context. As you are very well aware, we've been travelling the country. We've been talking to a lot of individuals. We've heard a huge amount from families who have been affected by HPTs and we are now nearing the end of our oral evidence. It's not complete because we want to finish by listening to the patient groups again. We're going to invite them back again. All our sessions have been screened, they

are on the website so people have been watching that. We intend to do that today and I hope that's alright with you. Great.

So just to stress that patients have really been the heart of our Review. I want to take this opportunity to pay a tribute to the courage, to the physical and mental suffering that we've heard, the impact, particularly of Primodos that has had on families. The guilt that mothers have felt in connection with this medication, unwarranted guilt, but nevertheless they feel it and they have told us about it. Then it's been about the struggling, the getting through life and also the worries about the future and they are very real indeed. So we've heard a lot of heart-breaking stories, but I have to say we've been really struck by the courage and dignity of those that we've met.

So to go to this hearing, it's really an opportunity for you to tell us what you think, as an All-Party Parliamentary Group; things that you think we really have missed that we need to know, and things that we should focus upon, particularly on the future because clearly that has been part of the statement that Jeremy Hunt made when he set up the Review, to look to the future. And, of course, you can raise anything else that you wish to comment on, on the evidence that you yourselves have received.

So, as I've said, we are recording this session. So it would be very helpful on that basis if I could ask you to introduce yourselves so that people watching on the website will know who you are and why you're here and if there happens to be a vote in the Commons, then, of course, we would expect you to go on the vote and we'd hope you'd come back as well after that. So is that alright? Is that all clear? Okay, so Yasmin if you'd like to start by introducing yourself and perhaps your colleagues would like to introduce themselves or you may want to do it.

Yasmin Qureshi:

Well thank you. I'm Yasmin Qureshi, the Member of Parliament for Bolton South East, Shadow Justice Minister and Chair of the All Parliamentary Group on hormone pregnancy tests. Can I just say on behalf of the All Parliamentary Group, to thank you Baroness Cumberlege and Sir Cyril and your team for the all the work that you have been doing on this Review and the considerable undertaking that you have taken. Thank you for giving us the opportunity to speak to you today.

I'm proposing to go into three aspects of the whole inquiry and my colleagues will deal with some other aspects. We are trying not to repeat ourselves. Although I know that inevitably some of what I may say today is probably repetition, but it is just important to set the scene. By way of background, the APPG was set up in 2014. Prior to that Marie Lyon and I

for some time were knocking on the door of governments but we were really not being heard. Indeed, we sent several letters and questions and as you have mentioned earlier in your introduction, questions, letters to different ministers, and we basically were getting no response.

Eventually we did have one Health Minister at the time, Daniel Poulter, who agreed to meet us and he then asked MHRA to set up a short review in to whether there was any link between Primodos and deformities. As you probably know that review found there was not. However, we did not accept that because clearly from the documents that we have seen, from the information we have, that we felt that that conclusion was completely wrong. Therefore, we continued, Marie Lyon and my office, and we have now an APPG which has 135 Members of Parliament on it and I'm proud to say, one of the largest and most active of these All Parliamentary Groups. I'm really grateful for all my parliamentary colleagues, not just the ones that are here today, and others because this is one of those groups where the MPs actually take an active, conscious role and participate in [whether it's urgent] questions or debate.

As you know yourself when you came to one of our meetings, how packed the room was, the committee room was. The amount of passion and feeling in this case. It's not party political, this is above anything to do with politics or any particular government because we feel that there has been a failure for many, many years across the board.

I think the reason the Members of Parliament are so concerned and are passionate about this is because we want answers on behalf of our constituents. This is very much constituent led. I think the first part of it is the historical evidence. There have been countless official documents and letters exchanged between government officials, doctors and the scientists, and I know you probably have seen some or maybe will be seeing some. What they show is that the gynaecologists, the paediatrics, the medical profession, people were raising the fact that this Primodos could affect the foetus or cause children to abort.

Some of these files, however, were classified until 2010 and only came to light a few years ago. Let me give one specific example. So in 1967, the then Committee on Safety of Medicine, was contacted by a paediatrician at Queen Mary's Hospital in London, Dr Isabel Gal, I'm sure you've heard about her, who said that there was a link between hormone pregnancy tests such as Primodos and spinal congenital malformations in new-borns.

The Minister of State at the time said, she has produced prima facie evidence that foetal abnormalities might be associated with the use of

hormonal pregnancy testing. Then that same year there's a letter from the Medical Research Council, which states, it looks like, in fact, that this could be another thalidomide story. The Royal College of General Practitioners then produced figures for, in fact, Schering, the pharmaceuticals, showing the high rate of miscarriages, stillbirths, infant deaths and abnormalities of babies whose mothers had taken the hormone pregnancy test. In fact the report's author, Mr Dean, concluded, and I know you've heard from Jason in his evidence session where he touched upon Mr Dean's evidence, and he actually concluded that the drug should be withdrawn. I would like to emphasise that the drug should be withdrawn.

In 1968 the Royal College of General Practitioners sent a letter to Dr Inman, who was the Chair of the Committee on Safety of Medicine, the regulatory body at the time, stating that 10 per cent of abortions recorded after Primodos were unlikely to be due to a chance. The same year Schering's lead UK scientists wrote to their parent company in Berlin stating, 'it is extremely disturbing that the results of statistics, human studies and other studies all point clearly to the possibility that Primodos may interfere with pregnancy'.

Despite knowing all of this, the drug still remained on the market. So we want to know why? Why on earth was such a drug kept on the market given the gravity of the severe congenital abnormalities? The drug should have been immediately suspended, pending a full clearance by the committee because unlike some drugs like Sodium Valproate which your inquiry is looking at, they actually have a medicinal purpose, but this has no medicinal or therapeutic purpose. So it could have been quite easily withdrawn from the market and the fact that it wasn't, in my opinion, and I think my Parliamentary colleagues, was a complete and utter moral dereliction of duty and not just moral, actual legal duty as well. Because I know people say, well things were different in those days and it may not happen again, but I'm sure the legal obligation and the moral obligation to protect patients would have been there just as much paramount as it is now. So why?

One and a half million pregnant women have been placed at unnecessary risk by being prescribed these drugs. Thousands of children were damaged, suffering from dreadful disabilities, many are brain damaged, some have spina bifida, others have heart and limb defects, cleft palate, deafness and other horrible disabilities. They don't need to have had those. This could have all been stopped and instead of taking action, the government said nothing. Nothing at all. Even though the evidence that Dr Gal presented, which was dismissed by the Committee on Safety of

Medicine - in a very interesting letter to his colleagues, Dr Inman actually said, 'I have had an exhausting meeting with Dr Isabel Gal. She believes she should have had more funding for research and that a larger number of abnormal babies may have been born in the time that has elapsed'. He said, 'we are defenceless in the matter of the eight year delay', and I know you are aware of the fact that it took eight years before the actual product came off the - is it Primodos came off the market. He goes on to say that Dr Gal is an intelligent, dedicated but rather sad little person. 'I dealt with her sympathetically but I do not believe that we have heard the last of this matter'. Can I say on this he is absolutely right because this isn't the last of this matter. We are determined to ensure that we get to the bottom of this and get justice for the victims of the drug Primodos.

On the issue of Schering and Bayer's role you heard from Jason, who as you know has also been investigating this matter. He gave in his evidence that in the '70s Primodos lost its licence to be used as a pregnancy test drug, but the Committee of Medicine, the regulatory body, failed to warn the doctors until 1975, and then in a letter it suggested that it may cause congenital abnormalities. In 1977, it actually stated that association has been confirmed and Bayer confirmed to Sky News that the drugs had not been licensed as pregnancy tests after 1970 and that anyone using it would have been doing so off label. So, again, there are serious questions. Why? Why were they still being given to women who they thought they might be pregnant even though the non-invasive cheap urine test was available, despite that it was being given.

It wasn't until 1975, as you are probably aware, that the label on the packet said, 'not to be taken during pregnancy'. A possibility exists of an association between the use of Primodos during early pregnancy and an increased incidence of congenital abnormalities. Because of this possible hazard, Primodos must not be taken unless it is certain that the patient is not pregnant. But, again, nothing happened.

Since 1967, in fact, I think there is evidence that shows that since the mid '50s the medical community had been aware of the fact that there were potential problems with this drug. All these years, nothing done again. The Committee on Safety of Medicine didn't even bother to inform the doctors that actually Primodos can no longer be used as pregnancy test. So doctors continued to prescribe this drug, even after 1975. That is evidence of malpractice at a very large scale.

Coming on to the expert working group, after a full debate in the big chamber, the Minister in 2015, George Freeman, set up an expert working group and he agreed in the discussions we had with him and on the floor of

the House, that this will be an independent review and that all the evidence will be released and reviewed. This is really important; all the evidence being reviewed and we mentioned to him about a document that shows the cover-up because if I may go back, when I first became involved in this case, through my constituent [REDACTED] I went to her home. I met [REDACTED] and there were boxes of papers. I actually went through quite a lot of those documents and it was when I was reading those papers that I thought to myself, there is, in my opinion, and I'm not a doctor or a scientist, but looking at the document, one thing was very clear, there had been a complete cover up here. People knew what was going on and they've done nothing.

We were very anxious for that information to be given to the expert working group. We were anxious that the evidence that was covered by Sky, should have been before them. We were anxious that the evidence that Marie had discovered from the Kew Archives, should have been before them. But it turns out that actually EWG never looked at these documents and as I understand it, and I hope you'll correct me, the MHRA were the persons who were controlling what they were supposed to look at.

Now to me, that is fundamentally wrong, because if you are setting up an inquiry, you can't have another body saying, you group of experts you look at this information but hang on, you're not going to look at 20,000 other documents. How are they going to arrive at any conclusion, a real proper inquiry, without sight of those documents?

We expect as matter of course, that the people sitting on the EWG, as well as the MHRA, are independent people. People, who, if they have any interest in the medical or have been sponsored or financed or worked for pharmaceutical companies, that they will be declaring that and, in fact, automatically almost perhaps rule themselves out. But the Chair of the expert working group told us that they had a system of self-declaration so people could declare if they wanted to but not if they didn't want to. It was Marie's research that led to at least one panel member being taken off the expert working group.

When we find out how MHRA is funded, by Big Pharma and then it only gives part of the evidence and papers to the expert working group, then we are bothered; we are concerned because we don't believe that that was therefore, a) an independent inquiry and b) and this is really important, that most of the substantial evidence, papers we wanted them to have looked at, they never looked at. Again, we've had no real proper explanation given as to why that sifting was taking place. Why pick and choose? That wasn't the purpose of it because otherwise, and I've said this

is Parliament, and I believe it, the EWG's work is really not worth the piece of paper it's written on because it's not comprehensive. It didn't look at all the documents. Had they looked at the boxes, thousands of documents, and every piece of paper available, I don't think they would have come to the conclusion they have.

Then, of course, we have the issue about how this evidence has been assessed by the Review team. Here I'm guided very much by what Professor Carl Heneghan set out, because, obviously, he's the expert in this matter. I have a lot of faith and respect in him because he's an academic, he's an independent, his funding doesn't come from pharmaceutical companies as I'm aware and he's at one of the most prestigious universities in the world. He sets out very clearly in his evidence session and I don't want to repeat myself, about how he thinks the methodology should have been; what the correct methodology should be, the meta-analyses, the way the analogies occur, and it appears that none of those methods was followed in this expert working group.

Then there is the issue of transparency. Why was it cloaked in so much secrecy? Marie Lyon, who in the end they agreed to be able to sit in in this inquiry as an observer, was not allowed to discuss her concerns with us because she had been made to sign a gagging clause which said that if she said anything, she could end up going to prison. Now when the Member of Parliament for Livingstone, Hannah Bardell and I tried to attend a press conference for the launch of the EWG report, we were locked out and told we couldn't enter. Two Members of Parliament representing their constituents being told you're not welcome. What has everybody got to hide?

Then, as we said, we have clear concerns about the finding of the EWG? We do believe it's a whitewash. It should have been peer reviewed. I understand that there is normally an industry wide expectation that some kind of peer review would be done. Not here. In fact, the only body that was going to carry out the peer review was the MHRA. Well the MHRA could hardly be considered to be an independent peer review body because they are the ones who set up the EWG. They are the ones who told them what they could even look at. It's like themselves policing each other.

I know my colleagues will go into some other aspects of this, I just want to sort of effectively conclude by saying that, as I said, I got involved in it because of my constituent, just as my other parliamentary colleagues and because of documents that I read. The way the ladies who took the drugs, the way they were treated, the methodology, the content of the drugs, and

the fact, and I know my other colleague Jacob is going to go a bit more into this, about the fact it seems that Primodos was being used in parts of the world to abort. It seems that the pharmaceutical company knew that as well. The medical community even knew that and yet despite that they carried on.

So, I am completely - and I'm trying not to be subjective here; before I became a Member of Parliament, I practised as a barrister for many years. I do believe in something called evidence. I do believe in causations and all those other aspects. Looking at it, looking at what Professor Heneghan has found and what Professor Abraham has said and what Dr Vargesson has said, what happened to the ladies, what's the constituent component of this and also the fact that this drug had been used in many parts of the country to abort, leaves me beyond any reasonable doubt that the drug a) caused the harm and b) medical communities knew exactly what was happening and c) there was a complete cover-up. Thank you.

Julia Cumberlege: Well thank you very much indeed. A very thorough exposition of the history and also your concerns which I think are extremely valuable and we may want to go into some of those a bit later on, but does one of your colleagues want to come and...?

Edward Davey: Okay, my name is Edward Davey. I'm here as a constituency MP for Kingston & Surbiton and can I first of all thank you for allowing me to give evidence and also thank you for the way you've been conducting your enquiry.

This issue was brought to my attention by a constituent, [REDACTED], who had a child many years ago [REDACTED] who has many disabilities, life disabilities as a result, we believe, of [REDACTED] having taken Primodos. That's when I got involved with the debates and reading about the subject and talking to Marie and the APPG, but I've got more incensed as I've got involved in this because I believe there has been a cover-up and there continues to be an attempt to cover up. I think it's therefore the job of Members of Parliament to blow the whistle along with others about that.

I have, in both my speeches, the most recent debates over the last two years, I have talked about that. The most recent Westminster Hall debate on 23 April, I went so far as to say I think this is a national scandal. I think it brings shame on our country and, indeed, on [REDACTED] It's a shame because we're talking about a drug, there is no medicinal or therapeutic value, it was known to be suspect of causing congenital malformations, stillbirths and miscarriages. It had many warnings of adverse effects and yet there was no attempt by the regulatory bodies to either suspend the drug or take

it off the market. One almost wonders what we were paying them for. Of course, that drug was the pregnancy test called Primodos.

Primodos was unnecessary, it was invasive and actually it was untested. It was promoted at a time when there were non-invasive and safe methods of diagnosing pregnancy. You have to wonder what was motivating them, though I think we know.

During my April Commons' speech, I referenced the scientific evidence by Professor Carl Heneghan and Dr Aronson, that has been published, of course, and had been peer reviewed at least twice. The meta-analysis by Professor Heneghan and Dr Aronson found there was a clear association between HPTs and congenital abnormalities. Both Professor Heneghan and Dr Aronson are acknowledged to be leading experts in evidence-based medicine. They have practical experience in the field of medicine. Professor Heneghan is still a practising GP and you've heard from him.

But, of course, his meta-analysis was criticised by members of the EWG during an interview session with yourselves. The EWG have published a study in 2017 which had not been independently peer-reviewed. The EWG used the same data Professor Heneghan used in his meta-analysis, yet the group reached a different conclusion. Except, actually, they had two conclusions because they changed their minds. In the EWG report it was stated there was no causal association, but what was not mentioned in the report was the fact that they agreed there was a possible association, a statement repeated many times by members of the group in the same oral interview session. Why was this change?

Could it be that admitting that there was a possible association, could point to a balance of probability, a very important legal term in these types of cases? By admitting there was a possible association, past regulatory failures would need to have been reviewed, and if that review had been initiated, the damning evidence, I believe, would have been revealed which would have proven that the government health regulators failed in their duty of care. The regulators took no action to either suspend or take the drug off the market, as I've said, despite hundreds of warnings from both the medical profession and Schering's own scientists.

As you know, the Commission on Human Medicines have been responsible for the recent critical ad hoc reviews on both the meta-analysis and Professor Vargesson's zebrafish study. This Commission was previously known as the Committee on Safety of Medicines whose Chair was Sir Derrick Dunlop. I hope I'm not going too far just to note that the same Sir Derrick Dunlop advised doctors that they could destroy medical records if

they were concerned about giving evidence relating to adverse effect. Quite an extraordinary statement.

But I want to look at these recent reviews of the work of Professor Heneghan and Dr Aronson because remarkably the cover-up that I've talked about over decades seems to be continuing. That means you've got a very difficult job because you're hearing different views from different experts. I'm no scientist but I'm trying to read this material and come to a view as an independent person. But I do think this cover-up is happening and it goes to the heart of the problems that you're having to wrestle with. I just repeat that a failure to prove the science would stop the review of past regulatory failures, and I think there is a lot of people with motives to prevent that review of past regulatory failures.

[REDACTED]

[REDACTED]

But your Review has been mandated to look at past regulatory failures and so for the EWG and others involved, it was essential for them to discredit Professor Heneghan's findings and his conclusion that there is a possible association. Indeed, since 23 April, you know there has been two expert working group reviews of the Heneghan, Aronson analysis. One by the Commission on Human Medicines and one from the European Medicines Agency. Given what I've seen throughout this sorry saga, I was not surprised to learn that both reviews contradicted the conclusions reached by Professor Heneghan and Dr Aronson. The question for you and for others, is was their review a credible scientific review?

Now I'm no scientist. I can only go by records that I can read and sometimes, even understand. It's difficult to assess the validity of the CHM review, partly because the recording of the discussions during the recent CHM review were destroyed immediately after the meeting and only a paper copy of the minutes was produced. Unlike this hearing that you're putting on your website; everyone can see it, it's permanently there. It didn't appear to be the case in this recent EWG review. The minutes, apparently, do not reflect the full contents of the discussions. We know this because that information was revealed by attendees at the EWG meeting. I think this is astonishing that this is still happening. This lack of transparency of people who are trying to undermine scientific evidence by some very respected scientists.

The two main experts selected by the CHM were not epidemiologists. I've probably got that wrong. During discussions, they heavily criticised the Newcastle-Ottawa Scale used in Professor Heneghan's meta-analysis and they promoted an alternative methodology, ROBINS-I. Now, again, I'm not

an expert, I'm not a scientist, don't please ask me to explain these methodologies, I would fail miserably. I would just point out two layman's observations on them.

The Newcastle-Ottawa Scale, according to what I've read, is a well proven and well used methodology. ROBINS-I is a relatively new methodology and it has been subject to some heavy criticism. What was interesting, I don't know if this has been revealed to you, but the two main experts that were selected by the CHM to criticise Professor Heneghan's work and criticise his methodology, were leading designers of the ROBINS-I methodology.

[REDACTED]

What is also astonishing is that Professor Stephen Evans, who confirmed he was the lead on the EWG review team, is one of the collaborators in ROBINS-I. Now this may be completely innocent. It's just interesting. And remembering this is Professor Evans who concluded there was no causal association, EWG report of 2017.

Now attendees of the CHM review of the meta-analysis, were informed by the Chair that the EWG report should not be referenced during the discussions of the review. They were told by the Chair that the review of Professor Heneghan's work would be totally independent, with no input from anyone associated with the 2017 EWG. We've already identified that Professor Evans was associated with ROBINS-I and was the lead member of the EWG. We've also discovered that an employee of the MHRA, who made a highly critical presentation of the meta-analysis to the attendees prior to the presentation by Professor Heneghan and Dr Aronson, has now been found to work closely with the scientist who was a core member of the 2017 EWG from 2009 to 2012.

In response to concerns being expressed about the close association, we were informed that the MHRA presenter had not had contact with the scientists since November 2016. But remember the EWG review commenced in 2015. I leave you to make your own conclusions.

I think it is hard to believe that the CHM can claim that it is totally independent in this Review, when it's been tainted by prior knowledge and possible bias. I can't prove that, but in this type of world, all these associations, all these relationships, at least raise the eyebrow. I wouldn't be making these frankly astonishing comments on work that has been carried out in this country in recent months if I didn't think there was a history of such problems going into the past; going all the way into the past. What has most astonished me was some of the evidence that was

found in the Berlin archives. I talked about this in my first speech back in, I think, December 2017, where you had the company scientists being interviewed by lawyers to give them advice on what they should or shouldn't say and whether their claim would stand up in court if they ended up in court.

Those notes of those meetings, some of them in the late '50s and early '60s are really clear that they knew at the time and they were warned by the lawyers that if this had gone to court, they clearly hadn't gone through the right methodologies that were accepted as normal practice at the time. So this cover-up is in [REDACTED] it's in this country and it's across the industry and a lot of people related to it. I have not heard a good defence from this collection of people. What we have heard is independent scientists, like Professor Heneghan, like Dr Aronson, who have come afresh, independently, and reviewed this material and had it peer reviewed and have found very differently from these EWG experts.

You asked Chair at the beginning, in your remarks, what would we like to happen? Well first of all we would like you to conclude what you believe the truth to be. It's not easy. You have a hard job given the different evidence you're hearing, but I hope that collectively we have sewn in your mind, there must be some serious doubt about the way different people have acted and doubt about their motives. But that's looking at the history. What should happen going forward if you manage to get to the truth?

First of all, the patients, the parents and the children, the adult children now, who have been affected, I think deserve redress. Redress I would say in two ways: compensation, but also redress for the care they need and the extra support they need. They have waited far too long and as we will hear, some are no longer with us. I think that should come from the government ultimately because I think there's been regulatory failure.

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[REDACTED]

I would also, this is my final point, want a review of the regulatory framework. I think it's found to be seriously lacking throughout this and as a Parliamentarian, someone interested in public policy, it clearly isn't the independent regulatory framework this country should have. Thank you.

Julia Cumberlege: Thank you very much indeed. That's extremely clear and the background is enormously useful to us. Thank you very much. So, Mr Rees-Mogg.

Jacob Rees Mogg: Thank you very much and thank you for allowing me to come and conducting this review. I am Jacob Rees-Mogg and I'm a Member of Parliament for North East Somerset. I became involved in this because a constituent came to see me. [REDACTED] came because his son had health problems which seemed to be linked to his mum taking Primodos in pregnancy. Then I spoke to Yasmin about it and understood that this was a much wider problem.

I'm a Member of Parliament. I'm not an expert in medical techniques or scientific procedures for testing drugs, therefore the role I have is to try and get answers for my constituents about the obvious questions. The difficulty here is in getting those answers as to why things happened as they did. Why the information that seemed to be known was not brought more widely to people's attention? So I think there are a number of issues here, which if I understand it correctly you're looking at.

The regulatory issue - there could be a regulatory failure even if it turns out that you can't prove that the drug was dangerous because the drug had another purpose, which we know about, it was also an abortifacient, which makes it a very strange thing for regulators to have approved as a test for pregnancy because there is an obvious risk that it could be problematic if mis-taken because of its alternative use. Even if you can't prove the abnormalities that many people think followed from using the drug, that seems to me a very clear regulatory failure in the first point.

The issue that I don't think has ever been addressed is the extent to which this drug's risks had never been properly tested before it was prescribed. I know from my business background, I once ran a fund investing in pharmaceutical companies, and many drugs failed to get through because they simply failed the poisonous test. Was this ever done with Primodos? Given the evidence that we now have in relation to mice and in relation to fish and some in relation to rabbits and to rats, do they show that actually if the tests that would now be done had been done then, that Primodos would never have been available for prescription as a pregnancy test?

Without applying hindsight to say we should have known in the 1950s what we know now, would it not be reassuring to people who think that there is this link with abnormalities to show that the drug would indeed have failed if that is the case and wouldn't it be right to research that rather than simply the discussions that we've had in relation to Heneghan and the metadata and the testing of the metadata, which seems to me to raise as many questions as it answers because if Professor Heneghan [unclear] because of the weakness of the underlying studies then isn't it the case that [unclear] those underlying studies can't be relied upon.

It's a most unusual place for these things to be going on. You'd think we were at Silverstone. [Laughter]

If the underlying studies didn't provide a base for Heneghan, did they provide a base for the EWG to say that there wasn't a causal link or were they overstating their predictions on the evidence that they had in front of them?

But I want to go back to some of the issues that came from [REDACTED] coming to see me and the causal link question, because although everyone accepts thalidomide is responsible for abnormalities, as I understand it a causal link has never been proved for thalidomide because of the ethics of doing the tests that you would require to prove the link. Therefore we are always dealing with a balance of probabilities and risks and back to the ethical question of could it possibly ever have been right to use, as Edward was saying, this test which had no therapeutic benefit to find out something that could be discovered in other ways when it was also known to have been an abortifacient, and isn't that a sort of very early indication that it was unsuitable?

The early date of some of the studies; the first warning was in 1958. It's not that we're saying that we know now that there was a risk but that people knew there was a risk really before this drug was even being properly marketed. The first major study was in 1967. In 1973 Schering were saying that a teratogenic effect cannot be ruled out. Now, with a drug that has no therapeutic effect, if a teratogenic effect cannot be ruled out, surely there is a regulatory failure if that drug continues to be used for that purpose?

In a way there is not a lot more to say beyond that, that once the drug company had that suspicion, even if the suspicion was wrong, it should only have been used for something that had a definite therapeutic benefit not for a test, even if there weren't any other tests available, but as I understand it there were other tests available anyway. So that, I think, in terms of regulatory failure, to reiterate my point, even if you can't make the link, the use as an abortifacient continues; the safety tests, there are only two tests to de facto determine its safety prior to it being marketed in 1958 and these as far as I'm aware were never updated.

Of course, I understand that you don't go back and test Aspirin, once it's been established as being a safe drug, but actually those tests were a lot better post 1958 with a drug that 15 years later was being questioned and in relation to the thalidomide problem which was happening at this time, surely to rely on two tests was insufficient and the regulators ought to have been thinking about that. They ought to have been looking back to see if

there was any history of safety. The issues that I've already referred to that other tests were available.

The issue of informed consent - that shouldn't patients have been told that this drug was an abortifacient? That many mothers, I would assume, would not have taken the risk of a pregnancy test that might have created an abortion. That's without Catholics, without coming on to the issues that Catholic mothers might have faced for ethical reasons that are almost certainly beyond the scope of this inquiry but nonetheless the issue of their informed consent, I would have thought is relevant and they ought to have been appropriately warned.

So what is the issue? What do we want? Well, we want answers for our constituents, and that's not to say what the answers ought to be, but it's to say that it's surely fair that constituents know why only two tests was deemed sufficient. Why informed consent wasn't required? Why an abortifacient was given out as a pregnancy test? Why, in spite of concerns years before the drug was removed, did it carry on being used? What are the answers and then what can be done to provide some reassurance that this won't happen again? That information will be made perhaps more freely available so that people know the risks of the drugs that they are taking and as Edward was saying, that there will be some acknowledgement for the people who were affected.

An acknowledgement that something was done that was wrong and that we can now look back and say it was wrong, even if we're not absolutely certain that it caused any deformities or abnormalities, but that there were so many regulatory issues that we know we wouldn't behave in this way today, and slightly throwing the onus of proof onto the producers of the drug to make up for the regulatory failures, rather than saying it's the people and the families where there have been problems who have to prove the causal link, which is almost impossible to do.

Thank you very much and thank you particularly, as great experts listening to an amateur because I am very conscious that I do not have the technical expertise in this area but I do have a concerned constituent who needs to have a voice.

Julia Cumberlege: Well thank you so much. I think it's really very interesting to hear from the three of you how our parliamentary system does work in terms of democracy and that your constituents have brought this to your attention and that you are acting upon it and I want to thank you for that.

I think there are several themes that actually cross all three areas that we're examining and Mr Rees-Mogg, just the one on consent that's come into all the three areas that we're looking at, but there are obviously some very important issues particular to hormone pregnancy testing. We need to go away and really think about what you've told us and how we can really assess, obviously, what you've been saying but to look at the value of what you said and how we can think about it when we're writing our report.

I would love to give you much firmer advice or firmer thoughts about what we're already thinking about, but we have been working really long and hard on this particular issue, particularly with patients, particularly with the patient group. So at this moment, we're not in a position to actually say to you, we absolutely agree with that, or we don't agree with that but you have been very concise and very comprehensive as well. I think that we will be looking at the transcripts.

I want to say about the transcripts that they will be produced before it goes out on the web because we have to be very careful that whatever anybody says, doesn't land either you or us in trouble and I can't think that it has today because you're very well versed in these things as politicians, but nevertheless this is the system that we've adopted.

So I don't know if my colleagues want to say anything but we've got another group, an All Party Group in about three minutes.

Cyril Chantler: No, I'd just like to thank you. We've raised with a number of people who have been to see us the general question, is these are three things that have gone wrong and the question I ask as a doctor, is why has it taken patient groups and politicians to draw it to the attention of the system and the profession? That is a question that we ponder.

Julia Cumberlege: Do you want to say something Simon?

Simon Whale: I'd like to echo Julia and Cyril's thanks to all three of you and to Marie and Mike and Jason as well for all the work that you've done which has helped us, is helping us enormously. The only think I would add to what has already been said, is the basis on which this Review was established was the concerns of patients as channelled through Parliamentarians and elsewhere. So we start from that perspective. In that sense we start with an inbuilt concern, a focus. I think, I hope, that would reassure patient groups and others with an interest in this.

Julia Cumberlege: Can I just say on the question of the expert working group, we're thinking very deeply about that. We will be thinking about what you've told us

today. Also, we really have to be very sure about things like redress and compensation and other issues. Sir Edward, you've raised today, we cannot actually - we're not competent enough to study the compensation or to put forward - we can make recommendations but we do not have the expertise to actually work through compensation because it's very difficult. But redress is something that is really important and you've all raised that in one way or another.

Of course, the regulatory frameworks is something again that has crossed all three of the areas that we've been involved in, so we will be thinking about that. So thank you so much for coming and I'm sorry it's not longer, but we've got another group coming in now. So thank you.

END OF TRANSCRIPT

Session 3: Valproate and Other Anti-Epileptic Drugs in Pregnancy

APPG*

START OF TRANSCRIPT

Julia Cumberlege: Thank you so much for coming this afternoon. We really, really appreciate it and I know you've come a long way to be here so thank you for that. As you know, we're talking about anti-epileptic drugs this afternoon and on the whole, we call it valproate...

Norman Lamb: Yeah.

Julia Cumberlege: ...is that all right with you? Yeah. Just - I want to say to you Norman, I really do want to thank you and your colleagues, your parliamentary colleagues, all on your group for all the PQs, for the debates, for all the times that you've raised this really, really important issue. We think that it is the work of the parliamentary groups that have really made this of such a national importance, and I want to thank you for that. But we also recognise that it is also the patient groups and the patient groups have been at it a very long time...

Norman Lamb: Absolutely.

Julia Cumberlege: ...and it's really so good to see Janet Williams and Emma Murphy here this afternoon. We know that you are the secretariat for the All-Party Parliamentary Group. Indeed, you've been talking globally, internationally, in this country, raising all sorts of questions and making it possible for us to meet affected people. That's been very, very important to us. We actually think that it has been so, so critical that we should put patients at the heart of our Review, and we have been trying to do that. We want to pay tribute to the courage, to the physical, mental suffering, to the impact sodium valproate has had on families and the struggle that people are having just to get through life and very much the worries about the future of themselves and mostly their children, now many grown up.

So, we've had some really heart-breaking stories and they've had a huge impact on us, and we just want to pay tribute to the courage and the dignity of all those that we have met.

So, thinking about the hearing this afternoon, it's really your opportunity to tell us what you think we should know, what you think we should be focusing upon and anything you wish to raise, comment on the evidence you may have seen on the website or heard or your personal experience of individuals who've been so damaged by these medications. So, this is your

opportunity. We are video-recording these sessions as I think you know, and I hope that's all right. They will be put onto our website. So, for the point of view of the website for the screening that is going to be on it, if you could start just by saying who you are so that we've got a record of that. So, Norman, if you'd like to start.

Norman Lamb: Okay, well thank you very much indeed for those introductory comments and your generous comments and I would particularly endorse what you said about Janet and Emma and their extraordinary campaigning skills and their resilience in pursuing this so impressively. So, I will say some introductory comments about what I think is for me the most important things that need to be confronted but also then hand over to the real experts in Janet and Emma.

So, I think we always talk about this in a sense as two big issues. One is to stem the awful flow of new cases coming through by getting effective robust procedures in place to stop more children being born with these problems and issues. Progress has been made but we're still not there yet and that - so that remains a massive priority and in a sense, the number one priority because to stop more children being born with these problems has to be the focus of everyone's attention.

Second point is - and I - this is obviously central to your work, is to learn from the experiences of this group and the other two groups that you're looking at to find ways of establishing procedures for the future that can more effectively allow government to intervene quickly to stop these awful long running sort of campaigns for justice that really take over people's lives. Impressive though Janet and Emma have been, they oughtn't to have needed to have done this. We really need to find a more civilised way of identifying problems early and then getting to grips with them. So that has to be a central focus for your attention.

Then thirdly, it's the need for justice for those people who have suffered as a result of this scandal. I think it's right to call it that. Now - and it's not just the children who have been born. You hear so many stories of mothers in particular who've ended up feeling a sense of guilt, misplaced of course because there is nothing for them that they should be guilty about - feel guilty about, but it's easy to say that but it's much harder to escape from a sense of profound guilt that by taking medication, you've ended up giving birth to a child who has issues.

The state has to confront that and there are - the regulator, the governments, successive governments, and the manufacturer all have had a role to play in so many people suffering guilt because of what has

happened to their family. It ought not to have happened and it could have been avoided had key players actually intervened as they should have done to prevent this scandal from happening in the first place.

But then it's also the children and whether it's 20,000 or whatever the number is, the numbers of people affected by this and often in quite profound ways. One of the things I think we've struggled with throughout all of this is that if you take thalidomide as another example of awful negligence and worse, in that case the outcome was so clear and obvious visually for people to see. Here it's not, not nearly so much, and yet developmental difficulties, autism, and all of the other impacts that this has had can have just as profound an effect on your life and your whole family's life because it affects siblings as well and the parents and ensuring that they get access to good and expert medical attention but also recognising that there is a significant impact on their - on the quality of their life and on their earning power as a result of what's happened to them. That has to be reflected in what government does.

Now ultimately, I know that that's a decision for government, not for you but in your advice to government I hope very much that you reflect on the extent of the impact that this has had on individuals. So, I think that's really what I wanted to say. So over to these two.

Janet Williams: So, Janet Williams, I'm the secretariat for the APPG for valproate. Early last week, I spoke to a lady in the office, I think it was Donna who asked me for a brief rundown of the history of the APPG and we've put that together for you here. I don't know whether you want me to just give you a brief outline as to what the build-up [unclear]...

Julia Cumberlege: That would be very helpful, thank you.

Janet Williams: Yeah okay. Right so I'll read it. We've put together a little piece and it just says, the APPG for valproate was originally set up with the support of the thalidomide group and their Chair in 2014 where we jointly became the APPG for harmful drugs. However, the - due to the Chair being inundated by other groups it was decided that in fact, it should set up its own APPG for valproate so as not dilute it or the information of it and the work of the thalidomide.

We had spent 12 months at that point with them learning how an APPG worked, and in July 2015, we set up our own with the support of Theresa Pearce MP as Chair and named it Anti-Epileptic Drugs in Pregnancy. During Theresa's Chairship we met with Health Minister Jeremy Hunt and Minister for Life Sciences, George Freeman and following - we saw the beginning of

the work towards the Valproate Toolkit which then was replaced by the pregnancy information programme.

In July 2016, Theresa had to step back from the APPG due to a shadow ministerial role and it was suggested at that time that we approach Norman due to the INFACT had met with Norman previously when he was Minister during the coalition government. We were delighted when Norman said yes.

Norman Lamb: Little did I realise what I was letting myself in for.

Janet Williams: That was in September 2016, and during his Chairship the APPG has had a change in name and it - October 2017, we were also able to arrange the Backbench Business Debate for valproate which was a huge success and we believe we sort of spring- boarded where we were at, at that point. Then obviously due to the change in legislation we had the pregnancy prevention programme. So obviously together the INFACT and the APPG - the members have all worked together to create the position that we're in now.

Norman Lamb: It's also worth noting that we had a Minister who listened to us.

Emma Murphy: Yes, we did.

Janet Williams: Course we did.

Norman Lamb: In James.

Janet Williams: Of course, we did yes.

Norman Lamb: Which was very significant.

Julia Cumberlege: So, Emma, do you want to add anything?

Emma Murphy: I'm Emma Murphy. I'm the Managing Director of INFACT and I'm mum to five affected children. I just want to echo really everything that Norman has said. This is a man-made tragedy. We shouldn't really be here, and I do think we have to stress that governments like to say lessons have to be learned. We really do have to learn lessons because we're seeing the new influx of medications that we're all aware of and there has to be tighter regulation.

We're meeting organisations up and down the country who are agreeing with us that not enough is being done. We're challenging it all the time and the numbers are just not falling. I think we've got to really work on that. I don't know how but I think we've got to introduce tougher regulations and

get real tough, because these are babies' lives. They're being born every day and it's a national disgrace.

Janet Williams: We did meet with the General Medical Council only yesterday.

Julia Cumberlege: Sorry you met with?

Janet Williams: We met with the General Medical Council yesterday. Like we expressed to them, it's all right sitting and talking facts and figures and banding information around, but it's when you get down to the nitty gritty of the real hardship that these families have gone through and you talk about the problems that the children have got, problems that those - those problems have put onto the family and onto mum with epilepsy and all the stress, creating more seizures, more medication and all the rest of it, and how that progresses.

It's not until you actually make them aware of that situation and you bring them down to that point where they actually realise the problems that there are with this drug. Everything was light-hearted, talking about facts and figures until we sort of dropped that yesterday and I think that's where all this should really begin from, like you say about, what the families have gone through.

Norman Lamb: So, you were instilling presumably the need for doctors to take much more of a personal responsibility for...

Janet Williams: Of course, yeah.

Julia Cumberlege: We've met some of these young people who've been affected and one of the things that really struck us was the way that they were so concerned about their parents.

Janet Williams: Of course.

Julia Cumberlege: I thought that was really interesting because I thought they would feel very internal about their own problems. No, they were thinking about their parents and I thought that was very interesting.

Norman, you've mentioned three different areas, organisations whatever you'd like to call them that had a part to play, the regulators, the government and the manufacturers, is there anything further you'd like to tell us about those three?

Norman Lamb: Well I just - I recognise how one goes about approaching the subject is important. But I do think that the manufacturer - the manufacturer is the only organisation in all of this that has made a substantial amount of

money from this. I think they have a responsibility and I think they have - they have to be confronted by that. I understand the need to address it in a sensitive way, but the bottom line is that they have known from the start that there were adverse consequences. I don't think that they've done enough, bluntly, all the way through this. I think the culpability rises as our level of knowledge increased.

They can always of course point to the fact that there is no legal decision against them in this country but I - if we're talking about justice and morality, then I think that they have to be part of a solution to this. There has to be some - there has to be a settlement that ensures that the families get financial assistance in my view. There has to be some recognition of the financial consequences for families of this scandal. The company should be playing their part in meeting that responsibility.

Now alongside that, the regulator - and all of my dealings with the regulator in the last three years have been constructive and they've been willing to engage with us and to listen, but over the course of the period since the drug was first introduced - when was it? 1970...

Janet Williams: '73.

Norman Lamb: Three. I don't think that the regulator has been in any way effective and if you think about the regulator's role it is presumably to protect patients from harm. It's a central purpose of the organisation and they failed in that and there has to be, I think a recognition of that in the conclusions that you reach.

Then of course there's government and I obviously have my part to play in this because I was the Minister who received a delegation, including Janet and Emma, and I knew nothing about this until that visit. But I was so horrified by what I heard that I instigated a process which I think in turn led to that European Review of the prescribing arrangements. Then I was out of office, unceremoniously dumped in 2015 and so couldn't play any further part. Government throughout this period since 1973, could have intervened and hasn't done, in the face of known harm. It is an extraordinary story how it's gone on for so many years, but it has, and that has to be confronted because people have been harmed as a result.

Julia Cumberlege: Right, Cyril...

Cyril Chantler: It is by my calculations, much of my information has come from you, 32 years from the time that it was known that sodium valproate cause congenital malformations, to the introduction of a specific pregnancy prevention programme. Why?

- Norman Lamb: Well it's extraordinary, there is no good explanation to that.
- Cyril Chantler: But you've just raised the question of the responsibilities, the regulators, government and manufacturers, but I've been - we've met a lot of people now formally, and as I said to the last people we were talking to, the question I've asked many of them is why has it taken patient groups working with parliamentarians to bring this problem to the attention of the National Health Service or system and to my profession. So, the question I'm seeking the answer to is - those two questions I need to know the answer because I'm not sure how the regulator, the government and the manufacturer can solve that problem. I think they could do more but I'm not sure whether the solution lies there or not.
- Norman Lamb: I suppose what I'm saying is that all of them could have acted and failed to act, and if we're trying to establish the reasons why this scandal has happened, that has to be addressed, their failure to act in the face of evidence. Now there was a lack perhaps of good lobbying and effective lobbying until these two came along. But that's no justification for the failures of government regulator and manufacturer.
- Cyril Chantler: But it shouldn't take lobbying to do that.
- Norman Lamb: No, it shouldn't, absolutely. That's why the second of the three things, priorities that I described, in other words, getting - establishing a mechanism that allows for a speedy assessment of a problem and resolution to it, is across the range of different medications and procedures is so important. That applies equally to the other two issues that you're looking at.
- Cyril Chantler: Do you think the patient voice is strong enough in the National Health Service?
- Norman Lamb: Totally not. I'm looking also - I was the Minister that established the Hillsborough-style review panel into deaths at Gosport Hospital. 456 people died having been prescribed inappropriately opioids. Why were those families never listened to? All over the place, you see examples of a bureaucratic system not listening to people. It's quite shocking. I think it raises very profound questions about - Bishop James Jones who conducted the review at Gosport talked about the 'patronising disposition of unaccountable power'.
- That was the - what he called his report that he was commissioned by the Prime Minister to write about lessons learnt from Hillsborough and I think that describes it perfectly. They're ordinary people - because ultimately, we're all ordinary people being systemically ignored, not taken seriously

and we've got to find ways of ensuring that public bodies are more responsive to people than that.

Julia Cumberlege: So how do you get the patient voice heard speedily, because there are mistakes made frequently within the National Health Service and some of them, are reasonable in terms that every operation carries a risk.

Norman Lamb: Of course.

Julia Cumberlege: Every medication carries a risk. How do we identify those risks early enough because usually there's been a lot of deaths as you were saying at Gosport. We can't wait for those deaths.

Norman Lamb: Yeah exactly.

Julia Cumberlege: So where is the mechanisms? Where is the opportunity to actually identify things early enough?

Norman Lamb: Well, I think this is quite a big subject. I'm not at all sure that the Health Service Ombudsman is an effective enough system for reviewing or hearing concerns raised by people about things that have happened in the health system. I do understand that you're dealing with often clinical judgements that sometimes go wrong and that has been accepted. But it's having somebody that is able to assess where it's different from that and where there needs to be a more thorough review without having to wait years for brilliant campaigners to emerge from the woodwork as it were.

There's no mechanism to systematically review evidence. We don't - but of course, I think it's becoming potentially easier with the digitalisation of data. We ought to be capable in a way that perhaps we weren't able to be in the past to identify trends and issues that may be of concern and we ought to exploit that ability more effectively than we do now. You don't want to create a whole new bureaucracy, but there has to be some - some body that has the ability and the responsibility for quickly reviewing and identifying whether something needs thorough investigation.

Simon Whale: It also needs to have as a predisposition a desire to protect patients.

Norman Lamb: Yeah, and a willingness to listen to what people are saying to them without too readily dismissing them which tends to be the culture in too much of the NHS.

Julia Cumberlege: Anything else?

Simon Whale: Could I just go back to - you - first things that you mentioned at the beginning around - I think you used the phrase stemming the flow of babies

born with valproate related disorders. Obviously, we've got the pregnancy prevention programme in place at the moment and I know the work that Janet and Emma have done, and others have seen and heard about has shown that's not necessarily working as effectively as everyone wanted it to. Have you got any further comments you'd want to make on where we are today in terms of efforts being made to reduce that number of babies being affected?

Norman Lamb: Well I think if the evidence is showing that it's not being effective, and Emma you mentioned that the numbers are still stubbornly high.

Emma Murphy: Yeah.

Norman Lamb: Inevitably it's a bit anecdotal because it's reports that people provide, then we have to look at what more needs to be done. I mean we can't just say 'well we've taken action, let's make the best of it'. That's not good enough. I remember when I met the specialist team in Norwich, and I think they've got a good team based in The Norfolk and Norwich Hospital, and they said that - I mean this was 18 months, two years ago now, and they said that every patient in Norfolk goes through that team and they make the judgment. But they said to me that there's very few patients that need to be on valproate, that in almost all cases, but not all, there is an alternative that is safer. The solution may be more restrictive ultimately, but I think we've got to look at how we can ensure that there is a specialist input in all cases to get it right rather than misjudgements being made by GPs.

Talking to GPs, I think the mindset has been, you know, valproate is the - they see it as the best - this is the most effective treatment for epilepsy, and their focus understandably has been on getting the best treatment for that person but not enough focus on the awful consequences of that for the child. So, I don't know whether you want to add anything about, if the current process isn't working, what step do we have to take to ensure that every decision is based on evidence...

Emma Murphy: I think at the moment; I think we've got to maybe think about doing a patient recall like with what was done with smear tests. Patients were recalled in and I think - because it's not working as effectively now, I think we need to be thinking along them lines because everyone is saying not enough is being done. Someone has got to tackle this because like we all know, this just can't continue.

Cyril Chantler: When we last met, we talked about the responsibilities of pharmacists, we talked about the responsibility of doctors and you saw the General Medical Council yesterday. But the conversations I recall ended by saying well, if all

this isn't working, maybe the people we need to be really involving much more systematically are actually the women, and setting up a register which we perhaps could do because there are records of everybody who's taking valproate, and contacting them directly which will then be the basis of the recall that has been suggested in relation to mesh] the difference there is in finding them - the women, but here that shouldn't be an insuperable problem.

Norman Lamb: One question I wanted to perhaps ask, and I don't know how much you've analysed the data from across the country but the impression I had was that it's quite variable, the rate of prescribing from one area to another. What I imagine may be the case is whether that - that that might depend on access to a good specialist team. I remember in our earlier discussions with James the need - talking about the need to ensure that the country is covered by a pyramid where there is always access to the right specialist team, rather than GPs doing their best but getting it wrong.

Emma Murphy: That's one of the problems that we're finding at the moment, specifically in the area that I live in, because where I am it covers three major areas and there isn't a neurologist at the moment. Me and my son were both due for an appointment. We haven't seen a neurologist for going on for two years and when I phoned and queried it, he'd retired, and they hadn't sent us a follow-up appointment. But I wasn't able to see a neurologist because they hadn't replaced him and the only have three epilepsy nurses covering this vast area in the North West.

Norman Lamb: Yeah, and therein lies a significant part of the problem. If the area is not well served, then bad decisions will result.

Julia Cumberlege: Then of course the huge manpower implications of getting more specialists.

Norman Lamb: There are manpower implications clearly but it's also a question of organisation and making sure that the system is properly organised with the pyramids of - we have cancer networks that work effectively to ensure that everyone gets linked into the appropriate level of specialism. Does more need to be done here to ensure that...

Cyril Chantler: We ought to be able to do it better than any other country in the world because of the nature of our National Health Service.

Norman Lamb: Exactly.

Janet Williams: Of course, yeah.

Julia Cumberlege: Simon.

Simon Whale: All right. I was just - I think we've been told by others that in the clinical world that they would expect, and are seeing to an extent, that prescribing of valproate has reduced. Regional variations is accepted by them but overall the prescribing levels, it is being said to us, should be declining. So, if the number of babies being born with fetal valproate spectrum disorder isn't declining, that runs somewhat counter to the prescribing volume reductions.

Janet Williams: Well when we first started this campaign, we met with the Minister for Life Sciences and at that point, we were told there was about somewhere between 13 and 27,000 prescriptions of valproate to women of childbearing age every year. There was also around about 400 to 500 babies born to valproate affected by it every year. We know at the moment that the figure for the prescriptions is around about 20 to 21,000.

Norman Lamb: So, it's gone down by about a third.

Janet Williams: It has gone down by about - yeah, yeah. The amount of children that are being harmed at the moment which was talked about at an MHRA meeting that we went to only recently and it was about 300. So...

Simon Whale: So, it's proportionally reduced.

Janet Williams: ...it has - yeah, yeah.

[Over speaking]

Norman Lamb: But still 20,000.

Janet Williams: Still a lot.

Norman Lamb: This is a - this is the women of childbearing age, so this is the core group, there's still 20,000.

Simon Whale: And 300 a year is still...

Janet Williams: It's not coming down fast enough.

Julia Cumberlege: Any other questions or anything you want to ask?

Valerie Brasse: Can I just ask one thing? It was just going back Norman to what you were saying about the lessons learned because of course the issue you've been working so hard campaigning for valproate and the impact on women of childbearing age, the new drugs that come along, are they learning the lessons? Is anyone picking up what should be being done for all of those

drugs that may also be teratogenic and for women who are taking the new generation of anti-epileptic. Do you feel confident now that the lessons have been learnt and the right policies are in place to prevent new [unclear]?

Emma Murphy: I truly don't believe that they are because we broached this topic with MHRA and their response to - about Keppra. I mean Keppra is a fairly newish drug. We know it's causing some harm, but to have the response of we're not going to deal with that until we've finished with valproate.

Norman Lamb: It's not a good answer.

Emma Murphy: It's - that is just appalling. These are the medicine regulators.

Janet Williams: Yeah there's needs to be more - they say - they talk about transparency all the time. I hate the word because there needs to be so much more of it with all the newer drugs that are coming along, if that transparency was there, then these women would be getting the informed choice, and at least receiving that information as to whether then they wanted to proceed to have children or not. With the newer drugs that's still not getting through.

Emma Murphy: They know about topiramate which is - it's very similar to valproate and there's no action on that. They're not learning lessons.

Norman Lamb: Of course, we're just building up a new body of complaints which is dreadful.

Sonia Macleod: I mean is there an issue - because obviously one of the issues you're going to have is drugs aren't tested for teratogenicity pre-market. There will be a period after they market it where there are going to be - they're going to be prescribed in pregnancy. If they are going to have a teratogenic effect, they will. But do you think it is that the lessons aren't being learnt quickly enough once that data comes in or that the data isn't being gathered?

Janet Williams: Well the data is being gathered through UK Pregnancy Register. So, the data is being - I mean granted it's - a low percentage but the data is being gathered by them. It's just not being worked upon.

Emma Murphy: We're not asking for these medications to be banned because we know that they are lifesaving. All we are asking is that women are warned of the risk...

Janet Williams: And get a choice.

Emma Murphy: ... and it's not a big ask when you're thinking of children. It's not a big ask. As regulators they're for patient safety supposedly, but it's not happening.

Janet Williams: The thing is with a neurologist - talking about patient safety, the thing about neurologists in particular is as far as patient safety is concerned, well that's what they're doing. They're looking after that patient. They're not thinking about what's coming in two, three, four years' time, whether she's going to have children or not. That's not their issue. I think that...

Norman Lamb: But it sort of ought to be.

Janet Williams: Yeah, of course it should. But I think that's another area as well that really needs to be dealt with.

Norman Lamb: Yeah, yeah absolutely.

Julia Cumberlege: Okay well we've covered our time I'm afraid.

Norman Lamb: Thank you very much.

Multiple speakers: Thank you.

Julia Cumberlege: I do want to thank you, all three of you for the enormous amount of work you do. It is so impressive.

Emma Murphy: We want to thank you all as well.

Norman Lamb: Yeah thank you. Thanks for listening to us, we appreciate it.

END OF TRANSCRIPT

20th May 2019

Session 1: Welsh Mesh Survivors

START OF TRANSCRIPT

Julia Cumberlege: ...very much welcome to you both, Jemima and your husband, Dr Williams, thank you very much for coming in today. Jemima, we know you as a very long-standing mesh campaigner and that you've worked beyond your own organisation and you've helped set up the Global Mesh Alliance, so you're looking very widely across the world, as it were.

Jemima Williams: Thank you.

Julia Cumberlege: During the last oral hearing, you brought a number of outstanding problems to our attention, and thank you very much for that. And also to your husband, Dr Dennis Williams, for raising concerns about mesh sufferers and the role of GPs was very helpful to us. Since the oral hearing we know that there's been a lot of correspondence and thank you again for that. And we've really looked at what you've been sending, and particularly the photographs, which are very good for us, and the online paper articles and the academic articles.

Jemima Williams: I'd edited them so that they don't include advertisements. [Laugh]

Julia Cumberlege: You don't need to apologise - it's all part of our learning, and we do want to thank you for that. So as I was saying, the newspaper articles and the academic articles, and also the FDA Adverse Events Report. So this session is your opportunity, bearing in mind that we are now near the end of our fact finding sessions, they're drawing to a close. But we have always put patients first - patients at the beginning, and now it's patients at the end. And you, I'm sure through the correspondence you've sent us, and also perhaps you've been watching some of the sessions on the website.

Jemima Williams: Yes, we have, yeah.

Julia Cumberlege: So it's you and your husband's opportunity now to tell us what particular issues you'd like us to consider, because we will now start writing our report after these sessions. So anything that you've got to tell us would be hugely valuable.

Jemima Williams: Well we've both written some things, but we promise not to get - we haven't overlapped, we've collaborated this time [laughs].

[Over speaking]

Dennis Williams: We've changed the order - I'm going to speak first on strict instructions...

Jemima Williams: Yes, if that's okay.

Dennis Williams: ...that I don't go on for too long, so.

Julia Cumberlege: Well that's absolutely fine. It's your session and you can run it as you wish.

Jemima Williams: Thank you - thanks all.

Julia Cumberlege: So, Dr Williams...

Dennis Williams: Thank you.

Julia Cumberlege: ...and perhaps you could just say who you are?

Dennis Williams: Indeed. I'm Dr Dennis Williams, a recently retired GP of 40 years and now an Occupational Health Physician, because I haven't stopped working yet, it's too early, yes, and I'm Jemima's husband.

Julia Cumberlege: And Jemima, do you want to...

Jemima Williams: And I'm the founder of the Welsh Mesh Survivors' Support Group and my name's Jemima Williams, as you know, yeah, so...

Julia Cumberlege: Right, thank you very much.

Dennis Williams: Can I just - should I start, will that be okay?

Julia Cumberlege: Yes, and I don't think I have to introduce our panel?

Dennis Williams: No, not at all - it's a pleasure to see you all again.

Julia Cumberlege: All right, good.

Dennis Williams: Thank you for inviting us back; I think it's a nice opportunity for us to sort of feedback. It was an excellent idea to put all the oral interviews online, because it gave people an opportunity to view them and actually see how widespread this problem is. It was really quite harrowing listening to some of the mesh survivors' statements, and I must compliment you for your compassion and understanding, and most particularly for your stamina and resilience in sitting here and just - because it's such a difficult thing to do.

I looked through many of the interviews online, but I tended to concentrate more on those from the health professionals. I must admit that I got quite upset and angry at some of them. It was evident to me that

many of these gynaecologists and urogynaecologists, all of whom are well-regarded, have excellent reputations, and most of whom were working in Centres of Special Excellence - of Clinical Excellence - they were really quite arrogant and often dismissive of the scale of the side-effects that their patients were suffering.

They seemed to be - they were playing Russian Roulette with their patients. If they looked even at the lowest quote of one in 10 individuals getting side-effects it seemed to be an acceptable level to them and that really upset me. There were several points that I picked up that, one that I thought was really difficult to understand, but some of them admitted that they had less of patients awaiting mesh surgery and that they were actually, indirectly, accusing you for delaying them being able to put the stuff in and saying that they were constantly in touch with these people and would tell them when the green light is for them to put it in again. That doesn't cause any understanding to me.

The other dig at the committee was that they couldn't wait for you to publish your findings. I just felt that they really weren't taking it - it was as if they - perhaps they didn't really think you were important and what you're doing do is important. That's the impression I got. Very few of them were promoting non-mesh surgical intervention above mesh intervention. The few that came on that were specifically anti-mesh were excellent in a way, I feel, but they're out on a limb. I just get the impression they're out on a limb - they're one of a few.

It concerns me that they admitted that many of their junior colleagues were unable to do things like colposuspension and other non-mesh operations, and admitted they required retraining. But there's no suggestion that they should commence. I just wonder how we're actually going to implement the changes that need to take place.

I was surprised that NICE decided to publish their guidelines before your report was issued and not only that, but they actually pre-empted your decision by putting mesh in there as one of the options for SUI. They didn't even think that you might say that it's going to be suspended for a longer period of time. I just wonder, if you look through the proposal or the NICE guidance that are out, but if you look through them I just see that they're going to be very difficult to put into practice, in my opinion.

When Dr - Professor Cardozo said that she has got this busy NHS clinic, she has so many ladies with SUI referred to her clinic, and that she does have a specialist physiotherapist and other members of her MDT Team, but that it was one physiotherapist in a very busy clinic, and the physiotherapist

waiting lists were long, how do we overcome that and follow the NICE guidelines - it's impossible. And what will happen is and I did write a timeline, but I'm not going to go through it, but I worked it out on the best sort of suggestion that I could make; the average time to get an appointment for a gynaecologist, certainly in Wales, is between three to six months, if you're lucky - it's often longer.

