The Independent
MEDICINES & MEDICAL DEVICES
Safety Review

The Independent Medicines and Medical Devices Safety Review

Written Evidence

Clinicians, Academics and Other Individuals – Pelvic Mesh

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Contents

Disclaimer

The statements made and the opinions expressed in response to the Independent Medicines and Medical Devices Safety Review's ('IMMDSR) Call for Evidence and in the video recording of the IMMDSR's oral hearings are those of the authors. They do not purport to reflect the opinions, views or conclusions of the IMMDSR or its members. The statements and opinions made do not imply the expression of any opinion whatsoever on the part of the IMMSDR concerning the truthfulness, veracity, accuracy or legal status of any statements or opinions made and published on the IMMDSR website. Nor does the IMMSDR accept any legal liability arising from any statements or opinions so expressed and published

WARNING: Please be aware some evidence contains descriptions, pictures and audio of the harm suffered by individuals. Some may find this distressing.

Submission from Dr Wael Agur MSc MD(res) FRCOG

Subspecialist and Lead Urogynaecologist | NHS Ayrshire & Arran
Honorary Senior Clinical Lecturer | University of Glasgow | Scotland

COI:

Name of Committee/Company/Organisation	Nature of interest e.g. Chairperson, member, advisor	If product related, please specify	Dates
Intellectual Interests			
My views have significantly evolved since 2011 and into 2016 during joint interpretation of scientific evidence, with clinicians and patient members, within the Scottish Government Mesh Group. I resigned from the Group in March 2017 and subsequently expressed the following views, both in private and in public forums: • Transvaginal **mesh for prolapse** has little or no proven benefit to women over and above the native tissue alternatives. With the highest risk of mesh-related adverse events, it should not be used - unless future long term research (particularly PROSPECT) suggests otherwise. • The risks associated with the **transobturator mesh tape for incontinence** (both the approach-related and mesh-related ones) outweigh its benefits, for most women. Therefore, it should not be used - except with approval of regional / national MDT. • The benefit **:** risk ratio and trade-off balance of the **retropubic mesh tape for incontinence** are probably less favourable than those of native tissue surgery, for most women. Therefore, it should be offered only to women who are fully informed about the non-mesh native tissue surgical alternatives.			
Industry Interests			
UCB Pharma*	Speaker Honoraria	Personal – Financial – Non-specific Kentera®	2007 - 2007
Pfizer*	Education Courses Sponsorship Speaker Honoraria	Personal – Financial – Non-specific Toviaz®	2007 - 2012
Astellas Pharmaceuticals	Financial support through a service development contract with A&A O&G Dept. Team training and purchase of equipment.	Non-personal – Financial – Nonspecific Vesicare® Betmiga®	2010 - 2013

* More details on amount of funds received from industry since the start in 2007 were published from January 2014 onwards on my personal page on ***Who Pays This Doctor?*** – A voluntary national register.
www.whopaysthisdoctor.org/doctor/33

Name of Committee/Company/Organisation	Nature of interest e.g. Chairperson, member, advisor	If product related, please specify	Dates
Astellas Pharmaceuticals*	Conference sponsorship Consultancy honoraria	Personal – Financial – Non-specific Vesicare® Betmiga®	2011 - 2015
Bard*	Education Courses Sponsorship Preceptor / Surgical Trainer Honoraria	Personal – Financial – Specific Nuvia®, Avaulta® and Ajust®	2011 - 2012
Boston Scientific*	Education Courses Sponsorship	Personal – Financial – Specific Uphold®	2012 - 2012
Neomedic*	Conference Sponsorship	Personal – Financial – Specific Remeex®	2013 - 2013
Johnson & Johnson - Ethicon Endoscopy	Education Courses Sponsorship	Personal – Financial – Non-specific Floseal®	2013 - 2015
Olympus	Sponsorship of Laparoscopic Urogyn Cadaver Workshop -Glasgow	Non-personal – Financial – Nonspecific	2014 - 2014
SEP Pharma / Contura*	Education Courses Sponsorship Speaker / Preceptor / Trainer Fees – Training surgeons on bulking agent procedures	Personal – Financial – Specific Bulkamid®	2015 - 2017
Research Interests			
Chief Scientist Office (CSO), NHS Research Scotland (NRS) & NHS Ayrshire & Arran	Career Fellow - Research Fellowship Programme	Personal – Financial – Specific	2013 - Ongoing
National Institute for Health Research (NIHR)	Co-Chief Investigator for PURSUIT study, a recently funded (£1.7m) multicenter RCT for surgical treatment of recurrent stress urinary incontinence in women	Non-personal – Financial – Specific	2018 - Ongoing
University of Stirling	Co-grant applicant	Non-personal – Financial – Specific	2018 - Ongoing