And that's assuming that they've already seen their GP, they've been diagnosed with probably SUI and they get referred. Then they eventually get seen, and if the consultant agrees that they've got an SUI and they need intervention of some sort, it's taken to the local MDT. One of the consultants says that their local MDT met every four weeks - well that's another month's delay. Then they have to make a decision, and if they decide on pelvic floor exercises or whatever, the recommendation is 16 weeks for that. And then - and that's assuming that the physiotherapist can see them straightaway which is extremely unlikely.

Is the physiotherapist going to have enough time to actually see the individual several times throughout that period of time, or indeed are they going to give them some exercise and say go away for 16 weeks. They might be doing it completely wrong unless they're followed up. And the whole time scale, from actually getting to the point of - let's assuming that these ladies require surgical intervention of some sort at the end, they eventually get to see a consultant who is considering surgical intervention, two/three years down the line - because that's what it will be.

And then they find out that the consultant is unable to do the operation that they choose, a non-mesh operation. And they get the option of going somewhere else and seeing someone else. If you're a patient, you're not going to want to do that. They are going to accept the option that's put in front of them because they don't want to delay it any longer. We all know these are non-life-threatening illnesses but they are very disturbing for some women, and I'm talking specifically about SUI now, and POP comes into it as well.

But it's an inconvenience. It's an embarrassing condition, but the bottom line is it's not life-threatening, and these ladies just want some solution. If they've been - if they've had medications, they've had physio, they've had medication, they've tried bulking agents, they end up seeing a consultant who says right, you need surgery, I'm going to put a sling for you, but it will be a mesh sling. But if you don't want that a consultant down the road might be able to do it, because there's no list of the skills of the consultants, who can put them in or not.

So I just feel a lot of them may decide to go privately, and I guarantee you that most of them will be offered mesh privately because that's the easy option. Perhaps I'm doing my - the consultants a disservice there, but that's the way I feel. We can shorten this period. In Wales, they've set up a group called WHIG - Women's Health Implementation Group - and they've taken a year to get off the ground really. Jemima and I go there regularly, and Jemima's the main voice, but I go along. But they're listening, just like you, and they're also trying to move forward and they're trying to help both the ladies who are now suffering from mesh problems and they want to try to stop some sort of getting it in the future.

They've proposed setting up pelvic floor coordinators, which they would have one in every health authority. We've put some literature in for you...

Jemima Williams: We've put some of that in here.

Dennis Williams: ...which, and this only happened at the last meeting, in fact which was last Monday. And basically these will be a first port of call - currently for ladies who are mesh-injured, but also hopefully for GPs who are referring ladies with SUI. So they can see a pelvic floor expert before they actually go and see a gynaecologist. This would lessen the timescale quite dramatically and it's relatively easy to set up as long as you've got the physiotherapists in line.

Obviously one pelvic floor coordinator is not clearly enough in one health authority. But if they can get physiotherapists on-board and they - not only are they going to send them to the physio but they will send them to any sort of agency, medical agency that can help them. So they are getting help. As far as mesh-injured are concerned, their intention is they're actually going to take individual stories from the individual, look at their treatment line, see what's happened to them...

Jemima Williams: I'm going to speak on that now.

Dennis Williams: I know - and then they will be treated in that area. They will be referred to people who they can - appropriate - early on. I think this is the sort of thing we've got to do. The NICE guidelines, just to go back to them a little bit, are far from being ideal but they do set out a pathway which is a good guideline to start. It needs tweaking. But I don't know whether you've seen the patient leaflets explaining the potential hazards that they've published. They're appalling.

They say that - there's one specifically for the potential hazards for mesh surgery and they will say that one in 10 patients may suffer symptoms from mesh rejection or mesh side effects. Then they emphasise again but that

means that between 90 and 99 people are not going to have problems and they actually put this in the leaflet. Now that's very condescending to the patients, for one thing, but it also takes away the message that they're trying to relay, that this stuff can be dangerous. They've got to emphasise how serious these things are and they're not doing it, and NICE are not doing it.

That's almost it, except that we - I saw the MHRA interview yesterday, we actually watched it yesterday. I was appalled. They were like rabbits in headlights - they had no idea what to do. It really came across to me that despite the fact that they're meant to be looking at the safety of these - of mesh and other implants, they are concerned more about the pharmaceutical companies than they are about the patient.

Jemima Williams: Yeah, I agree.

Dennis Williams: They haven't got the data, they just don't appear to understand what is going on. They're basically statisticians as far as I'm concerned. These notifiable bodies who actually, after one year can see a mesh implant, look at the research that's been done by the pharmaceutical company, and they're then given the kite mark, the CE mark. They can...

Jemima Williams: They can continue.

Dennis Williams: ...put it on the market. I just wonder, if the notified bodies were as diligent as they should be, would they actually still be in work? If they were being difficult to a pharmaceutical company, would they actually then - the pharmaceutical company then try and find another body that will actually be more sympathetic to their cause. That worries me greatly.

Having just a year, well maximum two, before they allow these things onto the market, and then there's no follow-up. That was the other thing I meant to say about the consultants - at least three consultants, including Professor Cardozo, said that follow-up of patients who have mesh inserted is not often done face-to-face. It's either done by triage with a nurse or over the telephone, and that's just the immediate follow-up - that is not the one year, five years, 10 years, perhaps which is what they should be thinking of doing.

So all-in-all there's an awful long way to go. I know much of what I said about the consultants trying to bully was addressed in the - your statement on the 16 May and I applaud you for that - I thought that was excellent thing to do.

Jemima Williams: Yeah.

Dennis Williams: Because there were lots very worried women out there who thought this stuff is now going to be - start putting it in again and everything has gone pear shaped and that this didn't matter anymore. And you certainly relieved their anxiety, and I thank you for that. There's just a few little things that I wrote down last night that - as a way forward possibly. I feel that all consultant gynaecologists and urogynaecologists need to admit that inserting mesh into patients carries considerable risk, and at the moment I don't think they do that.

I think they need not only to reflect on what they have done because of this review body, which some of them actually said, but to radically change the way that they use mesh for any procedures. They can no longer take risks with patients' lives. Information leaflets have to be robust, they have to be accurate, and reflect the severity of the side effects that mesh can cause. I don't want to frighten people, but at the same time they need to know the facts.

When we watched Mary McLaughlin's interview and she said about the consent form that she was asked to sign to have her mesh removed, but it said total removal and as you know, and I'm, not going to repeat it, but it wasn't going to be that. And if she hadn't questioned it - that is what she would have had. So I actually feel...

Jemima Williams: Partial removal is what she needed.

Dennis Williams: ...that the consultant is not the person to ask the patient to sign a consent form. I think it should be an independent individual, perhaps someone in the MDT team but someone with a knowledge of all the side-effects that are going on, with all the information to hand about side-effects, procedures, even have the instruments and the mesh there for them to see - that would be a way forward. That would actually be much more informed consent than they're having now.

You know about the records of operations and everything and the materials used, everything has got to be recorded - what's put in, the length of what they put in. It was interesting, some of the consultants said we can't say how long the piece of mesh is that we put in, because we don't know how much we're going to use until we - well they just measure what's left for God's sake, you know if you've got a piece - that's the main thing. Say where there's 25/26/27 centimetres has gone in, if you've whatever's left - so that seems unbelievable to people.

And long-term follow-up has to be mandatory. I think these ladies, if they go onto a database, and if they have side-effects, they go onto a database

and registry so we can report, they can be followed-up and they can be followed through and see if they have late side-effects. There was another thing that was said about if a lady had mesh eroding into the vagina and didn't complain about it, then she should be not bothered to be treated, because why fix something that they're not complaining about. The fact the mesh is coming through means that it is going to get worse as time goes on.

Jemima Williams: And the pain, the pain is intense.

Dennis Williams: But if they're not complaining, they haven't got the pain and what they were talking about, if you've got elderly women who have got mesh still inside them, should you follow them up? Well I actually think you should, because there may be something else going on, but because they're not having intercourse or because they have - elderly ladies would have vaginitis more often, or senile vaginitis, it's hidden.

Jemima Williams: Elderly people don't talk about these things anyway.

Dennis Williams: So I just feel that they have to take it more seriously, we have to look at a much broader spectrum of how we deal with people on mesh. I haven't even mentioned about taking out mesh from ladies who are already harmed; I won't go there today, because I think that that is another minefield...

Jemima Williams: Yeah, it is.

Dennis Williams: ...and I think that we'd be here for another two hours if I started talking about that. But that's all I wanted to say at the moment.

Julia Cumberlege: Thank you very, very much indeed.

Jemima Williams: Is it okay if I just read out...

Julia Cumberlege: Yes, Jemima, certainly.

Jemima Williams: ...a statement. These are thoughts and feelings from people in the Welsh group. I've brought along a folder of some of the things that I'm going to talk about, of evidence from our Welsh members, and I'll explain - but I need my glasses.

Dennis Williams: Which are here?

Jemima Williams: No, they're here.

Valerie Brasse: Sorry, can I just ask in the interim, Dr Williams when you were talking about the pelvic mesh coordinators and the group of work that's going on under the WHIG scheme, is that out in the public domain?

Dennis Williams: This is - the WHIG group was set up by Vaughan Gething, the current Health Secretary, he was put in a lady called Tracy Myhill, who is one of the Chief Executives on one of the health boards, and she has basically spent a year speaking to ladies who are suffering with mesh problems, around the table - sometimes it's a free for all and I really feel sorry for her. But they're starting to move forward, and now the ladies had got it off their chests and they've told everyone, they're starting to sit back and realise that we need to move forward. And they've come up with these ideas, there's not only Tracy, but there's a couple of others as well working with her.

Valerie Brasse: But are the ideas in the public domain, because I know about the group and....

[Over speaking]

Dennis Williams: The ideas are in the public - we've actually brought the publication...

Jemima Williams: The ideas are in the public domain...

Dennis Williams: Sorry, they are...

Jemima Williams: ...I'll talk a little bit about it in a moment.

Dennis Williams: We asked permission to present it, give it you and they said yes.

Jemima Williams: Yeah, we asked them at the previous...

Dennis Williams: At the last meeting and they said so that's why we're giving it to you.

Julia Cumberlege: Thank you very much.

Jemima Williams: So if I can just read this, because I'm terribly nervous and I don't want to forget anything. I may have to stand up and down because it's quite painful actually to speak in a loud voice for me. So first of all we'd like to take the opportunity to thank Baroness Julia and the Review Team, who many of us have come to realise that you have listened to UK mesh survivors and heard us.. And that you have already acted upon our evidence, and we thank you for your patience and your compassion.

We would also like to pay tribute to the Chairman of BAUS, Chris Harding, and also Professor Hashim for their excellent information and interaction with mesh injured patients on Twitter. I'd like to thank my rock, actually,

because without him I wouldn't be able to have done any of what I do because it is what it is. Welsh mesh survivors want to pay particular attention in thanking the Welsh Government in setting up WHIG, Women's Health Implementation Group, Tracy Myhill, the Chair, and the Coordinator Jody Stotanovich for their part in implementing a good strategy in pelvic health care pathways. Now recently in the trial of the mapping of mesh-injured patient experience so far and developing individual care plans to help us move forward. So that is being trialled with the working core group of the Welsh Mesh Survivors Support Group.

So many UK mesh injured people are experiencing great difficulty in finding the help we so desperately need, and busy consultants move on, forgetting to call us back with results and appointment dates et cetera, and we just can't get hold of them - unless, of course, we pay privately. Cross-border funding is desperately needed now, and health care pathways for mesh-injured need urgent development.

Trans-Labial scans. Mesh survivors have been encouraged by American groups that the Trans-Labial Ultrasound scans are the way forward in visualising mesh, but we know that only experts, experienced sonographers and experienced radiographers, can read them, leading consultants to dismiss the results.

Even so, there are many UK consultants and healthcare professionals that seem to be setting up quite lucrative businesses providing these scans, leaving mesh survivors feeling exploited and defeated. The evidence is enclosed - so that's receipts and things from different mesh survivors with the different levels of price ranges. And they range from between £250 and £425, only for those people then to go to their consultants and their consultants go 'oh that's not worth the paper it's printed on'.

During the evidence that you have made public over the last year, we've all been witness to the fact that some surgeons are being paid to put mesh in and then paid to take it out. Some also are paid to write expert witness statements in mesh litigation. In America this is known to be called Double Dipping - very lucrative. Mesh is never blamed - the inept surgeons are blamed, which brings me onto compensation.

In parliament, Lord Brennan made an excellent reference to this, stating that a levy should be paid by manufacturers, a brilliant idea. Jackie Doyle-Price also made reference in her statement to mesh- Injured to sue the surgeons. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] We want to be useful to our families, we want to be able

to live normal lives on the days that we can. There are many days when most of us, including myself, can't even get out of bed because the illness and the pain is so severe.

Many consultants' attitudes must change, the quote, you have to break a few eggs to make an omelette, is appalling. We are subject to eye-rolling by many consultants. The research into mesh, in our view, must be repeated, particularly as the FDA has just recently admitted to autoimmune problems being connected to surgical devices. And then we have alternative summary reporting set up for manufacturers, et al, to hide the true figures of complications. We have the CEO of J&J shouting 60/40 go - get that product on the market fast - that's in all of his inspirational YouTube videos. Meanwhile the broken eggs suffer and die. The mesh-injured, our sisters and our brothers.

The mesh world is surrounded by darkness, it's a lucrative business all round. We stand as a voice in tribute and honour to those without a voice, and to the dead. Shame on the manufacturers and healthcare professionals hiding the truth - they have blood on their hands . Gwaed ar eu ddywlo. Shame on the doctors who want to continue inserting mesh; survivors feel that consent is about protecting the surgeon from litigation - it's not about protecting the patients. The surgeons openly admit they haven't a clue as to how to do a full removal, including the fixings. [REDACTED] staples come with a warning that it's linked to cancer in patients.

We are having partial removals, and all of this crap is left inside us. There's also a contra-indication that those staples should not be used on arteries. My iliac artery is stapled because they perforated it at some point, and that

wasn't even found out until 2013. Shame on all of these people awaiting the green light for go - business as usual. That's all I've got say.

Julia Cumberlege: Thank you very, very much indeed. That's very compelling.

Dennis Williams: The work that you've done is fantastic, and I just hope now that once you have written your report and it's been published, it will have some impact upon particularly the consultants who insist that - the majority of them insist, that there is not a problem with mesh. I understand its uses, I understand that it can have beneficial results in patients - there's no getting away from that. But you cannot ignore the rate of the side-effects that are happening, and you can't use patients as guinea pigs and say well you should be all right; not you will be all right - but that's what they're doing.

Jemima Williams: Yeah.

Dennis Williams: There's always this doubt in their minds, and they're not prepared to accept the fact that they are taking the risk - they are telling the patients one thing but possibly believe another, or if they don't believe they're going to have problems...

Jemima Williams: Can I just interject just for one moment. I sent you the five-year period of the Freedom of Information that I had from the MHRA, talking - you know, the complications...

Dennis Williams: That have been reported.

Jemima Williams: ...that have been reported of the adverse events. There are at least 2500 pelvic mesh complications within that report, just the five-year period, which are mostly serious, and three deaths have been reported. And there's also the hernia mesh; I know that the Review isn't covering that, but this really needs to be investigated too - hernia and Rectopexy mesh. There were far less reports of hernia injuries, but there are even so, in that five-year period five deaths connected to that.

And there's just a list of questions, which I'd forgotten up until now, but I just need to ask you this; can the mesh-injured be assured of improved treatment and healthcare pathways by compassionate consultants? We need honesty, transparency and safety. Alternative summary reporting, which connects to the Freedom of Information; does the MHRA have such a register which hides the true numbers of, As, concerning devices, as the FDA have just admitted to having had? Since John Wilkinson has stepped down, can we be assured that there will be a rapid improvement in the regulatory system?

Can Jackie Doyle-Price assure the mesh-injured of help to sue the surgeons, as she suggested?

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Julia Cumberlege: The only other thing is, you asked us a lot about the questions of things that we could do. Can we just take note of those at this time and I'll consider them.

Jemima Williams: Even though I've handwritten my statement, and the questions, because my health is up and down and so I can only do certain things at certain times. So I've handwritten it - it's not too bad, and I'll leave you the questions as well, and this is all a present for you.

Julia Cumberlege: So if you'd like us to take copies of those, so that you have them returned.

Jemima Williams: It's fine. Sorry.

Dennis Williams: No, you can have them...

Jemima Williams: No, have them - it's fine. I've taken photographs of them to put on the group to explain what I was going to say. We haven't been able to cover every single thing, but I'm sure that you've had all of the details that people

have asked us to cover from other survivors. And so at the end of day, you don't want to hear it again and again, it's difficult.

Julia Cumberlege: Can I just say we've heard of new stuff...

Jemima Williams: Yeah.

Julia Cumberlege: ...in your oral evidence just now.

Jemima Williams: Right.

Julia Cumberlege: So thank you very much for that.

Jemima Williams: That's good then, thank you.

Julia Cumberlege: Yes, because we're always learning and we're always taking more and more evidence...

Jemima Williams: I'll always, always email you, unless you block me [unclear].

[Laughter]

Julia Cumberlege: We're very thankful. Cyril, do you want to...

Jemima Williams: Thank you so much.

Cyril Chantler: I was interested in the WHIG group that you set up; is there a link to that, do they publish minutes and papers? Are there terms of reference they have?

Jemima Williams: Yes, they do - well they have been doing. But until now, with what I've actually put in here, in this - they have now set up, as I said, a trial with mapping personal experiences and because some of us have been through terrible ordeals all the way through, and we stopped going to the doctor, we stopped going to our consultants because it's just really, really - it's difficult. We know that we're difficult cases - we know that now nothing more can be done for us.

I've been told that I've got this, this and this and I need a colostomy, but it will have to be done this way and I'll be in hospital for many weeks. And that I'm susceptible to sepsis, and so it would have to be done under the NHS, and I would want to choose the consultant that I gave my life - in whose hands I would be giving my life. Because I've been experimented upon enough - I've been a guinea pig and I don't want to be a guinea pig anymore. There was one removal that I had when I woke up from the operation, I'd had a trans...

Dennis Williams: A blood transfusion.

Jemima Williams: ...blood transfusion, and when I looked at my stomach, I looked as though someone had - some madman had been let loose with a staple gun - it was disgusting. And the way that I was treated after I won't go into, by a really - well there was no compassion from the male consultant - the female consultant was fantastic. The male consultant was horrible. I never want to go there again. So as things stand, many of us try and deal with our situations and our conditions in as best a way that we can and that's not ideal. When I use my - is this on camera - when I use my...

Dennis Williams: Peristeen.

Jemima Williams: ...Peristeen, my colonic irrigation, my bowel collapses around the catheter - sometimes the spasm is so great that the catheter bursts and you can't imagine the mess that that makes. And if I am really very ill, my spine - I've had recent MRIs and things - my spine is destroyed, my lower spine is destroyed, it's bone on bone. I can't have another implant, titanium rods and screws, due to the fact that I've already had a device that has rejected and that may be hosting - the residual mesh and staples may be hosting a bacterial infection which could then go on to become - infect another device. I've been told this by an immunologist.

And so I'm coping and I'm not always managing - I'm coping. There are times when my spine is in such a state I can't actually turn around to use my Peristeen and I won't allow Dennis to come and help me, so then I become obstructed. So it's...

Dennis Williams: In answer to your question, the...

Jemima Williams: Sorry.

Dennis Williams: The complex ladies involved in this meeting with WHIG, they've had the opportunity for a year to tell their stories and explain how difficult life is for them now, and they've difficulty in getting follow-up, they've lost trust in the surgeons that have put the material in them, and they keep hearing stories from - about different consultants who they've been recommended to, because other people have got horror stories about them.

So it's taken, certainly 10 months for these ladies to have their say and get it out there so that - and Tracy and the others...

Jemima Williams: Jodie and...

Dennis Williams: ...they're very sympathetic, very much like yourself - they listen, they take it on-board. And they've realised that they've got two things to do really.

One is to look after these ladies and try and find a pathway that they can have some form of satisfaction and actual help that matters with people that they trust. So by setting up these pelvic floor coordinators, they could literally have a one-to-one - they're individuals and so therefore they can go in there and say well we've got Dr So-and-So, Mr So-and-So who's going to do this, and they will be allowed to say no if they don't particularly want to go to see that consultant.

So they're trying to individualise it for the women that are suffering. What they're trying to do with the pelvic floor coordinator as well, is to create a system whereby there is a means of getting these ladies to have simple things, not just pelvic floor exercises and things by an expert and have it registered that they've actually been there and done it. So they are trying to move on now. But what they're doing is actually reducing the number of people that are going to these meetings, so Jemima and a couple of her colleagues would be representatives there, and more will get done.

But Vaughan Gething put forward £1 million to try and fund it...

Jemima Williams: A year, £1 million a year.

Dennis Williams: So they were actually at the last meeting saying how they intended to spend that money, and the plan is that that would be on-going, at least for a few years - as long as the budget allows.

Jemima Williams: So they said they'd put that into physiotherapy and so on.

Dennis Williams: So what they're actually doing now...

Jemima Williams: Trying to prevent...

Dennis Williams: ...is creating guidelines that GPs can use, that patients can use, and there'll be - I suppose it will be more specific to the needs of the individual and it will actually, hopefully, act as an education tool to lots of my medical colleagues who still feel that - if they've got a different pathway, they can go to the pelvic floor coordinator instead of straight to a gynaecologist. A, it's going to save time; B, it may be people who never need to go and see the gynaecologist then. So that's the way forward - they're going to try.

And I think that if they get it off the ground it could be something that could take off all over the UK.

Jemima Williams: Yeah, I do too.

Julia Cumberlege: Thank you very much. But I simply - Jemima, I don't want to dismiss what you've just told us, and all I can say is that we - we are so shocked by the

suffering that you in the past may have had and other people as well, but thank you for telling us that.

There's one question I'd like to ask you, which I'm afraid is rather managerial if you like. It's about funding cross-border treatment, and I think in the past you have just mentioned that...

Jemima Williams: Yeah.

Julia Cumberlege: ...and I believe that's a difficulty, so.

Jemima Williams: It is a difficulty, and the other thing, and I've put - I've actually put something in there, a few of our members suffering with Rectopexy mesh, because of one of the [REDACTED] surgeons, who is now suspended, their beacon of light and hope had been to come to [REDACTED] to have an operation with a [REDACTED] surgeon, who is now - [REDACTED] been stopped from doing operations, for whatever reason - because no information is coming through. But that light - that beacon of light has been completely extinguished and a couple of them are young mums with young children, one of the mums, two of her children are on the autistic spectrum, and her life is so difficult, and her beacon of hope has been diminished - it's been extinguished actually, with letters to say that their operations have been cancelled.

And some of these ladies are suicidal with the pain - it's horrendous.

Dennis Williams: The reason for stopping cross-border is obviously funding...

Jemima Williams: I was just going to say, Den, let me just say. Vaughan Gething has made arrangements with, I think it's a hospital in Manchester, for some of the North Wales survivors to be able to go to be seen and operated on.

Dennis Williams: It's hoped that the WHIG thing, again with this pelvic floor coordinator, will have the facility - because at the moment, what they say is if there's a consultant capable of doing the procedure in your health authority then you don't need to go elsewhere - that's their rationale. Whereas if, again if the individual has been upset or doesn't trust the consultant that's in their own area, requesting to go somewhere else is not a good enough reason as far as the Health Board is concerned. However, it is hoped that we can now overcome that and that Welsh patients particularly will be able to move around Wales should they find a suitable surgeon in another area.

Jemima Williams: Or even cross-border to Bristol.

Dennis Williams: As long as it is agreed and they have then got to try that further afield but obviously they have to coordinate with England in order to try and sort that

out. But that's the plan. Because - because they've lost faith in the local consultants, and that's true of English patients with English consultants...

Jemima Williams: Yeah, it's right across the UK.

Dennis Williams: So it's not that. Unfortunately, you know, surgeons are not gods, they can't get it all right all the time - some of them think they can - sorry. But I just feel that if we allow that - and if we look at these patients on an individual basis but they're not given a straight no. If they say well look if you fulfil these criteria and if WHIG is behind them, and if the pelvic floor coordinators are behind them, their chances of achieving cross-border funding are much higher. And I think that's a way forward at least.

Jemima Williams: Chris Harding has actually contacted Jodie Stotanovich who is one of the WHIG coordinators and has offered help with problems and questions and so on. So that's good too; it's good that these surgeons are now beginning to interact with patients, which they should have done all along, but you know - because of you - that's because of you they have started to do this, to interact with patients. And interact with each other, because I think that is really important. The consultants need to share knowledge and expertise in order to help us.

Every single one of the consultants have made mistakes - all of them, but some have had more positives than negatives, and so in the mesh community they are being looked upon as gods - almost. And I want to go to this particular person, because I think that he can do more for me than my local consultants can.

Dennis Williams: It was interesting that one of the urogynaecologists was saying about putting autologous slings in and that he was teaching his junior surgeons to put them in because they'd never put them in - they'd always put mesh in previously. I think there has to - you have to get back to the Royal Colleges and say look, if you're going to be a consultant gynaecologist in this current day, you have to have the skills across the board and not just concentrate...It's not a minutiae speciality, it's a broad band.

And putting in transobturator slings is unbelievable; they know when they put in them they can't take them out. They know it - and they've said on tape, 'I wouldn't go there', and they look absolutely petrified at the thought.

Jemima Williams: So they have no right using it.

Dennis Williams: So you're putting it into an area, you've no idea, A, what's there probably, because if you can't operate in the area, you don't really know the anatomy

that well anyway, and you're sticking something in there, and then you know you can't take it out. I think they have to either say, 'right that is banned completely - we just cannot do it - it's impossible'. Mesh is difficult to take out even if it's in the anterior vaginal wall, but let alone - and once it's cut, once the mesh is cut, it does contract and you can't trace the whole length of it. Because as they said you don't know how much they put in, because they don't measure it, then you don't know how much is there to take out. And so...

Jemima Williams: And even so, once it's cut, you can't find ends - you know another consultant can't find the ends to sort of follow it through and trace it through to remove it.

Dennis Williams: I know there's been a lot of media hype and hype, and sort of from press, particularly with the Scottish Mesh Survivors about trying to get some surgeons from America over who take out obturator slings regularly and have lots of experience, to come over. But there's some resistance; there's a resistance by the medical profession here...

Jemima Williams: It's arrogance and ego I think.

Dennis Williams: ...to try and accept, A, that they need further teaching from somebody outside the country, but if you haven't got the skills you've got to get them from somewhere. So I don't know.

Jemima Williams: So I don't think that [REDACTED] wants to come over here specifically to train consultants. His offer was, as far as I've been told by himself, that he would come and operate on those very difficult cases and to help with the backlog of people who are suffering. Some of them are really - you know [REDACTED], my friend, [REDACTED] she's really going through it - [REDACTED] - but they're only a couple of people; there are hundreds and hundreds of people out there who are desperate now.

Julia Cumberlege: Simon, do you...

Simon Whale: Could I just ask a question about one of the other subjects that you both raised which is regulation; so you both touched on it and I just wondered what your thoughts were about how to make the regulatory system better? And I know that's a very big question and we haven't got too much time, it would be good to hear your thoughts on that.

Dennis Williams: Well I think - sorry, do you want to go first?

Jemima Williams: I was just about to say truth, honesty and transparency - stop hiding the true facts. You cannot regulate or research unless you have the true facts

and figures. I mean it just stands to reason. Alternative summary reporting is evil because how can you know the true facts?

Dennis Williams: I think the - if you look from the surgeon's point of view, then they have to write up their surgical records immediately after the operation, that's always been the case. Then obviously what they really need to do is increase the amount of data that goes into that. All implants, whether it's mesh or anything else, has got to have some form of coding - a barcode or something attached to it that is put on to the operation records. They have to - if they're putting in tape, mesh whatever, they have to put in the size of what they put in - they have to say what they put in.

Jemima Williams: What goes in and what comes out.

Dennis Williams: And then they have to - I think then be - do a follow-up, and actually come back with more information after they've seen the patient. Let's say a week or 10 days post-op, whatever they decide is more appropriate, but then there should be a follow-up of a year or longer, I don't know one year, five years, dependent on the situation. Even if it's a letter to the patient and just say, how are you feeling, you had the sling a year ago, how are you feeling?.

They should - they'll have at least 50 per cent return, if not more hopefully. But if this information is available now within some of the hospitals, it's just not coordinated. And consultants don't talk to each other, they think they all use different materials, and if you go into the same hospital they're using four or five different sorts of slings - they're not using the same stuff that's going in. Don't get me wrong, I know they're busy, nobody knows it more than me, but it's extremely busy under the NHS, but they have to start sitting back and taking note of what they're actually doing.

And to deny the fact that there's side-effects, and to deny the fact that every time they put in a mesh, there's not a very good chance of a rejection, is so foolish, it's...

Jemima Williams: Yeah, it is.

Dennis Williams: And so they've got to be professional, they've got to want to put this right; and this is the bit that gets me - they don't appear to want to put it right because they don't actually think there's a problem. And in fact...

Jemima Williams: They're hiding the truth.

Dennis Williams: In some of the statements from some of the senior consultants online, I just got the impression we know what we're doing, we're doing it the right way, and you've just opened up a hornet's nest...

Jemima Williams: You've spoilt it for us.

Dennis Williams: And it's sad that they're not prepared to sit back and say there's obviously something wrong, how can we correct it?

Jemima Williams: Mesh survivors truly feel that the MHRA are not fit for purpose; how many have you heard that in your travels around the country?

Dennis Williams: In truth...

Jemima Williams: There needs to be a new regulatory system, a new body put in place above the MHRA, because they are funded by big pharma. We know that, and I'm sure you know that, and that's what's needed. That's the only way we're going to make a move forward...

[Over speaking]

Dennis Williams: I feel for the MHRA, that when you interviewed them, they really - as I said they were like rabbits in headlights, but they didn't have any answers because they actually haven't got a handle on what they're doing. They collect data but they don't seem to do anything with it. They really devolve responsibility for giving the CE marks to other people, and then they just rubberstamp.

Jemima Williams: And then they blame the surgeons as well, that's what I...

Dennis Williams: If you look at the figures that Jemima had on the Freedom of Information from the MHRA, at the end they've got little comments like cause and identified, device not...

Jemima Williams: Device incompatibility.

Dennis Williams: ...yeah, but they put device not incriminated or something like this at the end. But they've got all this online, but they haven't looked at it and thought well we've had all these - a lot of them are marked as serious, and I don't think...

[Over speaking]

Dennis Williams: ...when - what's their threshold for deciding that there's something wrong with a device. They didn't appear to have one. If you look, there's a total of 2500 plus on the list that we've got, and that's only for three...

Jemima Williams: I've only brought the hernia mesh stuff.

Dennis Williams: Oh yeah, all right, but you have the others. I just can't understand where their threshold is for actually thinking is there something wrong? They said, oh if we think there's something wrong we'll do something about it, and we do have the authority to withdraw a product from the market. But I, as a GP, we see it quite frequently the notes about a drug or something like that, that they've withdrawn or they suspended for a while. But they don't seem to look at the bigger picture of - A, they don't appear to accept that these devices have not been trialled enough before they're put into humans.

They are prepared, because it's a device and not a medication, they feel, what the hell, we have to take it back out again, but it can't be taken out, and that's the problem.

Jemima Williams: And the other - can I just say one thing; the other thing within the deaths, you know they say sudden deterioration due to infection. But the device isn't...

Dennis Williams: Incriminated.

Jemima Williams: ...incriminated. So we know that when mesh fails you have infection - and some of us have serious - you know we're under serious threat of sepsis and serious infections. Sudden deterioration due to an infection, and they died.

Dennis Williams: I think that what they've done, if you look at the data...

Julia Cumberlege: I'm so sorry - I think I'm going to have to...

Dennis Williams: I do apologise there.

Julia Cumberlege: No-no-no...

Dennis Williams: We've just gone on.

[Laughter]

Julia Cumberlege: ...because we're got other people...

Jemima Williams: Yes indeed.

Julia Cumberlege: ...waiting to come. But I really want to thank you both so much - it's been very interesting session...

Jemima Williams: No, we want to thank you.

Julia Cumberlege: ...and we have learnt a lot from it, so thank you very much.

END OF TRANSCRIPT

Session 2: Mesh Ireland

START OF TRANSCRIPT

Julia Cumberlege: So, thank you very much indeed for coming again to see us. I think last time we met with two of your colleagues and we've had an oral hearing previously, and at that time, you told us some of the problems that you face getting a full removal of mesh, and the same issue that has been faced by many other women, as well, including I think Fiona Bicknell who accompanied you last time, and she told us a lot about that. Since that last oral hearing, we've had lots of correspondence from you. Thank you very much for that.

In that, you were telling us about your concern that there could be a link with mesh insertion and squamous cell carcinoma and I think you went into that in some detail which was interesting and helpful for us and, of course, the advantages of a database and a registry. Also you mentioned concerns about the private sector. So we've had that from you and, as I've said, that's been very helpful to us, but also we've been thinking a lot about patients since we've been travelling around the country, and you will know that we started off with patient groups, listening to them.

people. So if there are particular issues you'd like us to consider, we would welcome that today, or anything generally you'd like us to consider before we write our report. So I hope that's clear...

Mary McLaughlin: Yes.

Julia Cumberlege: ...and if, perhaps, we could start with you saying who you are and what you represent, so that it's on the camera.

Mary McLaughlin: My name's Mary McLaughlin. I am the founder of Mesh Ireland. I would describe it as a one-woman campaign that has gathered followers. Maybe some clarifications which are helpful to how I've analysed the evidence that I've looked at. I have a Laws Master's degree in Corporate Governance and Public Policy, so I noted a lot of model discussions in the evidence, and I have a Politics Master's degree in Legislative Studies and Practice, so I am also interested in

how this whole - this Review will progress the plight of the mesh-injured.

I am in an interrupted PhD on access to civil justice and capability of laypersons, so that has fuelled my approach to looking into my experiences and that of other women. I've accessed mesh services in the Belfast Trust, in England and in the USA, and I had all my children in Germany so I've had quite an international reproductive pathway and post-reproductive pathway which informs my views, as well. I do know Mr Obolenski from FEG. He used to be a colleague of my ex-husband. I'll just declare that, just it was strange to see him in the evidence session.

Fundamental remit of the Review, you have pointed out to me that the Review wants to look at the healthcare system in England and how England responds to the problems, and one of the key points is, of course, that what happens in England cascades down and flows upwards, so it has great relevance not only for the devolved administrations but it also has great relevance for the global mesh communities and the other countries looking at reform. So the eyes of the world at the minute are on the current [unclear] Review.

So I looked at the evidence and thought I'd take it from an issues-based, and at the end of watching all of the many hours, I'd like to thank people for coming and giving their evidence. I know it's not easy and people get nervous, like myself. It's not a perfect situation, but at the end of it, I thought, so how does this shift?

How will this Review shift the burden from the patient back into the system, because no system's perfect and people have spoken about imperfections and flaws?

There was also a note of nobody seemed to be responsible, be it for the form that they're working in or professional bodies, that they just responded to professional bodies. Women don't understand that. Women don't understand how nobody can really be accountable, and I know this is what the panel is here to address. A lot has happened since we've been here. Mesh Ireland and the women that I speak to are very glad to hear of the continued ban, and I note that it's going to

take a year or two years to get the registry commissioned and up, so that is very helpful.

In Northern Ireland, the Chair of the All-Party Mesh Group, Órlaithi Flynn from Sinn Féin, handed in a letter of concern to the Human Rights Commission. I know we haven't spoken about human rights, but there is a general conversation with any mesh woman will say that they feel as if they're being discriminated against, that they're discriminated against because they're older, because they're non-reproductive, because of the presumption that the loss of their intimacy is not such a bad thing because they're not reproductive.

The impact of mesh is that certain groups of women are created and that they have a very hard ride for the rest of their lives potentially, be it in the benefits system, be it in the healthcare system, if everything is going to be who can pay for their health is going to get seen first, then that is very difficult. The disingenuity at NICE, I think NICE downplayed their significance and that they're non-mandatory to follow their guidelines because, of course, NICE is something that the courts use to determine whether a doctor has kept to the standard of care. So it might be a policy-based thing,

but for the women going to court, if the doctor has kept to the NICE standards, the doctor is going to rely on that. Therefore, it's a bit disingenuous to disconnect the two and say they're not - it has no consequence.

Ethics and informed consent, I'm still not convinced that the doctors have the best ethics. I'm not saying that there's - it's - when you watch the videos, it comes across as if, yeah, they know they dropped the ball, they know this has happened, but moving forward, we'll collect data and, for the women who are injured, it still comes across slightly disrespectful or blasé. You're a statistic. There has to be a difference between being objective and being sensitive to the people watching. I know a lot of people get angry when they watch medical professionals giving evidence and it's because they feel that they've been disrespected again, even if that is unintentional.

Then, the chilling effect of litigation, I'd like to speak something about that, in that I know it's outside the remit of the panel to discuss

people's access to justice in the civil courts. However, because everything in the system works as a defence for the medical profession when you go to court, the medical records they create work as a defence for them. Nobody cares what's on an informed consent form until something goes wrong. It's like the packet of - it's to guarantee your instructions in anything. If it goes right, nobody goes back to that document. If it goes wrong, people go back to the documents and start looking very carefully what was in it.

So the women - I'm still seeing this, that women are very dissatisfied with their medical records. There is a feeling amongst the women that the medical records are being written with the view, the prospective view that they might be used in court. We all know that doctors get medicolegal training in writing reports. One of the things that you notice is that, if you - it's usually the mesh injuries, patient feels. Patient feels her mobility is affected. Patient feels she has pain in her pelvis. Patient feels.

So it's a very weak formulation of what is real and it reinforces to the women that they're not being taken seriously. When they do try to access civil justice and go to their lawyers, the lawyers can't do a lot with those types of medical statements. So that is something that impacts on the mesh-injured women. So I'm really glad about the pause, but for the women who are already injured, there are a lot of things that we hope the system can maybe help us with, and I will give some suggestions or recommendations.

The standard of care, again, NICE and the GMC have a great role to play there. Patient registration or representation and PPG, I came across this PPG model where it says that there's patient participation groups, that the patient voice has to be represented, but not necessarily by the patient. I've noticed this has happened in Scotland where they formed subgroups now and the patient voice is being represented by doctors.

Now, we're not damning all doctors, we need them, they need us, [laughs] but I do think given the mesh crisis that the application of this existing model in a system is inappropriate because there will be no trust built to mesh or the mesh-injured if they're subbed in a committee by a doctor. Then, the question will be which doctor helps

the patient group? We all are aware of patient preferences for particular doctors. So I don't think - although that's an existing model, I think that should be disappplied in the case of any mesh patient groups.

The MHRA and adverse incident reporting, I wasn't going to talk about the MHRA because I know the panel has grasped that, but I did send up a document today and it was - in 2017, I followed the route to the very end with the MHRA to this [REDACTED] responding. The document was that, on - I understand that they look at a batch number and they see if there's a problem with the batch, and then they check whether anybody else has reported a problem with that batch.

On Section 11 of the page it says, are there any similar reported incidents? So, for example, if somebody reported pain. Then it says - it doesn't say in the batch, it says in the product. Then, there's a list of so many countries. I got it back and the thing wasn't ticked for yes or no whether there was a similar incident recorded according to the product and not the batch, so not a manufacturing defect with the product. Then, it said how many and it said zero, and then you've all the countries in the world where all this mesh litigation is going on and they're reporting back.

We did the - I have to acknowledge Mr Sergeant from the Northern Ireland Adverse Incident Centre. He corresponded very thoroughly and reminded them of their duty of candour and the - it went cold, correspondence went cold. So I think that that form has been filled out incorrectly, and perhaps the MHRA could follow up and see if they have reports according to the country and not a manufacturing defect, but a patient injury, because if they have those type of reports, they might be able to see some stats. I know you're all keen on stats.

So I'm going to do my recommendations first because I'm not good at time management, so I want to make sure I put them in. I heard lots of evidence on transobturator tape and they've got mine in the picture and I think, thank goodness it's out.

Julia Cumberlege: Sorry, Mary, can you go quite slowly and quite loudly...

Mary McLaughlin: Quite slowly, okay.

Julia Cumberlege: ...because these recommendations are really important to us...

Mary McLaughlin: Okay.

Julia Cumberlege: ...and I don't want to miss anything.

Mary McLaughlin: Okay. The first recommendation I have is that the transobturator tape is immediately banned and that an information sheet has to go out to the GPs and public bodies. The ban - I didn't hear any evidence in favour of the transobturator tape. I heard surgeons who said they never inserted it because they felt it's dangerous, and there's evidence that the system has rejected the transobturator tape, and when they realised there were problems with it they started to go back to the TVTs. So I don't think there's any mesh surgeons particularly attached to the transobturator tape and I think it would be good for the women who have been

damaged by it to know it's banned, just like the pelvic prolapse meshes were banned.

The information sheet to GPs and public bodies, I have encountered personally the problem that people that we interact with on a lower system don't understand the impact of the transobturator mesh on mobility, for example. So they just don't know how it affects, and it's not surprising when we have surgeons coming in to say that they didn't really link mobility to a transobturator tape injury. So we need some type of public information sheet that outlines for the relevant body the information they need to know and also, if somebody is going, for example, to a benefits tribunal, that they can provide a government information sheet about the injury.

I'm also aware that the benefits department haven't trained their assessors up on this thing, so I think a detailed information sheet would be very beneficial and help women who are left with injury, that they don't have to try and explain themselves because it's quite complex.

Cyril Chantler: Now, is this an information list to patients who have been damaged as opposed to an information list which would be part of the consent process?

Mary McLaughlin: Well, I would say that somebody needs to sit down and write a very detailed information booklet on transobturator damage.

Cyril Chantler: Damage, right.

Mary McLaughlin: Then, people who need it can tailor the source document down to the needs and the audience that it's for, but at the moment, women are just trying to lift stuff themselves off the internet and it's not really working. International and independent advisory body...

Julia Cumberlege: Can I just ask, then, about this information sheet? It's clearly different from the NICE evidence that's been put out or, sorry, the NICE information that's been put out to patients.

Mary McLaughlin: Mm-hmm.

Julia Cumberlege: Yours, as you have said to Sir Cyril, is about damage to the patients.

Mary McLaughlin: Yes, it's about how mesh affects the functionality and the day-to-day activities and making a journey, for example, which are frameworks. There are different frameworks where the evidence isn't about - it's not enough to say it causes pelvic pain. It has to be a little bit more that somebody can deduce how that impacts you on a day-to-day, and at the minute, we don't really have anything. Because the mesh women haven't been believed on mobility, then you as a patient are trying to tell somebody who's administering public funds that you can't walk and they can see you can walk.

Julia Cumberlege: So are you suggesting who should do that? You said the government, but that's a bit wide.

Mary McLaughlin: Well, maybe a leading mesh surgeon could write up a document and give it in to the Department of Health to say how a mesh tape in your hips affects how you walk.

Cyril Chantler: It's not just the Department of Health, from what you said. It's the Department of Work and Pensions.

Mary McLaughlin: Oh, the Department of - well, somebody in the government could maybe commission a leading medical expert to write a document to make it clear, and then that cascades down to the relevant departments. I think that's what I'm saying.

Simon Whale: Do you think - you're thinking of this specifically around - for TOT? Mary McLaughlin: Yes, yeah.

Simon Whale: Do you think there's a case for doing this with other forms of mesh, as well?

Mary McLaughlin: Absolutely, that the women don't have to - we have to shift the burden back to the system. The system has failed them. We've carried the burden too long. We're all tired. We need the system to kick into place. It's there, it's just not been activated properly. So that was my main thing, so the immediate ban of transobturator tape and information disseminated to the relevant public bodies, maybe formulated by an expert.

The next thing is the monitoring of mesh removals. I was pleased to see that the panel invited mesh centre clinicians and there was a large discussion after the Mesh Ireland session about mesh

removal and I was - I would like to thank the panel for doing that. So where do we go from here? There seems to be - the mesh myths seem to have been busted about shrinkage and splintering in most cases and things like that, so that's very good. Then, there's going to be specialist centres commissioned and the feeling is that who's going to monitor the specialists? Because, as you've heard many times, they haven't been doing a lot of specialist removal, and the skill and the competency of complex mesh removal is not won overnight.

So I thought long and hard about this and I thought, how can we gain mesh patients' confidence and trust in the system back again? There's a great distrust in the UK and I know some of the UK surgeons are working very hard to rebuild that trust, but...

Julia Cumberlege: Sorry, can I go back...

Mary McLaughlin: Yeah.

Julia Cumberlege: ...to the other one about monitoring the specialists?

Mary McLaughlin: Yeah.

Julia Cumberlege: Who are you suggesting should do that?

Mary McLaughlin: I'm suggesting that the UK should reach out on a global basis, and I'm suggesting it because there's lots of committees around the world, government committees looking at the same problems, and as one closes down, another one starts up. The women locally, as a country or nationally, as well, do not have trust in their national systems, and also because of the litigation and things that are going on in the background, there's a conspiracy theory to be proven or disproven in the minds of the patients.

So if there's several large countries that have this same problem and it's going through several governments and people like yourself are looking into this and people are coming up and giving evidence, would it not make sense that each country designates a specialist and that that specialist can go out once or twice a year to the other country and monitor the standards of surgeons in another country? So that the patients have the feeling that it's not the same

people, it's not the surgeon that injured them is now in charge of monitoring mesh removal.

Then, that the medical community in that country know that it's an international, independent person. They're coming in and they're going out. They're not...

Cyril Chantler: There are a number of international organisations, kind of specialities, so ...I was President once of the International Paediatric Pathology Association, and I know obstetricians and gynaecologists have World Congresses and there are structures around this. So you're suggesting that a body that is in this area might take the responsibility for overseeing on a worldwide basis this problem, but they are very much professionally dominated...

Mary McLaughlin: Yes.

Cyril Chantler: ...which is perhaps not quite what you would want.

Mary McLaughlin: Well, it's an idea, a seed that I'll put out there. I think we have to accept that we have to work with the medical community and we have to build trust again. I don't know if you put an international expert and two designated patient representatives that can look at the pictures of the mesh removal. We've heard now that the pictures

are going to be done and people are going to get pictures of their removed mesh and measured and pathology reports are going to be done. So the medical community seem accepting that patients need to see more evidence, and if they don't trust the doctors in their own country, then they're more likely to trust somebody who comes in and isn't dependent on that medical community for their own career.

I know everybody networks globally, but we can't bring somebody in from outer space to do these things, so we have to start moving forward. If patient representation is on it, then that is maybe a way forward, because it cannot be that the mesh advocacy groups advance one surgeon, their favourite surgeon. It's just creating problems already. So I think there has to be some type of bigger model and it's a sustainability thing, as well, because then, a country that's further ahead in the mesh crisis, they can shar

information with countries who are only starting to recognise and address it. I think that's a sustainable way to healthcare.

So that was - my third recommendation was the General Medical Council set up a dedicated investigation team. I looked into their models and I see they do a one incident follow-up, if a doctor has one incident that they follow up and see if they don't have to formalise the process so far if there's some remedial thing can be taking place. However, the GMC doesn't serve the patients very well. I've interacted with them a lot and you've got the data privacy thing going on, you've got limited - you've got - sometimes it's like a call centre type conversation you have. You can see people are reading from a script.

For patients who have concerns about individual doctors, I noted the gentleman from the GMC said we can get in touch with him and I think, no, he has to get in touch with us, in that he has to set up some service, that if women think that a particular surgeon has harmed them and it's a matter for the GMC, the GMC have to set up a dedicated mesh team because some of these surgeons are doing a lot of operations. Within groups, we have women who are injured by the same person. It would make sense for the GMC to see if it is a one-off incident with that patient, but whether there's other patients have had the same incident. I think they would then be able to evaluate

that better without having to discuss things that go into the data problem of sharing it with the patient.

my fourth recommendation is the expanded scope of commissioned services.

Julia Cumberlege: Before you go on to that...

Mary McLaughlin: Yes.

Julia Cumberlege: ...can I just ask you about the GMC and the investigation and all of that? Can you just say a bit more about that because...

Mary McLaughlin: Yes.

Julia Cumberlege: ...I want to be sure that that's within the remit of the GMC?

Mary McLaughlin: Yeah. If I take the example that I have - I've given you an example of my own pathway and I feel aggrieved by that - I know that there's probably - I don't know, I assume that there'd be other women who are grieved by the same problem and maybe the same surgeon, maybe a different surgeon with the same problem. At the minute, the only place that is filtering down to will be the court system, and that will go on the capability of the woman to fund litigation. So if the system is interested in addressing the flaws, there has to be a free-at-service or free-at-entry body that allows people who can't afford litigation and who don't want to litigate, but to be able to flag up the dangers.

So why can the GMC not get resources if they don't already have it? I suppose it's not a mediation type of thing, but the GMC advance the tribunal, the disciplinary tribunal, so it's not the woman that has to pay for that. They can see whether these are serious things that a good practitioner should not have been doing. Then, also, they can highlight to a woman if the woman is incorrect and the doctor hasn't done anything wrong, because I think it's important to not waste the rest of your life running down rabbit holes that nobody's going to listen to.

So it was my idea of letting the women feel a form of redress, that their individual complaint can be heard outside of the hospital system, because the hospital complaints system is just appalling. It is appalling. It is a paper production of cut-and-paste paragraphs which say, we

have looked at ourselves, we've done some navel- gazing and we have decided there's no grounds for your

complaint, or would you like to come and talk to us? Then, women are finding out that there's been recordings made of their telephone calls and there's already evidence being gathered and reports written, if you then end up doing a subject access request, you can see how there's documents building up.

Women don't want to complain to the hospitals. I've stopped complaining a long time ago. I've just given up on it. So I think it should come out of the Health Trust, because the Health Trust again, it's a chilling effect of litigation, and the Health Trust know what this could be a potential thing for their legal department.

Cyril Chantler: So you don't think the PALS system works?

Mary McLaughlin: Is that the complaints system in the hospitals?

Cyril Chantler: It's the advisory liaison service...

Mary McLaughlin: No.

Cyril Chantler: ...the Patient Advisory Liaison Service.

Mary McLaughlin: Absolutely not.

Cyril Chantler: Yeah.

Mary McLaughlin: Absolutely not. I've lost track of the number of complaints that have been...

Cyril Chantler: Because it was set up for that purpose.

Mary McLaughlin: Yes, but I think it doesn't work in the case of a potential mesh litigant. Our records are flagged that we're litigants. So everybody touching us are making sure that they're creating copious records just in case, but they're never - when people get them - and I only have several accounts of people I know - when they get their records, it doesn't match the patient's encounter, the patient's memory of the encounter. Some of them are very detailed. There's lots of details that don't match what the patient said, what the patient did, who attended the meetings with them, things like that. So the patients are beginning to feel like their documents are being manufactured, yeah. If you're not asking for your documents, you don't know this.

Cyril Chantler: You should get letters copied to you, all letters written about you.

Has that not happened?

Mary McLaughlin: No. We get a summary. You get a summary, dear Ms McLaughlin, we've lodged your complaint, we have spoken to the professionals.

Cyril Chantler: No, I meant when a doctor writes a letter to another doctor about you and your condition. You should get a copy of that.

Mary McLaughlin: Yes, we do. Like a summary letter, 'patient attended' and a lot of 'patient feels'. Patient feels there's something wrong with her bowel, patient feels there's something wrong with her legs, patient feels her tape has eroded. That's my letters, so I'm happy to share them with you. Patient feels.

Sonia Macleod: In terms of what you're suggesting with GMC...

Mary McLaughlin: Yes.

Sonia Macleod: ...would this provide over and above what they provide at the moment?

Mary McLaughlin: I think it would be from a different perspective and that it would de-escalate the conflict that the patient has for the doctors and the Trust that they feel have let them down. So if women are going to try and heal, they can't keep being sent to the hospital and the doctors that they feel have injured them. It's traumatic. Every time you come off the phone with the people who didn't want to know about your mesh, told you it was in your head and then, when you're trying to get your healthcare - it's just traumatic for the women. They have to get - the system has to direct them out of that conflict.

The doctors and the staff, they know your names probably. They're, oh no, this woman is on the phone, but who else can we phone at the minute? Who else can we talk to? There is a withdrawal of mesh population from speaking to their doctors.

Maybe not every mesh woman, but a lot of women have - I will not go down, I will never go back to my Trust for any gynaecological, never.

Julia Cumberlege: So when you've been thinking about this...

Mary McLaughlin: Yes.

Julia Cumberlege: ...which you clearly have in great depth and thank you for that, have you considered the whole of the complaints system that operates in the NHS? Clearly, you have been thinking about the GMC.

Mary McLaughlin: Yes.

Julia Cumberlege: People have told us that the complaints system is very complicated...

Mary McLaughlin: Yes.

Julia Cumberlege: ...and I wondered if there were other thoughts that you'd had specifically on the complaints system as it operates now.

Mary McLaughlin: Well, in Northern Ireland, we have two-year waiting lists for everything.

Julia Cumberlege: You have what?

Mary McLaughlin: Two-year waiting lists to see a first referral to a consultant on most health issues, unless you have cancer. That's the only - so the only other redress is through the complaints system. So I would assume that there's Trusts in England, as well, where they have very long waiting lists, so I would assume that the patient complaints system is overwhelmed and that there's template documentation that they sent out to patients and that the patients get these documents, often not within the 20 days or within the 40 days, often 60 days 'til you get a reply, and the reply is a standardised reply. By the time you get it, you can't even remember what exactly it was you complained about. That is the reality of it.

to make a complaint to - they don't want to complain about the appointment not being good. They want to make a complaint about the doctor. Not everybody would like to sue their hospital for many reasons.

So is the GMC not the body that deals with complaints specifically about their doctors? If I take my own case which I've talked about in

the previous session, if I think a doctor was going to take a scalpel to me, was going to give me anaesthetic and take a scalpel to me and do an operation that I had made quite clear I did not want, do - I can't process that through a complaints system in the hospital because the hospital is maybe phoning up [unclear] go to their legal department straight away, but then I'm thinking, if there are other doctors doing that, there are other women coming in who might end up not recognising that. Isn't that - hasn't the system to respond to that? Hasn't the system to create a special - this is a crisis. It's not...

Cyril Chantler: I think the GMC would say, and I think they actually said it to us, but I'd have to go back and check, that they do look at patterns of complaints about doctors. If they do get more than one complaint, they look at that. However, your point is, well, it's not working if that's the case.

Mary McLaughlin: Yeah, it's not.

Cyril Chantler: You've made a general statement right at the start which I wrote down, to shift the burden from the patient to the system.

Mary McLaughlin: Yes. I teach legal systems. I know systems go wrong.

Cyril Chantler: Yes.

Mary McLaughlin: I know panels try to put them right, but we have to move it from patient - the patient has to feel like they're able to heal. The patient has to be looked after, given the medical services and allowed to walk out of this mesh world and not have their life defined by mesh. Some women will have their scars, their emotional scars and their health scars, for their lifetime. I know that the remit of this committee is broad but narrow. It can't do everything, but I know that it can cascade down into other areas which will impact on the life of women when they've no more surgeries and no more consultant and they're at home living with other things that are an - but that - with this panel and the expertise that they've heard, we've had the best in the UK coming to talk.

Sometimes I've shaken my head at some of the things they've said, but it's not easy giving evidence.

Julia Cumberlege: Mary, I'm sorry. We've interrupted you and I think you were into your fourth recommendation...

Mary McLaughlin: Yeah.

Julia Cumberlege: ...before we interrupted.

Mary McLaughlin: Yes. The fourth was the expanded scope of the commission services.

Julia Cumberlege: Sorry, expand the...

Mary McLaughlin: Expanded scope of the commissioned services. So at the minute, there are specialist mesh centres set up in the UK, some working better than others. However, I think the selection of services that are within those special centres has been very doctor-filtered. For example, the women are not getting access to trauma counselling. When you talk - so there's no trauma counselling within those services. I think that should be part of it. The women are being asked to go to things like group therapy, CBT.

Firstly, I don't think any woman is wanting to walk into a group therapy with random strangers to talk about what's been going on with her vagina. I just don't think that is a reasonable suggestion. However, the health workers, that's all they're able to offer because there's no specialised counselling services within the trauma. Now, I asked for specialised services several years ago and I have been - waitlist didn't happen, and by the time they did offer me group therapy, CBT, I was already privately paying for counselling services. When I asked for those bills to be paid, it was refused because I had gone and got them myself.

I have been with a therapist for a year and then asked that those bills are paid because they're a recognised therapist, they're an accredited - but they're not some quack therapist down the road, the Health Service says no, you're going to have to come back in and we'll have to refer you within our things and that might take a couple of years. Then you think, but I'm in the middle of therapy. I've told something to somebody. It doesn't make sense.

So, again, it's if you have the economic means or not you get the therapy and, if not, the women are getting no therapy, and we cannot heal from this if we don't get counselling services. This is traumatic.

What I'm saying is, because of the part of the body that's affected and because of how they've been affected, a lot of us have been effectively neutered because nobody - sexual counselling would be another thing on the expanded scope of services. There has been no sexual counselling offered for women at all.

I think it goes back to the human rights issue, that there's a perception that when you've had your children that your intimacy is not so important, and that when you're post-menopausal that nobody asks you about it, they just assume that, if you lose your intimacy, well, do you know, you can live with that. I know the panel knows that's not the case, but this attitude is reflected in the current services. There is nothing to help the women apart from the women themselves. At the minute, there is a toxicity amongst the women and it's inevitable it's going to happen because you're just talking to the same people all the time because there's no professional person stopping this.

So that would be expanded scope of the commissioned services. I think the mental health and the sexual health area has been totally forgotten about, and also, if a mesh woman has an emergency, are they meant to go to their A&E? Is that - in Northern Ireland, you could bring your sandwiches and a flask now to A&E. Are you meant to go to an A&E service and start explaining to a doctor who's never heard about mesh what's wrong with you when you're bleeding, when you're in excruciating pain. They're not - can we

have an emergency service in these specialised centres that you're setting up, that there's an on-call system like we have for GPs?