Name of Committee/Company/Organisation	Nature of interest e.g. Chairperson, member, advisor	If product related, please specify	Dates
	and Principal Investigator for NIHR-funded **TOPSY** study (£1.1m).		
University of Aberdeen	Co-grant applicant and Principal Investigator for NIHR-funded **OPAL** (£1.2m) study. Principal Investigator for **SIMS** Studies and NIHR-funded **PROSPECT** and **VUE** studies.	Non-personal - Financial – Specific	2009 - Ongoing
The General Medical Council and University of Aberdeen	Referrer - to ensure accuracy and integrity of the **SIMS** pilot (short- and long-term) studies.	Non-personal – Nonfinancial – Specific	2016 - Ongoing
Surgical Training Interests			
Various manufacturers of medical devices and surgical instruments – Johnson & Johnson, Olympus, Applied Medical, Covidien, Vectec, June Medical, Bard and Neomedic	Supply of medical devices and surgical instruments for the Urogynaecology Cadaver Workshops - Glasgow, Manchester and London.	Non-personal – Nonfinancial – Specific	2013 - Ongoing
NHS Ayrshire & Arran	Lead faculty – Laparoscopic and native tissue Urogyn Workshops - Glasgow.	Personal – Financial – Specific	2015 - 2016
London Medical Education Academy (LMEDAC)	Course Director, Laparoscopic and native tissue Urogyn Workshops – Glasgow, Manchester and London.	Personal – Financial – Specific	2016 - Ongoing
Medico-legal Interests			
Central Legal Office – NHS Scotland	Provision of medicolegal advice, expert opinion and	Personal – Financial – Specific	2014 - Ongoing

Name of Committee/Company/Organisation	Nature of interest e.g. Chairperson, member, advisor	If product related, please specify	Dates
	report writing - mostly on mesh litigation		
Various law firms acting on behalf of mesh manufacturers, patient claimants and defendant clinicians – in Scotland, England, Wales, Northern Ireland, The Republic of Ireland, USA and Australia	Provision of medicolegal advice, expert opinion, report writing and/or appearance in court – mostly on mesh litigation	Personal – Financial – Specific	2014 - Ongoing
Oaklaw Consultancy Ltd	Own limited company dealing with medico-legal consultancy through a third party – Medico-legal Administration Service (MLAS)	Personal – Financial – Specific	2017 - Ongoing
Government and Parliament Interests			
Scottish Government - Short-Life Working Group, Expert Group and Independent Review Group	Clinician member	Personal – Nonfinancial – Specific	2013 - 2017
NHS England – Mesh Oversight Group	Clinician member - Information subgroup	Personal – Nonfinancial – Specific	2013 - 2017
UK Department of Health - Healthcare Quality Improvement Partnership (HQIP)	Clinician member – National Data Capture Group for Pelvic Mesh	Personal – Nonfinancial – Specific	2018 - Ongoing
National Institute for Health and Care Excellence (NICE) – Interventional Procedure Advisory Committee (IPAC)	Clinician member	Personal – Nonfinancial – Nonspecific	2017 - Ongoing
Westminster Parliament - All-Party Parliamentary Group (APPG) on Polypropylene Mesh	Clinician member	Personal – Nonfinancial – Specific	2017 - Ongoing

Name of Committee/Company/Organisation	Nature of interest e.g. Chairperson, member, advisor	If product related, please specify	Dates
Parliaments in Holyrood, Westminster and The Dail Eireann	Witness to Committees, signatory on patient petitions and/or participant in patient safety lobbies	Personal – Nonfinancial – Specific	2017 - Ongoing
Media Interests			
Social Media - Twitter	Active tweep with an account dedicated to public understanding of scientific evidence in relation to urogyn procedures (mesh and native tissue alternatives).	Personal – Nonfinancial – Specific	2014 - Ongoing
Mainstream UK and International Media	TV, Radio and Newspaper Interviewee (including BBC Scotland, BBC Panorama, Sky News, Canadian CTV and Aljazeera).	Personal – Nonfinancial – Specific	2016 - Ongoing
Various National and International Specialist Societies	Member of societies and various subcommittees	Personal – Nonfinancial – Specific	2008 - Ongoing

Submission to the Review

Introductory letter

24rd October 2018

Dear Baroness Cumberlege

Re: Independent Medicines and Medical Devices Safety Review – Pelvic Mesh

Thank you for the invitation to provide written and oral evidence to The Review. In this submission, I highlight my personal perspective on the matter, based on interpretation of scientific evidence, surgical experience with pelvic mesh devices and procedures and clinical experience in treating women with stress urinary incontinence and pelvic organ prolapse.

My evidence addresses the two approaches for placing mesh devices for pelvic organ prolapse (transvaginal and transabdominal) as well as the two approaches for placing mesh devices for stress urinary incontinence (transobturator and retropubic). For each of the four

procedures, I summarised the scientific evidence, described how my experience evolved over the years, commented on the current situation of the mesh device in the UK and proposed questions for future research.

In addition, I attach the following documents:

- **The Patient Decision Aid** (PDA) in current use by the Continence Multidisciplinary Team in NHS Ayrshire & Arran since September 2016. This document is based on 'What-Matters-To-You' initiative of NHS Scotland and has been used to document the shared-decision process between patients and clinicians since September 2016.
- **A Conference Abstract** summarising the initial results of using the PDA by 30 women considering surgery for stress urinary incontinence. The abstract poster is being presented at The European Urogynaecology Association in Milan, Italy this week.
- **My Declaration of competing interests**

I do hope you will find my evidence useful.

Kind regards
Wael Agur

Personal Perspective and Evidence for The Independent Medicines and Medical Devices Safety Review – Pelvic Mesh

Dr Wael Agur MSc MD(res) FRCOG
Subspecialist and Lead Urogynaecologist | NHS Ayrshire & Arran
Honorary Senior Clinical Lecturer | University of Glasgow | Scotland
24 October 2018

1) Transvaginal mesh for pelvic organ prolapse

a) Scientific Evidence:
Several small studies over the last decade, mostly industry-sponsored, had suggested benefit in reducing the risk of recurrence of pelvic organ prolapse. The largest and least biased trial (PROSPECT 2016), however, showed no benefit in **primary** surgery and, therefore, described the mesh-related risks as '*unnecessary*'. The *Scottish* 20-year retrospective study confirmed these results.

The largest European trial 2017 on **repeat** surgery showed no benefit either on the short or long terms (10 years). Level 1 evidence from the 2016 Cochrane review (Maher et al) criticised the MHRA for stating *'benefit outweigh the risks'* and proposed that transvaginal mesh procedures for prolapse are not offered to patients unless approved by an Ethics Committee i.e. largely within research context. In Dec 2017, NICE recommendation amounted to an effective ban on their use outside research studies.

b) Own experience with transvaginal mesh procedures for POP:
I was an early adopter of the use of transvaginal mesh for prolapse and I trained colleague surgeons too. Following the FDA warning in 2011, I significantly reduced my use of transvaginal mesh for prolapse. I stopped its use for primary surgery in 2012 and for repeat surgery in 2013; a year before the suspension of all pelvic mesh procedures in Scotland. At the time, I was concerned about the associated mesh risks but more about its failure to reduce the risk of prolapse recurrence in my own patients. The risk of recurrence following non-mesh native tissue surgery has been exaggerated. The Scottish 20-year retrospective study confirmed my own (and many others) clinical experience that the risk of failure of native tissue surgery is less than 5% in the first 5 years, not the 29% widely quoted in the mostly industry-sponsored literature.

c) Current situation with POP mesh devices:
The mesh devices used in the above research studies are no longer available due to several reasons: the manufacturers voluntarily withdrew them from the market, relabelled them '*for abdominal use only*' or ceased production altogether. Therefore, the prolapse mesh devices that remain in the UK market currently are relatively newer and had not been appropriately evaluated in robust clinical trials.

d) Questions that need answering:

- Are there any long-term benefits from the use of transvaginal mesh devices, over and above those of native tissue repairs, in women with primary and secondary pelvic organ prolapse?