It's a very specialised ailment if you turn up with mesh injury. I'm not sure A&E departments can do anything for people. Once they see that you're mesh-injured, nobody - it's hands off and you get paracetamol and sent home. So is that something you can maybe look at?

Simon Whale:

Sorry, just to - you're making quite an important point and I just want to make sure that we've covered all additional services or enhanced services that you're thinking of. Have we covered all the expanded services that you've got in mind?

Mary McLaughlin: Those were the ones that sprung to mind because we have colorectal, we've got gynae, we've got urogynae, some have orthopaedics in now, and - so I think - but we've nothing on mental health.

Physiotherapy, I'm not a physiotherapy fan, but if there's a role for it, I'll let somebody else deal with it. So there's physio. I know women are getting sent to physio, but on the mental health counselling, there's absolutely nothing, and sexual health, absolutely nothing. So, will I move on?

So, the next one is the updated medical record reflecting [filtering] gaps. So, what I'm suggesting is that - I've articulated there's a problem with medical records. Would it not be at a time where the medical community have recognised that the women's ailments have not been correctly attributed to mesh? Would it not be at a time that every consultant that has seen a mesh woman writes a thorough letter to the GP outlining the patient's history, the patient's complaints, why they're down to mesh and what the GP can do to help and what they should be looking out for, and that that letter is sent to the patient, as well, because the patients have a better knowledge of their medical history than the doctors?

the medical profession, that their ailments are related to - not patient feels, they're related - patient has read on the internet about mesh, none of these statements. They have to disappear from - they have to stop.

Doctors are still writing, 'patient has read from the internet about mesh'. It is disrespectful and it aggravates. I just think there has to be - if the doctors are saying they haven't recognised these things, then their records from the past may not reflect the true situation of the patient. I think patients could move forward if they knew that there was a patient that had a medical record that actually reflected, that acknowledged what had happened to them and why they're in pain, that they're not hypochondriacs going back and forth to their doctor.

Sonia Macleod: So are you suggesting a sort of retrospective look at people's records or are you suggesting different...?

Mary McLaughlin: Yes, well, not a summary of everything that has happened but just, say, at deadline X, 'Ms McLaughlin has presented with symptoms in

keeping with mesh complications. In Ms McLaughlin's case, she has problems with her bowel, problems with her bladder, problems with her mobility, problems with her intimacy. These have happened because' - it's highly likely that these have happened, probable, less likely, could be other reasons. I understand there are other reasons, other gynaecological conditions that can cause symptoms.

I heard the doctors. I agree to a certain extent that some patients have injury and think now everything is attributable to mesh, but the patients need to know to what extent their injuries - their current situation is mesh-related, and if it's not mesh-related, then patients need to know that, too, because they're not being referred to other doctors to address things that are perhaps not mesh-related, so there's things maybe dropping under the radar. I think - does that answer your question? Is that...

Sonia Macleod: Yes, it does. I can see that there may be difficulties in terms of attribution, and I suppose that's my question, is if we're dealing with a breakdown in trust in someone who feels that their symptoms are because of mesh and they're seeing the doctor who's saying, well, actually, no they're not, I think I can see that there may be issues around that.

Mary McLaughlin: Yes, well, that is the existing problem.

Sonia Macleod: Yes.

Mary McLaughlin: Now, what I'm saying is, if the system wants women to start to heal and start to trust the medical system, then they could write, 'is highly likely', 'is likely', 'is less likely'. They could use a framework. If somebody says they've got chicken pox, we say, well, it's unlikely to be related to mesh or it's impossible that it's related to mesh. If somebody says, I can't walk and the further I walk, the shorter my stride gets, well, I would say that would be definitely related to a transobturator tape injury. So I don't think that doctors - I understand that the attribution can be difficult, but they can't sit on the fence for the rest of their lives, in case a patient sues them.

This is the reality of it. What's the point in having a patient record or a medical record if it's written as a defence for a lawyer in a court? How does that serve the patient, who maybe will never sue the doctor and

will never get the treatment they want because nobody knows what's going on with their bodies? The doctors who have a very good idea of what's going on are not putting it down on paper, and how does that affect women's mental health? Why are women suicidal? They're suicidal not just because they're not - they don't have access to [patients], they're suicidal because they've been told for years that they're nutjobs. They come out of surgeries thinking they're nutjobs. They come out of disability assessments thinking they're nutjobs because nobody believes.

That is - I don't usually use that language, but that's when we're having a cup of tea with each other, when we go down and support each other and we go into the coffee room, that is the conversation we have. 'Did you see the looks on their faces? Did you see the way they were looking at us? Did you see the way they wouldn't acknowledge us?' I still encounter that. [REDACTED] I still encounter it, and it has to stop

Julia Cumberlege: So, Mary, is that the last of your recommendations?

Mary McLaughlin: There's one more.

[Laughter]

Julia Cumberlege: Oh right. Shall we go for that?

Mary McLaughlin: There's one more. We'll go for that. That's why I started. We're starting at the top. The public and private divide.

Julia Cumberlege: Sorry, public and private?

Mary McLaughlin: Public and private divide. So I have to declare an interest because I have switched between systems and there would be a legal argument as to whether I am in a no-man's land at some points in the system, because the doctors switch between systems and it's operated - in a private system, I was - did my pre-ops in a public hospital. So, from a legal point of view, it's difficult, but I noted in correspondence or press release or Parliamentary speech, I can't remember the source now, but there is a differentiation in the patient who's accessed private services.

I would go back to the human rights point of view. The mesh journey is a long journey for a lot of women. They may have started off in

work with extra private health insurance and they have shifted the burden from the public system by having insurance to pay for - so, for every woman that gets a private operation, there's an OR slot for a public patient. The doctors operate both in the public and private services, most of them. I know there are exceptions, but most of them do. So, the divide is very blurred because you can cherry-pick from both systems if you don't want to be accountable for one or the other.

So, if the Government is going to help people, the fundamental question is, should it make a difference whether the women were operated on in the private or public sector? Because the Government encourages private insurance, encourages waitlists to be dealt with through private health centres and with a lot of furore about the new London private mesh services clinics. So, is it fair that, if you are at a point in time, you're in a public system and you're on long waitlists, and then public money is decided to be

spent on commissioned services from the private healthcare system?

You could operate in the private healthcare system, but if anything happens to you, you're still under the liability of the public healthcare system because it's like a vicarious type of liability. But if you work or you pay privately for insurance and you're operated on in the private system, and then you're mesh-injured and then you can't work and then you can't afford private insurance, and then you become - you filter back into the public healthcare system and you're a public patient, is the Government any less responsible for you?

Is the Government - has the Government any, as a public authority - the public authorities use the private system, our employment system encourages employers to have private insurance. Surely to goodness it must be a case of all these activities are insurance underwritten.

Sonia Macleod: Are you -

sorry. Mary McLaughlin: Yeah.

Sonia Macleod: When you say are the Government less responsible...

Mary McLaughlin: Yes.

Sonia Macleod: ...are you meaning in terms of your provision of healthcare or in terms of potential compensation?

Mary McLaughlin: I don't think they're showing any less responsibility in terms of healthcare because I have experienced that myself. If you don't have private insurance, you can go to your national health system. I'm thinking in terms of any form of redress, yes, and compensation. We've had the Bristol hospitals scandal with the rectopexy mesh and the Spire hospital and there's patients, public and private. The private patients have had great difficulties accessing justice in the same way as the public patients.

The question is, if we want to move on and let the women - the women are injured the same way, whether they were operated public or private, and they haven't done anything wrong. They're operated on by doctors who are sanctioned by the government departments and standards of care procedures. The women haven't done anything wrong. So why, if the Government does a compensation scheme - I don't know what they're planning on doing.

Why should it make a difference that the woman was operated on in the private system? I don't think there's a good argument for it apart from an accountant's spreadsheet. It's less money to pay out if you can exclude a group of patients on the basis of where they got their mesh implant. It comes down to pounds, shillings and pence, doesn't it? You're looking at big numbers and thinking how can we limit the numbers here?

The other thing I would like to - in that public/private divide up, it's just Legal Aid. Legal Aid is not generally available to people for many things, and there's a question of whether this type of injury should attract maybe Legal Aid. I'll just put that in there. So, I think those are my - I'm sure I'm nearly up on time, am I, yeah? So, all the slides after that, they'll go with me back to Belfast. I didn't think it appropriate to comment in particular on any one person because there's mistakes in systems and systems have to be repaired.

A lot of people are very focused at the microlevel of this, of the micro-impact. When I go home, it's my micro-impact. I think the role of

patient advocates, as well, is to try to understand the system. I have the knowledge. I received funding for a lot of my degrees, so one of the reasons I've been involved in this is that I thought I had to step up and try and work my way through the system to help other people. So I'm not a brand or - I don't want to be associated with mesh for the rest of my life. I'd like to get back into my ordinary life as most women do, but there's a lot of hurt out there, a lot of very, very hurt people.

Julia Cumberlege: Well, Mary, thank you so much. It's been really useful. Thank you for the enormous amount of thought you've put into this. I think your recommendations are things that we will want to consider very carefully and think about the way forward. Of course, I can't say to you - I can't give you any definitive answers today, but just to thank you very much. Looking at it from a policy point of view has been really useful, and certainly know the interaction you've had with a lot of the women who have suffered, as we have. It is shocking. It is terrible, what's happened to people's lives. This sort of rigour that you've brought, the academic rigour has been extremely helpful. Thank you very much indeed.

Mary McLaughlin: Thank

you. Julia Cumberlege: Thank
you.

Mary McLaughlin: Goodbye,

thanks. Cyril Chantler: Thank you.

END OF TRANSCRIPT

Session 3: Association of Children Damaged by Hormone Pregnancy Tests (ACDHPT)*

START OF TRANSCRIPT

Julia Cumberlege: Can I welcome Marie and Mike Lyon, both of you here today. Thank you very much for coming to give us your oral evidence again. We have of course met in the past, but I just want to say that I think your outstanding commitment to the women and their children has been absolutely outstanding, and your energy and your diligence in finding out what has been going on in the past, and also caring for people in the present, that has been very impressive.

I just think about how you arranged for us our meetings in London, Southampton, and Manchester, where we met a lot of the people who had suffered through Primodos and hormone pregnancy tests, and that was very, very interesting for us. We heard first-hand exactly what people were having to cope with now, as well as what had happened in the past.

So, we know that you've been very involved with the expert working groups, both of them, and also all sorts of speaking engagements you've had across the world, I think, certainly across Europe and across the United Kingdom.

So, this session is for you. It's your opportunity to think about things that we should be thinking about for our Review. We are ending now the fact-finding sessions that we have been running. We started with the patient groups, and we're finishing with the patient groups, and so particular issues you want to raise, anything you want to tell us, any recommendations you'd like us to make in the report, we would love to hear any of that. Anything you want to tell us. You will know that we have the cameras running, and this will be screened on our website, and I hope that's alright for you.

So, if you could start just by saying who you are and your positions, that would be very helpful, thank you.

Marie Lyon: My name is Marie Lyon. I'm the chair of the Association for Children Damaged by Hormone Pregnancy Tests, and we presently have a membership of about 270 families.

Julia Cumberlege: And you are accompanied by your husband.

Marie Lyon: Oh sorry, yes. Yeah, accompanied by Mike, my husband who, quite frankly, if he didn't take me where I'm supposed to go, I wouldn't get there anyway. So, yes. Invaluable.

Julia Cumberlege: Right. So, over to you.

Marie Lyon: Today actually has been one of the hardest days to prepare for, and it's simply because there is so much to say, and it's knowing what to say, and what is being left out, and which is more important. It's been really, really difficult. I have, as usual, written it down because it's easier for me to do that, and it's basically a little synopsis of what has happened, the various areas that you're going to cover, and just to give a flavour, again, of evidence that maybe you haven't heard before. But I do thank you for all this, because it is a really good opportunity, and I just hope I do it justice.

I would like to summarise, really, the failures of the regulatory authority and the drug companies, and again that will be a short session. It's just, it is easier to tell it as a story.

One of the first things, though, that I would like to do, because this is really quite important, is reference the following statements.

They were made in the oral interviews that you've had with different people. One of the things that was said is that there was a possible association. The second thing was that we have always known there was an association. So, these statements were made by three members of the expert working group. They were repeated by the Chief Medical Officer of the UK, and supported by studies from Dr Inman, Dr Greenberg, Professor Vargesson, Professor Heneghan, and Dr Aronson.

Really, I think I would like to start by saying, would you agree that there has been recognised a possible association between adverse events and hormone pregnancy tests? So, that really is the first statement. To back up that possible association, and the failures that actually occurred to stop those tablets being taken off the market, is where I'll actually give some small pieces of evidence.

We know that the Committee on Safety of Drugs was set up in 1963 responding to the Thalidomide tragedy, and they also set up a year later, 1964, the Metabolic Research Reactions Unit. Now, this was incorporated, as I say, into the CSD in 1964, and the specific term of reference was, to assemble and assess reports of adverse reactions of drugs, and to study the mode of action of certain hormones. So that was the specific area that they were going to cover.

So, prior to setting up the Committee on Safety of Drugs, there had been a widespread concern about the number of deaths from thrombo-embolic events related to oral contraceptives. This information had not been shared with the medical profession, and could this maybe have been a reason why they wanted to focus on certain hormones within that particular unit?

Also, the Dunlop Committee, named after Sir Derrick Dunlop, who was chair of the new CSD, informed doctors at the time that they could destroy medical notes if they felt at risk from prosecution for prescribing drugs which had produced adverse effects, and he did qualify that by saying no matter how wrong that would be, but basically gave them permission.

The German state investigated, published an internal report dated 30 November 1961, which actually cited Duogynon, which is the German name for Primodos, as one of the possible causes of Thalidomide. So, again, could the new Safety on Drugs Committee have been aware of this report, which would further influence their decision to focus on certain hormones.

I have looked at a publication by the historian, Dr Jesse Olszynko-Gryn, because it does contain some good archival research which may shed some light on the documented historical evidence of the regulatory failures by the Committee on Safety of Drugs, 1963 to 1970, and the Committee on Safety of Medicines, 1970 to 2005.

Documents have identified that between 1961 and 1971, the NHS was facing a financial crisis, as laboratories failed to keep pace with the rising demand for tests, and this was including pregnancy tests, but these tests had doubled within that period, 1961 to '71.

Primodos at the time cost five shillings, against £2 for the organon-pregnosticon, which was a non-invasive test which they used small commercial laboratories for. So, basically there was a lucrative opportunity in the failing NHS, and that was soon captured by Schering and Roussel, who are now Bayer and Sanofi.

However, in 1966, suddenly Amenorone Forte was removed from the index without explanation, so there was no longer the opportunity to use that as a hormone pregnancy test, and it also had the same components as Primodos.

The government health regulators at that time were permitted to have financial interests in drug companies, either as shareholders or in receipt of research grants, but this introduced a possibility of conflicts of interest, and that will be more explainable when you look at the way that other countries actually operated. In Norway, for example, pharmaceutical products were assessed by expert valuation and not commercial potential, and that actually removed some of those conflicts of interest from the regulator.

Dr Inman had worked closely with Schering on their oral contraceptive because at the time, as I say, there had been quite a few deaths. So, he then helped them manufacture the mini pill, so he had a very close relationship with Schering AG and the UK subsidiary.

So, could his decision to endorse the discreet removal of the indication from Primodos in 1970 have been influenced by his collaboration on Schering's oral contraceptive pill? Was the government regulator fulfilling his duties as government Principal Medical Officer when he withheld the information of that removal from members of the medical profession and prospective mothers for five years after that discreet withdrawal? Could financial interests have been the motivation for his advanced warning to Schering about the shocking results of his own study into HPTs, a warning he did not disclose to the medical profession and the public for a further five months?

Dr Inman was Principal Medical Officer, between 1967 and 1978, and the government advisor responsible for deciding what action, or not, to take on Primodos and Amenorone Forte. Can we believe that Dr Inman mistakenly provided Roland Moyle, the minister, the

government Health Minister, with misleading and unfounded statistics from the German research foundation? Those statistics were quoted by Mr Moyle in parliament - they're on Hansard - to support his refusal for the public inquiry requested by Mr Jack Ashley. Instead of agreeing an inquiry, Mr Moyle advised parents that they would have to pay for research to provide a causal connection.

This obligation stipulated by the government Health Minister is still the same obligation we are facing today.

In his speech in the House of Lords in February this year, Lord Alton of Liverpool stated, they - the association - have faced the implacable determination of regulatory bodies, spending huge amounts of public money on ad hoc scientific reviews to cast doubt on the work of highly reputable scientists. Lord Alton is right to highlight the deliberately unrealistic obligation that we are under to provide a causal association for Primodos. The unrealistic demand from the Commission on Human Medicines, MHRA, and the European Medicine Agency, are put into perspective by a statement made in 2014 by the World Health Organisation.

The World Health Organisation stated, it is clear Thalidomide has an effect on the embryo, but no single effect has convincingly been shown to be the cause of the Thalidomide syndrome. Yet we are asked to provide a causal link for Primodos.

In Dr Inman's book, *Don't Tell the Patient* - quite ironic, really - he justified withholding information about Primodos by citing the possible impact on oral contraceptives. Dr Inman also supported the World Health Organisation concerns about a population explosion if the links between the pill and HPTs were made public. Dr Inman's lack of action was contrary to his defined responsibilities as Principal Medical Officer.

In 1968, an article published in Norway stated, the diagnostic method is so uncertain, which in itself is a reason not to use it. The Committee on Safety of Medicines would have been aware that Norway subsequently produced a study linking hypospadias and congenital abnormalities to the use of HPTs, and those findings increased the urgency for Norway to remove HPTs from the market. They even stated, 'even circumstantial evidence should exhort caution'.

In 1970, the indication for pregnancy was removed in Norway, and in 1972 an explicit warning against the use of Primodos stated it could cause foetal malformations. More European countries followed suit in 1971, 1972, and 1973, but no warnings were issued in the UK, and the hormone pregnancy test was still available.

In 1975, the FDA issued a notice - the risk of teratogenicity precludes the use of hormones as a diagnostic tool for pregnancy. With the overwhelming evidence from scientists in the UK and abroad, plus the results of his own study, Dr Inman was forced to take action, and the first warning notice was issued in June 1975, but only after first alerting Schering about the association he had found in his own study.

The CSM issued a second warning notice in November 1977 which stated, further results have now been published, and the association has been confirmed. Despite these warnings from the CSM, Primodos remained available in the UK until 1978.

I have previously provided a timeline of the historic scientific warnings received by the regulator, and you will be relieved to know I won't be repeating them. However, I will draw your attention to a small example of additional warnings you may not be aware of.

Brief notes written by Schering scientists who carried out the tests on Primodos include, a connection cannot be excluded with certainty, the substance cannot be ruled out, and there is a strong correlation. Also, on page 42 of the Expert Working Group report, there is reference to historic evidence which showed that Primodos had a teratogenic effect in mice, which was found to be drug related. Additional evidence was found in the Royal College of General Practitioners by Liz Lane from Sky News. Hand-written letter from Dr Norman Dean states, 'I have a bad conscience, though not really on my own behalf, about this whole business.' Dr Dean had asked Schering to withdraw Primodos from the market in 1969 after finding a high incidence of abortions in his study. Dr Inman wrote to Schering to advise against Dr Dean's request to withdraw Primodos.

Dr Fleming, also from the Royal College, stated that from his evaluation of the data, he believes that there is a distinct possibility that HPTs might cause abortion. If called into trial, he would be forced to mention

a possible connection between the drug and abortions. In a statement, Dr Fleming said, some of the cases in the Royal College records would probably provide better evidence for the plaintiffs than the evidence they already have.

Documents in the Royal College files also discuss fears of a claim for damages against the College because of negligence relating to Primodos. They stated, there is no way this data can be kept from the claimants. However, this need not be a source of alarm, as we have already given all our findings to the Committee on Safety of Medicines. We didn't see those findings. I don't know where they are. Dr Inman did not reveal the results of the study, and nor did Schering, who actually financed the study.

Could this be linked to Dr Inman's request to be subpoenaed by Schering to discredit his own study in court? If the Royal College report had been submitted, would this have provided Dr Inman with the opportunity to dispute these findings also?

Despite the weight of scientific evidence, the acknowledged warnings from the medical profession, the removal in 1970 as a pregnancy test in Norway, subsequent removal by other European Countries in '71, '72, and '73, plus the provisional findings in the Royal College study, and subsequent requests to remove Primodos as a pregnancy test, they all failed to mobilise the regulator to fulfil his obligations to take action on HPTs.

These facts are a damning indictment of the indisputable and catastrophic failure of the regulatory authorities, which brings us to the regulatory process today .

Currently, scientific evidence is from Professor Neil Vargesson, who produced a zebrafish study in 2017. The study was peer- reviewed and acknowledged as robust. Professor Vargesson did not claim his study was conclusive, but that it indicated evidence of harm. When the components of Primodos were added to the zebrafish embryos, there was clear evidence of abnormalities. The zebrafish are acknowledged to be similar to the human embryo, and are used in increasing numbers in scientific studies today.

When Professor Vargesson's study was published, he sent it to the Expert Working Group team. The response from the Commission on Human Medicines was to recruit another ad hoc group of scientists to review his study. The commissioner also sent the information to the European Medicines Agency with a request for a similar review. The European Medicines Agency did not ask to meet Professor Vargesson, and based their results on the information provided by the Commission on Human Medicines.

2018, Professor Carl Heneghan and Dr Jeff Aronson produced a meta-analysis based on the evidence previously reviewed by the Expert Working Group in 2017. The Heneghan/Aronson meta-analysis concluded there was a clear association between the use of HPTs and congenital abnormalities documented in the historic studies. This conclusion was completely opposite to the conclusion of the Expert Working Group.

After the publication of the meta-analysis, the commissioner recruited more scientists and another ad hoc review, and commissioned a further review by the European Medicines Agency. Once again, the medicines agency did not speak to either Professor Heneghan or Dr Aronson.

I will remind you of Lord Alton's statement in the House of Lords, the implacable determination of regulatory bodies to cast doubt on highly reputable scientists. Professor Neil Vargesson is chair and professor of development biology at Aberdeen University, has extensive work and research experience in embryonic limb development, thalidomide, and vascular development. He is independent and has not received funding for his work on hormone pregnancy tests. Professor Heneghan is a clinical epidemiologist and leading expert in evidence-based medicine. He is also director of evidence-based medicine, and a practising GP with years of patient contact, including pregnancy tests.

Dr Aronson is a consultant physician and clinical pharmacologist in the Centre for Evidence-Based Medicine in Oxford. Both Professor Heneghan and Dr Aronson are independent and did not receive funding for producing their meta-analysis. However, I will break off there, because what was suggested in the review on their study was that they

had had assistance from the Association. Now, what assistance we were supposed to give them, I really don't know.

So, Lord Alton's statement highlights that nothing has changed in the regulatory process since the 1960s. It is still a culture of protect and deny, while using public money to attempt to cast doubt on the work of highly reputable scientists. The Chief Medical Officer in the UK made a statement in her recent oral evidence which indicated that Professor Vargesson had stated that zebrafish recovered after being immersed in water. Now, was this another attempt to cast doubt on the independent scientific evidence, or was the CMO incorrectly advised? I would hope it was the second.

It is certainly at odds with the statement also made by the CMO that science only has value if we have the public trust, confidence in the process, and greater transparency. Well, that would be great if that was true.

I contacted Professor Vargesson, as my understanding from observing the review was that he had commented that the zebrafish made some recovery in the water, but did not reverse the damage. Professor Vargesson confirmed that the fish did not recover from the damage, which he says he made clear in the Expert Working Group meeting in 2017. He is also continuing his research, and at the moment finds that much lower doses are still causing subtle damage to the fish. He has said, if you wish to speak to him, he would be very happy to update you on his current progress, but obviously at the moment it's not published, so he would prefer that he actually has a conversation about it.

The review by the Commission on Human Medicines and the European Medicines Agency of the meta-analysis does not have public trust or confidence, and was clearly not transparent. We were advised that the ad hoc meeting would be recorded, but the recording would be destroyed immediately after the meeting concluded. Paper minutes of the discussions would be produced. The chair reminded those present to declare any personal interests in the drug companies - example, lecture fees, travel, accommodation, and consultancies. But the chair forgot to disclose that he had been chair of an ad hoc group who produced extensive work on oral contraceptives published in the *BMJ* in

2010. The work was financed by Schering AG, Schering Healthcare, Wyeth, and Searle, all companies listed as conflicts of interest.

Interestingly, he's also the guardian of the Royal College of General Practitioners oral contraceptive studies of 43 years ago, so he may know where the evidence is.

The chair stated there would be no discussions of the Expert Working Group report that was produced in 2017, and he confirmed that the participants in the review had no association with the 2017 report, or with the members of the Expert Working Group responsible for it. Based on the ad hoc review - sorry.

During the ad hoc review, two of the scientists consistently criticised the Newcastle-Ottawa scale used in the meta-analysis by Heneghan and Aronson, whilst at the same time promoting the ROBINS-1 scale as a better analytical tool. These two scientists were key to the decision-making process.

What was not disclosed was the fact that they were lead authors on ROBINS-1, or that the study was financed by GSK and Pfizer, both drug companies again listed under personal interests. I read a review of the ROBINS-1, and what it said was, difficult and demanding, even for raters with substantial expertise. What was also not disclosed was that Professor Stephen Evans, the lead scientist of the Expert Working Group review, is a collaborator on ROBINS-1, and of course it would be feasible that he would be in contact with the two scientists included in the review, and this calls into question the statement made by the chair that members of the ad hoc group would have no association with members of the Expert Working Group.

In his oral evidence to yourselves, Professor Evans was highly critical of the decision by Heneghan and Aronson to perform the meta-analysis, and declared that you should only perform a meta-analysis for randomised trials. Now, this statement was based on a publication of which he was the author. However, on obtaining a copy of the publication, it clearly sets out that Professor Heneghan met the conditions appropriate to effect a meta-analysis, which actually contradicts the oral statement made by Professor Evans. Maybe he's not read his own book.

The MHRA employee who presented a 20-page critical review of the meta-analysis before Professor Heneghan and Dr Aronson presented their findings worked on a maternity data project with another key member of the Expert Working Group from 2009 to 2012. When I contacted Dr Raine about my belief that this was another conflict of interest she replied, the presenter has not had contact with the member since November 2016. However, the Expert Working Group review began in 2015.

On receipt of the report from the Commission on Human Medicines, the name of one of the assessors has been redacted, and I believe this is the name of the person I disputed.

It is also of great concern that the chair of the European Medicines Agency - it never stops - who oversaw the review of both studies of Professor Vargesson, Heneghan, and Aronson, was employed by Bayer for 12 years, between 1989 and 2002. He was also a divisional head for the German Federal Institute from 2005 until 2016, and section head from 2016 to 2018. Now, the German Federal Institute is the former BGA, and they were the regulators who declared they were advocates for Schering, and requested

studies which did not contain malformations. The BGA are now known as BfArM. An observer from BfArM was invited to attend every Expert Working Group meeting, although requests for other experts to attend have been refused. We're nearly there. We're very nearly there.

In light of these findings, I think we have every justification to dispute the independence and question the transparency of the scientific reviews by the regulatory agencies, both here and in Europe. But nobody looks at the moral and ethical considerations. This is a statement from Tim Lewens, professor of philosophy and science at the University of Cambridge. There have been numerous suggestions that establishing a causal link with considerable confidence is a necessary precondition to establishing regulatory failure. A responsible regulator should take a precautionary approach, which often means taking measures to reduce potential risks even when causation has not been established with any certainty. This is especially clear in the Primodos case, where medical need was unclear, and alternatives were available.

I think that the opinion from Professor Lewens sums up the fault with the current regulatory process, which continues to focus on proving a causal association, perpetuating the moral and ethical failures of the regulatory agencies. I would like to reference a statement in the Thalidomide judgement, that was in case of severe damage, protection measures have to be taken even if the suspicious circumstances are relatively small. Extremely severe damage such as malformations forces the drug company - the drug manufacturer - to respond, even when there exists only the possibility.

With this judgement in mind, was it ethical to keep the pregnancy tests on the market when there were numerous reports of adverse reactions and the manufacturer is unable to provide any reassurance of its safety? Was it ethical for the regulator to delay eight years before issuing the first adverse reaction warning while confessing at the same time he had no defence for the eight-year delay, a statement which I feel would indicate he had full knowledge of the serious concerns surrounding HPTs?

You have been clear that your mandate is to review past regulatory failures if they exist. I feel the evidence presented to you proves that there were huge failings by the regulator. You have also been clear that you will not review the science, as you do not have the expertise available to you, and again, absolutely fine.

But what I hope you will review is the expertise, appropriate experience, and scientific qualifications of the independent scientists, the expertise, appropriate experience, and scientific qualifications of the experts chosen by the regulator to review the work of Vargesson, Heneghan, and Aronson, the independence and conflicts of interest of the experts chosen by the regulator, and the transparency of the scientific evidence provided by the independent scientific experts against the lack of transparency of the subsequent critical reviews by the regulators, for example missing information, the forest plots, destruction of recordings, failure to declare conflicts of interest.

I have lost a page, which I'm sure - no, [unclear]. Sorry about that. I will conclude before you lose the will to live, right? The conclusions our members would like to see are: an apology from the current regulators who have perpetuated the failures of their predecessors by refusing to

[REDACTED]

- it's a conversation that they've had about various studies, and it says, 40 per cent of the works collected would incriminate - I don't know if it's gestigens or gestrigens, I don't know how you say it, but it's basically the hormones. It was also again talking about the possible virilisation or feminising effects of deliberately separated from this assessment, because what they said was there were no adverse effects apart from virilisation, and then at the end it does say that through conversation, they were told that there could be 40 per cent of those tablets having an effect.

In 1978, from the board of directors - and this is actually stating that they will not remove Duogynon from the world - which is Primodos - but will continue distributing the product under the trademark Berlingen as a possible alternative.

They also talk about - to continue supplying Duogynon, which then will produce and distribute the product on its own, without mentioning the name Schering, so they were starting to distance themselves. This is another one, and this is relating to Korea, and again they're talking about, 'Duogynon has been and is being used improperly because of our omissions. Packages are still being sold with out-of-date instructions'.

So, again, this was another instance where they're aware that the tablets are still available, that they are actually being used, and we know what improperly means. It means that they were being used for abortion, and they're saying, 'to prevent situations that could lead to additional claims for damages against Schering, it was therefore decided that the Primodos committee would meet again in May 1978 to deal with these matters. There might be an issue of a possible worldwide recall of Duogynon'. But they didn't.

This one, again, is talking about the BGA, as they were, BfArM as now, where they spoke to Professor von Eichstaedt, who again had asked for the studies which did not yield a statistically significant correlation, and he also mentions somewhere in there about keeping the drug on the market.

The last one is quite interesting, because this is from David Finney, who was a member of the Department of Statistics, which of course was aligned to the commission on - Adverse Reactions Committee. He said,

he'd been asked would he actually cooperate with Schering, and his answer was 'it would be embarrassing to try to advise on problems which were likely to come before the sub- committee'. So, basically, he's agreeing, yes, actually they're going to come, because there is something there that is a link between the drugs and the adverse reactions.

That isn't all I've got. I've got so much. This is the problem. There's so much, and it's trying to find out what would be useful for you.

Julia Cumberlege: Well, thank you so much. So, can I just recap your recommendations?

Marie Lyon: Yes. Mm-hmm.

Julia Cumberlege: One was that you felt that there should be confirmation and acknowledgement of...

Marie Lyon: That is very important.

Julia Cumberlege:

From the regulator.

Marie Lyon: And the drug company.

Julia Cumberlege: You're saying from the regulator.

Marie Lyon: Yes.

Julia Cumberlege: The second one was about financial redress, et cetera.

Marie Lyon: Yes.

Julia Cumberlege: Again, from the agency. That's really, in a way, the same [unclear].
Were there other recommendations that I've missed?

Marie Lyon: I think we - I think we do deserve a statement from the government just to say, 'we made a mistake'. I think that's quite important, and it's just to confirm that there were regulatory failures in the past.

Things could have been done better. There are ways that we can actually try to improve what happens today, because obviously what happens today is still the same kind of culture, where we're looking at, how do we actually defend this? We're not looking at, what did they

find? Is this something that could actually harm people? Is this something that we should take notice of, do further research on? It just seems to be the initial way that they look at it, is to look at ways to actually say, well actually, this isn't right. The process isn't right.

They talk about biases, but they don't actually mention what the biases are. Confounding factors, but what are they? So, this is where I found it really frustrating when I read the records, from both Professor Heneghan's study and Professor Vargesson's, because there's no meat there. It's all a bit of an opinion and supposition. Particularly in the original Expert Working Group's report, where they actually omitted to mention that they thought that there was a possible association, but concentrated on stating there was no causal association.

So, if they knew, as they quite plainly said in their submission to yourselves, that there was this possible association, why was that not highlighted? Why was it then actually told to people, if you've taken an oral contraceptive when you're pregnant don't worry about it, it won't do you any harm? That really would encourage women to think, oh, it doesn't matter, I've already taken them now.

So, it's that kind of thinking where it's not just the fact that they're denying the past, but I feel that they're actually harming the future, because they're refusing to actually look at what we can do to make things better. That's the biggest concern that I have.

We need to have a process that is truly independent, that actually has scientists that are not aligned to either pharmaceutical companies or to the regulator, and this is what we've found time after time. The people who've actually joined these committees for the MHRA and the Commission of Human Medicines all have some form of prior link. In fact, I'm sure there's a little pool somewhere that they just dip in, take them out when they need them, and they perform in the way that they're supposed to perform.

That's an opinion from me, and that's the way I feel, but I know that's also how our members feel, that there is this determination to continue to deny that there was ever a reason to have even just caution, you know, don't take it off the market but caution people. Advise them that there may be risks, which we were never told.

Advise the medical community, you know, you must actually look at this and make a decision, an informed decision. Just suspend it, even suspend it, to actually say to the manufacturer, please go back.

But the other thing is, insist on seeing those documents. Because I do know, from all the documents that I've looked through, they have ghosting studies, where someone actually writes them and then they just sign up as if it's fact. I know that some of the studies they do never actually see the light of day, and we - somehow or other, our regulatory system doesn't have the authority, the legal authority, to say to those firms, we want to see your testing results. That is a dreadful, dreadful thing in 2019, that we haven't got the power to protect our people by saying, I want to see where the risks are. Those risks then can be explained, and it's up to the individual to say, I'm willing to take that risk.

I do know that some drugs are actually vital, because people wouldn't live without them. So, I'm not saying that we shouldn't keep trying to produce new drugs, but let's try as well and value the ones that we already have that we know are working. I think this is where it came with Primodos and with the hormone pregnancy test. It was a new thing, and it was lucrative, very lucrative. So, when you actually look at the spin-offs as well, with the abortifacient, because I did say, I think - I don't know if I'd sent it in writing, but there are today still these tablets on the market.

You're talking about Peru, France - I've forgotten the other one now.

Male: [Korea?].

Marie Lyon: No. Anyway. Lebanon. Lebanon, in 2017. There was a shipping order to Lebanon with these drugs. Now, I don't know if there's a patient information leaflet in there, or why Lebanon would need them, because if they're only used for amenorrhoea, why would you need a shipment in this day and age, when it's actually well known that amenorrhoea very often could be a symptom of pregnancy? So, we know that these drugs are still going. We know that Schering, or Bayer as they are now, are still manufacturing them, and part of that is simply because of the abortive effect.

We know that in Ireland, in 1997, there were 1000 packets a month being shipped to Ireland because abortion was illegal in Ireland, and this is one reason that I feel that we've so few people coming forward in Ireland because, bless them, if they genuinely went for a hormone pregnancy test and then found out what the usage was, they would not want to come forward. I think this is the problem with quite a few women that - I mean, I didn't know the other indication until I started looking into this, and I think, in fairness, the majority of our members didn't.

Cyril Chantler: Can I just interrupt you?

Marie Lyon: Yes.

Cyril Chantler: Because - I don't understand the abortion fully, because - was it the proposition that in the recommended dose for a pregnancy test it could cause abortion, or that they were taking it in much bigger doses? Marie Lyon: I think they were taking it in much bigger doses.

Cyril Chantler: How did they get hold of them? Because nobody would prescribe them for that purpose.

Marie Lyon: Amenorrhoea.

Cyril Chantler: That would be at a recognised dose.

Marie Lyon: I think they got - didn't they get something like four weeks? They had - it was more than two tablets.

Cyril Chantler: I see.

Marie Lyon: It was - I don't know if it was something like - it may have been two, it may have been four weeks. I know it's documented somewhere that it was for a short duration.

Cyril Chantler: It's a course, not just...

Marie Lyon: It is a course. No, it's not just two. But they were actually being sent over to Ireland for amenorrhoea at the time, in 1978, but there were an awful lot of women...

Cyril Chantler: But the recommended dose when it's used to amenorrhoea was not just one tablet, 12 hours apart?

Marie Lyon: No. I think it was every day for a certain period of time. So, of course, if you had those and you wanted to take three or four - and I'm not saying

that's what happened. I really don't know. It is supposition. It is looking at - trying to think, well, if there were so many packages going over, would there really be 1000 women needing these every month?

Cyril Chantler: When was this, by the way?

Marie Lyon: Ireland.

Cyril Chantler: When, though?

Marie Lyon: 1978.

Cyril Chantler: Thank you.

Marie Lyon: So, already it was known that they were a danger as a pregnancy test. I think also, it had started to be made aware that amenorrhoea was actually an indication that you could be pregnant, because I'm sure that later on they actually changed the advice to, you had to be certain that you were not pregnant before you were treated for amenorrhoea. So, that again changed the way that the drugs were used.

Cyril Chantler: Okay.

Julia Cumberlege: Can I just ask you, Marie, you, as I understand it, in your statement to us have made it very clear that we are not expected to re-examine the science, and thank you for that, because certainly that was in the Secretary of State's statement to us when he launched this Review. But presumably you are still interested in the way that the particular EM...

Marie Lyon: There's all these, EMA, MHRA...

Julia Cumberlege: EWG. The two EWGs, the working groups, the process of those, and that area you're still really very interested in.

Marie Lyon: Very concerned about it, absolutely, because I was at those meetings, and I know from the notes I took that actually it wasn't that everyone thought there was no link. You know, the conversations that occurred whilst I was in the room were definitely more, this looks quite interesting, and I couldn't confidently say I don't think there's a link. But the other big thing that came through was that the evidence that came was inconclusive, because there wasn't enough of it. That was said quite often. There isn't enough, we need more.

I know that there were nearly 7000 pages that I found in the Landesarchiv in Berlin. Those 7000 pages did not end up with the Expert

Working Group, and in fact the German documents that I desperately wanted to be translated were not translated until just before the next-to-last meeting. So, to try and take that information in in such a short space of time - one time, we got 2000 pages, and we had, I think it was, six days to look at them. That's a lot of - especially for a layperson, it's really difficult. But it had been said by one of the Expert Working Group, why are these documents being reviewed before coming to us? Are we not getting them all? The response was, well, we actually take a view that we will look at what we have, and decide what you need to look at. So, that was the biggest concern...

Julia Cumberlege: I'm sorry, I'm going to stop - who was saying that?

Marie Lyon: One of the Expert Working Group scientists.

Julia Cumberlege: Oh, right.

Marie Lyon: That was what...

Julia Cumberlege: So, they were choosing the information that was coming from...

Marie Lyon: The MHRA were choosing the information from...

Julia Cumberlege: The MHRA?

Marie Lyon: The MHRA, the secretariat. So, they had responsibility for actually handing out the documents before each meeting. That was a big concern to the experts themselves, I feel, because there was a distinct division. There was the decision-making group, and the participants who participated in all the discussions, they were not allowed into the small decision-making group. It was those people who were saying, we need to see more of this.

Another comment quite often was, why when you ask us to make a decision is it always in the negative? Don't you feel that this isn't... Why is it never, do you not feel that there may be something in this document? So, there were concerns from quite a few of the people who were there, and I felt from the first day it was a battle for me, because I'd had a prior meeting with the MHRA, which included Dr June Raine, and I think there were five people from the MHRA, and I battled because I had been told that I would be an observer and allowed to contribute with information I felt that they needed to know. When we

got to that very first meeting, prior to the group starting, I was told, no, you would be an observer only.

So, the ensuing discussions actually overturned that, and I was then advised that, yes, if you feel that there is anything that you feel is wrong, or you have a point to make, you will be allowed to speak. Unfortunately, the first meeting, there was some information which I put my hand up and tried to tell the Chair, and I was told to please put my hand down, it was not my place to ask to speak. I was not allowed to speak. It had been agreed at the previous meeting. I then tried to explain it had been overturned, and of course that was the first letter that went off to the MHRA to say, you know, hello, excuse me, there's the document that you agreed, you're now changing the goalposts.

It seemed to go from there that you had the people who were genuinely wanting to know, what have you got, and the others that were quite sceptical about what the information was and where it had come from.

Cyril Chantler: You represented the Association?

Marie Lyon: Yes.

Cyril Chantler: Were you on your own...

Marie Lyon: Yes.

Cyril Chantler: ...or was there another person with you?

Marie Lyon: No. They had allowed Nick Dobric. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

But he was sat, basically, at one end of the room, and I was sat at the other. So, yes, I was alone during those meetings, which was not a great problem most of the time.

I was concerned at the second meeting, and thereafter there was a barrister, and I did ask would it be possible that we could actually bring a barrister, just again to support, and the answer was no, this is not combative and it's not an inquiry.

Cyril Chantler: But the other person was in the meetings? He was on the group? Nick.

Marie Lyon: Yes. He was - no, he was like me. He was supposed to be an observer.

Cyril Chantler: He was there?

Marie Lyon: Oh yes, he was there. That was basically - the tenor of the meetings would generally be that you would have certain people that would drive the conclusions, and other people that would maybe not disagree with the conclusions but ask for clarification. That then tended to be overridden. The one concern I had was that because of the amount of evidence that hadn't been looked at, I wrote to - well, I wasn't allowed to write to the Chair. I had to write to the MHRA, who would decide if I was allowed to have the letter sent on. I asked if there was a possibility of a 20-minute spot to speak to the members of the Expert Working Group, and I had an email back to say, you have to let us know what you're going to say.

So, I said, well, I just wanted to basically update them on the information that we have, and it was a no. So, I decided to get this information and send it via email to each member of the Expert Working Group. I was then admonished at the next meeting by the Chair that I had basically overstepped the boundary. I was not allowed to contact them. It didn't actually matter, because they got it. So, that was fine. But the second disagreement came when I was told at the next-to-last meeting, which I didn't know it was going to be the next-to-last, that I had been given 20 minutes to actually give any further evidence, which was wonderful.

So, I started to give this, and I did exactly what I did today. I went to turn over the last page, and couldn't see it. The Chair just said, right, thank you. I actually said, 'I'm really sorry, I have got it, but I haven't finished'. 'No, I'm sorry, but time is up', and basically, 'sit down'. One of the experts that was very sympathetic came to me and said, how much did you have left to read? I said, it was only a page and a half, and she said, leave it to me. So, she went to the Chair and said, I feel

that Mrs Lyon should be allowed to continue with the presentation. The response was, 'you have two minutes'. I read very quickly.

So, basically, it was always going to be a difficult situation with some of the Expert Working Group, but particularly with the Chair, and that was a disappointment for me.

Cyril Chantler: Thank you.

Simon Whale: Can I ask about the EMA's investigation into anything because that was started at broadly the same time? They published on the same day as the EWG.

Marie Lyon: Coincidentally.

Simon Whale: Yes. You didn't get the chance to go to the EMA?

Marie Lyon: I wrote a letter, and then I rang them and asked, could I please observe? The answer was no.

Simon Whale: Did they give a reason for that?

Marie Lyon: No, none whatsoever. It was just a straightforward, no, sorry.

Simon Whale: When you read their conclusions, what are your thoughts about what they said as compared to the work of the EWG and what they had said?

Marie Lyon: I felt that they had strengthened a little bit. They had learned from the Expert Working Group's mistake, and they were more definite about the fact that there was no concerns for future use of the drug, that there was not basically a strong enough case. But again, I think that was towards the causal link. So, you have to put that in perspective and look at the fact that we can't have a causal link.

Thalidomide are still struggling now to actually get that scientific certainty. Well, I'm absolutely sure that Primodos will be in the same sort of position.

I think it's worth mentioning as well that there were millions and millions of Thalidomide tablets. There was 1.25 million Primodos tablets, and yet in this country, we had nearly 700 people affected. With Thalidomide there were 540, something like that. So, you have to think then of the percentages, and the other similarity is that with Thalidomide, because it was so apparent with the limbs, it was much more quickly identified, because with Primodos it could be quite some

time before that connection was made, particularly with heart disease or internal organs.

So, I think again there was a misstep there, because it wasn't something that we were looking for. I certainly didn't look for it, and I certainly did not think of it when my daughter was born. It never occurred to me it could have anything to do with those two tablets. We find today - I had two phone calls last week, again from two new people. This lady had taken it twice, and she said, I thought everybody did that. I said, no. She said, I thought you had to take it. That's what I was told.

First baby she miscarried at six months, and the second one died after two days, but she still hadn't connected it until she saw something on - I don't know if it was one of the - oh, I think it was the *Scottish Daily Record*. We've just done a big article in there.

So, again, there isn't the recognition that there was with Thalidomide, where it was an immediate and worldwide, obviously because some of the effects were just dreadful. So, you could understand why it became known very quickly. Primodos was always covered up, and it was covered up, as I said before, because of the impact on the oral contraceptive, and in Dr Inman's book he makes that very, very clear, where he said, don't tell the patient, which he didn't, that he was concerned - and the World Health Organisation were also concerned - about the fact that women would stop taking the pill or, if they'd taken it inadvertently and found they were pregnant, that they would abort the baby.

I understand that. I absolutely understand that that was a big concern, but that shouldn't have sacrificed the number of women who then went on, like me, to take the tablets without any knowledge whatsoever of what they contained.

So, again, you can see why this has happened, but it doesn't make it right.

Cyril Chantler: Can I go to your four recommendations again? The apologies from the current regulators, you made the point about denying the past harms the future.

Marie Lyon: Yes.

Cyril Chantler: The second point was that you want government acknowledgement and agreement of that first proposition, right?

Marie Lyon: Yes.

Cyril Chantler: The third one was financial support for your members.

Marie Lyon: Particularly the members who have still got really dreadful harms.

Cyril Chantler: I understand. The fourth one was financial redress from government and industry. Can you explain the difference between three and four?

Marie Lyon: Yeah. Three was for...

Cyril Chantler: Financial support for...

Marie Lyon: For the children

Cyril Chantler: For the children.

Marie Lyon: Yes. Number four is for the mothers who have lost their babies, who miscarried, stillborn. I would like to think that they would be recognised, because for them, they don't even have a child. So, that's why I made the difference between the two. We have members who are still caring for their children as you know, and have the worry of what will happen to them. We do know now that a lot of our members are actually finding life quite difficult, because it's accelerating as they age. [REDACTED]

[REDACTED]

But there are people who are far worse off, and it would make a massive difference to them. If they are unable to work - you spoke to Daniel and you spoke to Nicky, and again that is the calibre of the members, that they do not want to be - it's hard to put this, not reliant on the state. I don't mean that. But they don't want to feel an obligation, that they're taking a hand-out.

I think what we need to feel is, well, actually, this is something that you deserve, because there was an injustice done, and this now needs to be recompensed, redressed, whichever way that you want to say it. Again,

had this happened and, at the time, we had been told, good heavens, yeah, it's the drug, we didn't realise it, I can honestly say I don't think any of our members would have taken it any further. I think it would have been a case of, we were unlucky - and we were. But they recognised that we were unlucky, the drug company did something about it and took it off the market, and the regulator gave the necessary warnings and stopped the product from being used.

I genuinely think, even today, if a genuine mistake has been made, most people will accept that. But I think the stage that we are at now, we have battled for so long that we - I think we feel justified - and I am speaking for the members, not necessarily always my point of view - but I feel it is justified to say that there now needs to be some form of recognition financially. But the most important thing, and this is just for me, is the acknowledgement. Yes, we did know. I mean, we know they know, because we've got all the evidence. It's written down. But for somebody to actually say, once and for all, actually it was a mistake, it should have been rectified at the time, and we're sorry that it wasn't, but the people I really want to say sorry are the current regulators.

I think they've behaved abominably. I think that the way that these reviews have been conducted, particularly the last one which I thought was so stressful - the anger in that room was palpable, and that is not how you have a review. Again, it was - to me, it seemed a concerted effort to discard the tool that they had used, Professor Heneghan, and they just kept going on about - this is why I looked at ROBINS-1. What is ROBINS-1 that was so wonderful, and what was so wrong with the tool that they used? It's only when you look that - it's horrifying, actually, to look at that and think, how on earth could they have been involved? How on earth could they have had a link with Stephen Evans, a link with one of the presenters, even the Chair having a link with Schering? That's horrifying, and that needs to be stopped.

But I feel that we are justified in asking for an apology for the way that they are conducting themselves today.

Julia Cumberlege: Can I say that's very impressive, thank you. When we saw Daniel Mason...

Marie Lyon: Yes.

Julia Cumberlege: ...and Nicky Gubbins, they were extremely dignified. They were intelligent, they were brave, they were courageous, and I have to say I think we were all hugely impressed by them. But what I just wonder about it, in one of the other areas that we're working at, the medication may actually affect, we believe, the brain of the...

Marie Lyon: It did.

Julia Cumberlege: I wondered, just listening to Daniel and Nicky, they were so eloquent. Does the - and I should know this, but does the Primodos or those hormone pregnancy tests, do they affect the brain as well?

Marie Lyon: That was the first warning we had, actually, in 1958, from Dr Edwards who actually said that he had great concerns. I don't know if he was doing a study on the mental awareness. I actually can't remember. But he did say that he felt there could be an effect. We're not sure whether that would be an additional effect with someone like Daniel and Nicky, and we do know that quite a few of our members had children who were brain damaged.

Julia Cumberlege: I see.

Marie Lyon: Absolutely. But we also know that a lot of the stillbirths or the babies who died very soon afterwards, they had no top of the head. It was just all missing. That happened to quite a few, and in fact one of them was actually put on a trolley, covered with a cloth, and her husband found the baby an hour later, still alive, and lived for 48 hours. So, that unfortunately was the culture. Babies were taken away. The mothers could not see them - and this has been the despair, I think, of a lot of our members, and this is why I feel they need some sort of redress. They never even saw the babies.

I'm involved at the moment with a wonderful lady who's actually looking for the graves of some of the babies, because they don't even know where they're buried. She's been successful in finding two, which is just wonderful news. As one mum wrote to me - she sent a photograph, and it's under a tree, and she said, 'I'm at peace. I know where my baby is'. This is the dreadful things that don't come out in studies, that don't come out in reviews, that people, scientists, maybe don't always look at. I think we're lucky in that, particularly with Professor Heneghan who's a GP, he knows what the human cost

is. I think that's where he took exception with some of the evidence where they were saying, 'well, women only go for a pregnancy test when they're two or three months over'. No, no.

You go - well, we did. You go as soon as you missed a period and you're hoping that you're pregnant. This is where he feels that his experience, and Dr Aronson's, is that they have dealt with illness face to face, as well as being scientists. So, they know what the effects would be long-term as well. I think this is why he felt that he wanted to actually look at the Expert Working Group report, and it was only when he looked at that, and the documents were actually released to him that he just felt there was a great injustice, and that's what drives him on. Not money, because he doesn't get hundreds of thousands for what he does, but just the desire. As he was quite clear, which he said at the meeting a few weeks ago, when I rang him up, his response was 'I'll look at it. However, if the results are not in your favour, I will be publishing anyway. You have no control over that'.

That was - I mean, he's very direct, as you know. That was his response. I was more than happy to accept that, because that's what we want. We do not want to be patronised, as was unfortunately done in the Expert Working Group oral evidence, where they said, 'we actually thought about trying to find something'. What a dreadful thing to say. What do they think that we want? All we want is, did it happen, or did it not?

Simon Whale: Can I just go back to your fourth recommendation...

Marie Lyon: You're going to make me remember these now, aren't you?

Simon Whale: The recommendation about financial redress for women who lost their babies. Do you have any idea of numbers? [REDACTED]

Marie Lyon: The ones at the moment that we have, I would say, maybe would be a quarter, at the most, of the...

Simon Whale: Of your membership? Right.

Marie Lyon: Mm-hmm. They won't be a great number, I wouldn't think. But it's also people - [REDACTED], she was so dreadfully, dreadfully affected. She died three years ago. Now, her mum looked after her. She's now in her mid-60s, and she said, 'I don't know

what to do. My life has been caring for her for all these years'. So, she's no training, no pension - and this is the other thing with some of our members. They haven't been able to work to actually gain a good standard of living, to make sure that they have a pension in old age.

So, these are things, again, whereby it's not just the emotional impact. It's only when you actually start to speak to the members that you realise the financial impact, which I definitely hadn't factored in at all, I'm ashamed to say. But it's only when, as you know, when you're speaking to people and they say, I couldn't get a job, and I've no pension, and I'm really worried. It's shocking to think that this impact has lasted for 50 years, almost. [REDACTED]

[REDACTED] But when I look at some of the other members, they've had half a life, and that's been devoted to their children.

So, that is the difficulty, and I appreciate that. I don't know the answer. I really don't know how this would work, what kind of redress there would be. We're certainly not looking for millions. It's not that kind of resolution. The resolution must be that it's acknowledged, that the mistakes are acknowledged, that it stops happening again, which we know it's happening again. We know there's still that disconnect between something going wrong and the action, the appropriate action, being taken.

I have to say, I did watch one of the reviews from two people from NIHR, I can't remember now, and I was horrified, because they didn't seem to know what was happening. They didn't have a process. It's just simple things. Where something happens, there should be some kind of process that that's followed through.

One of the things that did impress me, actually, and maybe it doesn't - but I did try and push this towards the Expert Working Group, and this was on future recommendations. In - I don't know if it was Norway or Sweden - they have an advert. It's a fabulous advert. It's just a little face that comes on, and it bounces on the screen and it tells you if the drug is causing a problem. You know, everybody watches the TV. What a wonderful way, just to have a tiny channel somewhere that people can flick onto and find out, be careful, or make sure you read this.

Just that kind of information, because it's not getting through the doctor's surgery to the patient, and when it does it then - the drawbridge goes up again, and it's again a defensive mode as opposed to - really and honestly, I think you'll find with most people, if it's a genuine mishap, this could actually be resolved much more quickly. I don't know how that's going to happen. But certainly, the process, and looking at the people who were actually controlling that process, did not fill me with confidence at all. Quite concerning.

Julia Cumberlege: Right. Do you have any more questions?

Cyril Chantler: No, that's been very helpful, thank you.

Julia Cumberlege: Alright. Simon?

Simon Whale: No. That has been helpful. Thank you very much.

Marie Lyon: You mean I've just talked that much...

Julia Cumberlege: No, it has been extremely good, and I do want to thank you for everything you do for these women. You always go the extra mile. No, not the extra mile. The extra miles, and physically, because I know you go to Europe and Sweden and everything else, and you work with the parliamentary group and all the rest of it. Mike, thank you for what you do to support Marie, because I know she relies on you a lot.

Marie Lyon: Oh, I couldn't do it without him. Absolutely not. I wouldn't eat.

Julia Cumberlege: Can I say, we'll do the very best we can. We won't agree with everything that everybody's told us, you know, because we have to weigh it all up and then come to our conclusions and our recommendations.

Marie Lyon: I appreciate that. One thing I would ask is, do you - not the date, I appreciate you won't tell a date. Do you have a month or ish - you've no idea, have you?

Julia Cumberlege: What are you asking?

Marie Lyon: When it will be completed. Is it this year?

Julia Cumberlege: Yes. We want to complete by the end of the year.

Marie Lyon: Okay.

Julia Cumberlege: I would love to give you a date, but we've got a lot of work to do now.

Marie Lyon: I know, and I do not envy you.

Julia Cumberlege: We've been doing the very interesting things about taking evidence and all of that, and now we've really got to put our heads down...

Marie Lyon: And collate it.

Julia Cumberlege: ...yeah, and decide what we're going to say.

Marie Lyon: If there's anything that you need me to do, please let me know. Any information that you want clarification on, again, let me know. I know I did send you something on abortions that we found. That's the problem, there's so many documents all over the place that I'm so afraid of missing something that you really need to know about, which is a concern.

But thank you again for your time and your questions, and I hope that when we actually [unclear].

[Over speaking]

END OF TRANSCRIPT

Session 4: Scottish Mesh Survivors

Elaine Holmes and Olive McIlroy
Scottish Mesh Survivors
4th April 2019

The Independent Medicines and Medical Devices Safety Review
King's College London
Guys Campus
London
SE1 1UL

Dear Baroness Cumberlege and The Review Team

Thank you for allowing us to have a 'last say'.

We have been closely following the progress of the Review and would like to make the following comments:

- With regards medical device regulation, you have witnessed how several failed regulations have let down many patients in this country. If the MHRA had been fit for its purpose, the vaginal mesh disaster would not have happened.
- With regards to evidence on mesh safety, you have witnessed first-hand the failure of medical professionals to reassure you regarding the long-term safety of these mesh products. Such failure confirms what you have heard from many mesh-injured women – we are guinea pigs.
- With regards to surgeons' training, the NHS Digital (Hospital Episode Statistics) publication in the Journal JAMA confirms what we have been saying for years: surgeons' training and skills do not influence the long-term adverse events of mesh devices. The culprit is the device, not the surgeon. Please do not let senior skilled surgeons convince you of the opposite and do not let them blame junior less-skilled surgeons for the mesh disaster.
- With regards to NICE, you have witnessed the confusion in its recommendations on the use of POP mesh. We do not understand why NICE restricted the use of mesh to 'research only' in Dec 2017 and then recommended its use outside research in 2019. What new evidence emerged in the last two years that reassured NICE to the degree that changed its view on POP mesh? If you fully understand this matter, we would appreciate an explanation please.
- With regards to SUI surgery, you have seen the level of evidence that NICE relied on for their recommendations. The focus was on effectiveness rather than safety outcomes, the follow-up was only short-term and the influence of manufacturers is quite obvious. You have also seen how some influence from manufacturers went undeclared to maintain their revenue from the use of these devices and maintain the false doctrine that vaginal mesh is safe.