- What is the long-term severity and impact on quality of life of chronic pain and dyspareunia following transvaginal mesh surgery in comparison to native tissue repair surgery.

e) What I believe should happen:
Maintain the current suspension on the use of transvaginal mesh devices, including research studies, until **a)** long-term trials (especially PROSPECT) prove there is benefit over and above that of native tissue surgery, **b)** prove that the risks are comparable to those of native tissue surgery, **c)** prove that such benefit may outweigh the associated risks for at least some patients, and **d)** prove cost-effectiveness and willingness of the NHS to pay for such benefit.

2) Transabdominal mesh for pelvic organ prolapse surgery

a) Scientific Evidence:
Several randomised studies have confirmed benefit of the abdominal approach using mesh over and above the vaginal approach without the use of mesh. Abdominal placement of mesh appears to be associated with the highest success rates of treating prolapse and with the lowest rates of recurrence of symptoms. However, there are more systematic reviews than primary studies, suggesting a possibility of exaggerating the benefits and/or the effect size. Laparoscopic approach appears to offer a similar success rate to the open one.

The transabdominal mesh procedure adds further layers of complications that are not associated with vaginal native tissue surgery; **a)** complications of the abdominal approach itself, **b)** the use of mesh and its related adverse events and, if laparoscopy is used, **c)** the use of synthetic fastener (clips) adds the risk of a further medical device e.g. compromise of the intervertebral disc.

b) Own experience with abdominal mesh procedures:
I stopped laparoscopic surgery in 2014 due to the safety concerns of using two medical devices and the realisation that, in most patients, using native tissue techniques via the vaginal approach is enough. More recently, I further restricted my use of open abdominal mesh only to recurrent prolapse. This year, I voluntarily stopped offering the procedure altogether due to deskilling - as the numbers are too low.

c) Current situation with abdominal mesh devices:
There are several abdominal mesh devices available for use in women with and without a uterus.

d) Questions to be answered:

- What is the long-term severity and impact on quality of life of chronic pain and dyspareunia (as well as low-back pain and discitis if laparoscopy is employed) following transabdominal mesh surgery in comparison to vaginal native tissue repair surgery.

- Is the incremental benefit from the use of transabdominal mesh devices, over and above those of vaginal native tissue repairs, justify the associated risks of the abdominal approach, the risk of implanting mesh and, if laparoscopy is employed, the risks associated with the synthetic clips in women with primary pelvic organ prolapse?

e) What I believe should happen:
Restrict the use of transabdominal mesh devices to be offered for women with recurrent prolapse and in clinical circumstances, decided upon by a regional MDT, where vaginal native tissue surgery cannot be offered. While there is a good argument to justify the use of transabdominal mesh for women with recurrent central compartment prolapse, the argument for offering it as primary surgery is not strong and its benefit may not outweigh the risks, particularly in the presence of alternatives that do not involve the use of any medical devices.

3) Transobturator mesh for stress urinary incontinence surgery

a) Scientific Evidence:
Level 1 evidence from the 2015 Cochrane systematic review (Ford et al) of randomised controlled trials showed that, compared to the retropubic mesh tape, the transobturator tape is 6 times more likely to cause chronic pain and 10 times more likely to fail in controlling urinary incontinence and to require repeat surgery.

The review confirmed its main benefit to be a reduction in intraoperative bladder injury, however, this complication is believed by the vast majority of surgeons not to lead to long-term adverse outcome. The other benefit is a modest reduction of risk of voiding dysfunction that although may be statistically significant at population level, it is probably not clinically significant at an individual level.

Avoiding the retropubic space, particularly in previous abdominal surgery, is another anecdotal benefit, however, it is not clinically important as the alternative, the retropubic mesh tape, can still be employed. The single absolute indication of a transobturator mesh tape appears to be in a woman who had a retropubic femoro-femoral vascular graft and, therefore, any retropubic procedure is not possible.
Therefore, the possible benefits of the transobturator tape are probably not clinically important and outweighed by its inherent risks and by the high failure rates.

For the majority of women, unless removed in the first few weeks after surgery, the implanted transobturator mesh device cannot be safely removed in its entirety. Therefore, the adverse events, that had indicated surgical removal in the first place, are very likely to be irreversible and the woman's life is likely to change for good.

b) Own experience with mesh procedures:
After being an early adopter of this procedure since 2007, I came to the conclusion that the transobturator procedure is too risky for its presumed benefits and I stopped offering it altogether in early 2014.

c) Current situation with mesh devices:
There are several transobturator mesh devices from various manufacturers currently available.

d) Questions to be answered:

- Is conservative treatment a useful alternative or an adjunct treatment to surgical removal of the transobturator mesh tape device in women with chronic pain / dyspareunia?
- Is translabial scan a useful investigation tool prior to surgical removal of the transobturator mesh tape device in women with chronic pain / dyspareunia?
- What is the long-term success and impact on quality of life following surgical removal of the transobturator mesh tape device in women with chronic pain / dyspareunia.

e) What I believe should happen:
Maintain the current suspension on the use of transobturator mesh tape devices. This procedure is best not to be offered at all, except in the most exceptional of circumstances and following a discussion at a regional MDT. Such advice will reduce harm without losing any substantial value.

4) Retropubic mesh for stress urinary incontinence surgery

a) Scientific Evidence:

Level 1 evidence from the 2016 Cochrane systematic review (Lapitan et al) of randomised controlled trials showed that, compared to colposuspension, retropubic mesh tape has similar success rates in controlling urinary incontinence. While the perioperative complications were higher with the mesh tape, this was largely due to intraoperative bladder injury, which the vast majority of surgeons believe it has little or no long-term implications.

The 20-year Scottish look-back study suggested no significant difference in the number of longterm complications between mesh tape and colposuspension. Unfortunately, there were no data on the severity and impact on quality of life of such complications. On the other hand, here is strong evidence from patient groups that the long-term adverse events from the use of mesh can be severe and can be seriously impacting quality of life.

The largest randomised trial of retropubic tapes and the Cochrane systematic review suggested the risk of chronic pain following retropubic mesh tapes to be 1-2% but no good evidence on use of pain-killers or on impact on quality of life. Despite hundreds of mesh litigation in the UK, there are no publicised legal cases on the basis of long-term adverse events following a nonmesh native tissue procedure. In Scotland, there are 502 litigations in relation to transvaginal mesh but none in relation to non-mesh native tissue surgeries.

The benefits of the retropubic mesh tape procedures are short-term ones and are only recovery-related e.g. shorter time in operating theatre, shorter hospital stay and quicker recovery and return to normal activities. For most women, such benefits are unlikely to justify the mesh-related risks which are lifetime, cumulative, cannot be predicted, can be severe with significant impact on quality of life, difficult to treat, likely to be irreversible even after complete surgical removal and costly to the health service and patients.

This perception of the benefit:risk ratio was confirmed during my own initial experience of using an objective purpose-designed Patient Decision Aid. When 30 patients were well-informed of the benefits and risks of all mesh and non-mesh surgical procedures, 29 documented their choice of non-mesh surgery. Concerns about mesh-related risks were the main reason behind rejecting the mesh option. Further studies are required to unpack the effect of negative media stories from true appreciation of the associated risks.

b) Own experience with mesh procedures:

I stopped the retropubic mesh tape procedure with the suspension by the Scottish Government in 2014. I came to the conclusion that, taking the possible the benefit : risk ratio of the colposuspension, autologous fascial sling and bulking agent procedures is more favourable than that of the retropubic mesh tape one. Due to the long-term safety concerns that are beyond my control as a surgeon and due to the de-skilling as the numbers are too low, I have no plans to resume performing this procedure in the future.

c) Current situation with mesh devices:

There are several retropubic mesh devices from various manufacturers currently available.

d) Questions to be answered:

- How do long-term adverse events compare in severity and level of disability between mesh and non-mesh continence surgery?