- In 2006, NICE warned against the lack of long-term safety evidence on transobturator mesh. This year, 13 years later, NICE is restricting its use – but only after thousands of women were permanently and needlessly injured. In the same guideline this year, NICE is warning against the lack of long-term safety evidence on retropubic mesh. Please do not allow the injuries to continue for years to come until NICE decides to restrict the use of retropubic mesh.
- Please do not be convinced by the argument that some mesh devices are safe. Regardless of the type, all vaginal mesh devices, as a class, share the common adverse events that happen due to implanting permanent plastic material deep inside women's most intimate parts.

Our first request to you is to maintain suspension on all urogynaecological mesh procedures for SUI and POP, at least until evidence on long-term safety is available. Any patient 'consent' obtained to undergo these procedures without this evidence will never be informed. In the meantime, please give the opportunity to surgeons to develop their skills in surgery that does not use mesh. This is the true gold standard that surgeons dropped several years ago in favour of using 'quick fix' mesh. They should not have done so.

We started our campaign in 2012 and it has always been altruistic. After several years, we were successful in preventing other women from suffering the same fate we suffered. During that period, we have largely forgotten ourselves and focused on the campaign, especially as our surgeons told us they cannot do anything further to ease our pain and suffering. We now know that complete mesh removal is a reality and we are fully aware of many success stories. Our second request to you is to ensure that every mesh-injured woman is offered the option of complete, safe, surgical removal of her mesh device by a surgeon she trusts. For most of us partial removals have done nothing except worsen and prolong our agony.

Several decades ago the public outcry over the Thalidomide scandal effectively kick-started medicines regulation in the UK, and the MHRA was created. Your review has the potential to create a stronger independent watchdog to secure patient safety and public trust without any influence from pharmaceuticals or manufacturers.

The Mesh suspension you have recommended in the UK must remain for the following reasons:

- The risks from mesh cannot be mitigated. Clinicians and clinical societies have continuously failed to reassure us how they will mitigate the risk. Better training of surgeons doesn't work as the risk is with the mesh device, regardless of surgical skill.
- The risks from mesh cannot be predicted. Clinicians are unable to identify which patients are high risk of developing chronic pain and disability and which are not, it is Russian roulette.
- The risks from mesh are lifetime. There are reports where after several years of the good outcome surgeons talk about, women can start developing serious injuries later in life.
- Not all the risks of mesh are known. There are more reports of auto-immune diseases and cancer but the clinicians continue to deny them.
- The risks from mesh are irreversible. No woman goes back to her normal, even if the mesh device is completely removed. Clinicians continue to tell us the improvement rate after mesh removal is 50%. This is not good enough.
- The risks from mesh are entirely avoidable. The present alternative continence procedures, colposuspension and autologous fascial sling, are not associated with the irreversible adverse events of mesh, this makes mesh procedures entirely avoidable. If no mesh is used, a woman cannot develop mesh-related injuries.

We wish you all the best of luck.

Yours sincerely

Elaine Holmes and Olive McIlroy

<http://www.scottishmeshsurvivors.com/>

21st May 2019

Session 1: The Voices Today on Messed up Mesh (TVT MUM)

START OF TRANSCRIPT

Julia Cumberlege: So, I'm Julia Cumberlege and I've been asked by the Secretary of State whether I would chair this Review and we're looking at three different subjects: Primodos, sodium valproate - which we believe has affected children [unclear] in association with the medications that they took which resulted in disabled children. Then we've also obviously got - been asked to look at mesh, and particularly in the abdomen for women, women who've suffered from stress urinary incontinence and pelvic issues, so - organ issues.

So, we've been doing that and we've got a very small panel at the top because we had to do a lot of visiting, we wanted people on the panel and our support staff to come with us during all these visits so they could pick up as well and were very important in chairing different tables. We met people on tables, 10 to a table, and we went around, and we heard everybody's story. One of the things that has come back to us that people have been very grateful they've been able to tell their story and that we've listened and taken cognizance of that.

So, Sir Cyril Chantler on my left here is the Vice Chairman and obviously has been hugely involved in all this. Sir Cyril is a retired paediatrician and it has been really important for us not only to have a doctor but a doctor who's got a huge number of contacts throughout the service. So, we've been able to call on all sorts of people that he knows that I wouldn't know.

Then Simon Whale is on my right, and Simon is also a panel member. Simon's been looking at communications, which is obviously critical to this Review, and does much else besides, so that's good.

Then on his right is Dr Valerie Brasse, who you may have had contact with, I don't know, but certainly Lorraine has. She is our Secretary and does that extremely well.

Then Sonia Macleod, Dr Macleod, who is our senior researcher. So, that's us. Then we've got support staff here today just to make sure the session runs well, so I hope that's all right.

Hayley Martin: That's fine, yes, I met you over at Exeter, so I was at Exeter...

Julia Cumberlege: Oh, did you, at Exeter?

Hayley Martin: Yes, I was at Exeter.

Julia Cumberlege: Yes, of course. I'm sorry...

[Over speaking]

Hayley Martin: I wouldn't be at all surprised if you didn't remember.

Julia Cumberlege: Oh, well, thank you for that. I think Exeter was very useful [unclear].

Hayley Martin: It was very good. I think it was really nice. So, if I introduce myself; I'm a counsellor, psychotherapist, in my day job, so seeing those ladies have that opportunity to actually talk about it, it was therapeutic at the very least. But I was saying to one of your researchers before I came in that [do be] aware that all of you guys listening to that horrific stuff all of the time, you probably all need to be in counselling, I wouldn't wonder.

Julia Cumberlege: Could be right.

Hayley Martin: I'm hugely aware you've heard an awful lot, but yes, I did meet you all there, so thank you.

Julia Cumberlege: So, perhaps we could start the formal and what you want to tell us.

Hayley Martin: Definitely.

Julia Cumberlege: So, if you could start just by saying who you are and why you're here and [unclear] would be really helpful.

Hayley Martin: I'm Hayley Martin. As I've just said, I'm a counsellor psychotherapist in my day job. I'm also a former vice chair of TVT Messed Up Mesh. I was also the counsellor support person that people could call as well as Lorraine, and I'm a remaining member of TVT Messed Up Mesh and I've worked very closely with Lorraine since 2010. So, it was in 2010 that in sheer desperation, as a sufferer myself of pelvic organ prolapse mesh and a TVTO - so I had both worse types of mesh put in me - that I actually

scoured the internet to think, God, is there anybody else that's feeling like I'm feeling?

I found the website, and it was hugely important to me because it made me realise I wasn't the only person. The same, I feel, happened to so many other ladies then that then went on to find TVT Messed Up Mesh because it took, I suppose, Lorraine, one savvy, curious lady to set up a website, to put it out there just to see whether anybody would be interested or if there was anybody that was out there suffering as well. From that, it was very clear that there was a lot of ladies, and I suppose it needs to be acknowledged that Lorraine was actually the very, very first mesh support information website group that ever emerged in the very beginning. I know she had close links with [REDACTED] who ran the mesh group in America, and I think from that she started up her own group.

So, in that time of Lorraine doing all the research, sitting at her computer spending hours - you know, we would pass information between each other, we would find new things out - a lot of the stuff we were finding was coming from America. So, even from some sufferers in America; they were sending information and telling us this is what's happening here. It was all very new to us. We didn't have an awful lot of things that we could advise people for because we're not medical, but we came from the perspective of offering a shoulder to lean on, somewhere where people could come and cry and talk about what's going on for them.

From there, we opened up a message board which ladies then could actually put a topic on and talk about certain topics with each other. Some of the ladies then became members - so not everybody who actually went on the website became members, some of them used it just for information. But in total members, we had over 600 members who actually were members and we also - out of that, Lorraine and I have worked out that we answered 10,299 emails between us and that was in supporting ladies. I don't know how many phone calls. I wouldn't say it's as many.

But the email support was hugely important, but each email could take anything up to 45 minutes, talking to ladies about things other ladies had told us. Oh, they've tried this, maybe that might help you or just pointing

them in a direction where they could go and explore something else and actually encouraging them all to research themselves, because then they would become informed and they could make more choices being informed this time. So, I think I was quite shocked to find that it was that many emails. It never felt that many because it was spread out over quite a long period of time. But each one was done with care and with love and with support and we did feel very, very welcomed by those ladies.

They told us how much and how important it was to them and they don't know what they would have done without us back in those early days. I suppose as anything evolves, you're always going to find then break-off groups and splinters from what starts as the origin of a group. But I think standing on its own, TVT Messed Up Mesh; it actually did the beginning, it started all of this ball rolling as we sit here today, and credit goes to Lorraine for that.

Ladies would ring, and I would get phone calls on Sundays and bank holidays and weekends and the night-time, and sometimes it would be hours and hours of talking to ladies sobbing down the phone, trying to calm them down, trying to tell them that they will find a life even though it feels like they haven't got one now, trying to point them where they needed to go. Sometimes that was hard. It was really hard dealing with some of those phone calls, also trying to have a life of my own. I have four children. Trying to work with ill health, it was hard doing all that, but it was worth it because it was worth it to establish the fact that actually we all needed to have a voice, which is what this has all been about, really.

I felt that it's important to share some of those statistics because they surprised me, really. I think it was very clear in the early days that Lorraine and I realised this was a two-fold problem, really. It wasn't really just about stress urinary incontinence devices and pelvic organ prolapse meshes, it was also the fact that we were using deeply unsuitable materials to be putting in delicate areas of ladies' bodies and the fact that we all know that it was being put in an area that's a clean-contaminated area and therefore bacteria is being dragged through to the site where it was then to lay and that sort of stuff.

Also, the two-fold problem being the fact that at the time, the training was so minimal and the knowledge by surgeons was so minimal, and

both things are the most important points of this, that actually both of these things were wrong. It wasn't a good device, but the thing that made it more complicated, I think, was the fact that actually because we had multiple manufacturers - and a lot of the ladies have brought this forward, saying it would have been easier had it been something like hip replacements, had it been breast implants, you could have said, it's this particular manufacturer, that's the problem, deal with it.

It's complicated the issue the fact that there's been so many manufacturers and the fact that the devices have actually been manufactured here in the UK but also been manufactured in the USA. So, therefore it made it a global problem, really. We spoke to ladies from abroad; USA, UK obviously we supported, Scotland - an awful lot of ladies in the early days before the Scotland group was set up, we spoke to a lot of those ladies who were members of TVT Messed Up Mesh. Ireland, who've now got their own support group, we spoke to a lot of ladies and supported them in Ireland. France, Belgium - ladies were all contacting us, talking to us about what we knew.

Incidentally, an awful lot of hernia mesh sufferers, too, who didn't seem to have somewhere to go and there wasn't any support group, there wasn't anybody setting anything up for hernia mesh sufferers who were having problems with mesh, too. So, in those early days, it was a bit of a mire. We didn't know what we were doing, really, we were trying really hard just to support lots of people. I suppose the question that always emerges, and I know it's one that you have really not wanted to go down that road of because it feels futile, but it's like, who does the responsibility lie with?

It's a bit like, I know as a group you do not want to apportion blame, but for us sufferers it feels that, who is going to do this? Will

that ever happen? Will somebody or a group ever take responsibility for what's happened to all us ladies? Because that feels hugely important. It feels also I think important for a lot of ladies because of the lack of trust they now have in the medical profession and it also feels things like - without addressing the fault, it feels like it undermines the whole review process because it feels like you just then go to put medical professionals on pedestals and it almost feels like they're immune to regulation or culpability.

So, it's our hope that that won't be the case as a result of this Review. It will be something completely different. It won't allow professional bodies to hide behind rules and regulations that seem to change with a drop of a hat, and it won't allow them to close ranks like it feels they have done with us ladies. When I actually talked about coming to do this, a lot of the members spoke to me about the different factions which felt important that I mentioned the different factions that have been involved in this - I call it mesh debacle, if you like, or disaster. That went back to - I'm sure that you've talked about with many of the ladies and a lot of the professionals - back to the very beginning - and I know you spoke to Carl Heneghan because I listened to his - about the regulation of devices.

A lot of the ladies, including me, were hugely ignorant of the fact that actually, it was true that the meshes that they put in us were only ever tested on rats and sheep and of course the next line was to put them in us. So, therefore, we did become that first-level guinea pigs without consent, without knowledge, which is hugely shocking to you as a patient to find out that's been the case. A lot of those ladies I think still feel quite shocked by that, that that can be allowed to happen. The knowledge that we, if you like, picked out and found out to find out that actually a device could be put on the market simply by going to a panel and saying, well, I have this device, it's a stress urinary incontinence device, and them saying, are there any more on the market, and them saying, oh yeah, and they go, ok, stamp that through.

It was quite obvious that a lot of these devices were going out to the EU to be regulated and to get these kite marks and coming back into the country and being put into us without any knowledge that that was the case. It seemed that there were very little randomised control tests done, very little you could read about, really, because it wasn't there for you to read about. What was done? What was the preliminary evidence they had to suggest that this would be a good idea before putting it in ladies?

I think even in light of Brexit or not, whatever happens, there has to be for us ladies a thorough re-evaluating of the whole process of devices getting on the market in the first place. Not just stress urinary incontinence tapes, not just pelvic organ, but all devices.

There has to be a different way that this is done, it has to be safer. I'm not even sure that the medications are safe, but it almost seems like there's more regulation over medicines than there does over devices, and maybe that's my ignorance of knowledge, I don't know, but that's what it seems. I just wanted to express the shock that ladies had at finding out about regulation of devices.

The other thing that has been a huge topic that's come up with a lot of ladies is surgeons. The one question - if I had a pound for every time a lady asked which surgeon should I go and see, I'd probably be incredibly rich by now. It's really an impossible question, or it was an impossible question and it still is for Lorraine and I to answer that except to share experiences that we have had, experiences that other ladies have shared and treatments that they've had of surgeons. That's all we can share because we don't have the medical knowledge in order to recommend, if you like.

I think it's clear that many surgeons in those early days - I'd like to think it's not the case now, but in those early days, there were a lot of surgeons that were clearly putting in TVTs and pelvic organ prolapse meshes in one NHS setting and then the next day, they were in a clinic somewhere else that was either NHS or private setting, doing removal surgeries; performing those explant surgeries on ladies who'd significantly been injured by those

devices. But then, also going back to other clinics, putting them in other ladies in the knowledge that there were so many ladies that were injured because they were at tertiary clinics and tertiary clinics are set up when there's quite a lot of people suffering with a problem.

So, way, way back in those early days, it was there. The writing was on the wall, the evidence was starting to emerge, but it was hugely damped down and it was totally put away and not ignored. It seemed to me, and to a lot of our ladies, incredibly unethical that a surgeon can think it's okay to be actually doing massive amounts of implants in one setting and then in another, doing loads of removals. But the key bit being the bridge that meets the two is that the ladies who were then having them put in were not being told, well, actually there is a possibility this may go wrong, or there's a huge statistic at the moment, we do have tertiary - there wasn't that transparency and there needed to be that transparency.

Because many of those ladies would never have decided to have those devices put in them had they known that. So, I think right back at the beginning, surgeons need to look at why did they do that, why did that happen? How could they think that that was conceivably okay that they were putting devices in in one clinic and taking them out in the other? It was almost - I go back to something my husband said to me, and I remember talking to him about it, and he said to me, 'my God, it's a cottage industry'.

Because it felt that that's what it was like.

These ladies were having devices put in but not in the knowledge that that same surgeon was then doing explants or doing other surgeons' explants somewhere else. So, a huge lack of transparency and at the time and maybe still now looking back, it seems like it was a bit of a cottage industry. It seemed like some surgeons were set up for life, for the rest of their life to retirement doing explant surgeries. They could be in business just doing that alone. The other thing I suppose would be to say that I looked at the letter and it jumped out at me - the letter that went out from NHS Improvement and NHS England dated 29 March 2019.

Something that came up from the ladies, it said in section A the things that had to be met and it said 'surgeons should only undertake operations for stress urinary incontinence if they are appropriately trained and only if they undertake operations regularly'. I suppose the questions that I don't expect answers to, but the questions I and many ladies have in our head is, this feels like an acknowledgement - is this an acknowledgement for the fact that surgeons were undertaking these operations and weren't appropriately trained because that has turned out to be the case. It's turned out to be the case that significant ladies have been injured because these people weren't properly trained.

It wasn't really okay; I don't understand how it's ever been okay for any surgeon to operate on any patient at any time when not appropriately trained. What is appropriately trained? I think that's a word that needs to be defined. For each surgery, we need to know what appropriately trained for that is. Is it in hours? Is it in surgeries that you do? Is it - what is it? Because it's all very well now saying they need to be appropriately

trained after the event when so many people have been injured, and very harsh for us to hear when actually we've been guinea pigs, most of us twice or more over, even when it comes to explanting surgeries.

I don't know how surgeons become experts at something that was never intended to need an expert for. Again, they only become experts by practice and practice and practice, we all know that these medical devices are put in the body never to be taken out and they were intended to be a permanent device. So, therefore it was a new thing when surgeons decided that ladies needed to have some of this mesh removed. How do we do it? What do we do? I think some of them just dived in and started doing removals.

Some of them, in fairness, it was because they wanted to help the ladies. I've got no doubt they had an honourable thought behind that, but actually in reality, I do think some people got a bit carried away with themselves and ladies then went on to be significantly further from mesh explants as well. I think that it's shocking to think that surgeons would accept that they would go and be trained at a weekend workshop or that they would actually watch a video and that the first time they would put it in would be in theatre, potentially with a pharmaceutical rep present, telling them what to do with their particular device.

We know this is true. How do we know this is true? Because actually, ladies have told us. When they've got their hospital records or managed to get their hospital records, there on the notes it actually says who's present in theatre, and present in theatre have been pharmaceutical reps without the consent of the patient in theatre, which is quite worrying to think that us ladies didn't know that. I suppose the implication now is that how do we hone these skills? It's more practice on more patients and that does severely worry me, because the skills of the surgeons are key. It needs to be honed.

We need to grab any bit of information we can get from any source, any medical department in any part of the world - America seems to be quite ahead of the game, let's get some of these surgeons over. Let's get them training our surgeons. Let's get them looking at what kind of things are they doing that were helpful, that could help us here. Because I feel that - and maybe I've got it wrong, but the UK seems to do this, let's just close shop and put all our heads together and we'll come out with an idea, and

it feels to me if there's ideas out there that could help ladies, why are we not employing that? Why are we not getting that in?

Why are we not buying that support in to actually go, look, this is this guy, he's been doing these for 10 plus years, he's going to tell you how great it is and the pitfalls as well, and you're going to learn how to do this the best way you possibly can, instead of just having surgeons, as has evolved here, that have become - I suppose, quite a lot of them - self-appointed experts due to practice, practice, practice, practice, and along that way, some people have fallen by the wayside having been practised on again.

I'm always going to be, and I think many of the ladies will always be, utterly mystified that so many surgeons who we would consider to be intelligent, professional and ethical human beings, would train at a new procedure and yet be so utterly blind about it.

Without any personal research into it or looking at efficacy or adverse events, would just so blindly go in and do these treatments. It actually shows me what blind faith some surgeons have in manufacturers and pharmaceutical companies, and should they? Maybe they need to ask themselves that. Should they have such blind faith? Is a pharmaceutical's word going to be enough to a surgeon?

I'm trying to think, if I were a surgeon on a professional level, I don't think it would be. I think I'd need to know this was okay. I'd need to know it wasn't going to harm somebody. I'd need to know whatever it was that I knew all I needed to know about that device if I was going to implant it in somebody. In some respects, it feels like some surgeons have become automatons, not listening to feedback from patients or anybody else; colleagues or patients or reports, just going headlong.

I do wonder what pressure is put upon them from hospital trusts, also, in order to perform surgeries. If you like, bottoms in beds, ticks on boxes, okay, we can do 100 ladies with these mesh tapes as opposed to 20 colposuspensions. Versus money, it's cheaper and it's seemed easier. But it's not, it's cost thousands and millions of pounds to the NHS and will continue to do so for many years. I think for us ladies, we would like surgeons in the future to do their homework. We would like them to not just do weekend workshops.

We would like to know that when we're going in for a surgery and we're signing on that piece of paper, we know everything there is to know about that device before allowing anything in our body. I think it's a salient point that has been shared or is being shared by a lady that in her hospital Trust, there were actually over 50 ladies significantly injured out of 100 ladies that were taken to a clinical review. The interesting fact was, the clinical review was only put in process at the point when the first lady put a case - or a case was put in the court diary as a legal case - and then the hospital jumped into action. But that surgeon had actually been maiming people willy-nilly.

At what point - I suppose I've jumped on my soapbox now, but at what point does a surgeon realise that perhaps they do not have the requisite skills that's required to actually carry out these surgeries? It almost feels like there must be some really big, inflated egos out there that don't seem to realise. Because I'd like to think as a human being, if I kept doing things and I had people coming back, I might be thinking, I'm a bit worried. Is it me? Is it them? I need to find out because I can't do this. So, that was the bit on surgeons that was brought up by ladies.

I should go on to a short bit about hospital Trusts. At what point does a hospital Trust also take responsibility for those surgeons that work for them? Some sufferers shared the fact that they have an appointment to see the CEO at the hospital as a result of the clinical review, they felt that they would like to see the CEO. They put to the CEO and hospital Trust how could so many patients be so significantly injured by one surgeon and it go unnoticed? To which the CEO replied, 'I have 360 surgeons working under me; I cannot be expected to watch every single one of them'.

Now, that's a horrific reply because that's not okay. It's not okay that actually in a hospital Trust we have CEOs running hospitals that come out with a glib statement like that and think that that's actually okay. Because that's why we have CEOs, because they have people that work under them and they have people that work under them and we hopefully have a tiered system that actually watches people, monitors people, supervises people and makes it an okay thing, that everything is done safely. It's not okay to be glib and pass things off like that and say

that I can't watch. Of course you can't, that's why you have people working under you.

What systems are there in place for auditing surgeons and their outcomes? It seems very thin on the ground. Who is responsible for the buying process in hospitals, for devices in hospital Trusts? I really do think - and so do a lot of us ladies - is it buy one get one free or something? Because it does feel a little bit like that sometimes. All blindly taking the word of pharmaceutical companies without conducting any of their own research in-house, that I'm aware of, before they actually take and buy these devices in, sometimes changing manufacturers that they're buying in.

Where is the documentation to say why they chose one device and then suddenly a year later they've swapped to a different device? Is it because the other device didn't work, wasn't good? But they're not declaring that, they're just going to buy a different device in and start putting that one in people. What are those deciding factors for a hospital Trust in buying in devices? Is it based on good deals and money? I'm sure it probably is. There's probably something in that. But the questions us ladies have now are, who is regulating throughout all of this? Who is regulating it now and what assurance will we have in the future to know that hospital Trusts will adequately regulate the kind of devices that are coming into their hospitals? Because that's what we need to hear, we need to know that.

Also, I think part of the hospital's responsibility is obviously the keeping of things like theatre notes, and one thing that's come out time and time again from ladies - I'm absolutely stunned at how many of them, when they've tried to get their hospital records, have had a pile delivered to them, and in the pile they've gone through - they want to find the bit that shows their barcode, the manufacturer of the device that they have in them, and it so often is not in the pile. It's missing. One would like to think that's perhaps a coincidence, but I don't. I think it's far too much of a coincidence that that would be the case that so many ladies cannot access that piece of paper.

Because by not having that piece of paper, it prohibits them reporting their adverse event to the MHRA. The MHRA need to know what pharmaceutical company and all those details, barcodes, et cetera. They need to know that before they can take your adverse event, so that

prohibits lots of ladies being able to actually report their adverse event. The other thing is that these ladies haven't got this barcode, this pharmaceutical - these manufacturer details to then go on, and if they would like to pursue a legal case, they're on a sticky wicket.

They come up against hospital Trusts who are saying, I don't know what device we were using then, I can't tell you, we can't find it, or it's not in your notes, I don't know where that's got to. There's been ladies from same hospital Trusts having operations within a year, a year and a half or so of each other who have all come back saying - my hospital notes, I've got everything here, but the theatre note that shows it isn't here. So, there's been a lot of covering up going on and a lot of underhandedness going on, and that has prohibited a lot of ladies from - step 1, being able to report it to the MHRA because the MHRA always come back and say to us, well, we don't have the statistics. People aren't reporting it; we haven't got the numbers.

Why have you not got the numbers if there's so many ladies injured? Why haven't they reported it? Well, that's part of the reason why they haven't reported it, because they haven't been able to because the MHRA has told them, we haven't got your details. What can we do about that? That's been something that I've picked up with hospitals.

Pharmaceutical companies - for me, I feel it's a little bit like pharmaceutical companies would probably try and sell ice to the Eskimos, and regardless of evidence of devices and them being withdrawn off the market, what they tend to do was withdraw, tweak them, and remarket them under a different name and bring them back in the market, back into people, ready for use, despite them knowing failures, by tweaking poor sizes and adding this and that. That's what happens with pharmaceutical companies. Doesn't always feel ethical, doesn't always feel transparent or upfront.

We know in the past - I hope it's not happening now, but we know that hospital Trusts have been offered great enticements and so have surgeons. We also know that some of the largest conferences that have been held by some of the leading professional bodies - if you look, even on the website when they advertise them, at the bottom it will say things like, have been funded by various pharmaceutical companies,

which I find completely crass. So, they don't feature very highly in my opinions, really.

MHRA; this is a good one. I actually looked up the MHRA - I know what they're supposed to do - and I read a definition that said, 'an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe'.

Sadly, this is not the experience of any of the mesh sufferers. The MHRA did not ensure our medical devices were acceptably safe for us and I question whether they've done the same on many other devices.

Back in 2012, so two years after I joined hands with Lorraine to help the ladies, Lorraine wrote a letter which I'm sure you've got in the package of evidence that she's given to you. She wrote a letter to Mr Cameron, who was the then-Prime Minister and the Department of Health, a very comprehensive package giving lots of detail, lots of statistics, all our members, et cetera. Department of Health then passed it onto Dr Susanne Ludgate, who was Clinical Director of Devices and Medicines and Healthcare Products Regulatory Agency at the time, and she agreed to meet us.

We did in fact actually meet Dr Susanne Ludgate at Lorraine's home in Bristol, and for the first time it actually felt like somebody in authority was actually listening to us ladies. I'm not sure that that was something that at the time was being done. I think thereafter people from the MHRA did meet with other support groups, but I think that was probably the first time somebody had - she was brave enough to step out and face us. We made her fully aware, she was shown all the folders and files that Lorraine had. Look, these are all the members that we have, these are all mesh sufferers.

She heard about some of the phone calls we've taken, how many hours we were spending doing it, how exhausted we both were due to our ill health, and how we really needed help for these ladies. What could the MHRA put in place to help us? What could the Department of Health do to help us support these ladies who were withering because they just weren't getting the help? We were trying to give as much as we possibly could, but we were ill as well. She did say at the time that actually she

would go back and discuss with her colleagues and she felt that some sort of medical support helpline would be a jolly good idea and they would look into it. We felt elated. It was like, this is going to be marvellous.

Sadly, she went away, and she retired and that was the end of proceedings as far as we were concerned, despite we wrote to the MHRA again, despite we tried to speak to the new heads of devices. It felt like somebody had just pulled the shutters down. So, there we were, after that many years - here we now are seven years on from that date, thousands upon thousands of further injured ladies - even though that evidence was there in the early days, it wasn't really taken on board. I'm not quite sure why because TVT Messed Up Mesh became a registered charity. It was recognised and yet it seemed it wasn't enough.

What evidence did these people need? How much more did they need to actually act on it instead of keep throwing back, but the benefits still outweigh the risks, which is a quote that most mesh sufferers baulk at every time they hear it because that's just not the case? Because of the whole debacle about not getting your theatre notes and not being able to report it to the MHRA, and the fact that it was such a dysfunctional setup that you had surgeons who weren't reporting either, but then I get why they weren't because not many surgeons are going to want to report and make themselves look inadequate or not very good at their job.

It was a very perverse way of trying to get statistics and I'm sure if you've looked at the statistics, it was virtually zero people reported anything as a surgeon, because that just wasn't going to happen. So, there was a blindness of the MHRA; well, if we haven't got the statistics from the ladies, because they can't report it because they

haven't got their theatre notes, if we haven't got the statistics from the surgeons, then we'll plough on. Everything's still all right. It clearly wasn't. It was unfolding, this huge problem, that they continued to carry on and ignore, and I just cannot understand how the MHRA is still functioning.

I think we need to disband them, get rid of them, set a new agency up, one that seems to be far less infiltrated by pharmaceutical companies and that sort of thing, and actually for it to be totally, totally, totally

independent, because there's no way that the way they behave is independent.

I think that the other thing that ladies have asked me to bring is so many of them have spent vast amounts of money going privately; having private surgery. As we know, this has been a huge problem that medical notes - when you have private surgery, your private treatment from a consultant, those notes belong to the surgeon and you can't get access to them very easily very often. That's often been the case with ladies who've tried to get hold of notes when it's come to swapping from the NHS sector to the private sector, having surgery thinking, well, if I go privately I'll spend my life savings, this will make me better, I need to do this because I need to have a life, and then finding that actually the person that was operating on them wasn't really such an expert and they've now just swapped the problems they had with mesh for another problem or another level of symptoms.

The surgeons operating in the private sector - quite a lot of them weren't adequately trained in removals. They didn't know what they were doing, but it was a good way of making money and there was a lot of ladies coming thick and fast ready to pay their hard-earned cash to have these surgeries done. Then finding that they couldn't even get hold of the notes from those particular consultant surgeons when it came to actually trying to pursue a legal case because surgeons were being threatened with subpoenaing them to court because they weren't providing them, or they were going missing.

Oh, they're not in there, we don't know where they've gone, we haven't got them, and you can't have them. There did seem a lot of cover up going on there, a lot of cover up with ladies who were trying to find the evidence to support their cases in the legal term and actually not being to get the evidence from the next surgeon who saw what the last surgeon had done and just covered the back of the last surgeon and it would all be cover up. No paperwork, no paperwork, no case, and by the time you've gone through that whole procedure, you're probably - your period of statute of limitation has run out anyway and you can't pursue your case because it's gone beyond three years.

That's something that's been very sad for a lot of ladies because at the time of them realising 1) that they had a huge problem and that they

needed or wanted to pursue a case, it was quite hard to find solicitors that would take on cases because it was unknown to them and they weren't interested. Then of course the minute you had one that would take on a few cases, all the rest jumped on the bandwagon and suddenly you had every solicitor saying, we're experts in mesh cases and we take mesh cases on.

Moving on to that sphere of things, the legal side of things, lots of ladies were made lots of promises and lots of ladies joined solicitors, signed paperwork, were encouraged to evoke their household insurances which were sometimes in the region of

£100,000 or £50,000 to put upfront as a money for their case. Being told that in the long-term, that probably wouldn't be enough to see their case through, but not to worry, that they would manage to get an after-the-event insurance that would be in place by that time of the money running out, and their cases could carry on.

Sadly, that didn't happen and lots of ladies had evoked the household insurance, had put forward £100,000, £50,000 which then got all gobbled up and then they said - solicitors would then just come forward and say, we're really, really sorry, we can't get anybody interested in taking you on an after-the-event insurance and therefore you have no more money in the kitty and we can't take your case on. So, you'll have to find another solicitor and see if somebody will take you on on a no-win-no-fee basis or something to that ilk.

That happened to an awful lot of ladies and it was no fault of any support group because of course there's a lot of talk amongst support groups, oh, are you pursuing a legal case, who with, et cetera. It wasn't any fault of any - it was literally people seeing an opportunity, thinking it might be quite a good way to make some very quick money and actually it turning out to be a lot bigger situation than they ever thought and them thinking, okay, we've done our bit, we're not doing - cases have gone on now and people have pursued cases and things have changed on that front.

But it's very important to share that there were a lot of ladies lost and swallowed up in that process who never got the chance and did run out of their period of statute of limitations because they spent a vast amount of time...

Cyril Chantler: Do you know how many?

Hayley Martin: I wouldn't like to say. I'd like to just discuss that with Lorraine and ask her how many she thinks, but I know one particular company did that to an awful lot of ladies and it was quite shocking to know that's what happened. Because people were hoping - not because they suddenly wanted to become rich, but because they couldn't work as much as they perhaps might like to, they couldn't work at all, some of them, and they needed money to try and live off and function, and that's what they wanted compensation for, just to live. They were taken advantage of and they were let down bitterly and there was very little communication. It was grossly unfair and very, not transparent at all.

Lorraine and I have had our - I want to say our fingers in lots of mesh pies, but we kind of have, really. In 2014 we became PPV members for the NHS England working group, and I think the most shocking thing that I discovered at one of the meetings was to find that we were still going around in this circle of, why have we not got the numbers, say the MHRA? If there are so many people injured, why do we not have those numbers? Then us ladies saying, well, we can't report it because we haven't got the codes and we haven't got our theatre notes, and then them saying, right, okay, and then suddenly discovering that actually part of the reason why some of those ladies weren't getting the adverse events reported or didn't have the numbers for how many ladies were being injured was because there were no specific HES codes or OPCS codes at all for full or partial mesh removals. There weren't any.

So, what was happening is, they were being recorded under general urology and general gynaecology, which meant there was a whole plethora of ladies that have gone through the system having removals done, but actually it wasn't being recorded in the right place in order to give the statistics back to anybody like the MHRA or the Department of Health, because there wasn't any codes there. I found that actually quite shocking, that they were clearly coming through these surgeries but just being recorded under something different and so we lost all those statistics. They were actually lost in the [unclear].

I know now we do have those codes; they have been put in since the NHS working group, which is a very good thing. But in that process a lot of

valuable evidence was lost, and it was statistical data and proof. It could have been the proof for so many ladies of just how many adverse events there really were out there because look, this is the proof, these ladies are having surgeries one after the other. So much was lost and now we have those new codes, good, but I still feel really upset about the fact of the loss of that data. I would like to know if there's any way of getting any of that data back.

Can we look into that? Can it be looked into? Is there any way that somebody can go through general urology and gynaecology notes and find out how many were recorded under there so we can add them to all the ones we now know that we have? Because that would be really very good. Of course, yet again, the good old MHRA were still saying the benefits outweigh the risks. There was not a true reflection of the enormity of the explant surgeries due to this and due to the fact they weren't being recorded.

I think my experience - and probably Lorraine's experience - the NHS England working group felt - it was very new. It was something different that was set up. It was a chance for what we felt to be heard, but at times it felt like it wasn't a very cohesive working group. It didn't feel like everybody worked together or pulled together. I can only say that I sat in meetings there and felt - what can I say - members of staff coming in, some of them who weren't even introduced like you introduced everybody so we know who - just coming in with - trailing in with cups of coffee halfway through while we sat there without even any drinks.

We weren't treated very well. There were surgeons there who actually ignored us; didn't even look at us when we talked about the things that were happening to us. I found that really appalling and quite shocking. Whether it was they felt shame-faced, I've no idea. But there was only one surgeon, and I won't name him, but he was lovely. As the mesh saga was unfolding, his words were, 'please tell me if these devices are injuring ladies because I do not want to injure ladies.' That's what he was saying back in 2014 to the NHS working group.

Sadly, at the end of that, it felt that I think what we got back as a report was hugely disappointing. It didn't go anywhere near to expressing the enormity of the disaster, unlike - I want to say unlike when you got involved and the minute you did and realised the enormity, the pause

was put on. For me, that pause could have been put on then and that would have saved so many ladies if that had been the case, and it wasn't. There seem to have been a lot of professional bodies ducking and diving and ignoring and lying - which I'm going to say that word, because it was - and going on to further maim ladies. That's the way it is.

For me, I think the Department of Health have done a lot of duck shoving onto the MHRA and other spheres and places and professional bodies, and they don't live up to their gov.uk quote, either: 'we lead, shape and fund healthcare in England, making sure people have the support, care and treatment they need with the compassion, respect and dignity they deserve'. Well, I didn't have respect, dignity, compassion and I didn't get what I deserved, and neither did hundreds upon thousands of ladies. They didn't get it, either. The Department of Health's words are very cheap, and up to now actions have been almost absent.

The kind of things ladies have shared are things like they feel they've been lied to, overlooked, ignored, put down, let down, judged, laughed at - and yes, I have been laughed at - abandoned

- because that's how they've actually felt. The repercussions of mesh go far and wide and they will do for years and years to come. Ladies have been promised that they're having full mesh removals, and I know this has been brought up to you before, and then finding out they've still got mesh pieces in. Because quite honestly, I don't come from a medical background, but any sane person must be able to work out that if you put a device in that's supposed to be permanent, it's quite unlikely that you'll be able to get the whole lot out.

So, therefore, saying to ladies, you can have a full mesh removal, I think it's bending the truth slightly and I've always felt I don't think that's possible. It's certainly not possible to do removals without giving ladies another plethora of symptoms or problems as a result of it. I have spoken to ladies - there was one lady at Exeter saying, I feel so much better, I had my mesh removed, I feel great. I didn't want to be a dampener, but I said, ok, let's see you in a couple of months' time because really, I'm sorry, but the removal will cause massive scar tissue, there'll be lots of adhesions, there will be, sadly, further problems that may come your way as with

ladies who don't perhaps even know they've got problems of mesh. They know that they're ill, but nobody's picking up on it's the mesh.

So, back to the first level really is, what are GPs doing? Let's have GPs more informed. If they knew, they could send them the right way. We're never going to be completely free of mesh or pain or complications of having mesh within us. I think I've spoken to enough ladies over the years. I think one thing I found quite amusing was when you actually spoke with Mark Slack and he spoke about that mesh does not harden and it does not migrate,

and I was sitting there looking at him thinking, ok. I'm understanding the science behind that because it has to be oxidised and it has to be in the air, but how long does it have to be in the air before that happens or not?

Because if a device is in a package and it's opened up in theatre, the minute it's opened up, it's in the air, it's oxidised. Whether he's saying it's got to be for X amount of hours or how long, I don't know, but I do know ladies have shared with me that even now, 15 plus years - one lady I think was 17 years after mesh surgery, was finding that if she actually wiped herself down below after going to the toilet, she was having pieces of mesh come out on the paper. There it was, eroded through her vagina, breaking out on the tissue. Ladies were also getting abdominal festering spots on the abdomen, that when they came to surface and they bathed them and bust open, there were pieces of mesh.

So, ladies aren't lying. They have pictures of it, they have photographs, they have proof, they have it in little containers; this is the piece of mesh that came out of me. It's proof that it does happen. So, it's not necessarily true and yet again it's one of those things where sometimes amongst the professionals you feel like you're utterly disbelieved or that you're telling a tall story, because why would you? What would be the point of telling a tall story?

One of the more horrific things that we heard was from a lady who was a carer who worked in a residential home and she actually shared that there were many residents who had had mesh put in in years previous and were suffering horrifically when she was having to care for them vaginally with meshes that were protruding and sticking out and all sorts

of horrific problems. They had no idea that they'd even had mesh put in them, let alone what it was that was now protruding or causing them problems.

So, there are spheres of society that aren't getting a voice because perhaps they're just not able to voice that because they don't even know they had it put in in the first place and people that maybe are working with them don't know it's mesh and don't know what's happening to these people. So, that frightens me that there are out there that don't have that facility to be able to tell anyone and are suffering in silence, really.

The other thing one lady asked me to share with you is - and it seems really important because she isn't the only lady this has happened to - is that sometimes us mesh sufferers would like to go on holiday, and sometimes we think we might take a trip and then we try and get holiday insurance. One lady paid £800 for one single return trip to the USA on top of what a holiday cost her, because that's how much insurance companies are making out of mesh sufferers.

That's a lady who was a mesh sufferer, has suffered very severely, is having a life of sorts, wanted to have a holiday but actually because of her mesh problems, because she had to have surgery, because she has ongoing issues with her mesh, because all of these things that I thought would be relevant like, had she recently been in hospital? No, she hadn't been in hospital or hospitalised in many years. Had she been to the GP with anything to do with her mesh-related - no. But insurance companies are ramping up the prices of insurance policies on people like us who would like to have holidays sometimes.

It would be jolly nice to go away and just try and forget and have a peaceful holiday somewhere. But actually, when you're faced with an £800 charge just for doing something like that - or potentially less, it could be less if you're going to - I think I've paid in the region of £400 myself, £400 and something, to go on holiday because I'm such a risk. That's not right, it's not right. We're being taken advantage of even in the insurance sector. I understand if you've been hospitalised in recent months prior to going on holiday, I understand if you've been - you're at your GP every waking moment talking about mesh. But actually, a lot of

those ladies haven't and actually they're still being penalised, so I think that that's something that really does need to be brought up.

As far as other recommendations are concerned; some of the things that ladies have thrown at me for recommendations - so, availability of tertiary clinics, which I know is something that's been talked about. They need to be...

Julia Cumberlege: Sorry, availability of...

Hayley Martin: Tertiary clinics. They need to be within easy access and have shorter waiting lists, so we need enough of them because it is hard as a sufferer travelling any long distance, and it is hard if you've then got to have surgery very far away from home. A lot of those ladies have had to do that, so therefore having a tertiary clinic plus surgery somewhere more local would obviously be so much better. I know it's costly and I know all of those things, but there does need to be an availability. If hospital Trusts have actually put these meshes in, then the similar hospital Trust areas - I know they come under - some of them are under several - several hospitals under one Trust - they do need to provide tertiary clinics within their areas so ladies can be local, can go and be seen locally.

It's hugely harrowing knowing you've got a mesh problem and having to travel maybe from, I don't know, Hampshire or God knows where to actually have to go and see somebody about your mesh problem. It's bad enough having it without having to go miles out of your way to do so.

Robust systems for hospital Trusts. Properly audited surgeons with performance outcomes. It would be good to have independent auditing services regularly visiting hospitals to challenge and check that these processes are in place. I know it might be hugely inconvenient to surgeons, but actually if they're doing their job properly, they shouldn't have anything to worry about.

Provision of knowledge for ladies on how to report adverse events. Some ladies didn't even know they could report it in the first place and still don't know. I've said about greater knowledge to GPs. The lack of GP knowledge has created lots of merry-go-rounds for ladies where they've been sent for physio and various other things, all before anybody goes, oh, is it mesh? Oh, it might be mesh. So, better informed GPs.

Better informed accident and emergency departments, because there have been times back in the early days of mesh problems where ladies have actually ended up in A&E departments and you've been faced with - and I say poor A&E doctors because I realise just how much pressure they are under and how hard they really work - faced with somebody who's got mesh complications and then looking at you thinking, have some gas and air. Would you like some morphine? Ooh, I don't really know about mesh.

They've been really honest. Let's get the gynae reg down to have a look at you, and sometimes even the gynae reg hasn't actually known much about mesh problems.

So, there you go to the place where you want to be helped to find that actually they're all going, 'we don't know what to do with you. Let's give you some pain relief and just send you home because that's all we can do for you.' So, it's really, really scary that that's what happens.

Greater knowledge at pain clinics - a lot of ladies are sent to pain clinics - and greater knowledge at musculoskeletal clinics and other places that ladies get sent to. Sadly at pain clinics, quite a lot of ladies - and musculoskeletal clinics - you get sent to places like physios, and physios are great, but the minute you start talking about mesh they've got no idea what your mesh is, what it's done, where it is, and then they go and start trying to do their job, which is telling you you should do some exercise.

There's an implication that mesh sufferers are just lazy ladies who sit on the sofa all day and that's probably why they're in pain and they need to do more exercise. I was told that if I didn't go to see the physio that I couldn't carry on being seen by a musculoskeletal clinic and have painkilling injections because I needed to address the physio part of it, and once I'd done that, I could continue. But what I was trying to say and nobody was hearing is that when I go and I go and have physio, I'm in bed for two days because it exacerbates the problem and irritates the meshes and gets everything livened up. Nobody listens and nobody hears.

So, all of these departments - pain clinics - GPs, pain clinics, musculoskeletal clinics all need to have so much more knowledge about the fact that they will have ladies coming through their door with mesh

problems, so they're not actually making ladies worse, they're actually helping ladies. The other thing that's been a real bugbear for ladies is that when we go to pain clinics, you have to be psychiatrically evaluated, or they like you to be. I think it's part of the process of the pain thing.

Due to the treatment that we've had by some doctors and surgeons and stuff, it's really difficult because yes, of course it does affect you mentally. It does make you depressed, it does make you feel very low, and for some ladies, it's made them feel usually suicidal. But actually, the implication in making you do this evaluation - tick 50 boxes, whatever, these abstract questions and then give you an outcome, are you depressed, are you suffering, is that making your pain worse or better - the implication is that actually we're all mentally ill patients and that's all we are and we're not, actually. We're mesh-injured patients who do actually sometimes suffer with our mental health because it's a hugely horrific thing that's happened to us and that's the reason why.

The GMC; I suppose the processes that go on there. Lots of ladies know of their implanting surgeons, some of them who have been put in front of the GMC for treatments they've offered to people and things they've done, surgeries they've performed. There's never any feedback. You get asked if they - can we have your medical notes? We'd like to put them in front of the GMC. You go, yeah, anything that helps, of course, yes, you can take my medical notes and put them in front of the GMC. But then you never get any follow-up, there's no feedback, you're never told what the outcome is. I know you can go online and read, but quite often, the feedback from the ladies that I have known that have given up their medical notes to GMC over adverse events that have occurred to them is that the surgeons have been put back to do some retraining and they've been put under supervision or to work under supervision for a short period.

For ladies who've been injured, maybe those 50 ladies out of 100 who've been injured by said surgeon, that doesn't actually seem like a good course of action, really. That actually seems like it's not robust enough. That isn't enough to just say, well, we'll go and retrain you and we'll get somebody to watch you. That just doesn't actually seem enough for us ladies.

Robust regulation of pharmaceutical companies, which I mentioned earlier, I think needs to happen. We definitely need this proper registry so everything gets registered. I'm hugely aware because when my husband's grandfather had a heart pacemaker put in, they provide a little booklet with it. You get a little booklet every time somebody has one put in and it has your device number and everything on it, and I just think why can't that be the case in all medical devices, that you get given this booklet? It's your booklet, it tells you everything you need to know about your device, it's got codes on it, it's got everything you need. But somehow there needs to be this clear audit trail. It's no good saying, well, we haven't captured those numbers and we haven't got them.

We need those numbers to prove - and as it's been proven, how long it's taken to get to the door of this, people could have been saved if but there had been proper, clear audit trails with registries that were keeping these statistics.

Julia Cumberlege: I'm getting a bit

conscious of the time. Hayley Martin:

Okay, yes.

Julia Cumberlege: So, I do want you to finish but...

Hayley Martin: No, do tell me, how much longer have I got? Just a couple of minutes?

Julia Cumberlege: No, less than that. What I'm trying to do is to give each patient group roughly the same amount of time.

Hayley Martin: Absolutely, and

that's fair. Julia Cumberlege:

But if you've got other points...

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Hayley Martin: No, I just really wanted to say that I thought it was really interesting when we read - when I listened to the video of the Department of Health talking, and they were talking about their statement of regret and whether there would be one given out to the ladies, except to say that us ladies regret so much. We regret so much, a lot of it trusting. It feels like we don't exist a lot of the time. I suppose just to end really with a very short little statement which says: 'as sufferers, we've welcomed this Review and we would like to thank you all for this chance to have our voices heard; a chance to feel that what has happened to us is significantly horrific and important enough and does warrant investigating.

We also realise the enormity of such an undertaking and feel saddened that the Department of Health chose to ask you to conduct three reviews all at the same time, especially when all these reviews, including Primodos and sodium valproate, are as important and complex as each other. We can only hope that you have been able to gather enough information about each medical intervention and outcome and will be what each group of sufferers has always hoped for and deserves. Thank you...'

[Over speaking]

Julia Cumberlege: Can I just ask Kevin, you're here], do you want to say anything?

Kevin Martin: Yeah, I do. I think obviously Hayley's suffered from a number of years and all the other ladies as well and I do find it very surprising that you can have hospital Trusts that have no control over their consultants and how they operate or balances and checks on them. I don't know of any other industry that I've been exposed to that does that. As Hayley says about checking products, if you buy a lawnmower, you send your card off, they know exactly what one it is, you can have recalls on cars and things, but it seems a lot less controlled. I think also for me, having spoken to other husbands, partners, et cetera, it doesn't just stop with the ladies. It affects their whole family and extended family quite considerably, whether it means they're not going away, they're not going out at

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weekends or the normal social activities that people take part in. It obviously affects people's sex lives and the pressures on marriages and children of those marriages is quite significant. So, it doesn't just stop there, although that this is the main focus, quite rightly so. So, that's what I would just like to say.

Julia Cumberlege: Well, thank you for that, and certainly at some of the visits that we've done, we've had the partners, the husbands, come along and also the children, we've heard from the children as well. We've always felt it was family first and the families have to be considered, not just the woman but the extended family and how they have to cope with that. Of course, we've heard of break-ups and all the rest of it, so I'm congratulating both for you for keeping together. That's terrific. Hayley, thank you so much. That was a tremendous tour de force and you've certainly covered an awful lot of ground and we've taken notes.

If there are things that we would like to come back to - and certainly one of the questions I would have asked if we'd had more time is, how do we rebuild the confidence that women have in the medical profession, because that is really important. You may want to think about that and perhaps come back to us.

Hayley Martin: Yeah, I think some of the implications that - some of the things, if you put them in place as recommendations, some of the trust will come back hopefully.

Julia Cumberlege: Cyril, anything you would like to ask?

Cyril Chantler: It really was a tour de force, and thank you very much. Some of the things we've heard before going around the country from other organisations, but some of the things were new and we need to go away and think about it. I have huge respect for you and your family and all you've had to go through.

Hayley Martin: Thank you very much. That means a lot to hear.

Kevin Martin: Can I just ask one question? We have been discussing this on and off for the last few days: with the data that's been captured or not captured - and quite significant data hasn't been captured - is there no way that two

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hospital Trusts as an example, they could go back through all the operations and trace back to the patients and then ask them over a seven-year period post-operation what

symptoms or problems they've had, so that you could actually build up a set of data? I know it's only a straw poll in terms of data, but it would at least give you some idea of how many people have been affected and what percentage is a real percentage as opposed to those percentages that are quoted that the ladies think are totally inaccurate. Is there no way that that sort of survey could be done, perhaps to try and [unclear]?

Julia Cumberlege: I think that's a really interesting suggestion and perhaps we could go away and think about that because obviously one of our recommendations is - well, looking at the future, we're very anxious to look to the future and see what can be improved. You're so right that the data is so flaky, and we've got to ensure in the future that we make it robust so we really know what's happening. I think you and Lorraine have been amazing in the way that you've taken this in those very early days, and I think as a counsellor and psychotherapist, if ever I need one, [unclear].

END OF TRANSCRIPT

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Session 2: Sling the Mesh*

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Julia Cumberlege: As you are very much aware that we've been around the country and thank you very much for - Sling the Mesh for the - how you got your - a lot of your members to come and talk to us and meet with us and that's been really really helpful. Thank you for that. Of course, we're very aware about your organisation and the fact that it was set up at 2015 by Kath Sansom. I believe that when you first started it had something like 20 members. Now you're well over 7000 which is incredible.

Michelle Moffatt: Seven thousand six hundred.

Julia Cumberlege: The amount of work you must have put into that through various sources but social media as well as the ordinary media et cetera and of course supporting all the time women and their families and I think that's been incredibly impressive. So, I also want to thank you for the help you've given us and you've sent us a lot of material, you kept us informed of developments and that has been extremely helpful.

So, what we want to do today is really to listen to you. We are really at the end now of our formal sessions of oral evidence and they are going to be filmed and they'll be on our website and I presume that's all right with you? Yeah. Then - so that's been closing - really what we tried to do was to start with the patient groups, listen to them, what you and your colleagues had to tell us. Then this is the sort of final bit of closing the oral evidence sessions.

think it's really important that you tell us what you want us to hear. You will be aware that we're going to be writing our report, the recommendations. You will have had the opportunity to look at the website to see what other people have been saying et cetera. So, this session is your opportunity to help us think about the recommendations we ought to be making. But we're very happy to hear anything you want to tell us. Really very useful and we've got just about an hour to do that. Is that all right?

Jackie Harvey: Yeah.

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Julia Cumberlege: Great. So, I should welcome Michelle and Jackie and if you could say who you are and your position that you hold within Sling the Mesh, and Susan as you're here as an observer I'm afraid. Is that all right? Okay. So, we could start formally now. Can I welcome you here today Michelle Moffatt and Jackie Harvey from Sling the Mesh. Perhaps you could start by telling us who you are and your position within the organisation.

Jackie Harvey: Well I'm Jackie Harvey. I am an admin, help Kath run the Sling the Mesh group. I'm also founder of Sling the Mesh Northern Ireland, which is a group of Northern Irish women, approximately 550 women on that group at present.

Michelle Moffatt: I have been helping Kath with research and the writing of the submission to the Review, and also for today reviewing all - around 40 hours I think of oral hearings and also bringing together our feedback incorporating inputs from others in the team.

Julia Cumberlege: And you're Michelle Moffatt?

Michelle Moffatt: I'm Michelle Moffatt, sorry yes.

Julia Cumberlege: Yes, right okay. I don't know who wants to speak first.

Michelle Moffatt: I think I will start [unclear].

Julia Cumberlege: Right thank you.

Michelle Moffatt: Just to say that since I have been - a lot of our evidence and we have - there's a lot of issues that we'd like to discuss, we've actually come up with our statement to feedback which I think is around 53 minutes. So, it is a bit long but there's an awful lot that we would like to say. So, I'll start, to say thank you for providing Sling the Mesh with an opportunity to reply to the evidence presented to this Review. We have listened, as I mentioned, to 40 hours of evidence and this is the focus of the presentation.

The oral hearings have confirmed our concerns. Our submission of written evidence to this Review set out the case for a number of recommended actions to be covered by the Review, none of which

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have lost their validity in the light of all the oral evidence presented. We found little in the oral hearings that provides reassurance to enable a rebuilding of trust in the current health system in the context of pelvic mesh. We are shocked and appalled at how fragmented the health system really is, and how a multitude of national health institutions have been working in silos, in isolation. In our view they have been too pro industry at the expense of patient safety and with no effective accountability or oversight.

The oral hearings highlight to us the following: (1) There is shockingly weak evidence for the continued use of pelvic mesh. (2) There is a need to conduct a national recall. (3) There is an urgent need for a regulated and structured pathway to treatment for

mesh-injured women in a small number of accredited mesh removal centres with skilled and experienced surgeons. (4) There is no legislation for patient harm.

(5) There is evidently an urgent need for a reformed national information system with adequate funding to address the current fragmentation and vast underreporting of adverse events related to pelvic mesh procedures. (6) There is no single regulator taking lead responsibility for monitoring the uses and effects of implants. The current systems for ensuring patient safety are shockingly inadequate for medical devices. (7) That a number of institutions have been complacent in overlooking patient support groups and individual women's voices, ultimately ignoring patient safety in relation to pelvic mesh devices in which thousands of women have devastating injuries and some have even died. (8) The informed consent process is in need of vast improvement. There is an obvious need for a significant change in attitudes and communication relating to the informed consent process. (9) Greater controls are needed to mitigate conflicts of interest between device manufacturers and clinicians. There has been too much autonomy without sufficient monitoring. (10) Adherence to guidance issued by national medical institutions is not mandatory and is not monitored for adherence, compromising standards. (11) We

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acknowledge that in all the oral hearings, only one individual from one national body, BAUS, agreed that mesh-injured women should be offered an apology unreservedly. (12) It is worth mentioning here, our concern that recently published HES data records 16 TVT and TVTO surgery since August last year after the review's pause came into effect.

We would like to provide specific feedback and highlight key points relating to oral evidence in the context of our recommended key actions highlighted in our written submission of evidence.

Jackie Harvey:

Sling the Mesh action one calls for a full ban in the use of pelvic mesh devices following review. A full ban of pelvic mesh is justified given the clear lack of evidence for licensing pelvic mesh. No evidence on complication risks and the clear real-world evidence of extensive harm pelvic mesh has caused to thousands of women in this country over the past 20 years. A ban is the right thing to do.

It was clearly confirmed by national institutions including RCOG in the oral hearings that pelvic mesh is the only medical device that is inserted blindly. This is a medieval practice and must be banned. America's FDA has now banned the use of transvaginal mesh for anterior and posterior prolapse. Other countries are following suit. RCOG, BSUG, BAUS and The Pelvic Floor Society did not respond directly, yes or no, to the review team's question, is mesh safe?

We think it is telling that when BSUG, BAUS and The Pelvic Floor Society were asked whether women are wrong when they have told the Review that they have been treated as guinea pigs, the collective response was a wall of silence. If a full ban of pelvic

mesh is not achieved, then we advocate that pelvic mesh must be offered only as a third and final last resort option. This needs to be regulated and robustly monitored. NICE banned vaginal posterior prolapse mesh in December 2017, due to safety concerns and then effectively unbanned it in April 2019.

We believe the quality of evidence relied upon by NICE to produce its latest revised guidelines on pelvic mesh is unprecedented.

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Virtually all of the evidence is of a very low or low quality. There is no evidence to inform long-term safety and the real-world evidence and patient stories of harms have been overlooked. Professor Heneghan of Oxford University stated in the oral hearing that empirical evidence shows that low quality RCTs often overestimate benefits and underestimate harms. He said it is a mistake to believe that RCTs are top of the evidence hierarchy for harm.