- Which patients would trade off the uncertainty of long-term mesh-related adverse events for the short term benefit of daycase surgery, quicker recovery and quicker return to normal activities.

- What are the risk factors that could lead to the development of mesh-related adverse events?
- Is conservative treatment a useful alternative or an adjunct treatment to surgical removal of the retropubic mesh tape device in women with chronic pain / dyspareunia?

- Is translabial scan a useful investigation tool prior to surgical removal of the retropubic mesh tape device in women with chronic pain / dyspareunia?

- What is the long-term success and impact on quality of life following surgical removal of the retropubic mesh tape device in women with chronic pain / dyspareunia.

e) What I believe should happen:

Until the situation with regards the long-term mesh-related adverse events is clear, the safest course of action is to restrict the use of retropubic mesh devices to situations where the time-honoured non-mesh alternative procedures were either unsuccessful or were declined. A mesh medical device could be used if a patient's native tissue repair did not work. I believe such advice will reduce harm without losing any substantial value.

The Patient Decision Aid

https://www.nhsaaa.net/media/3152/20171109stressincon.pdf

The Patient Decision Aid - poster

Realistic Medicine

Patient Decision Aid (PDA) for Women Considering surgery for Stress Urinary Incontinence (SUI)

Christos Spyroulis, Inna Sokolova, Holly Bekarma, Sadia Khakwani, Wael Agur

NHS Ayrshire & Arran

In 2013, NICE[1] had recommended that women to be offered mesh surgery and its three alternatives. However the number of mesh procedures remains more than 10 times that of native tissue / non-mesh surgery.

9.8% of women developed mesh-related adverse events following mesh tape procedures for SUI[2].

In July 2018, mesh procedures for SUI were suspended by the five governments in The British Isles[3].

Patient decision aids (PDAs) are an important feature of the shared-decision making component of Realistic Medicine in NHS Scotland. PDAs have been shown to increase knowledge, accuracy of balancing benefit and risk and clarity of choice[4].

Design

- Prospective study of choice of SUI surgery after using the PDA
- 20-months period (Sep 2016 - May 2018).
- 30 women from urology and gynaecology departments read the national societies leaflets for the four surgical procedures (mesh tape, colposuspension, autologous fascial sling and bulking agent injection).
- Prior to consultation with their surgeons, patients were asked to read the PDA, indicate the procedure of their choice and provide reason(s).

Results

- 30 women, Age ~50.8 years, BMI ~32.3.
- * requested mesh tape surgery for quicker recovery.
- 24 women (75%) requested colposuspension for efficacy.
- * requested fascial sling for efficacy.
- 5 women (15%) requested bulking agent injection for being least invasive.

Procedure	Number (%) of requests	Commonest reasoning theme for acceptance	Number (%) of rejections	Commonest reason(s) theme for rejection
Mesh Tape	*	Recovery	24 (80%)	Safety (n=24, mesh complications) Blank (n=5)
Colposuspension	22 (75%)	Efficacy	8 (26.6%)	Safety (n=4, pelvic organ prolapse) Invasiveness (n=2) Efficacy (n=1) Recovery (n=1)
Autologous Fascial Sling	*	Efficacy	27 (83.3%)	Safety (n= 13, self-catheterisation) Recovery (n=6) Blank (n=8)
Bulking Agent Injection	5 (15%)	Recovery	25 (83.3%)	Efficacy (n=17) Blank (n=8)

* patient number<5 removed to protect confidentality

Conclusions

- Safety concerns were the only reason for rejecting vaginal mesh for SUI. Difficult to unpack true understanding of mesh-related risks from the media influence.
- Using the PDA improves understanding of individual patient values and choices.
- Adverse events associated with non mesh alternatives appear more acceptable leading to substantial impact on the patterns of SUI surgery.