BSUG states that it has relied on RCTs to determine the safety of mesh but have been short-term with none having long-term data on outcomes. BAUS confirms there are inherent flaws in all of the so-called high-level evidence and there are many blind spots in the evidence. BAUS states that RCTs were powered to look at success with outcomes centred around SUI treatment and not the nature of complications and so they do not know the outcomes.

The evidence gap prevents fully informed consent of patients with reference to risks. NHS England states that a reason why it did not take action to effect a pause in the use of mesh is that there was not the sort of evidence that is relied upon including very poor scientific literature with short term follow-up. Sling the Mesh questions then why this literature is being used by NICE to justify the continued use of pelvic mesh in its revised guidelines. We maintain that NICE cannot logically argue to continue using mesh when they are admitting they would have difficulties even recruiting women for trials because of the risks.

The revised NICE guidelines on bans previously banned mesh for posterior prolapse or rectocele that is considered so dangerous it was stopped by the FDA in America in 2018. Now that surgical mesh for anterior prolapse, cystocele has also been banned in

America recently, it is time for NICE to tear up its revised guidelines, give weight to the patient voice and do the right thing.

We are concerned that the NICE decision aids that accompany the revised guidelines do not cover all of the multiple mesh complications

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that are suffered by women. We are also concerned there were deficiencies in the revised NICE mesh guidelines committee.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

NHS England says there is a need to balance evidence with population cohort. In the absence of monitoring data, the real-world data is the evidence. Sling the Mesh alone has over 7600 members. Many of these are women still navigating a system searching desperately for help with their complications for which even today doctors and primary and secondary care do not link symptoms to mesh.

Indeed, a common theme throughout the oral hearings is that many of the institutions such as NICE, GMC and the Royal Societies that have an interest in patient safety have no power to mandate good clinical practice including guideline and reporting requirements. This needs to change.

Jackie Harvey: As our action two calls for a review of the structures and processes of mesh medical device regulation approval and adverse effects reporting, to enhance transparency and safety. So, let's go back to the flawed approval of mesh implants. The root cause of the pelvic mesh disaster

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began with SERNIP which gave mesh a C classification in 1997 meaning it was only to be used as part of research trials and there must be a register of patients implanted.

Vincent Argent stated in his oral hearing that in 2000 SERNIP reclassified mesh from a C to an A as a result of lobbying by manufacturers. The manufacturers submitted four papers; two were duplicates, two were excluded and two were conference abstracts of incomplete and uninterpretable results. There were no RCTs. SERNIP had not jumped from a C to an A for any other procedure. An A classification means pelvic mesh is deemed a safe and effective procedure. Mesh procedures took precedence and were promoted by manufacturers and surgeons societies as the gold standard quick fix.

MHRA stated in the oral hearing that they could not see any evidence to show why SERNIP changed mesh classification from C to A. MHRA said it was - is surprising to move from one risk classification to another unless there is significant data to support that. When NICE were asked if the category of mesh could be changed based on unpublished data from manufacturers, NICE responded that they would ignore such data unless the data said it was unsafe. Given this evidence, and the subsequent injuries caused by mesh to women over the past 20 years, the question remains why this classification has never been reviewed by the Secretary of State for Health, and responsible institutions.

We would like to go on to discuss regulation. We know that intense lobbying by the medical device industry has prevented an overhaul of EU and UK medical device patient safety regulations. As Professor Heneghan stated, the only reason a device is withdrawn is if a device is not functioning as specified. It has nothing to do with patient harm. There is no legislation for patient harm. MHRA said they would like to see more transparency in the area of safety but are constrained by the EU political process of regulation and that it does not go far enough.

MHRA admits that post-market surveillance has not been a priority and adverse event reporting is underreported and needs improving. MHRA also stated that the regulatory system has not focused on the difficulty

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of removing the device from the human body before clearing a device for use. This is shocking given that pelvic mesh is designed to be a permanent implant. We are very concerned that MHRA is on the side of manufacturers at the expense of patient safety. For example, a Director of MHRA said in a recent conference that they believe Brexit will present an opportunity to be more industry friendly. The parliamentary under Secretary of State for Health, Jackie Doyle-Price, made a reference to this in February at a House of Commons debate on medical devices.

It appears to us from the oral hearings that until recently there has been a lack of political will and resources to bring about change where the priority is patient safety. This needs to be more robustly addressed as a priority with new legislation for patient harm.

MHRA is confident that the new EU Medical Device Regulations or MDR will drive improvement in regulation of medical devices. Yet a review of the new regulations by Professor Carl Heneghan of Oxford University has found many flaws. He highlights that the language of MDR is open to interpretation allowing manufacturers and notified bodies to continue business as usual. To omit of evidence and allow publication bias in clinical evaluations and harmful data relating to safety and performance can go unreported.

In his 2014 MHRA review, Stephenson highlighted the link between public data and public health, arguing that publishing an injury and malfunction report would significantly improve the safety of devices by empowering patients and healthcare professionals and increasing scrutiny on industry and regulators. MHRA stated that the EU's revised database, EUDAMED is not expected to be up and running until some time after 2020. Crucially it has been recently reported in the media that the EUDAMED database is not expected to make injury and malfunction reports public due to commercial sensitivity. Therefore, we assume we cannot expect any change at all in patient safety reporting from EUDAMED that would improve transparency and accountability.

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We have no faith in a flawed business model for medical devices in which the NHS will now have to spend billions of pounds to address the fall-out of the mesh scandal as highlighted by Professor Heneghan in his oral hearing. Long term post-market surveillance of devices needs significant strengthening with a core set of outcome measures agreed with patient input. In relation to RCTs we are also concerned that if the mesh pause is lifted, flawed short-term trials will resume such as the halted DynaMesh trial. We are concerned that more women will yet again be treated as unwitting guinea pigs in short-term trials and suffer harm without monitoring for longer term complications.

Our action three calls for an overhaul of the HES reporting system and to retrospectively correct the vast underreporting of mesh complications to date through a national recall. Written evidence presented by the University of Leeds calls for a national information system to monitor the use of implants and devices including the use of pelvic mesh. We would like to see such a system include non-mesh procedures to allow for comparisons to be made. It should also include other mesh procedures, for example, rectopexy, sacrocolpopexy and sacrohysteropexy, since devastating injuries have occurred with these mesh procedures.

In the absence of a ban of pelvic mesh we agree that surgeons need to be mandated to input all relevant patient level data of all pelvic procedures on a national information system and crucially a registry established to interrogate the data. We note that it is estimated these will take two years to establish. So, at the very least mesh should continue to be paused until these and other review conditions are met, fully resourced, and operational.

NHS Improvement mentioned there are no figures available for how many people are affected by mesh complications. NHS Improvement said a full retrospective audit would be helpful. For mesh outcomes linked to safety, long-term data is needed in both the NHS and private sector. HES data has not been accurate due

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to the poor coding system. We are aware new HES coding for mesh procedures is now in place but there is still no code for rectopexy. New HES coding includes separate codes for TVT and transobturator mesh. Another code relates to a suprapubic sling procedure and we question whether this code is open to interpretation since mesh manufacturers also use this term for mesh devices. Is there a possibility that mesh procedures may unintentionally or otherwise be recorded under this code, therefore skewing figures?

Sling the Mesh believes a national recall of pelvic mesh is wholly justified given that the true figure of the number of women harmed by pelvic mesh is still unknown.

Action seven calls for the development of a registry of pelvic mesh implants. MHRA stated it is supportive of a registry to characterise long-term safety in relation to different surgical procedures using mesh and non-mesh alternatives. Our position is that if mesh is not banned then at the very least the current pause continues until such a registry is operational, along with a mandatory national database of required patient-level data.

Action four calls for a review of governance, accountability and effectiveness. The oral hearings highlight to us that every agency is complicit in a failure to coordinate and take timely action.

Everyone is responsible but nobody it seems is accountable.

Lack of mandatory guidance for clinical practice. BAUS, BSUG and Pelvic Floor Society stated that as professional organisations they can only advise. They are not regulators and therefore can only recommend what should happen in practice. NICE has no powers to act when their guidance is not followed. It is down to individual trusts and consultants and how they conduct their practice and therein lies a fundamental problem that needs to be addressed. All the professional organisations stated they need a stronger mandate from NHS England. Indeed, a common theme throughout the oral hearings is that many of the organisations who have an interest in patient safety have no power

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to mandate good clinical practice, including reporting requirements. We feel this needs to change.

Failures in governance and accountability. MHRA said there was a need to bring relevant authorities together for appreciation of priority for action. There is not enough coordinated action. This clearly illustrates that MHRA and all other relevant authorities have been complacent. Their risk minimisation systems have failed.

They work in silos. They do not know who has a mesh implanted and how many have been harmed and these failures have led to the mesh disaster.

When the Review team asked MHRA why has it taken so long to set up a system with a central coordinating body, the MHRA responded that it could not answer this question. The Department of Health, on behalf of the Secretary of State acts as system steward but clearly this system has failed in the context of pelvic mesh.

MHRA seems to be in denial over its role in the mesh device scandal. MHRA stated in the oral hearings that the final decision of what is an acceptable risk ultimately rests with clinician and patient. This is at the heart of the informed consent process and supported by information within the manufacturers' instructions made available to clinicians. We query how can MHRA justify such a fundamentally flawed statement that abdicates all responsibility for safety? Firstly, it is impossible for appropriate informed consent to be given if a surgeon does not have full access to benefit and harm data. Secondly, there are conflicted surgeons who are influenced by manufacturers and who do not explain risks because they are pro mesh, and their skills are limited to implanting mesh. Thirdly, it is well known that pelvic mesh manufacturers have omitted risks and complications in their instructions. They have hidden risks and this fact is being widely proved in lawsuits across a number of states in America.

America's FDA has banned mesh for transvaginal prolapse procedures because the manufacturers of mesh devices could not provide sufficient evidence that the risks outweigh the benefits. MHRA knows

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this. So why continue with a line, it's not for us to decide on mesh use, it's up to the clinician and patient.

MHRA admits there has been more complacency with medical devices and that patient voice on outcomes needs to be understood. There is a clear need for post-market follow up which needs to extend for the whole life of the product. The only outcome measure for success of pelvic mesh is continence. For example, a woman disabled by mesh but is continent is deemed a success.

Poor outcomes for patients have not been linked to the device.

MHRA did not mention in the oral hearings the considerable influence of industry connected to weak patient safety regulation as a major cause for these failures. As MHRA confirmed there is no body responsible for regulatory failings or in overall charge.

We maintain the view that MHRA is not fit for purpose in regard to patient safety because it and regulation serves the needs of device manufacturers at the expense of patient safety. This issue was referenced by Jackie Doyle-Price in February 2019 during a House of Commons debate on licensing of medical devices in which she said, regulation has focused excessively on what is in the commercial interests of businesses to maintain competition, rather than having patient safety at its heart. I think that when it comes to medical regulation it should have that at its heart.

NHS England stated that NHS improvement is overall responsible for patient safety. They admit that monitoring of patient safety is weak and that MHRA need to look at that. Such statements in the oral hearings resembled to us a game of ping pong in which institutions bat away responsibility for their failures. It is very confusing to disentangle who is actually responsible for what.

When asked by the Review team who was overall responsible for patient safety, NHS England responded that they recognise there is a deficiency and there is a commitment to improve patient safety. In relation to the situation of mesh where a rising tide of complications can arise years after implant, NHS England recognises that they have to

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be better at trying to spot this and that systems need to be more sensitive and committed to do this, but a different model is needed to pick up issues.

NHS England stated that its long-term plan is moving towards this. They stated that the reason that a pause on mesh was not instituted is because the system is complicated and joining the dots is difficult. NHS England stated they appreciate the Review's pause is the right thing to do and that they are still trying to understand the magnitude of the problem and they do not know how many patients have problems. They admit that the process has been too slow. The magnitude of this disaster is clear to see in the membership of patient support groups as well as studies highlighting the complications of mesh over the past 15 years. The real-world evidence of patient groups is still being overlooked.

We note that NHS England has recently recruited a Patient Safety Director. NHS England stated that there is a need for a model or structure that is biased towards patients, but they say they do not know how to do that.

Adverse event reporting. GMC urgently needs to be empowered to develop mechanisms to ensure doctors are monitored adequately for adherence in practice to GMC guidelines for adverse event reporting, informed consent, duty of candour and conflicts of interest. Our position is that GMC guidance should be mandatory, and this should form a key part of the appraisal system for clinicians. This will go some way to ensuring all surgeons meet standards and plug a gaping hole in monitoring.

GMC provides guidance on adverse event reporting but admits it does not know if advice is being followed in practice and if all clinicians have reported all incidents. GMC stated that there may be a gap in what is being reported and what they are being made aware of. This indicates to us that the GMC is currently failing in its role to ensure surgeons continue to meet standards set out in their guidance. GMC also stated it is difficult for them to identify trends in reporting. When asked by the

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Review team whether following GMC guidance should be part of a doctor's appraisal no satisfactory response was given by GMC. Our view is that all surgeons must be made accountable for ensuring they meet standards.

At primary care level GP awareness of complications of pelvic mesh must be improved. Even today some Sling the Mesh members report finding themselves in a position of educating their GPs on pelvic mesh complications. Women still report having to fight to get a referral to a specialist mesh-removal surgeon.

Reporting adverse events of medical devices. MHRA stated that very few patients know about the Yellow Card system despite its promotion efforts, and there is considerable underreporting of adverse events by clinicians and patients on medical devices.

They admit that more could be done to raise awareness of the Yellow Card system, but we questioned why flog a dead horse when Yellow Card is clearly not fit for purpose despite efforts to increase voluntary adverse event reporting over the years.

We believe a mandatory MAUDE type adverse event reporting system for all mesh types and related procedures with a central coordinating body is urgently needed. The Yellow Card has received increased reports from mesh injured women partly because Sling the Mesh alerted members to the Yellow Card system.

Dismissive attitudes of national institutions and some surgeons. When told by the Review team that patients stated they had been treated as guinea pigs and asked whether in effect the system of learning is from people going through pain, the MHRA responded, well to an extent that is an inevitable result of innovation in medical practice. There will be unexpected outcomes. This dismissive and cavalier statement is an insult to the thousands of women suffering and those who have died in this country linked to pelvic mesh. A system that treats patients as unwitting guinea pigs with a knowledge that the device can cause harm and even death of women is quite simply immoral.

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A surgeon from Oxford stated in the oral hearings, 'well the majority of mesh complications were bits of fibre in the vagina which were trimmed down fairly easily often without comprising the integrity of the sling. So, they weren't all major complications that were difficult to deal with'. This dismissive statement downplays a complication that has devastating far-reaching effects. It is another insult to women who are not told of the risks of this type of mesh harm in the first place. The statement trivialises the trauma of women having to undergo snips or trims of mesh in their vagina due to excruciating pain and loss of sex life.

Our experience tells us that many women who have mesh trimmed have had to undergo further surgery due to multiple complications that often ultimately ended in full mesh removal. Simple excisions only attempt to deal with part of the problem, thereby prolonging the suffering of women and presenting additional costs to the NHS. Partial removals can also make it more difficult for a surgeon to remove remaining mesh. MHRA stated further 'we have seen no clear evidence which indicate these products should be taken off the market'. So why is MHRA overlooking the real-world evidence of thousands of women injured and even killed due to pelvic mesh in the UK? Is this not clear evidence? We are wondering if it were thousands of men suffering with debilitating pain and loss of sex life and dying, would they be ignored?

There was mention in one of the oral hearings that 90 per cent benefit from mesh. But the measure for benefit relates solely to continence. So, we could present a mesh-injured woman in pain, in a wheelchair, who has lost her sex life, her job, her marriage. Yet in the statistics she has benefited from mesh because she no longer wets herself. This is a core weakness of the scientific literature when looking at benefits versus harm.

If we are to assume 90 per cent to be correct, and our position has always been that this figure is very likely to be lower, then what about the 10 per cent who have been harmed? Around 127,000 plus women in this country have been implanted with pelvic mesh. Ten per cent of

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these would mean 12,700 women have been injured and a number we know have died due to mesh complications. In the US last month, in a Pennsylvania Superior Court ruling, a Judge wrote that Johnson & Johnson subsidiary

Ethicon's Medical Director admitted that the rate of the TVT's long-term success as a treatment for incontinence was around 66 to 68 per cent. Ethicon however officially reported the success rate as over 90 per cent.

So, it would seem that the medical establishment in this country are quoting what the leading TVT manufacturer wants them to believe. Sling the Mesh was disappointed that the oral evidence given by NHS England, RCOG, BAUS, BSUG and Pelvic Floor Society did not give a satisfactory explanation why it did not advocate for a suspension of pelvic mesh given they have been aware women have been injured in the UK for the past 15 years.

Patients trusted the responsible institutions that mesh was a safe, gold standard device - a term we now know was coined by manufacturers not medics. We follow the trusted advice of surgeons, but women have been injured, maimed and even killed by mesh device complications as a result. MHRA know this. They have published data on pelvic mesh related deaths. Other deaths have been recorded in the media. These reported deaths may be the tip of the iceberg. Sling the Mesh believes the risk of death linked to pelvic mesh complications needs to be explicitly included in the revised NICE guidelines and informed consent process.

The Chief Medical Officer stated that the use of mesh spread because, "it seemed to be a quick fix and for a number of women it gave them relief but for too many they have ended up with disastrous outcomes". We question why then did the CM - the Chief Medical Officer also state that, mesh is something we want to keep on the books, when in her own words, too many women have been harmed?

Lack of informed consent. GMC stated they have extensive guidance on informed consent but there is a gap between what the guidance

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requires and how this is applied. When investigating reports about lack of informed consent, the GMC stated that it is very difficult to get to the truth, with opposing versions of the encounter between doctor and patient behind closed doors. We strongly believe that consultations between surgeon and patient should be audio recorded as a number of surgeons are failing to provide information on all risks, if at all.

Patients need access to, and explanations of, clinical recommendations in an appropriate form. We noted in the oral hearings that there is an acceptance that patients have not been getting adequate informed consent. The informed consent process needs to be improved if GMC are truly committed to its role of taking action to prevent a doctor from putting the safety of patients or the public's confidence in doctors at risk. RCOG also recommends staged informed consent to allow patients to ask questions with all documents given to them to allow them to make an informed decision and we agree with this.

A surgeon from King's mentioned, 'there will be a proportion of women who will be very much relieved to see the re-introduction of retropubic TVTs'. Other surgeons stated that women want a tape and are waiting for the pause to be reversed. We question how many of these women have been offered and given the opportunity for pelvic health physiotherapy as a conservative treatment? How many of these women have been properly consented with all the risks of TVT explained? We are extremely concerned that women are being lined up for pelvic mesh surgery to enable surgeons to return to business as usual if the pause is lifted with only a three- month follow-up and no capacity for long term follow-up when complications occur. Surgeons have significantly played down the complication rates to patients in order to promote mesh use and they went against RCOG's endorsement of the modified calvin score.

Duty of candour. We note that in relation to duty of candour, GMC could not say they know categorically that their guidance works in day to day practice. Sling the Mesh questions what is the point of issuing

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guidance if there is no effective monitoring to ensure it is applied in practice?

Lack of skills training in competence in non-mesh procedures. BSUG states there is a huge cohort of doctors in practice that have not been trained to perform non-mesh procedures and those who were have become de-skilled. RCOG's training programmes for student doctors do not include training in non-mesh open surgery options particularly colposuspension and hence there is now a skills gap in this country. RCOG states there is an opportunity to re-introduce colposuspension training and mentorship programmes at speed and that a recommendation from the review will help RCOG drive this forward. We welcome this news, although we would like to have heard from RGOG why it has not been proactive in recommending such action themselves when mesh complications emerged many years ago.

Action five. Improve processes to enable mesh-affected women to access fast-tracked quality assured multidisciplinary services for full mesh removal surgery. We know that HES data is inaccurate, and risk cannot be calculated through mesh removal rates alone. This is due to thousands of mesh injured women in need of mesh removal but the pathway to treatment is currently much too slow, meandering and ineffective. Our experience is that there is widespread denial or ignorance of women's injuries being linked to mesh and many women are going from pillar to post, prolonging their suffering, often for years. There are currently only a handful of trusted skilled and experienced surgeons in this country for complex mesh removal, and a mesh-injured woman who gets referred to one considers herself fortunate indeed despite her very unfortunate situation.

Politics should never prevent patient access to these skilled experienced and trusted surgeons. [REDACTED]

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We are concerned that surgeons should not practise on mesh- injured women in order to become experienced at complex mesh removal. We have been unwitting guinea pigs once with devastating consequences. We do not want to risk being guinea pigs again. Inexperienced surgeons should first undergo accredited training. We believe there is an urgent need for a regulated treatment pathway with a small number of accredited skilled and experienced surgeons and units with appropriate funding. Women need access to formal information on a surgeon’s skill, experience and outcomes to enable them to identify a surgeon of their choice.

Specialised pelvic health physiotherapy services. Pelvic health physio services need to be prioritised, expanded and adequately funded to enable all women that suffer with SUI and pelvic organ prolapse to mitigate the need for surgery in the first place.

Currently this service is massively under-resourced with long waiting lists due to resource constraints, as highlighted by a surgeon in one of the oral hearings. For women who have

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undergone mesh removal, pelvic physio services are crucial to minimise the need for further continence surgeries.

There needs to be an extension of post-natal care incorporating specialised pelvic health physio services post birth. If these services had been made widely available, we believe the vast number of so-called quick fix mesh surgeries would not have been needed for many SUI and some minor prolapse cases, and harm to many women would have been avoided.

Our action 10 called for consideration of the effects of commercial influence on the published research on mesh and the introduction of a Physician Sunshine Payment Act to ensure greater transparency. The Royal College of Surgeons said in the oral hearing, that there is a suspicion that a very active medical device industry is influencing surgeons to input mesh. It is a common issue that has been repeatedly raised in the media. It is not entirely fictitious. Not everyone behaves honestly, he said. There is no data on financial inducements. It is essential conflicts of interests are declared by surgeons online.

NHS Improvement's Patient Safety Director stated there has been a huge amount of influence from manufacturers directly on individuals that I think is unhealthy. There is conflict here. A surgeon said in the oral hearings that there has definitely been inducements from mesh device manufacturers for surgeons including meals, attendance at conferences. Another said free samples of mesh kits were handed to surgeons to try out.

GMC stated they support a mechanism such as a register of declaration of interests by clinicians and that if the Review recommended this, they would support such a mechanism. Sling the Mesh calls for a US style mandatory Sunshine Payment Act. We believe it is unethical that national institutions receive funding from industry. We believe manufacturers provide such funding precisely to obtain influence and/or market their brand. So why else would Ethicon provide funding to RCOG? Our view is that it is highly insensitive to mesh-injured women and unethical. Such funding does nothing to enable our

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rebuilding of trust in an institution that is supposed to, as one of its goals, improve women's healthcare. Sunshine legislation has been enacted elsewhere including the US, Australia and Japan and it's time the UK did the same.

Sling the Mesh has already provided detailed recommendations under specific actions in our written submission to the Review and these still stand. In light of evidence from the oral hearings, we highlight the following: (1) Pelvic mesh to be banned. If not, then it should continue to be paused at least until effective legislative and systemic solutions are in place. (2) A national recall of mesh with women contacted individually so they can give a clear report of their outcomes. (3) Regulated and structured pathway to treatment for mesh-injured women in the small number of accredited mesh removal centres with skilled and experienced surgeons.

(4) Medical device safety and patient harm legislation introduced to balance the scales of justice and allow people to hold device manufacturers to a higher standard of care. (5) Legislation to mandate national institutions to enforce guidance to strengthen transparency and accountability in the health system. (6) Clinical trials evidence should be mandatory for marketing authorisation of implantable devices. (7) Evaluation and regulation of medical devices improved. This should include core outcome sets with the lead being taken by patients not the manufacturers. (8) A MAUDE type database to be mandated and adequately funded.

(9) A legal requirement for mandatory data reporting by surgeons to input all relevant data of all pelvic procedures on a comprehensive national database covering both NHS and private sector. (10) A publicly accessible mesh registry of licence invasive devices with details of marketing status and linked evidence should be created and maintained to interrogate the data for short- and long-term complications. (11) Funding by manufacturers for the externalised cost of adverse event or adverse consequences to device users. (12) A US style Sunshine Payment Act. (13) Effective accountability mechanisms

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developed to ensure all Trusts and surgeons are held accountable for implementation of standards. (14) Informed consent process regulated. (15) Notified bodies to fall within the disclosure regime of the Freedom of Information Act.

In summary, we want to send a clear message to the Secretary of State for Health to take recommendations from this Review very seriously indeed. Ultimately it is for him and his department, along with other relevant institutions who have given evidence in the oral hearings, to examine their collective conscience and put patient safety first. We urge the Secretary of State for Health and all within the health and social care system to make this a national priority,

to work together to review the findings and the recommendations from this Review and publish a full response. A national action plan should then be implemented to coordinate implementation across the multiple responsible organisations.

If this Review's recommendations are not taken seriously and prioritised, then yet more medical implant scandals will emerge in which more people's lives will be ruined as the disaster of pelvic mesh, metal on metal hip and PIP breast implants have very clearly demonstrated.

Finally, to illustrate the life-changing negative impacts of pelvic mesh we want to end this oral hearing with a story of a mother's suicide due to mesh complications that her daughter has shared with Sling the Mesh recently. This tragedy illustrates the hidden cost of pelvic mesh that are devastating to women and their families and are far-reaching.

Many Sling the Mesh members have reported being told their mesh symptoms are all in their head. Many mesh-injured women who are in chronic pain feel suicidal. This appalling lack of recognition, and inappropriate treatment over the last 21 years for women suffering with devastating mesh injuries, and even dying, must stop with this review. We mesh-injured women will keep seeking justice including gender justice until the health system is fixed so that we in turn can all

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be fixed as best we can be. From now on there will be alternative solutions for our sisters, our daughters, all women. Investment in pelvic physiotherapy to reduce the need for surgery and if needed native tissue repair.

Pelvic mesh must be consigned to history.

Jackie Harvey: This is a story of a mesh-injured woman's tragic death as told by her daughter. 'I don't know where to start. My mum had a hysterectomy and subsequently after had three front and back prolapses. She had the mesh operation. In 2005 she took her life on train tracks. Her suicide note included the phrase, 'my operation gave out'. The pieces of the puzzle are now being slotted into place. She could barely walk. She complained about tightness and

pulling. Constantly went back for referrals, even had a repair done privately but the damage was done.

After the operation, it took over her life and she was house-bound. We, my family and I did everything in our power to save her. I am horrified that this has all come to light. I feel very angry. She suffered so badly. It won't bring her back but after her operation, it changed her. She lost so much weight and the shadow of her former self. Tried numerous attempts to take her life, in and out of secure units. No history prior to the operation for mental health. It was like a light went out. Her legs felt heavy and she was in constant pain. Said it was like someone was stabbing her inside her womb.

Tragic we lost her 3 - 4 March 2005. Miss her every second of the day. Only solace is that suicide is the end of the pain for her, but it's been a battle for my siblings and I. Picking up the pieces, you can never really move on. My brother told me about the mesh operation complications a month ago. It's opened up a can of worms in my head. I feel so guilty we could not save her. Now this rears its ugly head. Now that it's come to light, my mum wasn't imagining it. She did not have somatization. That's all the doctors could come up with. She constantly complained how much pain she was in to the doctors, consultants. It was not in her head.

We lost our mother two months before my only child was born. Sixteen years to conceive. Then to lose her just before my son was born. We named him [REDACTED] he's a photocopy of my mum, her traits, her looks, everything. My heart goes out to people having this life sentence, living with the pain on a daily basis. It practically made my mum disabled. Just tragic, that it was practised so loosely like lab rats. She begged me not to have it. I just put it down to paranoia. I feel so bad. Part of me believed her but the medical profession made us believe she had somatization. My mum no longer has a voice, but I sure have one to speak out.

Julia Cumberlege: Well thank you very very much indeed. That was very moving. Very tragic. Terrible for the family [unclear]. But, can I thank you Michelle and Jackie. You've been very clear, and you've done it in the time allotted and thank you because you had to go at some speed. We certainly of course will put that up on the web, so everybody can see what you are proposing. It has been very helpful, very comprehensive and I'll just ask my colleagues if they want to raise any questions. Simon?

Simon Whale: Well I'd echo what Julia said. I think it's very powerful what you said, and very coherent and well-argued and I think you've raised important questions about some of the evidence that we've heard. I think what we pledge to do is to carefully consider what you've said and make sure we reflect on that as we write the report, as we're about to start writing the report. So, thank you.

Julia Cumberlege: Cyril?

Cyril Chantler: That was really very, very good indeed. Thank you. To listen to the 40 hours is a real - so thank you. There's just one question I've got, and it came up actually during the hearings and it may have been with you, I just don't remember. It's the national recall - I think we've thought about, but the trouble is how to do it and we've been actually talking about it already today before you came in. The difficulty is to identify the women who've had the operation because we need to go back quite a long way because we know the complications aren't immediate. But I'm not sure how we can go back 10, 15 years to find the women. Do you have any thoughts about that, how it could be done?

Michelle Moffatt: I don't have any - it's really challenging because of the poor record-keeping. But there are records there but whether you'd be able to get all 127,000 women.

Cyril Chantler: I don't think we could because it's not recorded even necessarily in the notes because women have told us that. They've shown us their notes. We may well be able to do it as has been suggested in relation to one or two hospitals and that would give us some proportionality to the conversation, but anyhow we'll continue to wrestle with it. I just wondered if you had a solution.

Michelle Moffatt: No.

Cyril Chantler: But thank you [unclear].

Michelle Moffatt: But it needs doing.

Cyril Chantler: No, I - and in the future, there's no question and the points you make, it shouldn't be impossible now are well made. Thank you.

Simon Whale: There was one thing I was going to ask as you've got a couple of minutes. One of the recommendations you made in your summary at the end was about - I think I got it right - funding by manufacturers for the external effect of adverse outcomes. Can you just explain a bit about what you mean? Do you mean manufacturers should make payments or...

Michelle Moffatt: Yeah, I mean in other countries, in other European countries, they have a levy, like Norway and so on. So that kind of arrangement where they have to pay a levy and therefore anybody who is damaged or injured by an implant, that the manufacturer must foot the bill not the NHS, or the government.

Simon Whale: Because we know about the Norway scheme.

Michelle Moffatt: Yeah, I've read about it. To me, it's worth exploring that and I think that's feasible surely. I mean the problem we have in this country is that due to our legal system, it's not the same in the States, we can't take to court the manufacturers. We have not got a chance, not a single chance of winning and not even in group litigation. It's just not possible unless legislation was changed. So, it feels very unfair that the manufacturers who are making billions of dollars from harm, from harmful devices, are getting away with murder literally in our view. So, something has to be done about that surely. It's totally immoral in our view.

Julia Cumberlege: Jackie, can I just ask you something because when you spoke, you started off calling for a full ban, and then you talked about it being the third final option. So how are you relating those two things?

Jackie Harvey: Well obviously the ban is what we are really calling for but it certainly - if our voice, if our call is ignored, we just can't - we have to go for the next option which is a third - it has to be the very final last resort. We

won't change our mind about the ban, but we understand that this might not happen. So therefore, we need to be continuing to protect women by suggesting an alternative. In our view obviously at the moment with the new NICE guidelines suggested that was - mesh was on the same level as the other surgeries like the colposuspension and the autologous sling and for us that's just not good enough. We think it should be at the bottom of the pile and obviously preferably not at all. But if it isn't banned permanently, then it would have to be, and our suggestion would be that it is last chance saloon basically.

Michelle Moffatt: Yeah and even if it is last chance, we still have concerns, you know, that we don't trust that you know - so that all doctors can self-regulate because we've - we gave the example that since the pause, we're seeing that - we've seen from the HES data that very small numbers in comparison to before but there's still some doctors evidently inserting mesh during the pause. So, I think even if you have the last resort option, there's still a danger that there will be surgeons slipping through the net in terms of inserting mesh

- because some are very pro mesh and they do not have other skills. They only have the skills to insert mesh. So, their livelihoods are affected. We realise that, but there are medical ethics that they're supposed to adhere to. So, we are concerned that there are - that there is that situation.

Julia Cumberlege: Can I just ask you, looking forward, because that's been part of the remit we've been given. One of the things hearing what you've been saying - and it's been very powerful, I want to say that - what are we going to do about regaining some trust between patients and the medical profession? Because we know there are some very, very good doctors indeed.

Michelle Moffatt: Of course.

Julia Cumberlege: But clearly this has been extremely damaging and for good reasons that you've brought up today to tell us what has happened. But we just sort of want to think of the future because we're always going to need doctors. We're always going to need surgeons. How can we

actually - what we can we do to regain some of the trust that we used to have?

Michelle Moffatt: Well I think that obviously there are lots of very good surgeons and so we're not saying blanketly obviously, but there are obviously a good number of surgeons that are not adhering to the guidelines. So how do we address that? Because they're not being monitored as I mentioned by GMC. They're not being monitored for application of those guidelines, for all - for duty of candour, for all the things that I mentioned. So, I think there's a task that - there needs to be a change - big change there for GMC that they must be empowered to be able to ensure that their guidelines are being implemented across the board. Because it would appear that clinicians have too much autonomy in terms of interpreting guidance.

Julia Cumberlege: All right. Thank you very much indeed for that and for the exposition that you've given us this afternoon and everything else you've done in the past, keeping us informed of what's happening. I just want to say that we've heard a lot from a lot of different people and some of it conflicts and some of it doesn't at all and it strengthens what other people have said. But I think it very unlikely we'll be able to achieve everything everybody wants and so I just - I think perhaps it's wise for me to say that we really don't want expectations to be so unrealistic that our Review will actually not hold some ground. But we think it's going - obviously it's going to be very useful. Right, thank you very much indeed...

Multiple speakers: Thank you.

Julia Cumberlege: ...and thank you for coming.

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Session 3: Mesh UK Charitable Trust*

START OF TRANSCRIPT

Julia Cumberlege: We've been around the country of course visiting a lot of people, listening to a lot of mesh sufferers and their families. We've then had the oral evidence, which - you came last time and gave us oral evidence, and so we've been trying to start always with the patient groups, families first. Then we felt it very appropriate that we should finish the oral hearings, the formal part of our meetings, with again with the patient groups, the families. So this is what we're doing now, and then of course we will then go away and think very deeply about what we've been told and write our report.

So, for the point of view of - and you know the system that we're being screened today and it will go onto our website. So, if formally you could start by saying who you are and why you're here, your organisation, so that it's on the camera so that people will then know the context of this particular session. Is that right?

Candia McCullough: Yes, that's fine, thank you.

Julia Cumberlege: Okay, so if you'd like to start and then Joanne...

Joanne Davies: Are you okay?

Candia McCullough: Yes, I don't know why I'm really like - I think it's warm in here as well. So, my name is Candia McCullough, I'm the founder and trustee of Mesh UK Charitable Trust. We started off as a Facebook group because we were being stifled in secret closed groups. We didn't feel like we could voice what we were going through, like there was a control or something, and I didn't really know what I was doing. I'd never done it before, never had a group before, and I just set up this group because I figured that we needed a platform to be heard and we needed to be a public group. I was very sure of that.

It needs to be a public group but I didn't really know what was going on for me, it was a journey, so I didn't really have definitive answers at that point. But I figured that we needed to all come together somehow and be

able to discuss everything, nothing hidden, everything in the public eye, in real time as well so that you can - anyone can look. Anyone, doesn't need to be members, you can just all look in and see what's going on for members.

Obviously as members join they share their experiences. We're not doing anything.

It's what's happening and we needed to demonstrate that and I think that was really my heart. I think the other thing is, is that because of what we've been through as a family I felt it was important that I helped families in some ways and carers because in my own experience my carers were struggling to help me. I would have my own set of frustrations and it was neither of our faults but we didn't know what we were dealing with, what we had to contend with.

So they were struggling to help me, I was struggling to move. I was in so much pain they didn't understand the pain. The carers didn't understand how the pain medicines weren't helping me. I took them all, they gave them to me regularly. I was on maximum MSTs, Sevredol patches, everything. It was literally all in one go and still in this incredible pain. So I could see how it was like a whole myriad of problems even within my family. My children were witnessing those horrible screams that I showed you last time what I went through, and I don't think that anyone should have to go through that.

I felt that my group wasn't about me, actually, it was about all of us. Because there was something on the other groups, there'd be different groups for different things, like you'd have a sling group, you'd have a hernia group, you'd have - I don't know, I can't think of any others at the moment - vaginal. So everyone was like, is it this, is it that, is it the other? Actually I could really empathise with them all because I found out later that I had all these multiple meshes.

That's how I was able to say that there was a problem with anything like a hernia mesh because I had the big - something there that was put in there to support whatever. Then I found that one of the bladder slings,

so obviously I found on the images that I've got this sling type thing. Then there's one like the whole of the length of the pelvic floor and this is how I was able to understand you know what, everyone is suffering from the mesh. It's not that problem, this problem, it's the mesh.

I knew the group had to be called Mesh UK even though I wanted like a global one I couldn't manage that so it was like Mesh UK. I can handle all that then obviously when I got my records from France suggesting that I had the TOT and several others I really realised that actually - and it was instinct to set up a charity to help families. Because they've been wronged and it's about time that somebody I don't know helped them, help them in a way because it's through understanding.

I don't know what the word is for that but there is something about if you're all in this together and you're all working together you don't have to complain, compare, compete. Everyone understands how bad it is and then hopefully then by doing what we can do we can just give people a bit of a change from the routine of copious amounts of medicines, copious amounts of appointments, copious amounts of people not understanding, because it's not been understood because people are struggling to articulate this.

I think that it's also my duty then to try and make sure that people are being understood, because it was more harrowing not being understood. It was too macabre to go through something like this and not being supported by hospitals or doctors or any of the people that we have trusted to try and get the help that we needed. That's how Mesh UK then became the Charity, which was January last year, 2018, and since then we've done everything we possibly can to try and help raise awareness.

We've created a documentary where we gave a platform - again which we paid for ourselves - a platform again for all mesh-injured people to come together and the whole documentary was totally unscripted. We never scripted anything. Every word is from the heart, and it's what we've been trying to say to people but we've done it in a way that we would create the awareness, so that it can help make people understand

there are actual risks of this surgery as well as the difficulties that we are facing, and also the symptoms.

Whether it's carers, whether it's politicians, whether it's educators, or whoever. At the end of the day this is happening and the fact that it's unscripted is magical because there was no editing, it was so easy. It was so easy to bring them together because it was the truth. Does that make sense? I can't think off the top - oh yes, we've got...

Joanne Davies: You wanted to say about what we provide from the charity.

Candia McCullough: Oh yes, so from the charity we provide respite breaks. They're only three-, four-day breaks but I'm very realistic about how much money I can actually try and raise myself to send families away and it's not easy.

Joanne Davies: We're sending our first...

Candia McCullough: Our first family away, yes...

[Over speaking]

Joanne Davies: ...away next week.

Candia McCullough: Next month.

Joanne Davies: Next month, yes, sorry.

Candia McCullough: So it's like less than a month we get to send our first family away.

We got a GP referral which is excellent because obviously we never thought we'd really see that day happen but actually it's happened, so I'm really pleased. The whole myriad of symptoms came through about what this person was suffering. She was unknown to me. She's on the group but I've never really chatted to her.

She said to me, I've got two boys, they're teenagers now, I have a daughter, she was at home, she's moved away, got a child. I said, I tell you what, why don't you - because I said I know how this works with families and mesh and everything else. Why don't you include your daughter because I know she helped you with your boys? Why don't we

send you all away and she's got her own baby so it's like the first grandchild's holiday. A little respite, a change from the norm, and it's something that means something to her that she can travel to.

So she's chosen it, she's thought about it, we've discussed it. We're meeting the needs of people. It doesn't matter how small it is, we're making a difference I feel so, yes...

Joanne Davies: A big difference I think because I don't think people realise how important respite breaks are.

Candia McCullough: Oh my gosh, they're...

[Over speaking]

Joanne Davies: I don't think patients appreciate them until they've actually had one.

Candia McCullough: I know that because when I had my spine surgery two years after implant because my whole spine was just - I couldn't hardly walk after this thing where the spine [unclear] two years. I remember asking social services is there something where I perhaps can have a little bit of help and support so that whether I can't walk after my spine surgery if I could have something that could help. I just knew that that would be valuable then and that's why I've put everything through experience into what we do now. So, yes, I can't wait until they come back with their happy snaps.

But obviously even since then I think we were at 20 something mark for suicides. It's not something we promote that we do but for some reason because we've all been through it and we've got that experience of how we feel the numbers have sadly increased. I think we were at 48, 49, I lost track of my own experience - sorry, I got held up in my own so I did lose count. But I think it's 48 but I might be wrong, it might be 49...

Joanne Davies: Forty-eight suicide calls.

Candia McCullough: Okay, I would like to tell you about that and I think that's how I can help people with understanding. So the most recent one I'm going to tell you about and then come back to maybe my own. Joanne was the person who took the call thank God. The person I'm talking about has two small

children. She tried to hang herself and I have to have that on my heart and I'm not trained.

Joanne Davies: Can I continue while Candia pulls herself together...

Julia Cumberlege: Of course.

Joanne Davies: ...because we are fairly restricted for time? My name is Joanne Davies, I'm a Trustee for Mesh UK Charitable Trust, and my expertise is medical devices. Don't make me cry again. I've been consulting in industry for almost 20 years. I qualified at university in 1998 in Cardiff as a mechanical engineer in product design and manufacture. I have a history of relevant continuous professional development that includes practical training in surgical techniques.

I have personally created, compiled, and submitted marketing applications in more than 85 countries with a 100 per cent success rate. These devices include every device class from lasers to intracranial pressure monitors to linear accelerators and multi-leaf collimators. I've gained a wealth of experience and insight at every level in manufacturing and that includes the pharmaceutical and medical devices industry.

I've been hired by NHS Blood and Transplant Headquarters to audit their systems, and part of my work there included the interpretation and communication of compliance regulations to 32 UK satellite teams. It's also something I currently do on a daily basis. I've recently achieved verified professional qualifications in medicine as a patient healthcare coach to help Mesh UK Charitable Trust members.

I'm not aware of any conflicts of interest that I may have and am recognised across the world for my professionalism and integrity. If there is anything I say that isn't clear I'm happy for anyone to interrupt on anything.

Julia Cumberlege: Okay.

Joanne Davies: First of all, I'd like to say and put something in your mind, babies and people grow, plastic doesn't. I'm sure we all agree that the Review must be fact based but you may wish to re-evaluate the professional

authoritative and media evidence supplied to the Review so far. Due to time constraints I'm unable to highlight all

the inaccuracies that don't align with regulation. I've sent some to you already, but I'll give some significant examples.

The Permanent Secretary for the MHRA has claimed certain records don't actually exist but they do exist, as I believe I stated last November. These exist in the form of purchase orders, invoices, kitting lists, theatre records, audit reports, quantity records et cetera. These may not have a trail that leads directly to patients where they've been deceived but these documents will reveal to an extent the scale of the problem.

You may wish to question how NHS staff complete so much paperwork related to surgical procedures but cannot produce the critical evidence which is patient records and the scale of the use of mesh. I'll put it to you that these documents can be retrieved from the supply chain already as they are not protected by Article 20, which is the confidentiality clause within the directives. Even when I worked in the NHS in 2007, the *Data Protection Act 1998* was being used to justify them not creating database records.

However, quality management systems mandated these records and the *Data Protection Act* just specified how they should have been kept. Regrettably the introduction of the *Data Protection Act 2018* did not result in any improvement in the situation. When marketing a device it's mandatory for the manufacturer to consider the user's training - oh, sorry, I've skipped a paragraph there.

According to the Permanent Secretary, the safety of devices relies on the interaction of the user and the skill of the person using the product but this is actually controlled by the manufacturer. When marketing a device it's mandatory for the manufacturer to consider the user's training, ability, qualifications, or even any disability they may have, to ensure the device isn't rendered unsafe through reasonably foreseeable misuse.

You can find this evidence in the manufacturer's risk analysis, every technical document. It's also summarised in their CE mark application

and risk management report. This documentation is freely available within the supply chain and the requirements as laid down in law. When the CMO of England, Dame Sally Davis, was asked about post-market surveillance she had very little idea, which reminded me that until 2012 I was relying as part of my post-market surveillance for my clients on the MHRA's post-market surveillance reports, which were produced several times a year.

Then at one point I realised they weren't there and I contacted them and I said, where are your reports, I rely on them? They said, oh, we're running a bit late, we've decided to do them less often so they're going to be done - I think they've reduced them to twice a year or maybe once a year instead, but they would be ready by the February, so after the February came and there they were, the reports.

But then when I went to find them in 2012 all of a sudden they've disappeared so I contacted them and said, where are the reports I've been relying on? They said, we don't know what you're talking about. Now the evidence of this will exist all over the world because people have taken my records and used them in their marketing applications, so those documents that the MHRA is saying doesn't exist are referencing documents all over the world.

Other evidence has suggested that devices are brought to market based on substantial equivalence alone. This is not true, as every device needs safety and efficacy data according to applicable regulation. Excuse me, I've got a bit of a defect myself and a speech problem. Carl Heneghan informed the Review that a US FDA drug licence allows you to market any drugs anywhere in the world. This is also not true according to EC and UK law and US law and most other countries. This type of information, left sitting in the public domain is misleading, which could lead to serious consequences.

When I looked deeper I found more and more inaccuracies in UK GOV documents including scientific reports by expert committees. I understand the source of evidence gathered is from someone who says his qualifications include trying to get his head around regulations for

three or four years but strangely in an area that doesn't exist for devices. The same person is also presented as an expert witness on devices in the same document.

I tried to contact him by telephone in about 2012 when the post-market surveillance records went missing, and I'd seen a lot of information in the media that was inaccurate to discuss as I wanted to help but he was unresponsive. Some references about devices in Hansard contain inaccuracies and I submit that this conflicts with the ministerial code. Mesh UK Charitable Trust has approached both Hansard and the politician who presented these inaccuracies but we've had no response as far as I'm aware.

These errors still haven't been corrected.

The media tells many sensational stories and one is that the medicines regulations are more stringent than those for devices, yet they are not. There are a different set of rules for different products for very valid reasons. What I find most perplexing is when I disclose facts on online platforms they appear not long after in mainstream media stories but they're written without knowledge or understanding, and I've not seen one media article that's factual.

A witness has said that all mesh isn't the same device type due to patents but this is also incorrect. The patent system has nothing to do with differences in devices and the regulation of devices and it's not concerned with their safety, efficacy, classification et cetera.

It's about intellectual property rights.

Candia McCullough: Can I just say something? Obviously if the doctors are believing it's about patents I'm concerned because obviously they'll be using that as a loophole. They've got this patent and they show it to the manufacturer and then try and find a way to get it onto the market. I'm concerned because I'm a lay person and I just wonder if the doctors generally believe it's about patents.

Joanne Davies: Please ask them about it because a lot of clinicians - if you go into the patent databases a lot of patents are bought by clinicians. The Baroness

Julia Cumberlege asked John Wilkinson in one of the oral hearings, what does manufacturer's evidence show with regards to the safety and efficacy of mesh currently? Is that correct?

Julia Cumberlege: Yes.

Joanne Davies: Yes, he didn't answer this question acceptably. The law requires manufacturer's evidence to illustrate safety and efficacy in their documentation for a device to be legally CE marked. But as I've illustrated in my written evidence, such evidence cannot exist so it's difficult to understand how the MHRA's review of mesh could possibly have - it succeeded as claimed. The MHRA should have a record of this review that can be produced in evidence. Jeremy Hunt specified vaginal mesh as part of this Review. The terms of the Review also includes pelvic mesh. I've asked the Review team for clarification but I've not received any and this clarification is still needed.

Candia McCullough: Can I add something? The reason for that is it's been very hard to know how to help give you the information you need to make a fully informed decision in your report, so there is a lot more work still that we need to do to try and help you ascertain that information.

Joanne Davies: So, as far as I'm aware, we have two types of mesh. We have mesh that is intended to strengthen tissue or bone, and I believe this was brought to market as being substantially equivalent to sutures. Because I've read in one of the manufacturer's IFU's that sutures are safe so let's make the mesh out of the same material as sutures. But what they didn't consider was a suture is not substantially equivalent to permanent implant. A suture only stays in the body for a short space of time, the implant stays there forever. So they're not substantially equivalent.

But now all of a sudden we have a different mesh device. It's not a tissue or bone strengthener, it's become an organ holder which will raise that device to a Class 3. So we've got the surgical mesh, the skin strengthener which is a 2B, and now we've got the organ holder which is a Class 3. But I believe they've also moved the skin strengthener up to a Class 3, which is not right. They've based the classification of devices on the vulnerability of the human body. So if we manufacture a plaster and put it on here it's

Class 1, but if you want to put it inside your body forever it's a 2B, and if I put it inside your heart it's a Class 3. Does that make sense?

Candia McCullough: Well the other thing I remember you teaching me was this mesh was never meant to be used as an organ holder. That's a fact isn't it?

Joanne Davies: Yes, mesh has been brought to market as a strengthener - I don't know what the predicate is for organ holders. Where is the predicate for organ holders? I think that needs to be asked. I wonder whether it was brought in by clinicians as an in-house design which hasn't been through the CE marking process, or whether it's a piece of mesh that is being used off-label. I haven't heard these things coming up in the evidence at all.

I'd like to ask you all if you have any questions at all on the evidence I have submitted because I believe it tells you that these devices shouldn't be on the market. I'd like you to challenge me in anything that I've said because I won't tell you anything that is not factual. If I don't know something I will tell you I don't know. If I know I will tell you or if I know where it is I can tell you where it is or I'll go find out. So is there anything that I've told you that you think you can challenge or anyone would like to challenge?

Julia Cumberlege: Well I have to say, Joanne, quite rightly you've been at some speed to get through all this. So I think what we need to do is to look at the results on - when it's screened on the website and all the rest of it, and we've had people here taking notes, then we can go away and think about it and come back to you.

Joanne Davies: Okay, yes, so it's fairly rushed isn't it and very... [Over speaking]

Julia Cumberlege: ...it's fine at the time but we can then come back to you.

Joanne Davies: ...and Candia can talk for England. Is there anything you need to determine your decision on the safety and efficacy of mesh implants because for a device to be certified safe and effective it can't be safe, effective, and harmful?

Julia Cumberlege: Well we've heard a lot of evidence from a lot of different people. So I think a lot of what you've been telling us is quite similar to what we've heard from others, not all of it, and so it's been very useful for some of the points that you've made this afternoon. But certainly when you were talking about the different criteria, the A to C and all the - how that was all done, that's all been in the BMJ and we've read that.

Joanne Davies: Yes.

[Over speaking]

Julia Cumberlege: Yes, come on.

Valerie Brasse: Yes, just to say that obviously we're at this point now where we're coming to the end of our oral hearings . As you can imagine we have a huge amount of evidence that has now come to us, and our job as a team is going to be to sift through all of that, to look where there is consistency, where there are differences. We will want to explore that and it may well be that when I've gone through that or the team has gone through all of that and we say, okay, we have an issue here and this doesn't reconcile, we may well be coming back to people and in fact to the patient groups and saying, can you help us with this?

So, as you can imagine, as we're going along we're working - reading all this evidence that that process is about to begin when we finish the oral hearings. There's a very clear next phase where we begin to analyse everything, and I mean everything that we have received. There will no doubt be times where we have to say, there is an inconsistency here and maybe we should ask and we need to go back to others. So you won't be hearing anything from us, we will be back asking our questions.

Joanne Davies: Okay, there's another issue with the mesh. It's acting like a medicine on the human body. Devices don't do that. If you sit in a wheelchair it doesn't do anything to you, yes, and devices aren't supposed to do that. I mean really what mesh is doing and it should be in the medicines classification because of the way it's acting on the human body and we can't have both can we? It's either a device or a medicine.

Cyril Chantler: What about a heart valve?

Joanne Davies: A heart valve is a device.

Cyril Chantler: But it's acting on the human body.

Joanne Davies: No, it's - you shouldn't be having any adverse effects on the human body like nerve pain and...

Cyril Chantler: No, not adverse effects but it is bio-compatible with the human body.

Joanne Davies: It should be bio-compatible, yes.

Cyril Chantler: That's right.

Joanne Davies: Yes.

Cyril Chantler: So in that sense mesh may or may not be bio-compatible, that's one of the things to discuss. However, it's made of biological material or plastic material, an artificial material and it's inside the body. So I don't quite understand the difference between the device...

[Over speaking]

Cyril Chantler: ...I happen to have a heart valve made of cow pericardial.

Joanne Davies: Made of...

Cyril Chantler: Cow pericardial.

Joanne Davies: I haven't come across that material.

Cyril Chantler: Well it's from a cow.

Joanne Davies: A cow. Oh gosh, yes, I have come across that, I've looked it up myself a few weeks ago, yes. They're not bio-compatible actually.

Cyril Chantler: Well mine has been there quite a while.

Candia McCullough: Just as a comparison as I understand it as a lay person, there's a difference.

Cyril Chantler: I know, I'm not discussing that.

Candia McCullough: Yes.

Cyril Chantler: I'm just trying to understand the difference you're making here...

[Over speaking]

Cyril Chantler: ...we're not discussing whether they're good or bad that's...

[Over speaking]

Candia McCullough: ...no, it wasn't like I was suggesting...

Joanne Davies: ...I don't think I've been given enough opportunity to explain this and would it be better to write it? I can write it...

[Over speaking]

Cyril Chantler: That really would...

Sonia Macleod:: ...probably then we can get more detail, and a really thorough understanding, that would help.

Cyril Chantler: That really would help I would think.

Joanne Davies: I don't believe that anybody has presented any evidence to illustrate the efficacy and safety of surgical mesh, Primodos or valproate. I don't believe that you have evidence to review this. We have a process when we're bringing products to market and we haven't - I don't think you can pinpoint where the process has gone wrong. When we - even before devices are manufactured you have a materials manufacturer and he's got legal requirements as well.

So if I'm going to buy material from a manufacturer it's going to have to have a material safety status sheet and that is governed by a directive. He has to follow that directive and on his material safety data sheet it should say it's not to be used in the human body. So when a manufacturer buys that material in, did the system fail there because it didn't say that on the sheet? Or did it say it can be used in the human body, because someone

has made a mistake somewhere along the line and we need to pinpoint that mistake?

I've noticed as well in the oral hearings you've been asking people what they thought about the new regulations. They're absolutely awful and they stifle innovation. I was speaking to a manufacturer last night who has explained to me he's got 26 substantially equivalent devices. So these are syringes, 26 syringes, they all do exactly the same thing, they're made of exactly the same material but he's now being told that rather than have one clinical evaluation for all 26 he needs 26 of them.

Now these 26 have been sent out for Indian people to write, they've been reviewed by Polish people, and he's had them back and they've told him to sign them. He says, I can't sign them, I need to review them first. He's reviewed them and they're incorrect. This is how it's going to stifle industry. I don't think that when we leave the European Economic area we should be applying those regulations and using the notified body system. I think it's dangerous.

Valerie Brasse: What would you say we should do?

Joanne Davies: I think we need a new system and I think it should be built up from the 1993 42 EEC regulations, and just to make sure they are actually applied in their entirety because there's nothing wrong with them. We do have safe and effective devices on the market and most of them in fact are. The media stories on hundreds and thousands of adverse events, reporting things in [unclear] and all the other systems in the world is totally out of - what's the word?

Candia McCullough: It doesn't do anything does it?

Joanne Davies: It doesn't do anything. I could make a batch of 1000 needles and send them out and then realise oh no, I need to bring them back and do something so I'll report that as a matter of course. It doesn't mean thousands of devices have harmed people, it means I've just done my job to keep people safe. So it really does exaggerate things and that's not the way things are. I've noticed as well that we've put in medical doctors in the new regulations as being able to do my job.

They're not employers and I appreciate doctors but I actually asked a doctor to write a clinical evaluation for a client and it was like an eBay review. The doctor said it was nice, it felt nice, it looked nice. But we're not looking for that, we're looking for safety and efficacy and it really was a waste of a few hundred pounds.

Yes, I think that is a huge problem.

Sonia Macleod:: So I mean you're advocating really a return to the new approach and much more engineering based.

Joanne Davies: It is engineering isn't it?

Sonia Macleod: The approach [unclear] and strong...

[Over speaking]

Joanne Davies: Yes, it needs engineers and I don't mean biomedical science engineers, I mean engineers, mechanical engineers, electrical engineers.

Julia Cumberlege: You're saying that's relevant to mesh.

Joanne Davies: I'm saying it is relevant to mesh, yes.

[Over speaking]

Joanne Davies: Certainly all medical devices...

[Over speaking]

Joanne Davies: I'm not saying that a doctor can't be an engineer or an engineer can't be a doctor but you do need the correct training...

[Over speaking]

Joanne Davies: Manufacturers are having these certifications pulled, not through their incompetence but through the medical doctors' incompetence. They're coming out to do audits and they're telling you to do things that are incorrect and they don't align with regulation either.

Candia McCullough: I think the thing is how I see it is there seems to be a lot of clinicians in this whole medical mesh device - whatever you want to call it, and there doesn't seem to be the other people in it to make a balanced - does that make sense? So it's very weighted on clinicians and what they want for the needs of the business not necessarily - they might mean well but it's no balance for thought, and like engineers they'll think things through properly, they'll do it mathematically.

I think that's what I've seen even when I went to the MHRA. I was talking to clinicians and I also remember in that conversation as well they were quite happy to talk to me but they shushed her. I thought this was strange because it has to be a conversation for all of us. It's about all of us isn't it? The other thing that caused me concern and back to your earlier point was about the effects of the MHRA in Europe.

I know I mentioned that when [REDACTED]. Because if they've implemented the new regulations across Europe it is a grave concern for everybody so we do need to do something with it. Obviously I can't, she's your lady you know.

Joanne Davies: We're short of time, you need to say what you want for the patient. Candia McCullough: [Unclear] Have you got [unclear]?

Joanne Davies: We're ten to five.

Candia McCullough: Are we all right for time if we go a little bit over? Julia

Cumberlege: We've still got some time, yes.

Joanne Davies: I've still got loads to go through and I know you have as well.

Candia McCullough: She's regulations based, she's replying back to that.

Joanne Davies: [REDACTED]
[REDACTED]
[REDACTED]

[REDACTED]

Julia Cumberlege: The permanent secretary is accountable for the work of the MHRA...

[Over speaking]

Candia McCullough: He is accountable, thank you. We've got to take steps, we can't let this get in Europe and we just find it too much.

Joanne Davies: Do you know it's taken me until this week to find out who is in charge of the MHRA?

Candia McCullough: Well I thought I was talking to the right person... [Over speaking]

Joanne Davies: It's only because of this Review and I feel things like this need to be addressed as well so that when we look to the UK Government we can see a clear organisational structure and we can see who is actually accountable. Because if I could have found the permanent secretary in late 2000 I could have - sorry, not 2000 in about 2007, 2008, 2009, I could have been calling out to them then saying, hello, something is going wrong and I have not been able to do that.

Julia Cumberlege: Well we asked him specifically this question and the answer was that he is accountable for the work of the MHRA.

Candia McCullough: Yes, thank you.

Joanne Davies: Thank you. Shall I continue?

Candia McCullough: Yes, I think you've got a lot to get through and we need the information.

[Over speaking]

Joanne Davies: Jeremy Hunt stated that in many ways our regulatory system is world leading and I can assure you it isn't. When I started working in the industry the Medicines and Healthcare Products Regulatory Agency wasn't in existence. I relied on superior assistance such as US Food and Drug Administration to help me. The FDA helps and engages in global industry immensely. When the MHRA did materialise, the systems were weak in comparison to most of the rest of the world and still are today.

So I was trying to articulate the sort of problems that we go through. Do you mind if I just flip through?

So from the head, migraine, cluster headaches, sensitive scalp, under scalp thickened, can't wear my hair up, can't have hairbands, can't stand to have it brushed. Cognitive malfunctions, pathways for communication internally and externally are compromised. My ears - hyperacusis, sensitivities to noise that I can go from deaf to not being able to bear any noise at all and sometimes I can't hear at all.

I can't explain why I have these fluctuations. Swellings to the face, spasms to both sides of the face, numbness, tingling, especially below the mouth, pain in the cheek muscles from spasms. When they spasm they get so painful there's nothing that shakes it.

They're just - there's nothing that helps. Eyes - twitching involuntary, visual disturbances, central, peripheral, hypnagogic hallucinations, ORL showed that I was off balance.

I can't remember what it is 13 degrees off balance which shows that your core stability - it's your core stability this test was done. So it absolutely affects everything to do with your pelvic - absolutely. Stabbing pains, red eyes, very wet, overly wet, eyes struggle to move to positions. They get stuck and you can't move them. You can move your head but they get stuck - what's that? Pain also accompanying it, when I look up and to one side, so I was struggling to try and - anyway it got stuck.

There could be an overwhelming pressure behind the eyes, very, very painful. Nose - swollen, very sore to touch, redness comes and goes but it's relieved if I don't wear my glasses so it's all to do with the pressure of the glasses. Nasal drips, it hurts to breathe sometimes. Mouth - tongue swells causing slurred speech so people don't understand me. It goes blue to purple tinge, pain spasms and recesses right back to the point of nearly swallowing, which can last for hours, daily, every day.

Dribbling, breathlessness, slow tongue movement, dribbling, don't feel right, [unclear] affects drinking and eating too. Throat - redness externally, regularly sore throats, throat enlarges, sensitivities, difficult

swallowing and reflux. Shoulders - due to the falls because I was having falls, damage to the shoulder which has resulted in restricted movement. Sensitivity to pain particularly in this area where it makes them become rigid mostly on my right side though.

Arms - affected by shoulders and it feels like my bones are on fire, the lower right arm stabbing nerve pain, numbness, tingling, mostly left side but it affects right side too. I have involuntary movements like I can throw sugar and I didn't want to throw my sugar, I wanted to put my sugar in my cup, things like that, tremors, unsteadiness, and weakening sensation of strength. Sensitivities to food et cetera, difficulties with skin like severe hives.

Had breast pain, this doesn't - and this is probably the arms and wearing bras and then it affects your breast and the pain is so immense within your breast. I've been undergoing yearly mammograms for both. What was found in the mammograms was white matter AKA known as white mice. Hands - swelling, tightness, clawing where you're clawing up and there's nothing you can do, puffiness between the joints, reddening, thickening of palms, dyshidrosis, reduced sensations affecting grip, sensitive to cold, heat, cognitively I have accidents.

I do not register how something hot is - how hot it is, joint pain in wrists and affecting all hands. Ectopic type heartbeats which can be - [unclear] mentioning ectopic because I don't really know what that means even to this day. No treatment suitable. Diagnosed when pregnant and then I had to have a termination for that, so is it me or is it the fact that I'm sick?

Chest pains, shallow breathing, do not feel oxygenated, shortness of breath with little or no exertion, constriction around the chest.

Stomach - spasms, feels twisted, always feeling nauseous, rigidity in the stomach, extreme discomfort, have a sensation that something is pushing my ribs out to a point of breaking. It felt like this was enlarging and pushing my ribs right out. Bowels - spasms, excruciating pains, stabbings, slow and skewering pains, lower left side twitching, pulsing

sensation, rectum coming from lower [unclear], rectal bleeding, severe diarrhoea or severe retention, loss of sensation and throbbing.

I struggle to get to the toilet as my muscle sphincter is weakened and incontinence occurs. More recently though dairy - and this is not on here but I've added it as a note - having dairy and becoming allergic to dairy. What it is does with the mesh in situ the bowel then purges [makes a noise]. Imagine something sharp while your bowel is doing that, you just want to die, you don't want to live through that. That's what dairy does to me now. So obviously that was what was happening then, this is what's happening now.

Hips - hyper joint mobility, grinding pain in sacroiliac joint, feels like grit in the joints, feels like going to dislocate, excruciatingly painful. Genitals - photos available. As I've demonstrated before angry red connective tissue perhaps, prolapse visible, there seems to be a prolapse. Imagine that, that's what I reported back then in the [initial] tribunal, cause unknown, present to communicate, been left with a leakage, question mark, fistula I put in.

I have an acid loss and smells bad at times. The hysterectomy was a natural route, they've fixed a prolapse to whatever that meant because I didn't even know if they've fixed a bowel, bladder. I didn't know all of these things. This is just for this tribunal. I have an acid loss that smells bad at times. I went swimming this one time and - because I was told to go swimming, I should go swimming, I should do something that's positive to help myself.

Went swimming and as I went swimming I didn't feel very well but I pushed myself, I wanted to do it.

It was just gentle, it was a not very deep pool. So when I came out of the water I managed to get myself in the shower to wash off.

Going out for the evening meal three hours later after that swimming hot acid chlorine smelling came out in a gush from my inside of my body and it came through my vagina, down my leg all the way almost to the

ankle. So obviously the chlorine had got in and I questioned this with my doctor.

I said, is this osmosis, because I remember it from school when I was studying science or biology or whatever, could osmosis have occurred where the pool water would go into the vagina? I said, I've not had that before. No, don't be so silly, ridiculous, go away. I did not know I had mesh. It's important to note because these are not things that have been written before. Also contracted hospital virus three times, I was very poorly. No bacteria present at last swab, under gynaecologists.

Bed sores [unclear] occurring since over one year, further difficulties with swollen glands, groin nerve pain. That we know now is exit wounds from the product. Legs - loss of sensation, numbness, tingling, spasticity and restless leg, bones in upper legs on fire, searing pain, legs giving away for no reason to my mind at the time causing falls. [Unclear], involuntary movements in right leg.

Feet - cramped, loss of sensation, feels like toes aren't there, and cannot feel left foot more than I can with my right foot. Again spasticity and then we go into walking. Weakness, vision - I'm going to skip a lot of it just to give you a better idea of what's going on. Cognitive, falls, bladder and bowel, sexual problems, ruined our marriage. Spine, skin, and then several diagnoses I will read that.

Over a period of time severe chronic fatigue, ME type thing, fibromyalgia, chronic widespread pain, arthritis, query Von Willebrand disease because my blood wasn't clotting properly so they wondered if I had that. Luckily it got ruled out but it shows you it was affecting our blood. IBS, diverticulitis, chronic stomach and abdominal pain, bowel and bladder incontinence, post-operative amnesia, relentless fatigue leading to pain seizures, shortness of breath with little or no exertion.

Fistula spasticity [unclear], all of these are diagnoses, hypermobility, muscular dystrophy, adenomyosis was the start of all of this, angioedema with urticaria, dyshidrosis, sleep apnoea, [unclear] through dehydrated at the last MRI on my spine, previous x rays show scoliosis, hyperthyroidism,

obesity through lack of mobility, sensitive to foods, light, sounds, et cetera.

As you can see there is a great deal of - mentally to contend with just to name a few that I can recall. Best I can do with assistance for now, chronic lower back, and basically I worked up until this - this is what I was saying and I wasn't allowed to continue, no job suitable from me from the hereon in. So people in my life, I've wrote a whole list, all the medical people that were in there, there was quite a few at the time. Then there were other people that I looked to to try and get myself some help at the same time.

Joanne Davies: The ultrasounds.

Candia McCullough: Yes, the ultrasound scans. We want to talk about scans don't we?

Joanne Davies: People are saying that they're going for ultrasound scans and sometimes it detects the mesh, sometimes it doesn't. I've asked the surgeons on Twitter to go and check the frequency of the ultrasound scans. Because the way the ultrasound works is you've got a sound wave that goes and it hits something and you're going to get a different reading if it hits something hard, and maybe it's a piece of metal or a piece of wood the reading is going to be different.

So when you've got a piece of plastic in the human body it might be soft when it goes in, it might be like a crisp eventually and that may explain why some women who are going for scans and sometimes the mesh is showing and sometimes it isn't. I wanted to make that point.

Candia McCullough: When we went to that event though, I met with a radiologist and he explained to me because he does the scanning and he's freelance and he explained it to me. Basically the soundwaves or whatever hits the mesh and it can explain that there's mesh there and it might look like it's fine but it doesn't go beyond that to show what damage is occurring the other side, which I thought was very fascinating to hear that.

Joanne Davies: I also wanted to ask why people like notified bodies, manufacturers, organisations such as TOPRA haven't been involved in this Review, or

have they been involved in this Review? Because I haven't seen - because they are all part of this - well TOPRA is not part of the system but they are - they do have professionals working for them. I've been to some of their training sessions and you can't fault what they do. Whereas I've been to other training sessions and you just know that what they're putting into the public domain is misinformation. I've never heard misinformation coming from TOPRA. I think they teach the devices course in - oh gosh, I can't remember the name, my memory is dreadful. That's why I do this job because everything is always there for me, and I go back to it. But they do a Masters' degree in devices and I've been on one of their courses. They are excellent and you may wish to approach them.

Julia Cumberlege: Joanne, perhaps you could write to us on that.

Joanne Davies: Yes, yes, definitely.

[Over speaking]

Joanne Davies: With another issue that patients have asked me to raise, they're having mesh implanted with staples and things that are being left in. When staples are regulated they don't go under the same regulations as other medical devices, they're low, they go in, they take them out, they throw them away. I believe that these things are being left in them as implants and they need to be regulated as implants and not disposal staples. Another thing I don't think is happening is, are these staples being tested with the mesh because that is a legal requirement as well?

Candia McCullough: Do you remember last time I showed you a piece of mesh that we brought in? So we took images of [unclear].

Joanne Davies: That's what I passed over there. Some of these also said in their evidence that the mesh doesn't migrate and break off, and these are blown up images of the mesh that we have that actually shows the filament and we have one screen shot with it blown up so you can see it more clearly, which looks like a hair but you would not see that with the human eye.

Julia Cumberlege: Thanks very much. I have to say I'm afraid we are now coming to the end. So if there are final comments you want to make now is your moment.

Candia McCullough: Yes, I've got something to read here. I'm going to read it, paraphrase as it's been passed to me. We've mentioned on several occasions that an increasing number of cases are coming to light where the use of mesh in hernia and similar surgery has resulted in serious chronic pain and related issues. A member of our group was recently seen by one of the UK's top specialist in peripheral nerve injuries and the initial remarks made by the surgeon are very significant.

He said that 30 per cent of hernia repairs using mesh have unsatisfactory outcomes varying from minor discomfort to disabling pain. This of course is a far higher proportion than we had previously believed to be the case. He went on to explain that the team were reluctant to accept referrals because of such cases because if they accepted all such referrals they would never get time to treat any other patients.

In other words, those patients are still not receiving any care. What this fundamentally means is that limiting the scope of the Review as you have over half the damage and suffering caused by mesh has been excluded. If you are still precluded from including

it then we would ask for the safer, fairness, and balance, the extent of these cases be at least mentioned in your final report, and the urgent need for a similar review into the harm done in the cases made abundantly clear. I have something else that I'd like to say.

Joanne Davies: Can I make my final point if you don't mind? The regulations reported in 1993, we have problems the MHRA isn't listening, they're not removing mesh. We shouldn't be in a review, we should be following the regulations which are meant to deal with what's happening. So if we can't get mesh removed from the market by the MHRA where do we go? I want amalgam taken off the market as well so where do we go because we're at a loss, or do I approach the permanent secretary with this question?

Julia Cumberlege: This is a question to try and ban mesh is that what you're saying?

Joanne Davies: To get mesh off the market, yes.

Julia Cumberlege: Well [unclear].

Sonia Macleod: Well that would fall under the European Regulatory regime because of the way they are regulated, and therefore in terms of you would need I would guess - I mean only for the individual mesh product or mesh as a class.

Joanne Davies: Sorry.

Sonia Macleod: Are you talking individual mesh products or mesh as a total class?

Joanne Davies: I don't understand what you're saying.

Sonia Macleod: Are you talking about a particular mesh kit or are you talking about every single mesh product?

Joanne Davies: I'm talking about surgical mesh used as scaffold, that is one type of mesh and I'm talking about the ones they're using as organ holders which I don't know what that would be in - well it's to hold up an organ, that's the intended use, to get those off the market and amalgam. Last time I was here I mentioned that amalgam will be next and it was only last night I checked and I think about seven years ago they've started the mass claims in America for amalgam.

Now the regulations say that we don't use anything if a safer alternative exists and it does and I think it's important that that comes off the market. So where do I go because the MHRA isn't helping us and it's why we're here?

Sonia Macleod: Well we certainly - amalgam is not within our scope.

[Over speaking]

Sonia Macleod: Because we can't help with that.

Joanne Davies: All right. So where do we go?

Candia McCullough: I just wanted to say something before we do all sort of go and tie up, so I went for MRIs and I'll have to send you these images probably to upload to the thingy, your thing later. So that is mesh that's around the bladder

neck. I don't know if you can see that from there and you can see it's quite clearly - it's twisted and that was done with gadolinium in a local hospital close to me. The other one was when you see that you can see there's something that's not anatomically correct all along the pelvic floor at all.

You can see that it's like a strange shape there that doesn't match any organ within the human body, compared to when I went to France for a scan they did a gel with gadolinium enhance, they injected it into the vagina there and you can see it is flagging up something that's not anatomically correct as well. So that was what I wanted to show you because it's important. There are little bits of information I wanted to update you very briefly. Since I last saw you something not organic tore through my belly button and that's taken two months to heal.

Every time it heals something cuts through and it's excruciatingly painful, so that's in addition to my other injuries as well. I've found an image that gives you - it's not my image, this next one, I found it online. It's of a fella just so you know it's a guy picture, and what it shows is how his veins and everything are right on an edge. Now underneath my skin even now my legs and everything were all like that, I couldn't hardly move and I was in so much pain and struggling.

You can still feel them in my legs but this was affecting the whole anatomy to the point where I was feeling strangled by something like this that I could feel under the skin, so infections that sort of thing. The other thing I wanted to mention is BAUS have all of these mesh centres on their website, out of them I've crossed off all the ones that I've been to in my journey. So I've been to one, two, three, four, five, there's about five or six that I've been to since these have been on there.

In all of that time I'm still sitting here giving you evidence, telling you we're not being helped. So while it's a wonderful romantic notion that there's all these mesh centres actually I don't believe that they can do anything. Because otherwise I'd be saying, do you know there's a wonderful mesh centre, I've been helped, and they've done their very

best. I haven't found that. I've had two surgeries, one the day before I gave oral evidence, and another one since.

I am a BMI patient, a Nuffield, a Spire Health patient, and an NHS patient and across the globe as well. In all of those instances how come I'm still struggling and still in incredible pain. Do you remember I mentioned about suicide, [REDACTED]

Julia Cumberlege:

Yes.

Candia McCullough: Well, very briefly the pain was so bad as I tried to sit up I witnessed - I've never seen this before, I've witnessed my own suicide from the pain as an instant reaction to the pain. I don't think that way, I'm a very positive person but the pain is so bad you're seeing your - and literally an inch gash there, both sides, tidy - no blood because it didn't happen. It's what you're visualising at the time of pain. It's wrong. It's just all wrong that this is happening and we're not being helped.

I don't think there is such a thing because otherwise I would be sitting here telling you, yes, we've finally got the help, we've got - finally got the understanding. This is another reason why I think a ban should happen because I don't believe that we can be helped otherwise I'd be telling you differently. So thank you for being patient.

Julia Cumberlege:

I'm so sorry. I'm really sorry to hear all about that and how you've suffered and thank you very much Joanne for all the evidence you've given us. If we have any queries we'll come back to you.

Joanne Davies: I would like to hand this in if

that's all right. Julia Cumberlege: Yes.

Joanne Davies:

This is critical. They have just introduced endocrine disruptors as materials that can be used in medical devices. It's a new recommendation defining nano materials and we cannot verify what nano materials do in the human body and this is the next thing that's being brought in with the newer regulations. It's not good enough to add it to the...

[Over speaking]

Julia Cumberlege: I'm afraid we've got to call this to a close now. But thank you very much indeed and thank you all the supporters for coming as well.

Candia McCullough: Thank you.

END OF TRANSCRIPT

22nd May 2019

Session 1: INFACT

START OF TRANSCRIPT

Julia Cumberlege: Good morning, thank you very much indeed for coming today. Thinking about what you've been doing and the importance of INFACT in the way that the service is run, the way that you relate to patients and others, and just thinking that the organisation was launched in 2012, I think, and the purpose was to support families with children whose disabilities were caused by their mothers taking anticonvulsant medication through pregnancy. I have to say; we've heard through other sources that this support is so highly valued and thank you for that. Of course, you also raise awareness with the government and other agencies, and you supply the secretariat for the all-party parliamentary group, again which I know is highly valued.

In addition, of course, you run the association for families, and you've got over 700 families in membership, which is very impressive. In the November oral hearing you covered a number of important themes, and what you hope for the future. You kept us very fully informed of your concerns with the MHRA - with the yellow card system, the lack in the past of patient involvement, how the pregnancy register could be improved, and the personal independence payment and the way it's sometimes denied to people who previously benefitted. Of course, all of that is so important and there's a lot more as well, but perhaps the most crucial of all is the pregnancy prevention programme and how it is not comprehensively working.

So, I know also you've conducted surveys which have been helpful to us, and the case studies that you have supplied. I have to say, they are heart-rending, and thank you for that. Today, though, is different from the first oral hearing. This oral hearing is your opportunity to tell us what you've found in the intervening period, because the first oral hearing was in November, so we are five months on from now, and in the intervening period there's been a lot of information that's been coming through and a lot of views that people have expressed. So, it's up to you now to tell us what particular issues you would like us to consider when writing our report to the Secretary of State. So, if we could start, if you could just say who you are and your position with INFACT.

- Emma Murphy: Okay, I'm Emma Murphy, and I'm managing director of INFACT, and I've got five affected children by valproate.
- Janet Williams: I'm Janet Williams, and I'm the CEO of INFACT/FACSA, I've got two adult affected children.
- Julia Cumberlege: Thank you very much. So, now it's really over to you, whatever you want to tell us.
- Emma Murphy: Okay, so we've watched all the previous oral submissions and we have taken minutes of everything, and we would like to respond today to that. So, in our last submission we explained that at present we have approximately 2,000 people on the database who have been affected physically and/or mentally by valproate, the majority of which have neurodevelopmental disorders and are on the autistic spectrum with poor speech, memory and understanding. A large number of these children are now over the age of 20 years old and continue to require a huge amount of support from their parents.

The excessive stress that valproate sufferers experience to understand the outside world and the circumstances of their actions, in many cases has caused mental problems such as anxiety, depression and seizures. Since that submission, we have attended many meetings with the MHRA, Department of Health, General Pharmaceutical Council, The Royal Pharmaceutical Society, where the conclusions have been a very mixed bag of understanding what the pregnancy prevention programme means, the clear instruction given from it, and what can be done to ensure the new warnings are given.

Almost 12 months from the introduction of the PPP, we still find that some women are not receiving the warnings, whether it be from the pharmacist, GP or specialist. Some have still not been called in to see their GP or epilepsy nurse to discuss the topic, and all this showed in our survey which we presented to the MHRA in February. We have also carefully watched and noted the evidence given to the Review team from NHS England, the GMC, the CQC, MHRA, NICE, The General Pharmaceutical Council and NHS Resolution during which we recognised a number of points we would like to make today.

Firstly, on 28 January, evidence was given by the Royal Pharmaceutical Society where it was stated that, and I quote, 'this has been communicated but most probably not passed down the line or a possibility of it being forgotten about due to cards and booklets left elsewhere in the pharmacy'.

This alone is unacceptable, as we know since April 2018 and the introduction of the PPP, we have been contacted by at least six women who have become pregnant on valproate due to not receiving the information supplied through their pharmacist. We believe the pharmacy should have a set procedure which should be robustly followed, especially when legislation has been changed to ensure women receive the information.

The RPS went on to say in the evidence that not all pharmacists are a member of the professional body. Only half are on the register, so not everyone receives up to date information. There are warning labels that go on the box, the pharmacist would look at them, assess if there is anything that needs to be done, and the valproate warning label would act as a prompt to have that conversation. However, INFACT are now aware that this is not the case. Warning labels in some circumstances failed to be put on all white boxes, and so the pharmacist or pharmacist technician fails to have that discussion.

We are, however, aware that in a couple of areas, the new Sanofi boxes are coming through where there is only 28 tablets in a box in order to eradicate using the white chemist boxes eventually, although we are unsure as to how long it will take for the new boxes to become the norm in all areas within the UK. At our last MHRA VSN meeting, which the Royal Pharmaceutical Society attended, it was explained by them that the dispensing technician was not able to give instructions to patients when dispensing, and that only a dispensing pharmacist was able to do so.

Further information was sought, and we found, according to NHS Health Education England, the difference being that a pharmacist technician prepares medicines and other healthcare products and supply them to patients. They also take an active role in providing patients with guidance on taking medicines. We have since met with the CEO and registrar of The General Pharmaceutical Council who also gave evidence to discuss valproate, and the understanding is that a pharmacist technician was able to give the warnings, and that they were aware that every pharmacist had received the new PPP information of valproate.

However, in his evidence to you he stated that the difference between what standard procedures is to something that happens that afternoon, is that things don't happen the same way on a day to day basis. Although we understand his explanation, the routine a pharmacist has when communication and dispensing a prescription, should be written in

concrete and not rest on the day to day events. The GPC was very accommodating and has offered to involve INFACT and we look forward to working with them in the future. NHS England's evidence we found very sparse and protective of those he was aware had failed women in the past by not informing them of the dangers.

For example, on a number of occasions he said, we should take stock. When asked who should take stock, he answered by saying, that's a good question, implying that even though he had said it, he had no answer as to who should do it. He went on to say, the regulator, MHRA, have put in place the PPP and in the light of that they would expect healthcare professionals to react accordingly. As for pharmacists, the GPC have done everything right. I look at IT systems and flagging, and they have reacted appropriately. Community pharmacists' systems ditto, I'm just wondering if there is more to do.

At no point was it mentioned about how the GP or pharmacists have failed women on the delivery of the PPP, the reasons why this may have happened and what could be done to correct it. On 23 January, the Review team also met with Professor Helen Stokes-Lampard from the Royal College of GPs, and we were very concerned by some of their comments. Although we understand one or two things will be different to deal with due to the current system, some of the comments were not true to life as to what is actually happening during visits to your GP. For example, the RCGP is committed to patient safety and care, developing long-term relationships with our patients.

(2) Good practice states, anybody on long-term medication should be having an annual review of their medication. (3) We have a quality outcomes framework that came into effect in 2004, epilepsy is one of the conditions that is there. (4) If a patient came in and says, I think my child may have an abnormality related to a drug I took in my pregnancy, a GP knows right away that is definitely specialist care. (5) When in medical school, we were all taught pregnancy and epilepsy drugs don't go together. We are aware through our own experiences and that of our families that due to the struggles of getting an appointment with the same clinician repeatedly is near impossible.

That eight out of 10 patients are never called in for annual reviews. The quality outcomes framework from 2004 was withdrawn around 2014 which left female epilepsy patients with no chance of pre-conception counselling. It's only recently that a new quality incentivised framework is

to be introduced. However, INFACT find this insulting that GPs and specialists have to be incentivised before they can give particular warnings to their patients which comes under their job description as they have a duty of care towards their patients to do the task.

We are all aware, too, that a GP would not respond particularly well to a patient who insists that their child has been affected by a drug which they had prescribed, and the specialist referral which should be genetics at this point, is usually avoided by the GP in many circumstances. Our biggest shock was at a comment made by the professor when she stated that while in medical school they were taught that epilepsy drugs and pregnancy did not go together. Of course, we are not sure how long ago that was, but this makes the point that GPs were taught about this problem many years ago, yet still went on to ignore the problem and failed to warn their female patients without having to be literally forced to do so.

How many other GPs and specialists have the belief that the professor has, yet still to this day with the PPP in place, continue to fail to inform? Or were they instructed to ignore this fact by the Department of Health, bearing in mind as in our original submission we stated about the archived documents of 1973 from the Committee of Safety of Medicines. NHS Improvement's evidence was very much the same when it came to patient safety, as they explained how complex the system is when it came to a patient making a complaint about their treatment, stating that the system is somewhat administrative and bureaucratic.

However, when asked about why does the system keep changing, he stated that he thought it was due to the political interest the NHS received and people thinking they could do better and not giving things time to have the impact. But from our understanding of the system through the archive documents, we feel that constant change may well be to save money and cover up the truth about a penniless system and the bad decisions it's made. He went on to say that he agreed with how the serious incident framework hadn't been universally successful, and that there would be a new serious incident safety framework, however it wouldn't be called that.

But only a few more months earlier he stated that he felt change wasn't good, which again seemed a little contradictory. He stated that NHS Improvement had put guidance out to the prescriber concerning valproate in 2017. However, they play no part in the monitoring of the drug as it is not in their remit to do so, with the MHRA dealing with licensing and monitoring and NICE dealing with the guidance. However, on their website

there are study reports into diabetes and pregnancy and smoke-free pregnancies, but nothing whatsoever on epilepsy and pregnancy.

We did, however, do a search to find *Supporting the Safety of Girls and Women Being Treated with Valproate*, even though this was two years old and published before the new PPP was introduced. We noticed while listening to the evidence given by Sanofi that they interact with patient groups. However, on 12 October INFACT received an e-mail from Sanofi as we have queried information which had come through our sources about the shortage of Epilim at that time. In that response, we were told that Sanofi had changed their internal processes to ensure patient groups were informed as soon as possible about medication shortages.

We are unsure, however, as to who those patient groups are, as INFACT, nor FACSA, has never been informed of the Epilim shortages since the date of the email, even though we are aware this has been happening. Sanofi also mentioned to you about the quick response of QR codes now on patient information leaflets, which would give patients access to patient information materials. However, the majority of patients would not be aware or familiar with this. We know that in their evidence they showed you the smaller Epilim boxes which only hold 30 tablets and would ensure all patients receive the warning on the box.

This is something we do applaud, and have asked for, for quite some time. However, these smaller boxes still haven't reached all pharmacists as yet, and the pictogram on the boxes which had been there since 2015 took around 12 months to get through to patients due to the backlog of old Sanofi boxes which did not hold the warnings. This is a process which very much needs to be speeded up to ensure the safety of our patients and their offspring. Sanofi also talked about messages getting out since 2015 following the Pharmacovigilance Risk Assessment Committee (PRAC).

They noted there was a lot of discussion through the patient groups with the MHRA, and in turn the MHRA with Sanofi sent out concerning pharmacy messages. As for the patient guide, they stated, there wasn't a delay in getting these packs out to people. We had the final wording from the PRAC in February 2015 and were asked to come up with something more attractive than a sheet of paper, so the patient guides were submitted to MHRA, stating they worked with stakeholders, namely patient groups, on these materials.

However, this process took way too long to finalise with endless meetings with the MHRA and other groups, with the process becoming too diluted, taking almost four years to complete. During this time approximately 1,600 children have been affected by valproate in pregnancy, with the drug prescribed to approximately 28,000 women of childbearing age a year at that time. We understand there is always procedures to follow, however during our early talks with MHRA back in 2013, INFACT produced our own booklet for women which explained the complications when taking AEDs in pregnancy, and which was given to the pharmacovigilance team at that time.

It was then in October 2013 that conversation with the EMA began, and again it has taken seven years from that initial discussion to reach a finalised patient booklet to be released.

Janet Williams: The past work completed by INFACT, for example the PPP survey, shows that approximately 40 per cent of women never received a patient information leaflet inside a white chemist box. 78 per cent have never received a small pharmacy card, and over 60 per cent have never asked to sign the acknowledgement of risk form by their GP. Some women are still waiting for an appointment with their neurologist in order to change the medication, although we are aware that the system has changed somewhat when it comes to these appointments, with many women now not actually seeing a neurologist but an epilepsy specialist nurse in their place.

Some have struggled making an appointment with their GP or epilepsy nurse to discuss the possibility of becoming pregnant while taking valproate due to the sheer lack of appointments available, another area which the Department of Health and NHS England need to consider funding for to be able to correct this. Although all those concerned with the PPP are aware of the NICE guidelines, we are not surprised by the evidence they give to the Review team when questioned about the procedures and that of valproate.

Their deputy chief executive stated, guidelines are reserved for broad recommendations, not mandatory but doctors are expected to take them into account. If guidelines are not being followed, NICE have no powers to make them happen. NICE issue recommendations as where research is needed but can't commission it. Although we understand NICE work hard to put together new guidelines on numerous medications, et cetera, it's important to pay particular attention to the areas that they have no

control over, and find ways to ensure the guidelines are followed by healthcare professionals in order to avoid patients' lack of communication and understanding for their illness or prescription medications and the danger of them.

However, on 28 March we received an e-mail from the MHRA stating and giving the link to the NICE guidelines for valproate and other AEDs which have been released. This new guidance, however, is very contradictory stating, sodium valproate is first-line treatment to children, young people and adults with newly diagnosed juvenile myoclonic epilepsy, unless it is unsuitable and to follow all the MHRA advice on sodium valproate. Consider lamotrigine, levetiracetam and topiramate if sodium valproate is unsuitable and not tolerated. Be aware that topiramate has a less-favourable side effect profile than lamotrigine, levetiracetam and sodium valproate and that lamotrigine may exacerbate myoclonic seizures.

Follow the MHRA advice on sodium valproate. However, further down the guidance it goes on to state, discuss with women and girls of childbearing potential, including young girls who are likely to need treatment into their childbearing years, and the parents and carers if appropriate of the risk of AEDs causing malformations and possible neurodevelopmental impairments in the unborn child. Assess the risk and benefits of treatment with individual drugs. There are limited data on the risk to the unborn child associated with the newer drugs.

Specifically discuss the risk of continued use of sodium valproate to the unborn child, being aware that higher doses of sodium valproate or more than 800 milligrams a day, and polytherapy in particular with sodium valproate are associated with greater risk. Follow the MHRA advice on sodium valproate. Although the above states the danger of sodium valproate in pregnancy, the first comments above it on the subject of AEDs do not, and so any doctors most probably would not go down to read all the guidance on the AEDs due to the lack of time they have in appointments.

Due to this ongoing Review into valproate in pregnancy, we find the above an insult to the work completed at present, and feel it's necessary for NICE to meet and to review the wording and positioning on the statements as they give rise to contradictory and confusing guidance with prescribing valproate to women and young girls. Therefore, in some circumstances doctors may feel they have every right to continue to prescribe valproate without consulting or explaining the possibilities to their female patients.

The question is, why GPs are still not getting the word out to their patients, and why pharmacists are still not using the warnings when dispensing the white chemist box? We would also, through the Review submissions, that the founder of the UK Epilepsy and Pregnancy Register in March, and applaud the way in which he explained the system as he sees it with the honesty as to his feelings on other AEDs in pregnancy, saying that he felt we would have to come back and be in this same situation in five or 10 years' time. One of the questions he asked was, how did we miss this?

The answer to that question can be answered by the evidence in fact put forward from the archive findings, and that is that clinicians haven't missed it but the new [unclear] simply haven't been informed by the Department of Health of this devastation. Dr Morrow also noted that the yellow card scheme doesn't work, something we would tend to agree with, especially when 50 years on it still fails to be used fully by clinicians, and that most of the reports now are completed by the patients themselves.

Through all the evidence given by each governing body, the lack of ambition shown by each of them to follow legislation and ensure the PPP was in place for every woman prescribed valproate was very poor and it worries us as to how the halt in valproate affected children will ever be achieved other than a complete ban on its use by women, although as we understand this is not something that everybody wants. Since INFACT's last submission, we have worked with Lord O'Shaughnessy following his departure from the ministerial post and were very pleased when he suggested a debate in the House of Lords.

During his opening speech, Lord O'Shaughnessy stated that there is a tension between innovation and safety and that the principal idea that he wished to explore today, and how to balance that risk and encourage innovation, especially for those most in need of hope and help, but also act faster and be more agile, more compassionate when things go wrong. With valproate this has been a continuous ongoing battle for families of those affected, with more risk than benefit to us women of childbearing potential and their offspring.

Even with the introduction of the PPP, the resistance to carry out the legal instructions has continued within the medical profession and pharmacists with the need now more than ever for the MHRA to step up to the mark and look at other avenues such as maybe reclassification of valproate to class C. With this circumstance, as with pregabalin and gabapentin, it would make it illegal to supply valproate through a repeat prescription

scheme. Hence the GP having to have a face-to-face appointment each time a prescription is required by that patient.

This may well create complications on the doctor's workload; however, it would be encouraging GPs and specialists to ensure the PPP conversation is carried out and a change of medications completed where possible. As with the new guidelines for sepsis, hospitals now have to face financial penalties for failing to meet guidelines and this too is a necessary amendment. We are aware that the steps required are something which the government has been considering for some time, with the introduction of the long-term plan setting out two clear areas for the further progress on care, quality, and outcomes.

Firstly, enabling a strong start in life for children and young people, and secondly providing better care for major health conditions. This will improve safety recognition of deficiency, and the collection and linking of data and, as noted by Professor Willett in his evidence to the review as, commitment to start to move on that process and the long-term plan which is intended to start in 2020. INFACT have stated for a long time now that services need to work together to ensure information about women and their medication is filtered down from one department to another, through NHS, social services and education.

However, this has proved difficult over the years, with all three services refusing and finding reasons why this would be untenable in their eyes. As with the long-term plan, we hope this will be a factor that the patients and children affected by these medications are spotted and treated quicker, therefore stopping any possibility of them falling through the net.

However, in the long-term plan it states, over the next three years autism diagnosis will be included alongside work with children and young people's mental health services to test and implement the most effective ways of reducing waiting times for specialists.

We are all aware of the staff shortages for specialist services and expect the government to have implemented the employment of extra specialist staff to take the burden and to ensure that this happens. The plan goes on to state, as set out in chapter one, local areas will design and implement models of care that are age appropriate, closer to home and bringing together physical and mental health services. These models will support health development by providing holistic care across local authority and NHS services, including primary care, community services, speech and language therapy, school nursing, oral health, acute and specialist services.

There is nothing more as a parent you would like for your disabled child but to have these services on your doorstep, as we once did with the child development units and the Sure Start scheme. However, we all know that even though this sounds an exciting era in theory, it's up to the government to ensure the funding is secure and the staff is available to make these recommendations happen. As in the late '80s and early '90s, most children with special needs, with a diagnosed condition from birth were put through a child development unit and seen by a number of specialists ranging from paediatrician, occupational therapist, speech and language therapist, physio and social services.

However, that scheme was fizzled out at the end of the '90s and we are now finding that specialist services are few and far between, with only two or three speech and language units in the whole of Greater Manchester. It is going to be a hard line to follow to ensure children with a condition such as FVS are taken care of, with the lack of services and funding as it stands. Due to our involvement with families where a diagnosis has been difficult, we know that many have sought a private appointment where assessments and advice have been of a better standard.

However, these families, when going armed with a diagnosis to education, find that it's refused due to it not being through NHS England, and so once again finding themselves fighting for support. As we mentioned in our last oral submission, through the archived documents uncovered by INFACT in 2015 which date back to 1971, and medical research papers dating back to 1981 for valproate, we are fully aware that the issue of fetal valproate spectrum disorder, which is to be the new term of the condition, is not the doing of the NHS and its specialists and GPs, but that of MHRA and the Department of Health in their refusal to all women taking the drugs being made aware of the dangers in the first instance.

Some may say that it was a paternalistic view at that time, however as with the PPP, this continues to take place. We understand the concerns doctors must have when explaining the dangers of taking sodium valproate to female patients, and the fear of the patient stopping her medication to avoid any effects on the foetus. Recently released by the British Pregnancy Advisory Service was a briefing called *Sodium Valproate and Women with Epilepsy*, which lays out the figures of women from 2013 who have died as a result of stopping medication during or after the pregnancy.

The information is a sad reminder of how dangerous epilepsy can be without the correct counselling and guidance. It read, in 2017 national

maternal, new-born and infant clinical outcome review programme report on the severe links of investigation of maternal deaths found that between 2013 and 2015, eight women with epilepsy died during pregnancy or in the intermediate post-partum period. There was only one additional pregnancy-related death between six weeks and one year after delivery. In 2014 a report where epilepsy was also covered in depth, five of the nine women whose deaths were considered had stopped their AED and were not taking any medication during pregnancy.

Of these, two had previously been taking sodium valproate. This compares to the 2014 report where only two out of 14 epileptic women who died were not taking any medication. Some reports found that in only four per cent of women with severe morbidity from epilepsy received good maternal care. These figures of those children disabled physically or mentally as a result of valproate taken in pregnancy and confirmed by the MHRA are overwhelmingly high in comparison. From 2013 to 2015 there were 1,200 babies harmed by valproate in the womb, and in 2017 a further 400, bringing the total to 1,600 babies harmed in the space of a four-year period, and also a stark reminder as to how potent valproate is to the unborn child.

In some ways valproate can be compared to thalidomide, however the difference is very stark in comparison, with the physical problems you see thalidomide victims suffer. Valproate in many cases remains invisible, with many disabilities being of a mental nature such as autism and learning difficulties, memory problems and more. Many of the adult valproate victims have exceptional needs, with many of them not realising they do or what those needs are and completing a DNA or PIP form saying that they do things when they can't in order to please the assessor.

For example, using a microwave, which physically they can, but in circumstances this may seem possible to the assessor but mentally it's not, as many would forget they have to put the item in and forget to take it out, and not eating due to a distraction. Taking medication is another problem with the benefits system, these people may look capable and competent to remember their medications but explanation why it's needed and when you take it is a must. FVS people can walk but they are unable to use transport alone due to memory and distraction or confusion, and because of this are missing out on so much.

Responsibility for the number of children harmed lies solely at the door of the government for creating this monster of a cover-up and allowing

thousands of children's lives to be ruined in the process. All the evidence shows that valproate has caused so much damage over its lifetime with the damaged suffered by those exposed, many of which have suffered lifelong disabilities for over 40 years. We are all aware of the problem, also, with the benefits system, and the stress and pressure these families and their affected children go through every three years when the dreaded form comes through the letterbox.

Since the personal independence payment was introduced, the forms themselves have become a little smaller than that of the DLA form, however the methods of assessment and what PIP should be granted for is somewhat more distressing than it was. A person over the age of 18 who was once in receipt of PIP indefinitely has had that taken away and is forced to reapply for PIP, so immediately the worry of the family begins as they now have to prove that their son or daughter is incapable of caring for themselves or getting themselves around outdoors again.

The one thing which isn't borne in mind or asked about on the form is whether the problems or diagnosis which a person has is lifelong. Throughout the assessment particular tests are supposed to be carried out for memory, speech and physical ability, although not all assessors do these tests on every assessment. The fear of the family when it's waiting for the results and many found that either their explanation of the problems have been misinterpreted or not been sufficient for them to be in receipt of a care component.

We are finding that many people with epilepsy are being awarded mobility because they are unable to drive, yet being refused the care component simply because they have said that they can put something in a microwave with no thought of a person with epilepsy suffering a seizure while taking a hot substance out once it's heated. For a child or person with fetal valproate spectrum disorder, it's very difficult to process them to go through, as many of them on view what's physically capable, however having FVS and autism brings invisible problems which are lifelong and will never be controlled by medication or therapy.

This must be borne in mind by the DWP when dealing with a person with FVS, and once awarded given for life or an indefinite period of 10 years so the family doesn't continuously find themselves fighting the system for support that they are entitled to. So, during your summing up we ask you to consider the above and the many children affected, those especially who are now into their 20s, 30s and 40s, and the amount of pain and

suffering they and their families have endured as a result of the devastating effects of this medication. Let's also remember the many families who have experienced loss as a result of valproate in pregnancy.

The death of a child is unbearable as for any family, so it's important that you consider them too. It would be a terrible injustice to make these people suffer a moment longer and a moral conclusion to all the unnecessary pain and suffering is now necessary.

So, to summarise, when making your recommendations we ask you to consider a guaranteed future for children affected, ensuring diagnosis. For their education purposes, ensuring that teachers and tutors are taught neurodevelopmental problems caused by valproate, when studying.

That the present geneticists train the new generation to ensure the diagnosis and constant knowledge of FVS, and that medical students in all areas are taught about valproate in pregnancy and the symptoms of the condition. In future planning make it easier to replicate guidelines to forge a pathway for other AEDs in pregnancy, and to ensure NICE follow strict instructions on valproate when it comes to guidance. That the funding to allow the form of a diagnostic clinic is ringfenced so as to stop any government withdrawal.

That the benefits system recognises fetal valproate spectrum disorder, or FVS, for benefits such as employment and support in PIP, awarding the funding for life in these circumstances. That a respectable care plan is offered to those affected to support them through their lifetime, allowing them a mortgage or a sustainable life, and that a lump sum is given for their previous pain and suffering. That families that experienced bereavement due to valproate exposure receive a posthumous payment.

Julia Cumberlege: Thank you very much indeed, that was extremely useful, very comprehensive, very powerful. So, thank you both very much for that. Not only have you been very professional in the way that you have researched this, and you speak all over the world. I know you've been to New Zealand and other countries. But I think the way that you approach it is, as I say, very professional and we're grateful for that. Can I pick up just one thing, that Emma you were talking about? It concerns the Royal College of GPs, and you were saying one of the problems was that the quality framework in the past had been withdrawn, but they are now going to produce a new one. Have we got a date for that? Has it been published or are we still waiting for it? Or we can go to them and ask them.

Janet Williams: Yeah, well there wasn't a direct date given as we are aware. It was supposed to be put in place as soon as possible to ensure that the PPP was used, but there was no definite date on that.

Emma Murphy: That was discussed at the valproate stakeholder network group, but no date was given.

Julia Cumberlege: No date, well we can always go back to them because I think that would be useful to have that for the GPs. The other thing I just wanted to mention was about PIP, to say that we are meeting the Department of Work and Pensions to actually discuss this and go through it. So, all the time we are still listening, and we are picking up points like you've made today and especially your summing up the particular things you want to see. We're listening to all of that, and in the meantime we're still talking to other agencies and putting your points to them.

Today, certainly where you have mentioned certain agencies, organisations, we will be taking that up with them to see if there is a response from them on that, but then of course it's their choice whether they want to come back to us or not. So, I'm going to ask my colleagues if they have any questions [unclear].

Cyril Chantler: You very powerfully made the point of the gap that you've identified between what the system has promised, or what the professions have promised, and the reality of what you are measuring now - your members are drawing your attention to. It would be very helpful to have a table of that if that's possible for our purpose. Would that be possible?

Emma Murphy: Okay, yeah.

Cyril Chantler: The other thing you drew attention to which I hadn't realised, this is the hospital where child development units were first introduced by a man called [REDACTED]. So, the notion that that service is no longer available for children with development needs, do you have chapter and verse on that, because I didn't realise that?

Janet Williams: The majority of child development units did come to its conclusion around about the '90s because both my sons went through the child development unit, seen by many surgeons in one particular place.

Cyril Chantler: Quite, that was the idea.

Janet Williams: Yeah, and then obviously the Sure Start came along as well, and that's completed too. So, at the moment...

Cyril Chantler: I knew children's centres' funding had been diminished, but I didn't know the child development units no longer exist. There's certainly one still here, or at St. Thomas's.

Emma Murphy: I've never gone to a child development unit, and mine are all at the younger end now.

Julia Cumberlege: I remember them very well, and in fact in our area it was social care that were doing it and they had a number of professionals involved and they were highly, highly valued by the parents who were talking to this wide range of professionals there. I remember them going, and the cry of despair from people who had used them, but as you say I think the idea was that they would be taken up with other agencies, or taken up with other organisations but I'm not sure that there's anything as comprehensive now within the community...

Cyril Chantler: It was very much a medical thing, though...

Janet Williams: Yeah, it was.

Cyril Chantler: ...because that was ■■■ idea that rather than having to take your child to see an ophthalmologist or an ENT specialist or an orthopaedic surgeon, or paediatric neurologist. They would be in one place and together as a multidisciplinary team assess the needs and plan the care of your child. So, I need to look into this.

Janet Williams: Everything seems to be done separately now, your GP will refer you on to a paediatrician or whichever specialist that you need, but there's no actual particular multidisciplinary team as there used to be.

Cyril Chantler: We will look into it, thank you.

Julia Cumberlege: And it did include social care.

Janet Williams: Of course it did, yeah.

Julia Cumberlege: Right, Simon?

Simon Whale: Yes, thank you both very much, it's been really helpful and as others have said, very powerful. One of the things I was just going to ask about was the contradiction you highlighted in the latest NICE guidance. Have you discussed - because you've said to us, quite understandably, that you want NICE to clarify. Have you discussed that with NICE, and what did they say?

Janet Williams: Yes, we have. I'm glad you brought that up Simon, actually. Yes, we have, we've met with the MHRA and NICE and that is being corrected.

Simon Whale: They are going to correct it?

Janet Williams: Yes.

Simon Whale: Do we know how they're going to go about that? Do you know how they're going to go about that?

Janet Williams: Well, it's a matter of updating the updates.

Simon Whale: They're going to correct it in a way that you'd be comfortable with?

Janet Williams: Yes, they've gone through how they're going to do that and what sort of wordings that they're willing to use which has been agreed.

Simon Whale: Do you know when?

Janet Williams: In around about three months' time, hopefully.

Emma Murphy: They were suggesting maybe a year; we didn't find that helpful in any way, so they have agreed three months.

Simon Whale: Okay. The other thing I was just going to ask about was, you raised this point about pharmacy technicians and whether they can provide warnings verbally to patients at the point of dispensing and the apparent difference between what the Royal Pharmaceutical Society said and what the GPhC told you. Has that been resolved, that difference between those two organisations or is that still a...?

Janet Williams: That's still an ongoing issue, yeah. We met with the General Pharmaceutical - well, we've met with them a few times now, the General Pharmaceutical Council and in the first meeting that we had with them we said that that really shouldn't be an issue. Whoever dispenses the medication to the patient should be able to give that information to them and it shouldn't really be a problem.

Simon Whale: Sorry, the GPhC agreed with you about that?

Janet Williams: Yeah.

Simon Whale: All right. That might be something we follow up on.

Emma Murphy: They did say they were going to send an update round following that meeting and they would put more information out just to bump it up and encourage...

Julia Cumberlege: Agreement is terrific, to have reached that. It's then the implementation that is actually the challenge, always isn't it? Valerie?

Valerie Brasse: Yes, I did have one question. You've been very active in monitoring what's been happening with the pregnancy prevention programme and your work's been fantastic. You talked about maybe what is needed [unclear] is the short sharp shock which says, actually you withdraw it. But that the community is divided because the alternative would be reclassified and therefore that prevents renewed prescriptions automatically, it has to be done with a review. How divided are the community?

Janet Williams: Well, the one thing we don't want on this is a ban, we've never wanted that; we don't want that at all. However, we've pushed and pushed as far as we can go now with this, and other than a reclassification I think from there onwards the next step would be to look at - you have got a small minority of people that are always going to need this drug, that have tried everything else and that nothing else works for them. That's why we don't want the ban, but to do the reclassification, that would be our way of finding out which people haven't tried a drug, which people can use other medications other than valproate and finding that small percentage.

Valerie Brasse: [Unclear] reducible minimum?

Janet Williams: Yeah.

Valerie Brasse: It's interesting, because I know that you had concerns about that because it's not convenient, for example, to have to go to a hospital or whatever to get that drug prescribed for you.

Janet Williams: Yeah, of course.

Valerie Brasse: Are you feeling that that might be an acceptable compromise if we really can't make this work any better?

Janet Williams: It's - acceptable compromise? There's nothing else left to try.

Emma Murphy: No, we've tried everything and like Janet said, we've pushed and pushed the regulators, we've met with absolutely everybody and they all have a different excuse and I think it needs some sharp shock. We don't want that, but we've got to safeguard these babies.

Janet Williams: The only other alternative would be if - and it's like we had this discussion with the GMC, and if you've got a doctor that's prescribing but not passing on the PPP and not asking women to sign the acknowledgement of risk form, it's alright for that doctor once. It could be another surgery down the road where it's happening with another doctor and it's looking at that area rather than just the one surgery that the GMC don't seem to be taking on board. It's all right one doctor doing it in one surgery, but if you've got 10 in that area then that's 10 doctors not passing on the information. 10 women not getting it. We've already got six women that have become pregnant since the PPP came out.

Sonia Macleod: Are the women that have become pregnant since the PPP, are they in one geographical area?

Janet Williams: No, they're not, no scattered, unfortunately.

Julia Cumberlege: So, there's an issue about spreading good practice.

Janet Williams: Definitely, yeah.

Julia Cumberlege: They must have networks and things that - well, Cyril knows an awful lot about primary care, but you would think that they could, at their meetings, local medical meetings, whatever.

Emma Murphy: Well, we would hope, yeah. We do hope that, but it doesn't seem to be happening.

Cyril Chantler: When we met recently, we discussed the issue of every woman of childbearing age being on a register which we could with their permission obtain from the prescribing of the medicines, perhaps. That would then mean that they could directly take responsibility to be contacted. Do you still think that's...

Emma Murphy: Yeah.

Janet Williams: Yeah, we've discussed this before and I think, like with the UK pregnancy register, for example, there needs to be something - you get a letter when you need your smear test done. You get a letter when you're due to go and have your mammogram, say for example. So why can't they do it for this?

Cyril Chantler: Because while medicine is a very complex area, somehow putting the patient more in charge of their own destiny is perhaps a different way rather than just relying on the system and the professional.

Janet Williams: It's all about getting the information out there, Cyril, it's just not filtering through. So, it's a case of finding out the reasons why that information isn't filtering through. There's got to be a reason as to why the doctors and pharmacists are not doing this other than just saying, well at the backend of the day sometimes you don't do it because you've had a long day or whatever. You can't do that with this.

Cyril Chantler: Systems are complicated and they...

Janet Williams: I understand that.

Cyril Chantler: ...depend on people, and sometimes the people are not wanting to do a good job. I can't imagine anybody who does the job without wanting to do a good job.

Julia Cumberlege: Do you think with new technologies coming in, communication systems, something like that - that we could harness them in a much more productive way for particularly the people that you represent?

Janet Williams: What do you mean? As in...

Julia Cumberlege: Well, with GPs for instance we know that one of the things that they have are the alerts and one of the problems with the alerts is that they have too many...

Janet Williams: Yes, I understand that, yeah.

Julia Cumberlege: ...and that's a bit difficult. But I was just thinking when Cyril was talking about women having their own notes, a bit more control over their destiny and their families and the rest of it. Do you not think that - well, I'm just thinking we've got a Secretary of State at the moment who is very keen on new technologies and how we can harness that to the benefit of the people of the people you represent?

Emma Murphy: I think at the moment we've got to try everything, absolutely everything. We would encourage anything at the moment.

Janet Williams: The one problem you may have with that is that valproate can - well, all these AEDs can affect thought processes and short-term memory. We come across that all the time, so if you're going to put it in the hands of the patient, you may have one or two that struggle with that.

Cyril Chantler: Remind me how many women there are of childbearing age taking - with epilepsy?

Janet Williams: The last time we spoke to the MHRA it was about 21,000.

Julia Cumberlege: How many?

Janet Williams: 21,000.

Cyril Chantler: So, a database of 21,000 people who, with their permission is accessible by e-mail or Facebook or on Twitter. If an organisation like INFACT had access to that, you could do a lot, couldn't you?

Janet Williams: [Laughs] Yeah, definitely, and we'd do our utmost to make sure it was done, too.

Julia Cumberlege: Right, okay. Is there anything else that you would like to say before we draw this to a close?

Janet Williams: That's everything with regards to this, but we want to thank you as a review for hearing all our voices. It's been 40 years too late, but we really thank and applaud all of the work you've done because it has been needed and a lot of our parents are overcome that this is happening, so thank you so much.

Julia Cumberlege: That's very generous, thank you, and can I say I do think the amount of work you put in, as you say you meet so many people and at the same time you have to care for your families. I think it's hugely impressive, thank you.

Janet Williams: Without the husbands we couldn't do it.

[Laughter]

Julia Cumberlege: Thanks very much.

END OF TRANSCRIPT

Session 2: Young People Affected by Valproate

START OF TRANSCRIPT

Julia Cumberlege: Well Branwen, welcome. It's very good to see you here today, and I know that you've been very determined that you shouldn't hide behind your parents, that you young people who have experienced the results of sodium valproate should be able to speak, and speak for others. So I do welcome you here today. When you came to the previous oral hearing, you raised a number of concerns, that adopted or foster children may be unaware of their medical histories. That was one of the concerns you raised and, arising out of that, that they may remain undiagnosed and unable to access appropriate support.

You also emphasised the difficulties in assessing appropriate medical care, education and broader social support, in particular due to cuts to some regular services, so we understood that and took that on board. You also raised the whole issue about young carers, and a number of young people are carers to patients and indeed to their siblings, but this isn't often acknowledged. You were very worried that these people don't receive any support, support that they should receive, and this is about counselling, respite care, mental health and how that impacts on young carers. Then a number of key questions you raised with us which were really interesting and, subject to all of that, we have listened to what you've said.

But today is your opportunity to tell us what you have heard in the intervening five months since the first oral hearing, and anything you want to say to us that would help us with composing our recommendations - any further research you think we should be doing - we would welcome any thoughts you have. Perhaps we could start just by you saying who you are and why you're here.

Branwen Mann: Well, my name is Branwen Mann and I represent young people who are affected by sodium valproate and I do have fetal valproate syndrome as well. I'm here to be a voice for everyone who don't really have a voice, who have fetal valproate syndrome. I've actually been given a job recently, which is quite a huge one, which is being a lay person on the Children and Young People with Disabilities and Severe Complex Needs Guidelines Committee with the National Guideline Alliance and, to be honest, it's pretty huge. I still can't believe it to this day, but yeah, I'm really looking forward to helping with the guidelines and changing them and helping with

the benefits and National Health System - Service - and everything else. I'm really looking forward to it. [Laughs].

Julia Cumberlege: Has that been difficult, finding a job?

Branwen Mann: Yes, actually yeah. It was a very long process with the Guideline Committee because they - I don't think they had many people applying and stuff, but after about three or four months of me sending the application they finally gave me an interview. I spoke with them on the phone and they said, 'we'll give you a call in about two or three weeks to let you know the results'. Two days later they phoned me back saying, 'you got it'. I was like, oh okay, great, thank you. But yeah, it's been really hard, but thankfully with the Committee they only meet up once every 10 weeks or something like that and - which is amazing because of the health with me and stuff and I'm not really good with travelling. Yeah, I'm looking forward to it to be honest. It's not happening until July but still, yay [laughs].

Julia Cumberlege: Do you hear that from other people?

Branwen Mann: Yes. I hear about stories - well, I'm not - obviously when it comes to the Guideline Committee I'm not allowed to speak to organisations or anything because of policies and stuff, but I do speak with young children who are affected by fetal valproate syndrome and I ask them how they would like me to change the guidelines, or to maybe help them in the future, or maybe their children in the future. I've been hearing a couple of little things that I could probably improve. One of the main things is PIP and the system and stuff, because wow, I still can't believe the stories that I've been hearing about PIP, yeah, basically...

Julia Cumberlege: You've got some things there you'd like to read, yes?

Branwen Mann: Yeah. Like I mentioned last time, I would like to acknowledge the group of children that did not survive. Since speaking last time, others have shared their stories with me - so many valproate families are devastated by this experience. There were two million late miscarriages, neonatal deaths and stillbirths and early deaths related to valproate. Again, I want to acknowledge my own dead brother and sister, Keverne and Trelissa. Before I begin - I just realised at the top of the page - I want to say a huge thank you to my mum who has actually helped write this for me the past week, actually, because I've been doing a lot of babysitting and stuff, and she's just been a godsend. I mean, she's helped me write this up, so thank you mum.