References

1. National Institute for Health and Care Excellence (NICE). Urinary Incontinence in Women. Clinical Guideline no 171. September 2013.
2. Keltie K, Elneil S, Monga A et al. Complications following vaginal mesh procedures for stress urinary incontinence: an 8 year study of 92,246 women. Nature Scientific Reports, 7: 12015 (2017).
3. Surgical mesh for stress urinary incontinence to be halted immediately in England. BMJ 2018;362:k3035.
4. Stacey D et al. Decision aids for people facing health treatment or screening decisions (Review). Cochrane Database of Systematic Reviews 2017, Issue 4, Art No.:CD001431

NC18-0064.2

Submission from Dr Vincent Argent

Consultant in Emergency Medicine

COI

Advisor to APPG on Surgical Mesh – no renumeration

Submission

I was a Consultant Obstetrician and Gynaecologist at East Sussex Hospitals NHS Trust from 1987 - 2006. Now I am a Consultant in Emergency Medicine with a special interest in the immediate care of obstetric and gynaecological emergencies in the community. I have also had a long standing interest in pelvic pain. My degrees include chemical engineering and I am a member of the Institute of Chemical Engineering with an interest in medical plastics. I have a law degree and am a expert in the evolution of consent in clinical practice and the author of many articles on risk management in obstetrics and gynaecology. From 1997 - 2005, I was a member of the NICE Women and Children's Guideline Review Panel and gave advice to SERNIP. I am an adviser to the APPG on Surgical Mesh and I have given advice to the mesh campaign groups including Sling the Mesh. In 1997, I strongly opposed the decision of SERNIP to give TVT a Grade A rating because of the limited case cohort studies and the lack of long term data. I recommended that the TVT (and later the TVTO) should only be used as part of robust RCTs. SERNIP was set up in 1997 and had limited impact and was entirely voluntary and therefore inadequate for the regulation of medical devices. The work was later under the MDA and then NICE NIP. IN 2003, I advised NICE on the document ' Consent for procedures for which the benefits and risks are uncertain ' (attached). I strongly advised that this should be used in the case of the new SUI surgical procedures. In 2006, the NICE Urinary Incontinence Guidelines stated that, for SUI slings, ' women are made aware of the lack of long term outcome data. ' The NICE advice was not generally followed. Most women were not warned of the long term risks but were mostly told that TVT/O were ' gold standard ' procedures and a ' quick-fix ' cure. The SUI slings were highly aggressively marketed to gynaecologists as in the Ethicon ' buy a Lamborghini ' and ' Surgery is the Cha-ching thing ' campaigns. These procedures became highly lucrative for private surgeons.. In 2009 and 2011, I contacted the MHRA and the RCOG telling them that there was serious under-reporting of the risks of SUI plastic sling operations and was almost non-existent in the private sector and that there should be a national register with mandatory reporting of complications in the NHS and private sector.. The MHRA and the RCOG were slow to act. It could be said that doctors were in denial of the problems

I suggest:

1. Consent Women must be fully informed of the benefits and risks of SUI sling surgery to the standard of the Montgomery decision in the UK Supreme Court and the subsequent case law suggesting a greater onus on consent for elective procedures. This is the case retrospective to 1999 under Montgomery. It would meet the requirement of the NICE 2003 Consent Guideline. Women should have the opportunity to talk and meet with others who have benefited or have had serious life changing complications. They must be told that it is impossible to predict who will suffer life changing complications.

2. There should be a comprehensive national mesh recall to ascertain the true figures for risks and benefits, These figures can then be used to give women accurate information..

3. Future SUI procedures in both the NHS and private sector must be recorded on a national register with mandatory reporting to the MHRA of all complications.

4.There should be a rigorous scientific analysis of the effects of mesh in the body to examine the extent of physico-chemical and biochemical degradation activity.

5. The marketing of SUI operations with uncontrolled and unregulated private surgeons websites should cease or at least be controlled for objectivity with accurate descriptions of risks and benefits using the nationally accepted risk grading rather than vague language.

6. The NHS must provide full funding for surgical mesh removal centres with multidisciplinary teams including pain management.