When a baby dies early, not everyone wishes to talk about it. The experience gets swept under a rug as if it never happened. These babies are a part of a story too. I'm acknowledging all the babies that did not make their first year. Conditions such as epilepsy and mental health disorders, and even migraines, can bring an element of stigma. I have been disgusted to learn of how some of our mothers are treated during pregnancy because of this. It is forgotten that they take medication that affects the mother during pregnancy. Other health problems can come to the forefront during pregnancy - these are clearly vulnerable women. It is understood that labour and the birth may be problematic, yet staff are not always prepared.

I was horrified to hear some of the stories as to how mothers were not listened to when they expressed concerns regarding their babies. One baby spent a day in the special care unit before being taken to her mother. The baby would not feed properly and staff from the special care unit showed her how to feed the baby. She was naturally distraught as she was made to feel she was unable to feed her child. She'd thought herself to be a terrible mother.

Visitors expressed concerns about the baby, still no one looked at her child. Two days later, her child was not breathing properly. Still no one looked at her baby. Then when bathing her baby as she prepared to take the little one home, a midwife stepped in, her baby was rushed to the Harefield Hospital. The baby had two holes in the heart and needed an operation at six months old. I think it is disgusting that this sort of thing happens at all.

One baby died because a doctor refused to believe that the mother was in labour, because she was early. Because of this she went through labour and gave birth with no support. Her baby died as it had needed an incubator. Most of these mothers do not complain as so many of these women have been put down most of their life. They are insecure and have learnt not to. There are hospitals that fear to be sued and close ranks. All women need to put things into place, the new mother in such circumstances.

One mother was lucky. She approached her solicitor who by chance had been a midwife. The solicitor told the mother to focus upon special needs baby and deal with everything - and dealt with everything. The hospital was not sued as all the mother wanted was recognition and support for her baby's needs. There needs to be an independent body that is clearly advertised, to help women in this situation.

Something else I noticed in these stories was that those who underwent this type of experience were watched carefully by social services with regular visits. There were some that were forced to attend places that taught the mother how to care for her child. I know some of these mothers. These - this is perhaps correct for the situation for some but there are others who are always there for their child. They give loving support and fight hard for their children's needs. I don't know how any mother might cope when she's under such scrutiny.

Education. When I was in primary school, I had to be pulled out of class in the middle of the day to do exercises with my teaching assistant. She had to be trained to ensure she could do my exercises properly and safely. Today, that school has benefited with a teaching assistant that has been trained in this way for free. The school has invested in further training. That school now welcomes children with medical conditions, some of which are disabled. It is set up as a place that can provide appropriate care and works closely with the local health community. This is not always the case.

Organisations that independently support children with special education needs have told us policies are often in place that will provide the children appropriate support. Parents and carers are not always aware of these policies and are not always - are not informed by them. If they are aware of these policies, they often have to fight to ensure that they are put into place in a way that supports their child. Families with special needs children do not always have the time and energy to give what is needed to themselves to do this. Many parents and carers are not always aware of which organisations are best-placed to support them.

Education is one of these areas that you hear most complaints about. The process of assessing a child is not always appropriate to a child's needs. We have spoken to parents that they were told - that they had been told by professionals that the money is not in place to give the necessary time to assess their child. This can have devastating consequences for the future of these children who do not access appropriate support.

Bullying is another problem that I've heard a lot about. It is something that I have experienced myself. The best provision to improve this and raise our self-esteem is whereby the school has a base where special needs students can go to during the day. Any additional medical support can take place there without being obvious to other children. Additional support for schoolwork and socialising and [unclear] needed is so essential to our

wellbeing. Schools that have a base find it easier to offer additional opportunities for the children. At my secondary school, we attended the National Children's Games at Stoke Mandeville every year.

Two brilliant initiatives include prefects. A prefect oversees a part of the school, such as the junior playground. One child at the special education needs schools provided support for the younger students, going to senior teachers if a child was having difficulties at school. The other is a mentor who may be given a child - a named child - who may have been identified as needing social support within school. Mentors also provide an awareness of the resources within the school, or help them to approach someone where they're finding things difficult.

Inadequate resources are clearly why parents and carers and the children themselves have not been heard. This can mean that a child is not accessed properly - assessed properly. Inappropriate equipment is used instead of the recommended equipment, due to costs. Equipment that might be used to support the learning at home is rarely supplied. The SEND system introduced in 2014 did not fix the old system, but have added a new set of problems.

The evidence taken in by the Education Select Committee and a hearing witness from Ofsted and Quality Care Commission (sic) and local government confirm that children with special education needs are being failed. It was found that many councils do not comply with the law and the social - and with supporting children with special education needs. Parents and children are not consulted regarding decisions, and hurdles are placed in their way, making it more difficult to access resources. The money is not being properly used to ensure that we get resources that we need.

Another thing that I'm going to talk about is home schooling. Not surprisingly, a number of mothers have given up, and turned away from school education system have decided to home educate. They have become frustrated as they watched their child decline because of a lack of necessary resources in place for their child in school. The authority has a duty to review a child's statement or EHC plan annually. If your child has an education healthcare plan and a personal budget, they'll still be eligible for this.

All children with EHC plans can request a personal budget. As long as home education is specified on your child's EHC plan for educational provision, the child should get money. However, each local council has its own policy

on this and often make it a difficult or impossible process. I have spoken to mums who have funded - who fund home education out of their own pockets, which is actually quite common. The ability to home educate, money is important as it can be used to purchase and manage services that will ensure that their child can access the resources needed to ensure the child has a good education.

Some parents believe that their child cannot access the medical support, such as speech and language therapy, that they will be able to access if in a school. If your child requires special medical care - such as hearing tests, speech therapy - this should continue as the NHS service follow the child not the school. The NHS may not refuse treatment to a home-educated child on the grounds that the service is normally provided within a school setting. I am concerned that there are home-educated children that have fallen through this net and are not aware that the child can still access these resources. We need to ensure that the home education - that the home-educated children receive the financial support, that they ensure that they can access the resources that improve a child's education.

Boarding schools are another alternative to the education system. It is an easier - it is easier to access funding for this but it is not an easy process. It can be possible to find a school that supports a child's needs. A lot of research for this is needed. However, in many cases a family's life is greatly improved. The time with a child is a joy. The stress in the home life is reduced. When a child has complex needs that are difficult to meet, sometimes this is the best option.

[Aside discussion].

Branwen Mann: The importance of our families. Our families are important to us. Many of our siblings will also have a fetal valproate syndrome. We live in diverse family units where we rely on our parents or carers to ensure that our needs are met. Many of our families are also single-parent families whereby our - where our mother is the sole carer. In some families both mother and father are disabled. In some separate families, the father is still a strong parental figure providing support for the mother. In my family we function as one unit - when one of us is ill it affects how we function as a unit and as an individual. I expect a lot of families have a similar system of coping.

Those with fetal valproate syndrome are often anxious or have depression and we cannot always grasp what is happening around us, too easily

panicking when something does not do as it should. Our family is our lifeline. Our wellbeing depends upon the wellbeing of our family unit. Their health, their stress levels, their mental health - the carer's assessment is not meeting our needs. Social prescribing - a brilliant initiative - has the ability to provide us with some areas of support. However, it leaves a family with areas of need that are easily dismissed and some form of support [unclear] all he has in place.

As we grow older, we watch the health of our parents and carers deteriorate. They will not always ask for help as not many - as many no longer trust those professionals that oversee the welfare of the family group. My mother once tried to explain it all to me. She shared that different mums are likely to have been - she shared that some mums are likely to have been ostracised at some point within their life. It is a very demeaning experience that leaves you totally disempowered. It is the experience that a person who had epilepsy, mental health problems, migraines and pain faces the world. All have invisible health problems that are disabling in their own way.

The challenges are faced and just - and not just related to health conditions, but also upon the effects of the medication upon them. They can cause a greater risk of sleepiness, difficulty with thinking clearly, reasoning skills or ability to remember and solve problems, coordinate their bodies and communicate effectively. Even the weight gain. Much of their health problems are dismissed as a side effect of their medication and rarely explored.

As individuals affected by anxiety, it is essential to our wellbeing that the health and wellbeing of our family is recognised and their needs addressed too. We need to be empowered in so many ways. I have imagined an epilepsy nurse sitting with me and my sister, answering our questions and explaining to us what we are seeing, and then giving us the tools that will help us care for her when she has a seizure. Even though that - even those that find it difficult to communicate with experience emotion in these circumstances. This does not happen and we are left disempowered and worried.

Those with mothers affected by bipolar, migraines and neurological pain live with challenges that leave a child with similar fears. As our parents grow older, we wonder what will happen when they die. Who will care for us? Will they be competent to care for us? Will they even be able to assess our needs?

Medicine safety. My life experience has ensured that I have a great interest in medicine safety. Myself, my mother and my grandmother have all had negative experiences regarding medical prescribing, which is surprisingly common in those with chronic health problems. Medicine is too easily used to counteract the side effects of other medicines, to the degree whereby some of the doctors prescribe medicine to counteract the medicine they have just been prescribed. Not all professionals use the Yellow Card system to report side effects.

For me, more importantly, are medicine-related patient safety incidences being reported on the National Patient Safety Alerting Systems. It is the analysis of the national reporting and learning systems that new risks are identified and communicated via the use of medicine safety alerts are carried out through the NHS England. We need a greater policy - policies of how medicine is used and abused in this country.

Medication overdoses and the practice of prescribing medicines and medicines that are contra-indicated. One of my consultants introduced me to the postcode lottery system for the access of medication in the country. I asked one of my frustrated consultants to explain this to me when he found that, yet again, I was unable to access medication to help me cope with the chronic migraines. In the UK, formularies there have been decentralised. Each CCG has its own local formulary. In my area I am unable to access medicines recommended by the hospital I attend for migraines, as it is not on the formulary for my local CCG.

Previously, contra-indications and or known effects of medicines has greatly limited my choice. For three years I have been without adequate pain relief. Now I've been put - I have now been put forward to a scheme whereby I can access medication that has not yet been licensed in the hope that the access in form of pain prevention. My mum does not like this process, but I have both migraines and arthritis. My life is blighted by pain. I just want something to help me. I don't understand the formulary system but I do know that I am not the only one that experiences this. How much does this system affect ourselves and our families?

One last thing that I'm going to talk about is PIP. There are many, many challenges related to PIP I wanted to draw your attention to. If you have DLA or PIP, you are able to access other benefits, including a disability premium such as the one coming with - such as the one that comes with housing benefit. Not every parent understood that they would have to pay this if they are not getting PIP. A number of mums were hit greatly by this.

To lose their DLA and to have to pay additional cost for housing has had consequences amongst their lives, many going into debt. One was at great risk of losing her home. After a tribunal they began receiving PIP going unnecessarily into debt, living life during this period in severe stress, seizures, illness, sleeplessness. This is not acceptable.

In some families you can go down the process of preparing the PIP forms for one person, then you begin the cycle that there will be another child. Sometimes others. Then the parent forms will need doing, then the ESA forms come. If the PIP is not successful, you may or may not get it, and you face another cycle without financial support until you have successfully appealed at tribunal. It is a cycle of stress that ensures a disabled person, especially one with epilepsy, will spiral into worsening health problems and even death. For so many reasons I cannot fathom how the country does not lose out financially upon this abuse-ridden system.

Does anyone have any questions? [Laughs] after all that?

Julia Cumberlege: Well, thank you Branwen, that was a great tour de force and thank you to your mother as well. You've raised so many different issues and certainly some of the young people we've talked to about education, some have gone to a school for special needs but others have gone to mainstream schools. I presume that depends on the choice of the parents and the child et cetera. Both seems to be successful in some cases and in other cases not, so that I think is a matter of choice. But I think the way you've highlighted the issues in education have been really, really good for us to listen to and to hear.

Can I just ask something about families? You were talking about families, and today and through the oral evidence that we're taking now from patients, you are unique, because you are the only person who has been affected - young person - who has come to talk to us about it. So, for us that is very, very useful and helpful. Thank you. I just wondered, because I think we've heard from other young people in a more informal setting, they have real concern for their parent. I wonder if you've felt that with your mother because after all she has epilepsy and whether that's another burden that you carry?

Branwen Mann: It is. Very recently, mum's health has gotten even worse - she's been having more seizures. For some reason, she's been discharged by the neurologists. Me and her are trying to push the GP into letting her back in to see the neurologist. He's one of the wonderful people who has always

listened to me as well as my mum, because he knows what I've seen, he knows that I've seen her almost die.

Actually, within the last five months I've probably had to phone an ambulance three times for her, which is really heart-breaking because at one point I genuinely did think she was going to die because - I was only out for about 10 minutes and when I got back she had the biggest bruise on her face. She could not remember me; she could not remember where she was. Thankfully - this is going to sound ridiculous - but thankfully we have cats and they were able to comfort her and somehow, she was able to remember where she was. It took a good two or three hours until the ambulance came. Yeah.

That is one of the scariest things though, is not knowing what's going to happen to your mother - or father, saying that. Because we live far away from my nan, my aunts, my uncles - because they live up west - what's going to happen with us? Because I know I'm going to be fine, but what's going to happen with my sister because, yes, she is still under adult social care services, but what sort of home will she be put into? Because there's loads of talk of her being put into a - I don't know what they're called, it's a block of flats where you're with a load of disabled people. I have no idea what it's called but I don't know.

Julia Cumberlege: I think we know what you mean.

Branwen Mann: Yeah.

Valerie Brasse: A supported...

Branwen Mann: Yes, that's it. Yeah. Me and mum have been talking about it and we don't think that she'd ever be able to cope with that sort of thing because of my sister's hearing. She - if she has any form of different pitch or anything, it would cause my sister to have a sort of echoing effect in her brain and it would take her a while to calm down. If that sort of thing happens, she'll probably have to phone me to settle her down and it's just really difficult to be honest. But yeah, I mean, I don't know what's going to happen. Touch wood if anything happens to mum...

Julia Cumberlege: I think your courage is amazing...

Branwen Mann: Thank you.

Julia Cumberlege: ...and the way you're coping with all this, and coming here today. I know it is another added tension perhaps. But certainly, that was very, very good indeed. I'll just ask my colleagues if they would like to ask some questions.

Cyril Chantler: Yeah, I just want to say thank you because it's been very interesting and very useful for us. Thank you.

Branwen Mann: Thank you very much.

Julia Cumberlege: Simon?

Simon Whale: Yes I'd agree, I mean it's very enlightening, Branwen, thank you, because as Julia says, you are unique in terms of these hearings. We met other young people alongside you a few months ago and that was really valuable as well. But the one thing - one of the things I was interested in was what you were saying about the benefits system and PIP in particular. I think you used the phrase, cycle of stress, to summarise how it feels, which is - probably echoes what other people have told us about having to deal with the benefits system. I just wondered what you're - whether you've got any thoughts about, well how could you make it less stressful? What could the Department of Work and Pensions do for someone in your position to just make it a bit less stressful?

Branwen Mann: Well, I understand that there's literally two separate categories, it's care and mobility. The thing is, I understand the care side but the mobility is just - it's not that it's tight or anything, it's just I've tried to fight for it myself and it is not easy, because you literally have to, I think - what is it, walk 200 yards with support or something? That's what stresses us out, is that it's not as flexible as it was with Disability Living Allowance.

With PIP you could either get lower care and higher mobility or you could get high care and low mobility. That's what stresses us out, because with the DLA you always got middle-rate care and middle-rate mobility and it was always something in between, but with PIP I think it's just higher or lower, I don't think there is an in-between.

Simon Whale: So, if they had a bit more flexibility that would help?

Branwen Mann: Yeah, it really would to be honest, it really would.

Simon Whale: Okay, thank you.

Julia Cumberlege: But I understand you also have a healthcare budget, do you?

Branwen Mann: Yes.

Julia Cumberlege: That doesn't disqualify you for PIP?

Branwen Mann: I don't think so, no.

Julia Cumberlege: No, right. We've got a colleague who knows a lot about that so we'll probably ask him. Right, Valerie?

Valerie Brasse: No, it's all very informative, and thank you Branwen. I'm perhaps interested in your conversation about the education and healthcare plan and the notion - are you suggesting that if you - if a parent opted for home schooling that that child would be disadvantaged by the way the education and healthcare plan operates? In other words, can you get the support if you opt for home schooling?

Branwen Mann: Well, like I mentioned, it depends on the council and the sort of area that you live in. I, like I've mentioned, I've met loads of different families.

Valerie Brasse: So some do, some don't?

Branwen Mann: Yeah, it's hard to tell, and one of the things that the families ask me about is if there is a way that they could possibly get the care plan or the budget and stuff, and I'm just like, you need to fight with your council because there's nothing I can do. Me and mum try and help them but there's so much that we can do when we're just sitting behind a computer.

Valerie Brasse: I might have a look at that.

Branwen Mann: Yeah.

Sonia Macleod: Do you know people who have gone for a more flexi-school approach, so they're not completely home-schooled and they're not completely schooled within schools?

Branwen Mann: Actually, I know of one family. I think the little one was home-schooled but then they switched her to education by teachers and stuff because it was, I think it was too hard for the mum to do it. But I don't know if there's anyone who's actually split it down the middle.

Sonia Macleod: Okay, I was just curious.

Branwen Mann: But I don't know. My mum spoke about doing that with me one day but I don't know if that actually happened, to be honest. Sorry, that's making

me think now [laughs]. But yeah, I don't think there is a down the middle with that one actually.

Sonia Macleod: Okay.

Julia Cumberlege: I'm sure your mother will watch this...

Branwen Mann: Yes.

Julia Cumberlege: ...and she probably will help us and also supplement. But you've read it all so clearly and that's been really, really helpful, so thank you very much again.

Branwen Mann: Thank you.

END OF TRANSCRIPT

Session 3: FACSaware

START OF TRANSCRIPT

Julia Cumberlege: Well, can I thank you very much indeed for coming? Emma and with your son Andy and also David Body, very good to see you here this afternoon. Emma, first of all, I want to thank you for the visit you arranged for us when we went to Leicester. That was very interesting for us because we met a mother and her children who had been affected by sodium valproate. Indeed, I remember very clearly listening to one of the young men who was at university and that was interesting. Others were a bit more disabled and so we saw a bit of a spectrum. That was very informative to us.

We, then, of course, had the oral hearing on 20 November and I'm conscious that things may have changed since then in your minds and what you want to tell us. But just thinking about that, I mean first of all FACSaware of course was launched in 2013 by you and you've been with it all the time. You've produced a number of reports for the media, for regulators, for politicians, and they're based on the views expressed through your networks.

That has been very interesting, and I know that you have 375 members on your Facebook page and 400 followers. So, it's quite a cohort of people who you relate to and inform and indeed help when they need some help from you. Obviously signposting local support services and represented by Leigh Day Solicitors, we know that, and David might be saying a word about that later.

First of all, just thinking about your hearing in November, you set out six different aspects that you would like us to listen to. They were interesting and we've taken those on board. Then you wanted to explain to us what you wanted to see going forward. Again, we've been examining that; your top three priorities. Some of the things that have concerned you since that call for evidence has been about the closed archive files. We can say a word about that, the NICE guidelines and some other issues that you raised. So, it was a very full meeting and extremely helpful to us.

Today, what we would like now is for you - thinking about what took place in November, five months further on now. This is your meeting. This is your opportunity to tell us things that you think we ought to know. Because we're getting towards the end now of our fact-finding sessions, and of

course writing this report is going to be a herculean task and we're ready for that. We realise that not everybody's expectations will be possible for us to recommend because they may not be things that we can see should be implemented.

Because we are very anxious that it should be a practical report, that what we recommend can be implemented. It's not just something pie in the sky that we wish for, but it needs to be grounded. There are particular issues that we know you certainly want to see in the report, and we want to hear from that today. So perhaps you would like to start off, Emma, and tell us what you'd like us to hear. What you think again should be recommended in the report. Particularly things that might have changed in the intervening period.

I know that you did raise some through Twitter and other things about how you would like things to be slightly changed. Things like, well I haven't got them quite here at the moment, but it came through social media or something, and you wanted for us to know. But it was about consent, it was about expert witnesses. It was about interest and it was about product liability in the future. So, it's over to you.

Emma Friedmann: Okay, thank you panel for posting this, facilitating this.

Julia Cumberlege: Could you just start for the screen to say who you are...

Emma Friedmann: Yes.

Julia Cumberlege: ...and why you're here.

Emma Friedmann: Hi, I'm Emma Friedmann, campaign director of FACSaware. I have epilepsy. I was prescribed sodium valproate, Epilim, and was not told that there was a substantial risk to my child. This is my son, and he has fetal valproate syndrome.

Andy Friedmann: [Unclear].

Emma Friedmann: Would you like to introduce yourself, Andy, or do you want to wait until you've finished your mouthful?

Andy Friedmann: [Unclear].

Emma Friedmann: If I could read this little bit and then well, David, would you like to introduce yourself?

David Body: Yes, of course, I'm David Body. I'm a lawyer who's had quite a long association with this subject. I first acted for clients in this topic in 1999 and I continued to do so, certainly until 2010 when the litigation [died] [unclear] had to be discontinued. In the aftermath of that, I continued to liaise with the families. When I retired I kept two interests alive; one was actually finishing up the administration of the litigation with the legal aid agency, if I tell you that I completed that in February this year, you understand that is quite a long time in fact.

Of course, I've maintained links with support groups, particularly with this support group, because Emma wouldn't let me retire in peace. So, my continued interest is maintained. But I think it would be fair for me to say that since I retired, I have regarded this as unfinished business and I'm hoping you're going to help me finish it.

Julia Cumberlege: All right, thanks very much indeed. We've got just about an hour.

Emma Friedmann: Right.

Julia Cumberlege: If you would like to start...

Emma Friedmann: Yeah.

Julia Cumberlege: ...Emma.

Andy Friedmann: Hi everybody. My name is Andy Friedmann or Andrew Friedmann. I'm here from FACSaware.

Emma Friedmann: Okay.

Julia Cumberlege: Thank you. Right.

Emma Friedmann: I wanted to, first of all, seek consensus from the panel on this executive summary, just the one page. I'll read through it for the sake. So, it has been proven beyond doubt and accepted by the pharmaceutical industry that there is an increased prevalence of physical and neurodevelopmental birth defects when valproate is taken during pregnancy. Would you accept that?

Those exposed have lifelong disabilities and have been unable to access justice in the UK courts. The services required by those affected and their families are highly specialised. The taxpayer is paying for the services required and the pharmaceutical industry is not contributing. Our regulatory system is broken and needs to be fixed, hence why you fine

people are hopefully going to move some stuff in the right direction. Andy, would you like to read the wish list now?

Andy Friedmann: Immediate additional funding for local education, health and care services. Immediate and lifelong financial security for those exposed to valproate who present symptoms of valproate syndrome. Appropriate services delivered coordinated by professionals who have an understanding of valproate syndrome. A judge-led public inquiry into medicine and devices regulation to focus on valproate.

Emma Friedmann: Thank you, Andy. This is included in the written submissions. What I've noticed from watching a substantial number of the oral hearings, is that you've had a really, really nice conversation with the groups that have sat before you, the professional groups in particular. I've been able to see from that where your particular areas of expertise, knowledge, and interest is. I've designed what I wish to talk about today based on the idea of having a conversation with you rather than me reading a script. I have little bits for each of you.

But generally, the requests, pictograms on the outside of the medicine boxes, so if any medicine has been shown to cause harm, it should have this circle with a pregnant woman inside. If there is inadequate knowledge about a medicine that will be prescribed to women who are pregnant, then to have the triangle outside of the box. This is now there on the medicines in France. So, on the French anti-convulsant medications, they either have the circle or they have the triangle. It's just there as a visual prompt. I would also like to see a symbol developed alerting men of the fact that medicines do affect sperm as well. So, this is something I found and just got printed off because I just thought it was quite sensible really.

Patients who are receiving their medications in a dosette box - so from a pharmacy and they're putting all the pills in - they're not receiving the original packaging. Many are not receiving the patient information leaflet. So, they don't know exactly what it is that they are taking. Their carers do not know. They are unaware of the side-effects. They are unaware of what to do if they are experiencing a side-effect. I feel that's something that you can make a recommendation. The pharmacy bodies have been very helpful in this whole process. I feel that they would step up to that challenge of providing that.

Cyril, if I may come to you first? I very much enjoyed watching the conversations you've been having about the registries and the database.

It's something I feel really quite strongly about. After speaking to GPs and other healthcare professionals in my local area, GPs would very much welcome there to be a tab on the SystemOne GP software to immediately upload things to the Yellow Card. Their time is pushed and if they could just click that link and it would send through to the Yellow Card, obviously the systems have to make sure that they operate with each other.

There are other computer systems that GPs use, but if that could be implemented then the Yellow Card information would be a lot more thorough. The GPs wouldn't be spending extra time trawling through it all thinking, okay what's relevant, what's not. Then hopefully that Yellow Card information would feed into the general database that you've been discussing, and that would then feed into these registries that could be set up when there was a product of interest.

Now the Enhanced Summary Care Record, this is the copy of what I have in my area in Leicester. I've signed up to have my details and Andy's details on the Enhanced Summary Record, but it's not being promoted enough. I feel that to get a database of national - everybody's national record - is going to take a huge amount of time and a huge amount of additional information governance, and legal frameworks and ethical questions around that. Enhanced Summary Care Record is something that exists now and if it could be promoted, that would be brilliant.

The Chief Medical Officer mentioned the ICD coding and the challenges that she has had trying to raise with this with the World Health Organisation. Now the World Health Organisation doctor Margaret Chan recognised the valproate toolkit in 2016 as being a leader, a really, really good piece of work. So, they are aware of teratogen-related syndromes.

Now I raised this issue of ICD coding back in 2014 at an APPG that Alec Shelbrooke hosted. I don't feel that there's been movement. That's five years ago. I raised the issue then, I've raised it since. The CMO is aware of it and if these databases and registries are going to be effective - UK is the global leader in health and whatever, we should be able to influence the World Health Organisation. If that coding was there, it would greatly enable the process.

The thing about whether a registry should be mandatory or voluntary - you've had the conversations with the National Joint Registry and the National Congenital Anomaly and Rare Disease Registry and the Epilepsy and Pregnancy Registry. Obviously one of them is mandatory and two are

voluntary. I know for a fact that Andy, despite my obstetrician and neurologist having conversations while I was pregnant and they were discussing valproate syndrome, I know that he was not added to the Epilepsy and Pregnancy Register - it was there. Whether that backs up what Doctor Morrow was saying about the concerns over litigation, or if I forward, if I put a child on there then I'm at risk of litigation and my Trust is, and all of that.

But it strikes me that there needs to be - in order to get that sensible evidence base, there has to be something mandatory. If you want to be treated with a medicine then you should - I believe, maybe this is for Valerie to look at the ethical side of this - but I believe I would want my information about how I get on with the product to be added to the safety data in order to help other patients. But that's a conversation that no doubt you will raise both sides within your recommendations. Cyril, would you like to ask me anything?

Cyril Chantler: I really wanted to listen, to think. You raised the question just very quickly on how you mandate a registry; that is really quite tricky.

Emma Friedmann: Mm.

Cyril Chantler: But we have been taking advice about that under GDPR and we've been talking to counsel about that. So, we're on to it, but we've not yet reached a conclusion.

Emma Friedmann: Yeah, I think the opt-out - I mean I think the National Joint Registry said that 95 per cent of people were happy to be on the registry. So, if there's only a 5 per cent opt-out...

Cyril Chantler: I agree with you.

Emma Friedmann: ...then so long as that option is there, I would agree with most of the people, that if presented with information to you, that having an identifier as the national - your NHS number, that would be sensible.

Julia Cumberlege: Can I just add to that because we have drawn a distinction between a database and a registry.

Emma Friedmann: Yes.

Julia Cumberlege: The database would be mandatory but the registry, at the moment, we take up what you're saying, and we have to think about that.

Emma Friedmann: Yeah.

Julia Cumberlege: But certainly, in order for us to get accurate information, we need a proper database to start with...

Emma Friedmann: Mm, yeah.

Julia Cumberlege: ...and then draw on that for the registry.

Emma Friedmann: Yes, definitely. But I think something that the Congenital Anomaly Register were saying the fact that they don't get back in touch with the patient, because they have taken the opinion the patient is going through an emotional time. Therefore, they wouldn't want to be disturbed about it. Well, I'm sorry, but that's again somebody else making a decision on behalf of patients when they haven't consulted the patients.

Cyril Chantler: I'll say one other thing, if I may, about the Summary Care Record, because I've been involved with that for some years. But if you look at – I'm not obsessional about reading government documents but if you look at page 94 of the long-term plan you will find there is a proposition there that people with chronic illnesses should own their own health care record.

Emma Friedmann: Mm.

Cyril Chantler: The whole record.

Emma Friedmann: Mm-hm.

Cyril Chantler: That would be a care plan and a record which would be interoperative with all the other records, which are held on people who have long term conditions -likely be their hospitals or GPs SystemOne, Vision or [IMIT] or whatever.

Emma Friedmann: Mm.

Cyril Chantler: The notion there is that...

[Aside Discussion]

Cyril Chantler: But the notion there is that enables health and social care to be coordinated by the person who is affected not just the disease. So that would be an extension of what you would propose.

Emma Friedmann: Mm.

Cyril Chantler: I can speak out with this Review that I very strongly favour that personally.

David Body: Certainly when I was a trustee with the Patients Association, one of my co-trustees who works with [REDACTED] was then working on an app you would have on your phone which would contain a lot of that information for precisely that purpose.. to identify.

Cyril Chantler: Yeah, he's shown me his.

David Body: Yeah, well whichever healthcare need, you were then confronted...

Cyril Chantler: Well this goes beyond this because it's got to be interoperative with everybody else.

David Body: Yes.

Cyril Chantler: Anyhow, so...

Emma Friedman: Yeah.

Cyril Chantler: Okay?

Emma Friedmann: Lovely.

David Body: Back to the list.

Emma Friedmann: Yes, back to the list. Right, Simon, quite a few bits and pieces about communications. I have a bit of a bee in my bonnet about communications. But I think something that has upset me and my involvement, which has only been really since 2010/11 has been the misinformation presented. This is from a wide range of sources, but there has been the misinformation, which is denying that informed choice, in effect. It's not really supporting developing scientific knowledge to misinform people. It's not - it's just - there are just big issues around it.

I understand the concerns people have about fake news and this quack saying this and somebody else saying that. This person - I understand that there's all those concerns but at the end of the day, it should be for the user to decide, the person who is having that information to make that decision. But when the information comes from an authoritative body, so whether that's a government, a big national charity, an organisation associated with the government, that needs to be tackled. The whole evidence base and how we establish - if you don't know, if these bodies

don't know, they need feel free to say, 'I don't know'. There's inadequate evidence. This is what some people say, this is what others say.

Something that I hope that you will be able to deliver in all of this is a change in the format the patient information leaflet that comes inside the boxes for all medications. At the moment it's tiny print. After I've had chats at the community centre that you came and visited, I've had conversations with patients, and I've said 'do you read the patient information leaflet?' 'Oh no, I don't bother, it's tiny words', they all say the same. They're just not taking it in.

I think if there could be some work around the format of the patient information leaflet and yeah, just some workaround that would be really useful. Speaking to a wide range of patient groups, from people with learning disabilities to people who are struggling with their vision, like I am a little bit at the moment.

The format of the drug safety updates and guidelines; so, the MHRA will put out their drug safety update, and NICE will put out their guidelines. What I've found with the drug safety updates from the MHRA is when it comes through on emails - I've subscribed to various things that I am interested in - when it comes through to my email box, the first half of the sentence taken up in the subject box doesn't mention the product. So, if you're looking at it on a mobile device, you've got to click into the whole thing to read it all. So, there's little bits and pieces like that.

Also having a summary box, the top five things you need to be aware of; the cohort who are using it – well, the name of the product, the cohort who is using it; any contraindications changing to restrictions, places to go for further information, probably some other bits and pieces with that.

Also, to have an auto-link in the prescribing software, so with these GP systems, SystemOne, and the various others, if whenever you clicked to prescribe the medication or renew the prescription for somebody, a box popped up and said, have you read this alert? For it not to be two pages A4 that you've got to read and if you want the evidence that backs up what's in the statement, you've got to click to four other research papers. That's the way that it is at the moment and it's not practitioner-friendly. We need to make these things a bit more friendly. So that's on communication. Would you like to ask me anything about comms?

Simon Whale:

Well you've raised some quite important practical points actually. You will have seen some of the things we've said to other people throughout the

hearings over the last six months, have been around the system, in all those different guises, being clear about what it doesn't know about a particular drug or device, as well as what it does know.

So, to your first point about women being given the information they need to make an informed decision, to exercise proper choice in a safe environment, absolutely the system should be clear about what it knows but also what it doesn't know. I think that is a culture change for the system. We've explored that; you will have seen us explore that [unclear]...

Emma Friedmann: Oh definitely.

Simon Whale: So hopefully you get a sense of our thinking, emerging thinking about that.

Emma Friedmann: Yeah.

Simon Whale: I think as far as patient information is concerned, they're not user-friendly, as you say. It should not be beyond the wit of the system, manufacturer and regulator combined to be able to get it more user-friendly. I think that's something that goes way beyond sodium valproate, it goes way beyond any particular individual medicine. I'd say it's just true [of unclear]...

Emma Friedmann: Mm.

Simon Whale: ...in general. It's not just about the size of the font, the print. It's also about making it a language that people understand.

Emma Friedmann: Mm.

Simon Whale: Things have improved over the years a little bit now but there is still a long way to go.

Emma Friedmann: I mean the MHRA and when we've worked with them on the valproate toolkits and the wording to go on the outside of the box, the wording for the information booklets in 2016 and 2018, they have consulted us as patients and said 'you lead, patients you lead on what it is that you feel is sensible language and presentation of this'. That has been very welcome. MHRA asked me to have a read through the Dear Doctor Letter and make any changes that I wanted. So, I did that, sent them back. I haven't gone back and checked whether my edits were used or not but it's the fact that they communicated with me, Emma, what do you think to this wording?,

There were a few bits that I changed. But it's just them asking, which is really nice. The Yellow Card, these leaflets, I had to wait six months for a box of 500 for my FACSaware stall up in Leicester and for the various presentations that I do, because they were waiting for a print to be done. Six months, which is outrageous. These need to be in all waiting rooms, just to prompt the patient, to make the patient understand that they are part of the process; empower them in a sense and obviously to provide the regulators with greater, more useful information.

Now, this is something that the Medicines Communication Charter put together to promote a conversation between prescriber and the patient. I can share a copy of this with you, but this was shared with, such and such, on the date, by – 'I would like to help you to get the best from your medicines and to achieve that, we need to work together. Though I am your doctor, you are the expert when it comes to things affecting you and your life.' It's a great prompt. If all GPs were actually having that kind of conversation, then I think it would really, really help.

But the fact that these things already exist, they're just not being promoted, and they're not being used. So, I think rather than completely - you know just design something completely new - let's see what's there first and are we using it as it's been designed to be used?

Misinformation, all right, I had a neurology appointment a month ago, these are still there in the waiting room, 2013, they're out of date. They don't highlight the risk of valproate. Just for them still to be there in a neurology outpatient waiting room, it's unacceptable because there is no other information there. This is a symbol that was designed, now personally - all right, I mean have you got any ideas as a panel what that...

Valerie Brasse:: What is in the circle, the red circle, I can't see?

Emma Friedmann: It's a...

Male: Interesting...

Emma Friedmann: It's a foetus.

Julia Cumberlege: So, it's thinking about future children because they're fainter in the woman, as it were, so it's the future.

Emma Friedmann: Mm. Okay, well this is what was suggested by a charity when patients had already put forward that symbol and when that is the recognised symbol. This symbol was pushed repeatedly at the valproate stakeholder meetings.

Repeatedly. It's that kind of thing that, well the patients have said this is what they want. Yet somebody else is trying to dictate and push something on us. All right so just need to be aware of that. That's kind of it on the communications side, but if you have any questions then I'm happy to respond.

Baroness, a real challenge is irresponsible prescribing. It was Mental Health Awareness week last week, it's epilepsy week this week. When you just read through tweets that people are putting out there, and they're giving these huge long lists of five, 10, 20 medications that they're being prescribed. They're not being given information on them. I cannot believe that 10 medications have been tested against each other for short-term, long-term impact.

It is causing a lot of patients to completely lose trust in their medical professionals. That is not good for the profession. It's not good for us patients, so that really, really needs to be challenged. The overdosing. The overprescribing. The, here's a pill before a therapy. Sometimes you need the pill, obviously, I'm only alive because of the pills I take. But I feel that this is something for the GMC, for them to put something in place and for them to actually start accepting what patients are saying, I think that's a responsibility.

On to a political sort of point - when there was the development of the *Health and Social Care Act*, were there discussions about the dissemination of safety information? Did that come into play? I haven't read the whole Act; I've seen bits and pieces of it. What I have seen with the private providers and the public sector, NHS providers, there is an inconsistency. Private providers will do something voluntarily. There will be a mandatory requirement or there will just be a loose guideline for NHS. It's sensible to bring it all together but was this discussed as part of the *Health and Social Care Act*?

Julia Cumberlege:

Do you know, I have to say, Emma, I can't remember. I, in my loft I have got the whole of the Bill, every single - it was the longest Bill that they'd ever had for a health issue. You remember we had the pause in the middle of that Bill? Then people brought in a whole lot more issues that they wanted to discuss.

What started off as quite a simple Bill then became a Christmas tree because everybody hung on everything else they wanted to see in the Bill. So, I would like to go back and look at that and certainly think about safety

in the context that you've put it. To be perfectly honest, I cannot remember all the debates that took place...

Emma Friedmann: Mm.

Julia Cumberlege: ...because it went on for a very long time, months and months and months. I would have to look at that. Of course, what really matters is not so much the debate that took place when the Bill was being debated, it's what's enacted. It is actually the Act that is the most important part.

Emma Friedmann: Mm.

Julia Cumberlege: Because that is what Parliament decided. Again, one would have to go right through the Act again.

Emma Friedmann: Yeah, okay. I suppose I saw back in - when I gave evidence at the European Medicine Agency in 2017, the thing that I have noticed, the failure of valproate toolkit in 2016 to actually get out to the frontline where it was needed, was this challenge of the dissemination of this package. It wasn't just the UK, it was right across Europe. But the fragmentation of the NHS, the increased use of private providers to provide NHS services, the move towards a privately-run NHS, the lines of communication need to be properly firmed up.

Whatever your view about a privately-run NHS, versus a publicly run NHS, that's political and I'm sure there are differing views here in the room. But there must be - private patients going to the private sector must be protected. NHS patients must be protected. It does all need pulling together, and it's not happening at the moment. Anything that you can do collectively to pull the systems together will greatly aid that.

Julia Cumberlege: Can I just say about Bills that come before Parliament?

Emma Friedmann: Mm-hm.

Julia Cumberlege: Usually they start in the Commons. Sometimes they start in the Lords but usually in the Commons, and you've got a first reading, second reading, committee stage. We had, in the Lords, days and days and days of committee stage. Which enables anybody to come in at any time to debate it. Then you've got the report stage where votes are taken. Then you've got the third reading and then you've got, this Bill [to now] pass. So that takes place in the Commons then it takes place in the Lords.

When we made alterations, modifications, which we do quite a lot to Bills, it then has to go back to the Commons. They have to agree to our modifications, or they don't. If they don't agree it comes back to the Lords. If we consider it again and say no, we want to stick to what we want, it goes back again to the Commons, then it comes back again to us. Passing a Bill is a huge task.

Emma Friedmann: Mm.

Julia Cumberlege: To remember every strand that was discussed during that...

Emma Friedmann: Mm.

Julia Cumberlege: ...and I wasn't involved in the Commons, I was only involved in the Lords, and in fact put down a number of amendments, some of which were accepted, some of which weren't. In between all of that, there's a lot of negotiating going on with the Department, with ministers, to see if they will agree to these amendments. Usually, you try and get cross-party support, so you've got in the Lords, of course, you've got those who don't have any party affiliation, independent. So, you have to think of them. It is a huge task. It is extremely thorough and as I say, I mean to remember every strand that is debated, I can't do that now.

Emma Friedmann: Mm. All right, okay. On to another point, a big movement lately has been towards online providers of prescriptions, delivery services and also online providers of, speak to a GP, speak to a health professional. This area needs a lot more regulation. Lots of us patients with severe medical conditions, we need to have that delivered prescription. We also need, though, to have some face to face contact with our pharmacist. Our pharmacist needs to really be checking that we are still a functioning human being.

My concern with the online providers is that you're just being dispatched this medicine and you're not having that opportunity to chat with the pharmacist. There's been this wonderful push to get people to recognise the professionalism of pharmacists and the importance of going to a pharmacist before going and seeing your GP. This is kind of like bypassing the professional. Pharmacists are so important in this - in medicine safety and providing that information about the medicines you're taking and being that first point of call.

I have a lot of concerns. I've raised this with the MHRA, I think the community pharmacy groups have raised these issues as well. I'm very lucky that I've had the same pharmacist for almost 20 years now. But when

he retires, will that small community pharmacy be seen as a sustainable business? I very much hope so because that one to one - he's seen me at some terrible points when I've had really challenging times with Andy. I've been in a real state of mental ill-health and he's been there as that person that I can just go to the top of my road and speak to. There needs to be some kind of protection of those people.

Valerie Brasse: Emma, can I just ask what sort of feedback you've had from the MHRA because that's a very important point. I've just received a notification on my system to tell me about my local online pharmacy. Of course, it's one part of the system sort of spearheading, isn't it, it [away] with modern technology, whereas actually leaving behind really quite important parts that need to be all knitted together.

Emma Friedmann: Mm.

Valerie Brasse: I just wondered whether the MHRA have been back to you...

Emma Friedmann: The...

Valerie Brasse: ...with any...

Emma Friedmann: Yeah.

Valerie Brasse: ...consolation or consoling words that makes you feel that this is going to be managed very well?

Emma Friedmann: They are very concerned. I haven't been given an update on action. But you get a mailshot come through, advertising that the company - it's got the NHS logo, you assume it's an NHS service; no, it's not actually. The MHRA are very concerned. Pharmacy bodies are very concerned. It's something that needs to be factored into these regulations. If they are going to provide a one- to-one, face-to-face contact within their service, let's see what that is going to look like. These things all have to be assessed on their merits. I hope you'll be able to follow that up really because it is affecting a lot of people.

Now, for Sonia, a couple of research points really, you've probably found out the answers to these already. What is the social and market impact of our current regulatory system? What research is being done on valproate and abnormal sperm and the outcomes? I think I may have mentioned before that when we had a lot of media publicity after the European Medicines Agency public hearing in 2017, I had three women contact me in the space of a week saying 'I've just seen these children and heard this on

the TV, our children have signs of this valproate syndrome, but it was just the dad that took valproate'.

I took it up with Doctor Ian Hudson, CEO MHRA, back in 2013 and he confirmed to me that infertility - that was mentioned in the patient information leaflet - was actually about abnormal sperm. So, I know that the MHRA are aware of that. The European Medicines Agency will be aware of that, yeah.

Sonia Macleod: I know certainly when we looked at the active measures of research the EMA put forward, there's as you say, they are aware of it. In terms of going forward, we have asked them for an update on where we're at from actual manufacturers. So, we are waiting for that. It's on our radar, we are aware of it. It is something that we haven't a definitive answer to yet. I suspect that may be because the research is ongoing.

Emma Friedmann: Mm.

Sonia Macleod: There isn't a definitive answer yet.

Emma Friedmann: So, this is something that needs to be incorporated in the database and for the registries to extract the data off. This acknowledgement that there are environmental factors that will affect sperm. Somehow that needs to be extractable from a database.

Sonia Macleod: In some ways, it's much - it's not straightforward to track teratogenicity when it's mothers ingesting it. In some ways it is more straightforward as a study. It is more difficult when it impacts on fathers. That's not to say it can't be done. It is just that bit more complicated.

Emma Friedmann: Mm.

Sonia Macleod: It's always very obvious with the mother of the child, it's not always so obvious with paternity, so that does add an additional issue.

Emma Friedmann: I've had questions asked in the House of Commons about this, and the response that I've had from the Department of Health and Social Care or their representative, has really not acknowledged the importance of that. If we want to promote family planning and the idea of being responsible before you become pregnant or before conception, take responsibility for your body, then these things have to come out.

Sonia Macleod: I think it is also - it is partly being caught up with the fact that this is an area that is a relatively recent idea that actually sperm quality has substantial

impact on children. It's not something that's been around an awful long time. We've known for much, much longer about the maternal impacts of medicines, taking them when children are in utero. The impact of sperm quality is something that just hasn't had the same impact in the same sort of profile.

Emma Friedmann: Mm.

Sonia Macleod: It is beginning to get even more so now; we are beginning to get more and more studies that do show the impact of paternal age and things like that also. I think it is an emerging area. That may also be why the research is behind, it just simply is.

Emma Friedmann: Yeah. Well, anything that you can do in your research searches to find systems that have been effective in monitoring that, and obviously anything to do with valproate and the abnormal sperm studies, then that would be great. Because a lot of people are seeking clarity on that.

Sonia Macleod: I can absolutely see why.

Emma Friedmann: Yeah. The intergenerational effect of valproate. You've heard Branwen talk probably on several occasions, she wants to know.

Sonia Macleod: Yes.

Emma Friedmann: Her friends...

Sonia Macleod: Want to know.

Emma Friedmann: ...want to know. We have these reports about children of women who were exposed to valproate, how their children are showing similar signs, that has to be established, yeah.

Sonia Macleod: Yeah, I mean again, absolutely it is within the research that is going to be looked at going forward. EMA, MHRA are aware of it.

Emma Friedmann: Mm.

Sonia Macleod: But that's no consolation for people who want an answer now, is it really? But it will be done, but at the moment it just isn't there.

Emma Friedmann: Yeah. Now I just want to make a statement. I am vaccinated, my son is vaccinated. I am not an anti-vaxxer, I am not an ex-vacser. I like to ask for evidence. After hearing Doctor Raine, the MHRA, mention the importance of the monitoring of vaccine safety, in any database or research or

registries, for that to be properly looked at. I've blanked out the inflammatory comments on this, but this is from the US, but that was the vaccine schedule...

Andy Friedmann: US stands for United States.

Emma Friedmann: It does, yes - 1962, 1983 and this is 2019, child vaccination schedule. Now I have looked for information on impact of having this number of vaccinations in your childhood. It's a minefield. I'm not finding anything. But in my local GP surgery I'm seeing leaflets promoting a vaccine during pregnancy and where you look to see the safety data - obviously I'm a lot more vigilant and I'm immediately, right where's the safety data on this - it just says this product has been used in the US for a couple of years.

That's it. It provides no links to a research study. The vaccine in question is something that most people have during childhood. Whatever happens in this process, the monitoring needs to be looked at. There's lots of - it's such an inflammatory issue. It's so challenging. If I put a tweet out or something, questioning a research paper, the abuse that I receive back. It's similar the other way around. Somebody advocating a vaccine will get abuse from anti-vaxxers. Then people that are anti-vaxxer, mixed up with the ex-vaxs which are mixed up with people like me that just want some clarity in the area.

But we can't have this being the thing that we're all sat round again in 10 years' time saying - we just need to be aware and we need to be vigilant. Free trade agreements and whatever being set up post-Brexit and whatever; are we going to have the US vaccination schedule with no supporting evidence to show that it is actually improving child health and child outcomes? What are going to be - are these things going to become bargaining chips in the - but that's just an in the air kind of question.

Sonia Macleod: I think in terms of things being added to the vaccination schedule, we do our own assessments, they are national assessments, they are not international assessments. So certainly, when you look, nothing would be added to the vaccination schedule without a thorough national assessment of it. That will be the data. So, I don't think - regardless of Brexit I can't see that changing because that is just the way that things are added to the schedule.

Emma Friedmann: Okay.

Julia Cumberlege: Emma, I'm very conscious that we really have taken just an hour.

Emma Friedmann: Okay.

Julia Cumberlege: I know we started a few minutes late so...

Emma Friedmann: May I say three...

Julia Cumberlege: ...if you'd like an extra five minutes.

Emma Friedmann: That would be wonderful because I just have three points for Doctor Brasse and then I'll answer anything and allow David to speak if he wishes to. Sorry, David.

David Body: I think we've run out of time.

Emma Friedmann: Doctor Brasse, okay, there are various ethical dilemmas that you will have seen in this whole process. The things that spring to mind to me are; is current practice ethical? But looking forward the fast-tracking of medicines and devices and the precautionary principle, that minefield. The regulation of herbal remedies to be considered as part of this regulation review. Herbal remedies including cannabis and non-invasive therapies.

The things about cannabis and epilepsy and how it helps people who are in severe pain who haven't responded to various things. There are huge questions around that because it's a criminalised product, but if there are so many health advantages to it, if it is helping so many people where conventional medicines are not, all of that I think there needs to be some more proper conversation about that. Basically, maintaining precautionary principle.

[Aside Discussion]

Emma Friedmann: Any questions?

Julia Cumberlege: Right, well, thank you very much. I just want to thank you. I hope we've met your exam questions with at least thoughts, and they've been really good, stimulating questions that we've had. I'm very sorry David, I know you probably wanted to speak but I'm afraid we've got other people coming.

David Body: I know you have. I'll take two minutes of your time. First thing to say is you have a written submission which [unclear]. I think the - to my mind, the acknowledgement that you...

Cyril Chantler: David, can you speak up, please?

David Body: I'll do my best. The acknowledgement I think you have to make in your Review of this is that the immense contribution that has come from the patients, and I believe it was an unsuspected contribution, and it is right to say the patients by themselves have done far more for the patient cause than lawyers have ever managed to achieve. As you can imagine from someone who practised for 37 years in medical law, that isn't an easy admission to make. But it is to my mind essential to this Review coming into...

Julia Cumberlege: Well, that's why we designed it as we did.

David Body: I think it is also something which having set that agenda, having contributed so much to it, it is critical one of the things that this Review disseminates is that good practice about patient participation goes far further than simply valproate..

Julia Cumberlege: Very much accept that, thank you very much indeed.

David Body: I shan't say the controversial things now.

Julia Cumberlege: No, right. Well, thank you so much for coming. I have to say for all the work that you do when you're out of this room, working with all your members and all the rest of it. David, I'm sure we'll hear from you again sometime.

David Body: Yes, I'm sure.

Julia Cumberlege: But thank you all very much and thank you, Andy, for coming. Andrew, bye-bye.

Andy Friedmann: Bye everyone... .

Cyril Chantler: Thank you very much.

Emma Friedmann: Okay, thank you.

END OF TRANSCRIPT

Session 4: OACS, OACS Ireland*

START OF TRANSCRIPT

Julia Cumberlege: So perhaps if you could just start by saying who you are and your organisation and why you're here so that it's on screen.

Carol Lapidge: So I'm Carol Lapidge, I work with OACS alongside Jo and obviously Karen as well. We represent parents of children who have got or been damaged by sodium valproate.

Julia Cumberlege: Thank you very much - and Karen?

Karen Keely: I'm Karen Keely, I work alongside Carol and Jo, and I do Ireland as well which we have a board of eight people and just - it's not all about the parents, it's all about services and all about doing the right thing for the children. So that's what I do in my role.

Julia Cumberlege: Thank you very much and for mentioning Jo but we understand she couldn't be here today, quite understandable. So it's over to you really, I think Carol first and then Karen.

Carol Lapidge: I'll just read off what I've written because I'm not very good at... Julia

Cumberlege: That's fine.

Carol Lapidge: Our daughter was home with us last weekend and we chatted about making the speech. Her advice was, take deep breaths mummy, relax, or you will panic and have giggle fits and your brain will go kaput. So she knows me so well. I do apologise, it just jumped on me.

Cyril Chantler: Take your time.

Carol Lapidge: Jo is very sorry she can't be here today to deliver the speech and we've worked on this together and I hope I can do her justice. She is much better than I am at delivering speeches and I'm more of a sit back and listen and make notes and ask questions kind of person. We spent a very long time listening to and reading the evidence and there has been much talk of the commitment of the governing bodies to make changes

and to learn from the decisions around valproate and we feel this is commendable.

However, there has been little talk of what the future holds for our children and in finding the lost children which is very disappointing. It is clear from the written and oral statements given by the manufacturer and the regulators that information was available and they were aware of the teratogenicity of valproate from day one of licensing. It appears to us that the results of the tests carried out on the rats were disregarded.

Why this is the case we cannot know for sure but, given the history of what appears to be constant cover ups, we would suspect that all they were interested in was treating the patient with no regard to the long-reaching consequences. In the first few decades there were papers published from individual researchers that warned of malformation, and neurodevelopmental concerns. It appears to us that this did not suit those [unclear] prescribing valproate as they took a 'carry on until proven' rather than a cautious approach.

There was no apparent follow-up or tying together of any information gained through the individual researches. It took about 20 years before studies began on malformation and another 30 to 35 years before neurodevelopmental delay was considered.

OACS feel this was a total disregard to patient safety by both the regulators and the manufacturer. We would like to be assured that the papers from the '70s and '80s have been brought forward and considered.

We find it unprofessional and careless that the manufacturers and regulators did not monitor the children born to the first mothers prescribed valproate throughout the whole of their development from birth, through school, and into adulthood. It is suspicious that the early reports were not brought together and studied more closely.

Throughout Sanofi's evidence it appeared they stated that there was

not enough scientific evidence in the '70s and '80s to warrant a concern with regard to neurodevelopmental delay.

Surely the smallest amount of evidence should have been enough to warrant a closer inspection. We would like to point out that not one party in this whole saga was proactive in their research or monitoring. We've been given to understand that the recommendation of the manufacturer from the beginning was to prescribe valproate when no other medication works, and it appears that the regulators ignored the advice. As a collective, the healthcare professionals prescribed valproate without any clinical trials on humans, and ignored the evidence of the animal trials.

As this was a joint decision it can be perceived as being made in the best interests of the patient, however, we feel this isn't the case. We feel that what has actually happened is the right of freedom of informed choice was taken away. We were reassured we were taking a safe medication when in fact we were pumping poison into our unborn child. In the written evidence we have seen presented by Sanofi in December 2018 there are paragraphs where sentences have been redacted.

We have been asking for transparency throughout this Review and while the documents have blacked-out sentences we cannot be convinced we are being allowed access to all the facts. Surely in 2019 it is time for transparency. We have a right to know the full truth and historically this has not happened. Sanofi had a moral duty to report any issues regarding valproate and should not have been content to accept the regulatory guidance especially as they are experts on their own product.

There appears to be no consistency or commitment in research of valproate in the early years when it should have been a priority and this is a huge failure on the part of Sanofi and the regulators. It was admitted during the evidence given by the MHRA that in 1972 the then CSM knew about the teratogenicity. It is beyond our understanding as to why the MHRA did not initiate warnings regarding valproate,

knowing that there was strong evidence at the time of the harm valproate can do.

In 1968 the ICI documents discussed damage to the unborn child, and I believe Karen has more information regarding this and the history of valproate. I mean, what hope have we seen in the historical documents stored in the National Archives that may hold vital information regarding this Review. It's the charity's view that without the redacted documents in the National Archives a full and honest assessment and decision cannot be reached without adding these documents to the statements from the victims, manufacturers, and evidence that our legal team has provided.

Every piece of evidence must be considered no matter how small it appears to be. OACS and their members want a judge-led inquiry to expose the full extent of the catastrophic events that have taken place since 1972. OACS has recently found that one Trust in Wales has put together a recall of all women taking valproate, and so far out of 14 cases seven of those were found to have children harmed by the medication. Out of those 14 cases there were three miscarriages and one pregnancy lasted through to 33 weeks.

At this moment in time, the PPP - there is no counselling in the UK for these women and that's just not acceptable. We cannot stress enough the importance of finding the lost children. This will highlight the future of those that are still children today, it will give us clearer understanding of the care our children will need throughout their life. We will gain information on how FVS impacts every aspect of their lives, not to mention giving those that are now adults without diagnosis the chance to find the most appropriate support.

Government and/or Sanofi could fund local CCGs in researching and finding the lost children via the GPs, hospitals, and schools. We are aware this would be a mammoth task but we feel that this is the least they could do. I know approaching schools has been put forward before and we feel that this is a great start but we have to be aware that some children may be missed if we are not careful.

Just as an example, some of these children may be on the autistic spectrum but treated as being naughty and would not have been registered disabled. There are also those who may have been adopted and have no idea their mother had taken valproate. If there were to be a two-pronged approach from the health authority and the education department I am sure, given the right support, and funding many of these children will be found. If some of them are missed then at least we know every possible action was taken to find them.

The lost children are now adults and may not have obvious symptoms of FVS. Some will have grown into adulthood functioning as best they can and with perhaps what will appear to be little idiosyncrasies when in fact if they had been appropriately assessed they may have been found to be on the autistic spectrum. I cannot stress enough how well those who suffer with any kind of LD manage to develop coping skills that then mask their needs. It doesn't take very much to change in their life for them to fall apart.

Some may have shown aggressive behaviour and be considered to have mental health problems but never assessed appropriately. If they have extreme anxiety leading to panic attacks and then aggression it would be safe to assume that they could be assessed without full knowledge of their medical condition. FVS can manifest itself in a destructive way and, not knowing why they are behaving in this manner, they will not receive the appropriate support and it makes them incredibly vulnerable.

There is the concern that they may turn to drugs, alcohol, or be left open to abuse and in danger of suicide. Sadly, as FVS is not well known, or possibly not even taken seriously within the health profession, the above issues can relate to those who have actually been diagnosed. I recently attended an event in North London regarding the LeDeR, I don't know if you know about the - it's a learning disability morbidity review. It was quite scary for me as a mum with a daughter with LD. I did not realise that men with LD statistically die 26 years younger than those without it and women die 29 years younger.

They discussed the high rate of death caused by epilepsy and constipation. Constipation was the biggest shock to us, especially as so many of our children suffer with it. It highlights the concerns we have regarding the unknown medical problems especially this, which is a health problem that is never talked about, no one wants to talk about their bowel habit, and quite frankly if a person has suffered with constipation all their life they wouldn't think it unusual.

When it is brought to the attention of health professionals their first instinct would naturally be diet. Our daughter was put on special diets but nothing changed and her consultant sent her for a barium enema. I know that this is not a very nice procedure and our daughter is a superstar for agreeing to do it. It found she had a slow processing colon and her bowel muscles were weak causing acute constipation and a high risk of infection. This test is not automatically ordered and there are not many hospitals that can do it. It is more likely that sigmoidoscopy or colonoscopy will be performed when it may not be necessary.

Our children have such complex needs it is difficult to truly understand what support they require without a full MOT, both physically and mentally. We feel this must be arranged immediately. As they grow older their needs and problems change and it is sometimes hard to keep up with it. There is a history of parents being accused of Munchhausen by proxy because they appear to be going to the GP all the time with different complaints.

If a full MOT is performed on a regular basis we will know how best to treat or work with the current problems and how to prepare for the future ones. The families need support now and the evidence is clear that valproate has damaged our children. They need support with medical reviews, assistance with claiming benefit, and appropriate support packages now, rather than sitting on waiting lists.

The importance of starting assistance early in life is paramount for anyone with problems in order for them to reach their potential, and our children are no different. The longer they wait the greater the risk of medical and educational developments. While at the event I spoke to several community nurses who specifically work with adults with LD. One of the conversations highlighted that the patient needs to be listened to so the patient feels safe and that the parents often know how best to handle a situation but we're not listened to.

The nurses felt that there was not enough time spent on ensuring the patient felt safe. Some hospitals have a hospital passport but they're not always looked at. One of our members brought their daughter to

a hospital for a procedure and the anaesthetist completely disregarded the mum's advice. The situation became very difficult for both mum and daughter. This is not uncommon. A hospital passport should be given to all our children. On this should be a list of their problems and their phobias and the complex issues that arise.

I have examples, a young man with LD has a fear of black mattresses and would walk out of the hospital rather than have treatment if he saw one. How simple would it be to ensure that the black mattress wasn't in the room? A young lady who has an obsessive fear of heights that cause panic attacks but she had to be pushed back to her room in a hospital bed following a procedure. How do you get around it? One hospital porter said, no problem, and brought her a recliner chair with wheels to the recovery area and sat her in it. She thought it was highly entertaining and there were no panic attacks or aggressive behaviour.

It is a simple thing to put in place but the professionals have to adhere to it. We have another case of a young man who appears to be high-functioning but struggles quietly. He should have had support when travelling to his studies but this was not available and his mum had to stand in, taking time out of work. He needs to have a procedure that requires a request for funding and the waiting list is very long. His parents are now planning on paying for this privately. This should not be the case. This should have been dealt with years ago.

Some of our children appear to be high functioning as well but this doesn't mean their understanding of consequences is as competent as people are led to believe. We may be asked why the health and social care available is not sufficient for our children and why we feel it may not meet their needs. It is not sufficient full stop. There are such long waiting lists for accessing all therapies and when you finally get an appointment other issues have arisen due to the delay. Funding is constantly cut and spread thinly, and with an ageing population we will not be able to meet everyone's needs.

Our children are not receiving the full appropriate support now so who knows what the future will offer. The future does not look bright and there are massive battles ahead for many parents.

Families are struggling to cope with the issues they are facing today. They have no emotional or mental capacity left to look at how to resolve the problems that will arise in the future. We have battles every day with our children just getting them ready for the day ahead, and then when we turn to the professionals for help we face further battles.

We all at some point as parents of children with FVS have to look to the future. Residential homes are being closed and in some cases, such as the big institutions, this may well be a good thing. Or they are being turned into supported living accommodation which is financially complicated. In the 1980s much of the social housing was sold off and not replaced. In another conversation with LeDeR events it was highlighted by the community nurse that there is not enough social housing to provide supported living for elderly adults.

Where our children will live when we are gone and how they are going to survive are just two of the biggest fears we have for our children. Some of us are lucky in that we own our own homes and will be able to leave them to our children, providing we don't need to sell them to pay for our own care when we're older.

However, many have to rely on the state and there is still the concern of who will watch over them and ensure they continue to receive the appropriate support, physically and financially.

Many of the social housing offered to our LD adults are in areas of deprivation and crime. We can see vulnerable adults being moved into these places where they are not fully protected because the carers are not there all day, as is the nature of the beast that is supported living. Again, you have FVS adults left vulnerable to drug, alcohol, sexual and physical abuse. There is growing concern for the psychological effect valproate has had on the children regarding suicidal thoughts. Many of our children say they want to end their life for one reason or another.

It may be that the reason sounds flippant and eyes may roll, unfortunately our children do not fully understand that if they commit suicide they can't come back. All they know is that whatever trauma they are going through will be over. They don't see the bigger picture and it is very difficult to make them understand. I know this is true of

anyone feeling suicidal but then you throw in the mix of the autistic spectrum and the developmental delay it becomes far more complex.

A mum reminded earlier in the week of how difficult it is when you have a child with the mind of a three-year-old combined with the hormones of a 16 year old. Sometimes we forget that our lives are not the norm. We have families that have...

Carol Lapidge:

We have families that have lost their homes and are relying on private accommodation to rent. The rent is extortionate and the mortgage would be cheaper but they can't afford to save the deposit. If a family are relying on state benefit rents an accommodation privately the council will look at the property and decide what the rent should be. If the landlord decides it should be higher the tenant has to find the difference. How do families manage this? How does an adult with FVS complications manage this?

There are constant battles to try to ensure adults have the most appropriate care package. If we were not here to do this we worry about what may happen. Families are coming to the realisation that at some point they are going to have to face the same issue. We have put a Will in place so that any assets left to her are placed in a trust fund in order to prevent it from being swallowed up completely by her placement in the residential home. This type of Will costs money to put in place.

How does a family who may have their own home but are living from hand to mouth going to afford to set up this kind of Will?

Then benefits - claiming benefits is a massive problem. DLA is now being replaced with PIP and this is causing all sorts of issues. There is no one to assist them filling in these forms and getting an appointment at the Citizen's Advice Bureau is impossible. Our support is only online and we are limited to what we can do.

We have had feedback from parents whose children were in receipt of DLA but have had PIP declined. They do not understand what is different but they are so exhausted they do not have the energy or drive to appeal. Any young adults claiming ESA are being placed on the

return to work group instead of the support group. The system is broken and there is no sign of it being fixed. It makes sense to have a return to work group but what doesn't make sense is when an applicant has been deemed to fall into the support group are then moved over to the return to work group when they are required to reapply in three years' time.

There is no consistency and why should they have to reapply if they have been deemed unfit for work permanently. People will lose their benefit and we already have a case that we know of where a family lost their home and went bankrupt because they couldn't pay their mortgage. The amount of DLA they could have received would have made all the difference. Another parent has been told that the funding is simply not there for her daughter to attend residential college. This is a college for special needs adults as well.

We find this unbelievable. The residential colleges for adults with learning disability may make amazing changes to the young adult. They are a foot in the door to independence and can lead to work depending on the ability of the young adult. I have personally seen a massive improvement in the quality of life of many young adults who have attended these colleges. How unfair and sad it is that this young girl will never get that opportunity.

Looking at the evidence available to us as a charity and the families it appears that there has been a consistent neglect and indifference to the damage valproate is capable of. We are very aware that valproate is a good medication for controlling certain types of seizures and that there are times when there is no alternative. However, as we have stated earlier, the decision made all those years ago took away the opportunity for a family to make a clear and knowledgeable decision on whether they should take the risk of having a child with some form of disability, and putting plans in place should their child have a disability.

We want assurances that the appropriate PPP plan will continue to be in place. Part of that choice should be that women taking the medication for whatever reason are given the opportunity to stop the

medication altogether and supervised closely by the healthcare professions. I strongly feel that this Review has the chance to set out common-sense laws and legislation surrounding teratogenic registration. Any or all teratogenic medication prescribed to women of childbearing age and the healthcare professional prescriber needs to have PIP in place.

Following the emerging compensation allocations in France it is quite clear that OACS and their families do not want a similar compensation scheme, as it is unfair, totally inadequate, and an insult. Ideally it would be in the best interest of the child and adult affected to receive a lump sum and a central trust fund be set up that they can access should their needs change severely and their lump sum dwindle due to unexpected complications in their health.

We would welcome any other suggestions and ideas on how the trust funds are run or a hybrid version of the Thalidomide Trust modified to suit the families of valproate. At the end of the Review OACS trustees do not want a situation where all the government does is ring-fence the valproate children so they get priority treatment and it stops there. This should be the start. If money goes into the pot of health and social care it will be swallowed up and used elsewhere.

Our understanding of funds given by the state is that if the money is not spent by the end of the financial year they get less the following year. Because our children's needs change so dramatically from year to year it's difficult to predict what they will require funding for. We will be in the same predicament where we to fight for our children's rights. Over the decades families have been unable to establish justice for their children because of the legalities of providing an expert witness to give supporting evidence.

It appears that there has been a closing together of neurologists and healthcare professionals who knew the risks to protect themselves. We would like everyone involved in this Review to take off their business head and use their imagination. Think of your children and their achievements from learning to walk and talk to going to university if that is what they have chosen to do. Now imagine your precious

children having a disability that prevents them from achieving everything they have achieved.

Imagine the anguish, devastation, and heartache you will feel knowing your child will not be able to achieve what they have. Think hard about how different their life would be, the struggles they will face and the lives they will have when you are no longer here to protect them, and ensure that they...

[Aside discussion]

Carol Lapidge: ...the struggles they will face and the life they will have when you are no longer here to protect them, and ensure they have all the support they require. Now think about the fact that this could have been avoided. This is a manmade disability caused by a decision made by a fellow human being, not something that life has unfortunately thrown at you. But another person made a decision that changed everything. In all conscience, how can you not believe they have been cheated out of a life they should have had?

These victims are going to need lifelong support. Those who made this decision may no longer be around but it was continuously covered up and they continue to prescribe valproate. Someone should answer for this, and the only way forward where we can hope they will be compensated financially, because that is what we need, is by a judge-led inquiry and we would ask that the review team put this forward to the Government.

The damage that valproate has caused is devastating. The lives it has ruined and continues to ruin is heart-breaking. Families are torn apart and they live with frustration and anger every day. Just one day is a rollercoaster of emotion, and no one should experience this kind of trauma. OACS Charity fully supports the final submission of Leigh Day and David Body, and they express how grateful we are for all their support and hard work. Karen Keely has worked tirelessly, finding research papers and random documents that we would never have had time to find. We wouldn't be here today if they hadn't been behind us all the way.

I've got some questions. I'll try to make it quick so you can get a go.

1. Does the Review team feel the robustness of the answers in relation to the papers from the '70s and '80s was sufficient?
You don't have to answer that.
2. Why when there was some evidence to show malformations and neurodevelopmental delay did the manufacturers and regulators not monitor the children born to the first mothers prescribed valproate throughout the whole of their development from birth, through school into adulthood?
3. Sanofi took over the company in 1981, and in 1982 there was a small amount of research regarding neurodevelopmental delay but this was disregarded - why?
4. Why were the earlier reports not brought together and studied more closely, and were they anything to do with kick-starting the most recent researches that have confirmed neurodevelopmental delay?
5. We would like to know what research Labaz passed to Sanofi when Sanofi took over.
6. During Sanofi's evidence they continually cite that they informed the regulators and that the regulators did not follow the advice. We would like to know the response of the regulators to this information.

7. Why did the monitoring not start until the 1990s, and why was it that they only followed the children up to the age of three months when there was previous evidence of neurodevelopmental problems?
8. Why has it taken so long for research to become public knowledge and why have most families only discovered the devastating news via word of mouth?
9. How can we be sure the evidence and information given by Sanofi is open and honest if sentences in their submission have been redacted? Even if it isn't relevant at least we will know nothing is being kept from us. Considering the history this only seems fair.
10. What hope have we of historical documents that were redacted and stored in the National Archives, what hope have we of them being opened? Surely these are essential for the Review team to know the whole story.
11. In 2018 only 74 reports were made via the Yellow Card and most of them were from patients. This shows a serious underreporting via the Yellow Card system from professionals. What can be done to rectify this?
12. How many times were concerns raised and discounted as not having enough evidence, and were historical researches brought forward every time to compare when a new research was started? Why did it take 20 years to restart? Surely comparing reports that show similar findings are evidence.
13. What evidence is there to prove that not taking medication during pregnancy is more dangerous than taking valproate? We agree there are some who would not be able to manage without the medication but there are many, that with bedrest and listening carefully to their bodies, would have made it through their pregnancy without tonic-clonic seizures. Is this not the action taken by many who suffer with other medical conditions during their pregnancy?

14. Do we know how many deaths there have been due to valproate by miscarriages, stillbirths, childhood illnesses, and illnesses that develop into adulthood, and suicide?

Julia Cumberlege: Well, congratulations, a real tour de force and you were worried that people would not be proud of you. I think they've got every reason to be proud of you, thank you very much indeed.

Carol Lapidge: Thank you.

Julia Cumberlege: You've asked us a lot of questions and I have to say a lot of those resonate with us, sort of the questions we've been asking. At this moment we can't give you the answers. We want to go away and think about it and then obviously we'll come back and talk to you about it. But I think it would be a good idea if we go on now to Karen. Karen, I don't want to cut you short as happened last time.

Karen Keely: I'm going to just slightly pick up on the history. I know I've sent a lot over but there's some - I would like to pick up in more detail the issues that need to be highlighted to the Review team. OACS Ireland has gathered a lot of historical research. We are here to provide the Review team with all the historical documents of the PILs and the SPCs on valproate in the UK, Ireland, and France.

We have also found some discrepancies in the said SPCs that went out to healthcare professionals and the PILs that went out to patients.

We have given the Review team many worldwide documents regarding this issue. We note that the Review team asked Sanofi and the MHRA for the history of the PILs and SPCs. We also note that the full history was not provided by both the MHRA and Sanofi, however, they referenced many medical articles in relation to the SPCs and PILs. Basically, what mother can get hold of medical articles when you know - so I just didn't understand that part? So that's why I ensured I got all PILs and SPCs for you.

It was licensed in many countries, France in 1967, Belgium 1971, West Germany 1973, Netherlands 1971, Spain 1970, Switzerland 1972, Italy 1973, UK 1974, however it was used beforehand, Finland 1972, and Japan 1975. The chronology of events from 1971 to date is provided.

The valproate chronology which also provides copies of relevant committee minutes and communication documents, the chronology outlines all the significant regulatory considerations, communications, and updated product information relating to this issue.

As outlined in the chronology, the possible risk of congenital malformations was recognised from the time of authorisation based on animal studies. Clear warnings about the risks of birth defects associated with valproate were present in the information for healthcare professionals at the time of licensing. The first data sheet of valproate in the UK stated that in women of childbearing age the product should be only used in severe cases or in resistance to other treatments, and this compound has been shown to be teratogenic in animals. Any benefit which may be expected from its use should be weighed against risk.

I've brought over the 1974 UK data sheet in case you didn't receive it from Sanofi. The 1971 original licence application for sodium valproate in the treatment of epilepsy was submitted to the Department of Health in the UK. This application was considered by the CMS and its subcommittees. Valproate was initially restricted to use in hospitals and/or centres specialising in the treatment of epilepsy before it was approved for general prescription in 1974.

Animal data available at the time of authorisation indicated that sodium valproate was teratogenic and the first data sheet dated 1974 indicated that valproate should only be used in women of childbearing age in severe cases or in those resistant to other treatments. In March 1974, the CMS advised on a variation of product licence for Epilim to delete the requirement regarding the monitoring. The requirement to limit promotion to hospitals, other centres specialising in treatment for epilepsy, on the conditions - on the indications of use reads, as generalised for focal or other epilepsies in women of childbearing age.

I've just read that sorry. I'm going to - 1973, 1974, Kew National Archives. We would like all archive documentation to be redacted

on valproate released to a judge-led inquiry. 1974 Drug chemist with no warnings of any type of the teratogenic effects it states the following on page 788. Anti-epileptic agent sodium valproate, Epilim, is said to be effective in the management of some cases of epilepsy which have failed to respond to other anticonvulsants.

Sometimes its use has enabled other drugs to be reduced or withdrawn. Side-effects reported included ataxia, gastrointestinal upset, and hair loss. These occurred when sodium valproate was given with other anti-epileptics. It is advised that the latter should be reduced rather than the sodium valproate. [REDACTED] 1974 - no warnings went to doctors, no warnings went to pharmacists, and this is from the CMS.

In 1982 the CMS considered a paper on sodium valproate and its teratogenic effects and advised that there was a need for a specific research into anti-epileptics, and that there should be an article issued to healthcare professionals in a bulletin, current problems in pharmacovigilance warning about valproate and birth defects.

This was issued in 1983. This was produced by Abbott Laboratories Pharmaceutical Division. Why did Sanofi not produce one of these 'dear doctor' letters for the UK and Ireland and other European countries that they supplied valproate to?

While regulators were meant to update healthcare professionals with SPCs the relevant information did not go out, why was this allowed to happen?

[REDACTED]

[REDACTED]

The teratogenic effects of many anticonvulsants present a serious dilemma in treating female epileptics. There is a small but definite risk, about two or three times normal, of foetal malformations. Recent evidence suggests that valproate has a higher teratogenic potential than most and is absolutely contraindicated.

However, both foetus and mother may suffer from anoxia. Women with low seizure frequencies might be advised to stop taking the medication but unfortunately pregnancy itself seems to lower the seizure threshold. On the other hand if treatment is continued further problems may arise because pregnant - it increase - arise in pregnancy. It increases the clearance of many anticonvulsants so serum levels have to be monitored carefully.

There may also be a direct toxic effect on the foetus, such as sedation, neonatal bleeding, and even neonatal withdrawal seizures. Drug chemist, 5 September 1987, 1987 October, Drug chemist, A Clear View for Epilepsy, in this article on the treatment of epilepsy, the CND September 5, we implied that sodium valproate is absolutely contraindicated in female epileptics of childbearing age. However, this was an unfortunate overstatement.

The manufacturers of Epilim, Labaz-Sanofi have kindly drawn our attention to the Committee on Safety of Medicine's view that there is no clear evidence that any one anticonvulsant is safer or more dangerous than any other in epileptic women. We are grateful to them for giving us this opportunity to clarify this. R.G. Green, King's College, London.

Sodium Valproate 2, 1987, Sweden - The National Board of Health and Welfare has additionally approved the use of sodium valproate for the treatment of generalised epileptic attacks associated with petit mal, myoclonic, or atonic attacks, and for tonic-clonic attacks, grand mal that are inadequately responsive to other drugs.

Treatment of focal epilepsy is also approved when other therapies fail. That's in 1987, no warnings from WHO. This is the World Health Organisation. What I don't understand is, where did we go wrong in all this? So many children are damaged.

I'm going to move on to 1990. In addition to this information on birth defects and neural tube defects, and recommendations on the diagnostic screening were added to the production information. 1983 - An article on the risk of neural tube defects was published. In the

current problems in pharmacovigilance, that's 10 years after Abbott did their - sent their 'dear doctor' letter.

There is a 10-year gap from 1983 in the US and 1993 in the UK one.

Patient information leaflets became a legal requirement for

all medicines in 1999 and in 2000 warnings in product information for valproate were expanded to reflect the available evidence on birth defects, to state that women should be informed of the risks and benefits of continuing treatment. In 2004 the information is revised, contraception is advised, and unplanned pregnancy is not desirable.

Malformations, other than spina bifida, are not included and polytherapy is a risk. In 2006, a very careful evaluation is called for in certain cases. Epilim may be an appropriate choice for women in childbearing potential provided that an informed choice has been made. Epilepsy specialists are mentioned for the first time for the risk of development delay. This is on the PIL, however, in 2006 the French had put autistic disorders - I translated this one. I translated the pregnancy part of it so I'm just going to read out the autistic part.

In addition to several isolated cases of autism and related troubles have been reported with children exposed to sodium valproate in the womb. Why didn't they do it in Ireland? Why didn't they put it on the UK? This is Sanofi, and the regulators. I don't - that's...

Cyril Chantler:

Sorry, what date is that?

Karen Keely:

2006, that's the date they didn't give you the PIL – I've got the PILs as well.,

[REDACTED]

[REDACTED]

So in 2009, the information is revised and a greater focus is placed on communications with the patient's doctor, and more information of potential disabilities is provided

including autistic disorders. Why wait until 2009? From 2012 women of childbearing potential are advised not to take Epilim unless advised to do so by their doctor.

From 2015 a new boxed warning is introduced in the leaflet for the first time, and more detailed information as mandated by the ruling of the EMA in 2014. There's one aspect I would like to bring you back to and that is 1977. In 1977 Sanofi [REDACTED], a

statement he wrote. This has got to do with Abbott. He went over to - from the UK with Abbott with labs and all. Just one thing, there is in fact in the United Kingdom a record of pregnancy and valproate. Forms have been completed if you have a patient who becomes pregnant whilst on sodium valproate and these forms are all sent to [redacted] I recently suggested this at Nottingham [redacted] central point of proof. Of course we're not going to be answered this but at least we have the information whether they will be considered reasonable here I do not know. He was actually talking to Abbott in the worldwide marketing of sodium valproate. I brought the graphs of the second

- the first meeting I sent to you, you have. This is the second one where they're talking about all graphs and some of the research that was taking place. So that's that.

I then brought this because this is the national plan nationwide action on epilepsy, this was 1977. If you want earlier ones I can bring them as well. I have all the epilepsies because I - I don't know how I found them but I found them and it's just saying the same thing over and over you know so sorry, all my questions. Sanofi stated that they updated regulators with the appropriate information of the time.

In 2006, the French PIL and valproate, [redacted] mentioned autistic disorders. Why wasn't autistic disorders mentioned in the UK in 2006 and Ireland in 2006? Why weren't healthcare professionals sent a 'dear doctor' letter yearly? I mean they're dealing with pregnancy register so shouldn't they have updated the doctors on that?

We have previously sent the Review team the 2006 SPCs and PILs from UK and Ireland and France. Why did the MHRA or Sanofi not give a full timeline on valproate to the Review team, or did they? Did they give all the PILs from UK?

Sonia Macleod: Yes, we've got all the PILs. Karen Keely: All of them?

Sonia Macleod: Yes.

Karen Keely: Why didn't Sanofi not produce the same 'dear doctor' letter that Abbott Pharmaceutical Division produced in 1983? Only one 'dear doctor' letter on valproate went out to healthcare professionals based on the [unclear] research. At this stage Sanofi produced sodium valproate worldwide. Regulators were meant to update healthcare professionals with SPCs with the relevant information. This did not happen in the UK and Ireland to my understanding.

Sanofi was involved in the funding of the UK and Ireland pregnancy register, why did they not inform the healthcare professionals that were involved in the said register of their findings, of the teratogenic effects and neurodevelopmental delay at the time of their findings? Do we know how many...

Carol Lapidge: [Unclear].

Karen Keely: ...1977 the pregnancy forms. It appears from the oral evidence that the Review team has not asked Sanofi about the 1977 pregnancy forms. We feel mothers have a right to see such forms and we would like Sanofi to produce the conclusion of said forms, along with the blacked-out part of Sanofi's submission, as OACS Ireland has already requested this information via an FOI and was currently turned down.

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

The HSE has established the Valproate Response Project Group which oversees eight different work streams relating to the issue of valproate. Representatives of the FACS Forum including OACS Ireland sit on the Valproate Project Group, as well as the steering group. The project group

has a number of working streams. Future examination is required to establish liability but regardless of the cost the committee - sorry, I'm talking now about the health committee. We went to the health committee in 2017 and now this is some of the things they've stated in that health committee. So further examination is required to establish liability, but regardless of the cost the committee is of the opinion that the state has a responsibility to assist all those affected by FACS, stated by Michael Harty TD, Chair of the Irish Health Committee. One work stream has been responsible for producing the rapid assessment report and I passed that on to the Review team. The rapid assessment report, it quantified the extent of the problem. This report has been completed but has not been yet made public. Oh, it's made public now.

The data is based on a variety of the national and international data sheets, and while it estimates prevalence, it acknowledges that the true impact of valproate on women and children will only be apparent as the data is collected through [unclear]. Regarding independent investigation, the FACS Forum has received communication from the Minister of Health that indicates that he has not ruled out an inquiry/investigation.

The Irish public deserves answers too so that changes can be put in place to avoid similar occurrences in the future. A full investigation needs to take place so that the families can move forward and we need to know the truth. Families also need a system of redress established so that they can ensure that their children have the best of care when families are no longer around to see their loved ones. Some of these complexities have arisen in relation to the issue of compensation and would also be best addressed via an investigation, which you are doing now.

We have had many meetings with TDs and ministers regarding the issue and we hope to go back to the health committee shortly.

The HSE progress to date - I haven't wrote everything down because we have done so much throughout the year. The HSE has established their valproate response project oversee [unclear].

This is the steering group. I've just brought it all over to you so you have all - you'll be able to see and our workstreams. We have already had women in counselling now for a good few months since November, December, not

[REDACTED]
sure. We've had them all in counselling and I cannot tell you the benefit that they are getting from that counselling. Yes, they come out in tears, I agree, they [unclear] but it is a benefit and it should have happened from day one.

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

If a mother can see something is wrong surely a doctor can see something is wrong, surely a nurse can see something is wrong.

I know nobody is looking for blame but somebody has to be accountable, somebody has to be accountable for all of this. Children have lost lives.

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

I need to know the truth so I can move on and so the families can move on, and I will never know the truth unless all these documents – or Carol or any of us, nobody will know the truth unless Sanofi is 100 per cent transparent, and we need that from them. That's - they owe us that. Why this 'dear doctor' letter from Abbott, why wasn't this produced every year

to a doctor, to a neurologist, to a pain specialist, to a cancer specialist? I mean they use them for everything.

I just don't get why this wasn't produced - I'll never understand it, and every year Sanofi - to my knowledge because I won't speak if I don't have true facts, but to my knowledge they were part of the pregnancy register in the UK or was it a UK and Ireland pregnancy register? It wasn't only Dr Morrow,, which is in that document here [REDACTED] as part of the pregnancy register so - and as for Topiramate....

Julia Cumberlege: Topiramate

Karen Keely: Everybody knows that's out years, that's not a new drug. I mean I was on the edge of my seat when he said it was a new drug coming out that was teratogenic but when he said that I was like, everyone knows that's been out years. I don't get that, you know Phenytoin. The MHRA sat in front of you and stated to you that they licensed valproate because it had the same effects of Phenytoin. I'm like, is this for real? I mean I didn't get that. I mean I don't know it's probably because - I just don't know why.

If you know a drug is teratogenic and whether it's animal, human, or - I don't care. But if you put a strong warning on that and a warning that in layman's terms that women -

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] I don't understand it. I don't think - I'll never understand it and that is why I have produced all the Irish PILs, licences.

You have all the UK's, all licences, and I go back also there was something with [unclear] Europe. This is in Europe. This is where they licensed, you can have a look, they licensed this throughout Europe and the day to day licence and the amount they licensed. Winthrop is also Sanofi. Do you have any questions?

Julia Cumberlege: Well, thank you so much, both of you, that was just amazing, thank you very, very much. I just want to ask you, Carol, you did talk about support packages and I do understand that but you said it was difficult to assess. Has your organisation thought of the elements of the support package, and of course it would vary according to the family circumstances and the young people involved, but I wondered if you'd thought through it and what you would really like?

Carol Lapidge: The care package used for – well, it varies obviously as you said but it depends on the need. But they need, as I said in the statement, a full MOT to decide what that care package would need to be because some won't need as much support as others. So they would have to be looking at what the health problems are, social problems from day one right through to, well end of life really I suppose, especially with the adults. The adults are a real issue because when you have a child your parents look after you and they push, they look for stuff.

But when you're an adult you need more support really and someone to be able to take you to the hospital, you need someone to make sure you eat properly, drink properly, whatever. So it's - actually if you just think about what you do for your children when they're little, that's what the care package needs to be as an adult as well. I suppose, I don't exactly what you want me to say here, but a care package would be decided through the family and social services.

Julia Cumberlege: So there'd have to be an assessment.

Carol Lapidge: Oh, absolutely, there always is, that's what... [Over speaking]

Julia Cumberlege: All right, well thank you for that. Because you talk about adults and of course some of them must be 50 now or something like that.

Carol Lapidge: Yes, [unclear] and other ones we don't know about.

Julia Cumberlege: Yes, so that's quite a difficult thing. Going back to the children, I thought one of the ideas you put forward was this health passport that a child

should have so that they don't have to keep explaining repeatedly in schools and other social care. Do you know if that's been trialled anywhere?

Carol Lapidge: I hadn't heard of it until the other day when I went to the events that I went to. One of the nurses mentioned it, so as far as I'm aware it's in a hospital - it's like some hospitals have it for the young adult or the child as well I suppose. I don't think it's widespread, no, I don't think it's everywhere because as I said I've never heard of it. We've been to a few hospitals over the years, haven't we?

Julia Cumberlege: So it actually needs to be beyond health doesn't it?

Carol Lapidge: It does.

Julia Cumberlege: It needs education, it needs social care and it needs to be quite a neat little document that would...

Carol Lapidge: Yes, the biggest problems are the anxieties and the phobias of the children and the adults. The procedures are fine if you sit down and talk to anybody and explain what you're doing. That's great because that's automatic now, it's quite open with what procedures you're going to have done and what could go wrong and that's great.

But when you have an adult or a child that comes into your surgery or your consulting room and you don't know that person, you don't know what their phobias will be. Like I said, the black mattress, how would you ever guess that? That's just so extreme. There are lots of phobias like that that just stop them from going in. If they were aware of it then they can work towards making it easier.

Cyril Chantler: The summary of care record is now accessible on the secondary user service when you attend at an A&E department, I think I'm right in saying.

Carol Lapidge: They see that now do they?

Cyril Chantler: Yes.

- Carol Lapidge: But what if it's not on there, just if the information is not on there?
- Cyril Chantler: Well I thought it - well I'll check but I think it's the case that in A&E you can access, with permission from the patient, the summary care records. Our summary care - yours and mine are now available too.
- Carol Lapidge: Yes.
- Julia Cumberlege: But I think it's particularly important for education because these children can behave quite unusually and the school needs to understand that. So they're not naughty or whatever, this is the way they are and I think the passport would help hugely.
- Cyril Chantler: Well, we raised that with the Permanent Secretary because it's being able to link using the NHS number and gaining permission for the health record, and plan with the school. He did actually tell us that he would contact his successor, the permanent secretary for education about this and we're following up on that.
- Carol Lapidge: You've mentioned that before and I thought that was a great idea because working with the surgery and trying to get information from the schools is really difficult when we're looking at anybody with a CP on their records. We have to get information from the school and make sure everything is running fine and what happens is we - connecting up is really, really difficult. So the NHS number would be fantastic if we could just give that. It's a brilliant idea, I think that's a great idea, I really do. I know that you can access some of the records as well and I'm aware of that but sometimes on those records it's not got the phobias. It's just the condition...
- [Over speaking]
- Cyril Chantler: But, no, I - absolutely accept that it's got to be. Can I ask another question?
- Julia Cumberlege: Of course.

Cyril Chantler: Karen, thank you, I mean it's a monumental amount of research... Karen Keely: I'm [unclear].

Cyril Chantler: I'm sure you have, but thank you for all the work that you've done on everybody's behalf. But you did in the course of your presentation mention a series of questions that you think that the manufacturers ought to answer.

Karen Keely: Yes.

Cyril Chantler: Have you yourself put those questions to the manufacturer? Karen

Keely: Not these particular questions but...

Cyril Chantler: But I was going to go on to say that it could be quite useful if you could set down on one sheet of paper the questions you think are particularly pertinent...

Karen Keely: [Unclear].

Cyril Chantler: ...and let us have it, okay. Karen

Keely: They're all done.

Cyril Chantler: Thank you.

Karen Keely: There is another question I would like to put on the [redacted] question I [unclear] I can do it in an email you know. So again because the pregnancy forms.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] will send anything you want over if you feel you don't have all the documents because there is a list of these and you will

be surprised at what is in - this is only the second. You'll be surprised at what goes in for the first, second, third, fourth, fifth and sixth.

Julia Cumberlege: Thank you. Simon, do you have anything?

Simon Whale: I've just got two points actually, one for Karen and for Carol. Carol you mentioned the health Trust in Wales that has contacted you retrospectively as it were.

Carol Lapidge: Yes.

Simon Whale: I don't know if you've got any more information on that that you could send us - if you have that would be really helpful.

Carol Lapidge: That would be Jo. I'll speak to her tonight and I'll ask her to send it over.

Simon Whale: Great, and also whether you know of any other Trusts in England or Wales or elsewhere that have done anything like that.

Carol Lapidge: No, not that I'm aware of.

Simon Whale: Right but further information on that would be really good. The thing I was going to ask you, Karen, and I'd echo what Cyril said about all the work you've done, an extraordinary amount of work. I'll speak up a bit. So, you've done an extraordinary amount of work. One of the things I was wondering was whether, on the points about inconsistencies between the different PILs in different countries and the different SPCs in different countries, have you raised those inconsistencies with UK authorities? Have you asked...

[Over speaking]

Karen Keely: No, I've been waiting for something like this all my life, to tell you the truth, and I asked the UK authorities, the MHRA for the PILs and the SPCs and I was turned down due to a lack of - I'd done an FOI and I was turned down. I got I think a 2009 one, however, I then went digging as you do, and I found another one. When I asked the Irish - I went to Ireland, when I was in Ireland, and I asked for what date it was licensed, I was told 1983. Now I knew that wasn't right and [REDACTED]

they even stated this to more people than me.

[REDACTED] didn't know about off-label licensing, but I just researched papers. But in fact it was actually licensed in 1975 and then licensed again in 1980 and relicensed again in 1983. So we have 1983, 1980, and 1975 documents here of the licence.

Simon Whale: The French PIL, the French PIL that talks about autism in 2006 have you drawn that to the attention of the regulator here or in Ireland?

Karen Keely: No, I'm just waiting to do that. I'm sure they've been watching [unclear].

[Over speaking]

Simon Whale: I think you just have drawn it to their attention.

Karen Keely: [REDACTED]

Valerie Brasse: I think what was I going to say, Karen, is there's a lot more homework for us to do and I feel actually we will be looking at all those comparisons, and if we've got the questions we will take them back to the MHRA.

Karen Keely: Thank you so much. Julia

Cumberlege: Sonia?

Sonia Macleod: I'm all right thank you.

Julia Cumberlege: Can I thank you both and [REDACTED]

END OF TRANSCRIPT

Session 5: Valproate Victims

START OF TRANSCRIPT

Julia Cumberlege: If you'd like to start by just saying who you are and why you're here.

Susan Cole: Yeah. My name's Susan Cole. My daughter has fetal valproate syndrome. I've been running a Facebook group since 2011. I've been campaigning since my daughter was born or asking questions since my daughter was born. I have also been involved with OACS Charity early on before 2005 or so and more recently as well.

Trish Greenhalgh: My name's Trish Greenhalgh. I'm a GP by professional training. I'm professor of primary care health sciences at the University of Oxford.

I suppose it's worth saying how I got into this. I'm not an expert on valproate. I've written books on evidence-based medicine, so I'm a sort of pluripotent, take-a-look-at-the-evidence sort of person. I work in the same department as Carl Heneghan. But the reason I got to know Susan was because my son, who's now a junior doctor, at the time was a medical student, had written an essay on valproate and fetal effects and wanted to turn it into a paper. I got into writing and co-authoring a paper with my son, which then got picked up by various people and groups. Through that, I got to know Susan. She asked me to come along today, but we've already said that most of the hour is going to be hearing from Susan. I've got some comments on that.

Julia Cumberlege: Right. Thanks very much.

Josephine Tapper: My name's Josephine Tapper. I am a woman with bipolar that was prescribed valproate for a number of years against my wishes and was actually threatened with sectioning in 2006 when I questioned its teratogenicity. I spoke at the European Medicines Agency from my point of view and sat on the ad hoc scientific advisory group there around valproate and bipolar. I'm a member of the MHRA valproate stakeholder group.

Julia Cumberlege: Right. Thanks very much. I'm not sure we're going to be able to have the full hour, but we will try.

Susan Cole: Okay.

Julia Cumberlege: But we've all got other commitments we have to honour.

Susan Cole: Sure.

Julia Cumberlege: Susan, are you going to kick off?

Susan Cole: Right, okay. Right. First of all, I'm representing - rather than - I don't consider myself to be a representative of a membership group as such. I consider myself to be a person with a lot of allies through Facebook, Facebook groups and social media. That's the way things have evolved. I've been quite involved in the development of this process. I was very pleased when it came along. Right, where am I going to start? The area that I want to focus on today is patient group engagement, although I wouldn't mind telling my story. But it's a long one.

But when Jeremy Hunt brought the Review about, he stated that the long struggle for justice for victims added insult to injury to the victims. That's what I want to focus on. I think the Review has been fantastic, because we've got lots of important information and data and facts and figures through that. I've got 50 pages of references to the evidence that's already been given. That's in a document that has been presented to you, so I'm not going to focus too much on that information. I'd rather focus on the insult to injury aspect of this, how hard it is. I don't think it's quite - people don't understand how hard it is to be working for 20 years on this. That doesn't just apply to me, it applies to everybody. Next one.

Yeah, one of the - sorry, I want to talk about the good practice in patient group engagement and bad practice as well, what I've experienced in that. I'm not an expert on this at all. Probably Josie's much better at this and is versed in that. It's interesting that despite all of the letters written to MPs over time and despite parliamentary debates on valproate as far back as 1983 - something we've discussed in this submission - I consider that the catalyst for this Review was our protest outside the MHRA offices in 2013. We've been writing letters. OACS Charity from 2005, if not earlier, have been writing letters for about 15 years to try to get information through.

It was that protest, I believe, that tipped the balance. At that protest, we had a handful of mums, some with their children. It was loosely organised through Emma Friedmann and various people involved and Jo Cozens. We all just said, you know what? We're fed up with this. The only way we can get our message across is to literally stand outside the MHRA offices. Somehow that worked, so yeah. One of the things that Trish talked about is... [aside]. Well, she mentioned it as being...

Trish Greenhalgh Go on.

Susan Cole: ...a thing about public speaking.

Susan Cole: What I want to talk about is public listening. I think that it's about time there was more public listening. I want to just go into that, but I don't know if this is where you want to take off. But (a) we didn't have the facts. Nobody listened to us, because we didn't have the facts. Nobody listened to us, because we didn't have any credibility or integrity or we weren't believed. Nobody really cared, because they didn't put themselves in our shoes.

Some of the reasons that have come forward to us, to me - and as a person that has a Facebook group and goes on Twitter, and also to OACS Charity. One of the reasons is because they didn't want their disability being exposed to the public. They've also been put off joining groups for whatever reason or they've been excluded from a group, a patient group. They don't have the time to work on things or they don't feel they have the education or the knowledge and the understanding. I think accessibility is a big problem in getting heard. Then there are others who are afraid for their professional reputation, so you have those who have a good job and they don't want to present themselves too loudly. Right.

Right, good practice. Valproate Stakeholders Network, others may have talked about this, but that's been an inclusive way of bringing people together. That started again after the protest. It began as a small group of a handful, I think about five people in the room at the Department of Health to discuss this. I didn't get involved at first, because I thought it was a damage limitation exercise. I was completely cynical and didn't want anything to do with it. But over time that process, the Valproate Stakeholders Network process, has been really useful. It has moved people forward. I think that's probably partly why we're here today.

To have representatives from the MHRA, obviously from all of the different bodies, professional bodies - I can't list them now, but you probably know who they are. They're largely the people that have given evidence to this Review. To have them all around a table has been incredibly interesting. There are good things that come out of that, I think. There are lots of really bad things that have happened as well in this process. Yeah. Yeah. Sorry, I'll just have a pause now. I'm just trying to work out where I'm going. Right.

[Aside discussion]

Trish Greenhalgh: Of course, being a doctor and a professor sitting on the patient side is - I need to know my place. I'm not here to give an expert opinion. I understand that. I

wanted to amplify and comment on really what Susan said already today and with the previous stuff that she's presented to you, from the perspective of someone who's done all sorts of things like expert witness work and been involved in inquiries before, so here's some comments.

Firstly I am struck by the clarity of the evidence. Nobody's in any doubt that this drug is teratogenic, that it's known to be teratogenic for decades. As Susan says, we don't need to go into that, but it was quite striking that this isn't something that people were arguing about the evidence.

The second thing I wanted to comment on, first of all, I'm absolutely in awe of Susan's leadership of an extraordinarily difficult patient campaign. This is not the kind of top-down leadership, start a campaign, everyone follows you. It's a classic sort of female leadership really. It's like herding cats, because the different patient groups and perspectives are so diverse. The different groups, in inverted commas, represent different clinical conditions, different interest groups that have been set up for different reasons, different levels of engagement with this particular issue - some are actually not that interested in it or don't have time to support it - and a different set of claims to represent valproate victims or whatever.

I think I am very struck by the heterogeneity in the different patient groups and different individual patient perspectives and the way that Susan has managed to respect those and, to a large extent, pull them together. She doesn't speak for them in any simple sense, but I think she does an incredible job of synthesising something that's not easy to synthesise. I wanted to comment on that.

The third thing that strikes me, as someone who hasn't been involved in this and has come quite recently, is that patient involvement - patient discussions, the shared decision-making discussions in these two main groups, women with epilepsy and women with bipolar disorder, seem to me to have slightly lagged behind what might be called accepted practice or best practice compared to other conditions that I've seen. That is a subjective impression. I haven't explored that in great detail. But it just strikes me that, hang on a minute, why exactly were neurologists not having the conversations with women when there was quite clear evidence of teratogenicity? That is an impression.

Susan said, I think quite clearly - but I'm going to repeat something that she was talking about earlier. She said before we came in here, 'this is the most

Susan Cole: No, you've done brilliantly in terms of making things concise, which is something I'm not brilliant at myself. [REDACTED]

Josephine Tapper: [REDACTED] I would just like to reiterate that the issues of certainly women with - it's a word I would use as well - stigmatising conditions, and also the fact that we are having to manage serious conditions whilst trying to engage with groups in an articulate, eloquent way, and the MHRA have been very supportive in that. I know that there's been issues along further back. I also - and I suppose that I sit - one of the issues has been that valproate has not necessarily been - not considered on a - it's been considered within the parameters of epilepsy initially. That is because there's been a failure to engage by mental health charities and by psychiatrists.

If I can just talk about my personal experience within the MHRA stakeholder group, I don't sit here representing all women with bipolar. As I said at the EMA, my input is based on my experience. It's not evidential, although I've done a lot of work around it.

We're seen as - charities are seen as supportive of patients. That actually hasn't been where I've come from. I've tried to engage charities and the MHRA have tried to get charities to engage with me. I am an individual. I've actually suffered - my bipolar has come to the fore again, so I've found it difficult to manage. I've had responses such as, 'oh, well, we're a small charity, so we can't help you'. Well, I'm an individual woman. I've found as well that the learned societies, the Royal College of Psychiatrists - so neurologists seem to have been quite engaged for good or for bad. The Royal College of Psychiatrists have often been slow to engage, in fact with the MHRA as well.

The other thing objectively that there has been an issue with is that within particular conditions - and I'm observing epilepsy - there has been almost a - there has been a protectiveness amongst certain patient groups that they don't want to engage with other patient groups. I liken that to - it's divide and rule. I don't think that that's helped the process. It certainly doesn't help PPI, patient and public involvement with which I do some work.

I think that that has been a real stumbling block that if you have - it's almost like - I come from the corporate sector. It's almost like you have sort of oh, well we can't - there's intellectual property rights and commercial property

rights that you might say within the corporate sector. Some patient groups have operated like that and I think to the detriment of the women who've suffered from valproate disorder and the families themselves. I think it's been a missed opportunity and a bit sad, to use an emotive word.

Julia Cumberlege: Okay. Well, thank you very much for that. Shall we go back to the issue of the public inquiry? Do you want to say a bit more about that?

Susan Cole: Well, yes. I was involved in the FAC litigation which is the fetal anti-convulsant litigation. That finished. We lost legal aid funding in 2010. That case was against Sanofi. [REDACTED]

[REDACTED]

Through that process, the lawyers found a lot of redacted documents, heavily redacted documents where pages and pages have been redacted. The simple reason is we need a public inquiry because we need to actually find out what happened and learn from the past. It will also be a way of bringing together any question about any payment or compensation. We also need somebody to bring all these elements together.

We made a submission recently to the Department of Justice, which was to - and I think I've sent you a copy where they're going to set up a system of having a public advocate, an independent public advocate for public inquiries but particularly inquests where there's a sudden loss of life, say like Grenfell, for example. That would be great to have something like that, because it does bring everything together. I think that a public inquiry's essential really for us. I speak as well for OACS Charity, because they were - I've represented them for quite a number of years as well. But that seems to be across the board. I don't know if all of the groups feel that way. I think a public inquiry is the only way we can really learn from the past. Yeah.

Julia Cumberlege: It does mean, of course, a great delay, because they take time to set up and to run.

Susan Cole: Yes.

Julia Cumberlege: They are very costly. But I can understand that some people want a public inquiry.

Susan Cole: Yes. We would like some form of interim compensation if that's at all possible. I'm not saying - that is what women are demanding. You could ask every

woman on my Facebook group and they would say, I want something now. I want some compensation now. But it's easier said than done. It's a hugely complex issue. When you're talking about compensation schemes, they have to be worked out very carefully. I haven't got the knowledge about that, but Emma Friedmann and David Body I think are speaking or have spoken today. They're much more knowledgeable about that sort of thing.

Julia Cumberlege: But we're not equipped to assess compensation.

Susan Cole: No.

Julia Cumberlege: You need some real expertise in that and we don't have it in the team, but certainly it's an issue that we obviously would want to address in principle.

Susan Cole: Yeah.

Julia Cumberlege: It may be about redress or whatever.

Susan Cole: Yeah. I do think there's an inequality of arms as well that you haven't got - so that you do have lots of patient groups struggling. There's sometimes groups around a kitchen table. There are charities. The structures are difficult and lots of people aren't trained. These groups need support. I think if we could do something to help victims get together, all those affected get together and have some kind of mediatory process with some funding, that would be wonderful.

There's a [REDACTED] that supports charities to - they're consultants really and they will facilitate things. A mediator or a facilitator to bring - not bring groups together but to enable people to get support. That would be excellent. Most women want somebody that is experienced in the condition rather than a telephone helpline from somebody that doesn't understand, yeah.

Julia Cumberlege: Any questions?

Cyril Chantler: Since we first met - which is a while ago now - we've been all over the country. We've met, in the three areas of the Review, a very large number of people - mainly ladies - who've suffered terribly. One of the questions - as you may have noticed - I've been putting to the people who've come to these hearings and regulatory bodies and professional bodies is why is it that this has been going on for so long? My profession didn't seem to know and the National Health Service didn't seem to know, so why is that? What should we do to make sure that this doesn't happen in the future?

Susan Cole: Yeah.

Cyril Chantler: Do you have any answers to that?

Susan Cole: I think there's a cultural problem in that women aren't believed and they're ignored. Primarily there's - you could just say there's an institutional sex discrimination, discrimination against women and women's health, so there's a big problem with that. I would like to propose - in fact some of the other groups I've been in touch with, [REDACTED] Network, have proposed a women's safety and health type of committee that would specifically look at women's issues.

Then the second issue is because we have disabilities. With us as valproate users, if you like, we have a disability. We've been institutionally ignored at best of times. Many of us older women have grown up in an environment where even our families didn't really take us that seriously. We were slightly put aside, if you like, because we have a disability. Epilepsy in many cultures is still seen as you're possessed by the devil and that - globally. This is a global issue, so we're still dealing with that.

Why it didn't come forward? Well, it must have come forward to doctors, I think. I think it did. I met recently with my daughter's paediatrician who diagnosed her in 2001, [REDACTED] He was at [REDACTED] hospital when he diagnosed her. But he told me at that time - I was a bit of a fog, but he told me that he had written a letter to all the GPs in [REDACTED] warning them about this. He knew how serious it was. He'd seen lots of cases in India. Doctors did know. I don't think there was really an excuse. I think the data that they had, the statistics, the numbers were a bit vague. I think at best they were vague. I think it was probably too much...

[Over speaking]

Cyril Chantler: No, no, I think Trish is right. The evidence has been there from decades.

Susan Cole: Yeah.

Cyril Chantler: But it's taken patient groups working with politicians to bring this to the attention...

Susan Cole: Yeah.

Cyril Chantler: ...[unclear].

Susan Cole: I have a group of envelopes here...

Female: Oh. Ooh.

Susan Cole: ...going back a long time.

[Over speaking]

Susan Cole: That hasn't worked. As I said, I do think that us protesting outside the MHRA is what kicked this off, because we've had plenty of letters from Members of Parliament all across time and across governments.

Trish Greenhalgh: I'm also struck by the difference between the length of time it took anyone to do anything about this versus thalidomide which was once - once someone blew the whistle, something happened very, very quickly. One would have thought that lessons would have been learnt more quickly. I wonder if it's partly because of the nature of the effect on the foetus, which is - I wouldn't say it's nonspecific, but it's neurodevelopmental delays. It's not as if you're born without any arms. Do you know what I mean? It's less visible. It's quite pervasive. It affects the individual and the family quite profoundly and for the rest of their lives, but it's not quite as dramatic as something like thalidomide. Maybe that was one of the things to think about.

Sonia Macleod: I would say the penetrance isn't as high.

[Over speaking]

Female: Yes, I think that's probably true. That's probably true, yeah.

Sonia Macleod: ...if you look at the statistics on actual physical malformations on valproate, they are much, much lower, the physical manifestations. As you said, the neurodevelopmental ones are so much less visible.

Trish Greenhalgh: The women may have been on more than one drug, so then there's questions of can you trace it back? Whereas thalidomide was given for morning sickness. It was usually only for the mums taking that kind of thing.

Julia Cumberlege: Yeah. Yes, we did interview the Thalidomide Trust and all that. That's actually on the website.

Trish Greenhalgh: Yeah.

Julia Cumberlege: But I think you're right. It was a very visible consequence of taking thalidomide. One could see it. I think that this - it's much more complex...

Trish Greenhalgh: Indeed.

Julia Cumberlege: ...as you've discovered, so [unclear] really. Simon, if you've got any...

Simon Whale: I'm not sure it's a question. I've got more an observation about what we've heard. It chimes with some of the things you've said. As you know, we've been around the country and we have met hundreds of people including many families affected by valproate. I suppose one of the messages that comes out of what they've told us - which has been echoed today and via others in patient groups - is the desire for something to happen sooner rather than later. But there's been this enormously long period in which the system collectively has failed to even listen, as you've said, and then recognise that there's something that should be done. That's spanned 30 more years.

Female: Yeah.

Simon Whale: There's an almost [unclear] completely understandable weariness on the part of people affected with - it's just the time for something to happen. I think that plays heavily on our minds when we come to think about what we should be recommending and what influence we can have over what happens next. It also comes back to the point about the public inquiry, because whilst we need to think about whether there is good reason for a public inquiry, we also have to balance that with a desire to try and do something to help people sooner rather than later. As Julia has said, public inquiries can take years...

Female: Yeah...

[Over speaking]

Trish Greenhalgh: This is what we were talking about in the café, isn't it?

Susan Cole: Yeah, but I think you could do both. I think...

Simon Whale: Yes, if you...

[Over speaking]

Susan Cole: ...you can have a public inquiry. As I said, if you can have some support - and I know Rebecca Bromley and Peter Turnpenny have talked about specialist centres. That would be a godsend, because we constantly have people saying my son has this, that and the other. Is this a feature of fetal valproate syndrome? We don't quite know. There's so much guesswork in terms of the actual medical support. I don't see why it should be an either/or situation.

- Simon Whale: No, I think you may well be right.
- Susan Cole: Yeah.
- Simon Whale: But I think you've touched on something very important that access to support which is both clinical, medical support but also educational and social support...
- Susan Cole: Yes.
- Simon Whale: ...is lacking. Where it does exist, it's haphazard.
- Susan Cole: Yeah.
- Simon Whale: Something could and should be done about that.
- Susan Cole: Yeah.
- Simon Whale: Giving families that opportunity to access the support they deserve is something that shouldn't hinge on whether there's a public inquiry or not.
- Susan Cole: Yeah.
- Simon Whale: It's a separate point.
- Susan Cole: Exactly. I think others have mentioned getting an MOT for the children. It's not a brilliant way of putting it. But for somebody to be able to look at my daughter and have a good, thorough examination on a holistic level - so they're looking at the whole body and mind and support in that way.
- Cyril Chantler: Yes. That's entirely right and proper for anybody with a chronic illness, particularly a child. You need a multidisciplinary assessment on a regular basis and a care plan and then a system for delivery.
- Susan Cole: Yes.
- Julia Cumberlege: Can I just say...
- Susan Cole: [Unclear].
- Julia Cumberlege: I don't know what our conclusions are going to be about a public inquiry, but certainly we wouldn't set it up. The government would set it up, because it's up to them to do that. Then it's up to them to decide what they want the public inquiry to look at. It may be that they would want them to introduce the issue of compensation, in which case it would be very difficult to do much

before that public inquiry had resulted in its findings. But it's all open at the moment.

Susan Cole: Yeah.

Julia Cumberlege: We just need to think about it more. Valerie, have you got questions?

Susan Cole: Sorry.

Valerie Brasse: More so, I suppose, a comment really. It's going back to what you started by saying, Susan, which is there's three points, the first two of which were no-one's listening, we don't seem to have the facts and maybe we haven't got credibility because we're women. If you think about the three interventions we're looking at, actually that is absolutely the same across the piece...

Susan Cole: Yeah.

Valerie Brasse: ...because we don't have the facts about any of them. Really it plays back into this point about justice, social redress, however you want to look at it. We don't know the numbers involved, which is quite extraordinary across all three. We don't know how many children are affected....

Susan Cole: Yeah.

Valerie Brasse: We don't know how many were affected by implanted mesh. We don't know how many hundreds of women took Primodos.

Susan Cole: It's complicated, isn't it? Yeah.

Valerie Brasse: That link between the three is really quite interesting.

Susan Cole: Yeah.

Valerie Brasse: Maybe that partly explains why it has taken so long. Actually here we sit, after all these years, still not knowing the numbers...

Susan Cole: Yeah.

Valerie Brasse: ...because we weren't recording them.

Susan Cole: I've watched lots of the video evidence. I've seen how many, many organisations have stood up. I'm talking about the main medical organisations. They don't know. They're trying. NHS Resolution was an interesting one. It's so complicated to pick apart those massive structures that have been there for

possibly hundreds of years, some of them. Those institutions, it's so hard for them to work together. That's not my problem. That's not my issue. But something can be done, because we're all grown-ups. I'm sure you - I think that would be really helpful to just keep going with this.

In terms of how to stop this happening in the future, I really strongly believe that if you have a good way of listening to people, when these things come up, when there are questions - if anybody goes to the government, sends their MP a letter saying this is happening, I don't like this, it's not right, something needs to be looked at. That Member of Parliament should not be going to the health minister and saying, what do you think of this? They then say, well, this is the party line. This is what we're going to say. There needs to be a little bit more thought and connection with the departments that are supposed to deal with this sort of thing. It's not good enough to say, oh, we'll deal with that within the next parliament.

Sonia Macleod: Do you think the MPs - because it's interesting that you've chosen MPs as a group obviously that is [unclear]. But where do they fit into the overall picture?

Susan Cole: They fit into the overall picture because they're our last resort. They are the...

Sonia Macleod: The defence.

Susan Cole: They're the structure that we have for democratic process. When nothing else works, that's where you go. You go to your MP if you really need help. They're elected. They're representative. That's why.

I did want to mention all-party parliamentary groups which I think need work as well. I don't think they are particularly - well, needs to be work on all-party groups. Sometimes the secretariat is funded by pharmaceutical industry. They can often exclude people, so I've never been - well, I think I've been invited to one of the valproate all-party parliamentary group meetings, despite being very close to Norman Lamb who's the chair - not close in that way, but I've had meetings with him and he's a brilliant person. I want to use this opportunity to thank him for - he's really stuck his neck out and really gone beyond the call of duty to actually pick up on these really difficult, tricky issues where other MPs didn't. But yes. Yeah, is that...

Sonia Macleod: No, I was just interested you picked them, because they - I was really interested in what you said, because to me they are sort of - like they are the last line. They're the people that you shouldn't get to.

Susan Cole: Yeah.

Sonia Macleod: If the systems work, you shouldn't get there. That was why I was just curious and why I said, how do they fit into the whole picture?

Susan Cole: Yeah. Ideally every medical institution should be listening. I could go on for weeks about - and Josie and Trish could probably do a lot better job of talking about how to engage groups. But that's what my main focus is, as I said, wanted to get across today, because I do think that's the answer is a really good, solid structure that doesn't leave people on Facebook and Twitter to share information. They're brought together. I think that can happen. I don't think that would be very difficult. I think we've seen from the MHRA stakeholders network that these things can happen. I think you've - yeah.

Josephine Tapper: I'd say human factors is - I know it's a fashionable word at the moment, but I think that's an important factor. You've got institutions or you've got learned societies or royal bodies which have traditionally been very resistant to change and slightly reactive. I think that there is work around human factors and how it can be better communicated.

Julia Cumberlege: Well, I think you've put it across very well. Thank you very much indeed. It's been a really useful session. Thank you for your colleagues here supporting you. It's very good. Thank you.

Trish Greenhalgh: She's done really well, hasn't she?

END OF TRANSCRIPT