7. There should be a national compensation scheme for patients affected by mesh complications.

8. All Class III medical devices should be subject to controlled introduction by the MHRA in keeping with the new EU regulations. 'Substantial equivalence' introduction, if permitted, should be strictly and closely monitored.

In conclusion, I would like to give oral evidence to the Inquiry. Dr Vincent Argent FRCOG FRCA GMC No: 1731437

Attached documents:

NICE Guideline 2003. Consent – procedures for which the benefits and risks are uncertain.

https://www.nice.org.uk/guidance/ipg56/documents/consent-procedures-for-which-the-benefits-and-risks-are-uncertain2

NICE Guideline 2006. Urinary incontinence: the management of urinary incontinence in women.

https://www.nice.org.uk/guidance/cg40

Submission from Professor Carl Heneghan

Professor of Evidence-Based Medicine, University of Oxford

Synthetic mesh for use in abdominal and vaginal pelvic mesh procedures

Conflicts of interests: I declare that I am Director of the Centre for Evidence-Based Medicine (www.cebm.net) at the University of Oxford and a clinical advisor to the All-Party Parliamentary Group (APPG) on surgical mesh. I have received expenses and fees for my media work, and grant funding from the NIHR, the NIHR School of Primary Care Research and the NIHR BRC Oxford, and I am an NIHR Senior Investigator. I have received financial remuneration from an asbestos case and given free legal advice on mesh cases. I work as an NHS GP work in urgent care, and I am Editor in Chief of BMJ Evidence-Based Medicine.

Executive summary:

If safety signals and recommendations had been acted on - many of which were available fifteen years ago - the failings that underpin transvaginal mesh could, and should, have been avoided. Patients have often been badly-informed about the risk of procedures, and the lack of evidence gathering and the slow response of the multiple agencies involved in safety have let patients down.

Because of the systematic failings there is a need to establish: 1) a robust approach to registering conflicts of interest of doctors; 2) a consent system that has impartial, informed decision making; 3) a clearer defined roles and responsibilities for the multiple agencies involved in patient safety; 4) clarity over who has the legislative capacity to ensure recommendations are enforced; 5) a national registry for all implantable devices to protect patients, improve outcomes, and identify best practice; 6) establishment of an independent review group that has the skills, knowledge and the independence to undertake thorough, transparent evaluations and demand better data to inform patient safety; 7) a greater emphasis on recognising harms when they occur, and 8) ensure the patient voice is foremost in any solutions with a focus on restoring public trust in medicine.

This report reflects research, investigations and reviews of the evidence I have undertaken while employed at the Centre for Evidence-Based Medicine, University of Oxford.

This summary is based on the following observations:

1. Summary of evidence

Year	Source	Evidence
2003	FDA	FDA receives over 1,000 reports from nine surgical mesh manufacturers

2003	NICE	NICE approved TVT for the treatment of stress urinary incontinence, but did so recommending the procedure as only “one of a range of surgical options for women with uncomplicated urodynamic stress incontinence in whom conservative management has failed.”
2003	NICE	NICE also recommended that observational data on effectiveness and safety of the procedure should be collected over at least 10 years. Preferably, “this should be nationally co-ordinated in the form of a registry of audit data to include both the numbers of procedures carried out and measures of outcome and adverse events.” https://www.nice.org.uk/guidance/ta56/documents/final-appraisal-determination-tension-free-vaginal-tape-gynecare-tvt-for-stress-incontinence2
2005	Cochrane	Review of surgery for stress urinary incontinence recommends the need for studies with longer term follow up. Few trials report in a complete fashion, and most information comes from annual meetings. https://www.ncbi.nlm.nih.gov/pubmed/1603486
2007	Cochrane	Surgical management of pelvic organ prolapse in women published. 22 RCTs (8 new trials). Findings still report there is insufficient robust evidence to support the practice. Concluding there is an urgent need for adequately powered trials. https://www.ncbi.nlm.nih.gov/pubmed/17636742
2008	FDA	Letter alerts health care practitioners to the medical complications associated with transvaginal mesh. http://www.amiform.com/web/documents-risques-op-coelio-vagi/fda-notification-about-vaginal-mesh.pdf
2009	Cochrane	Surgical management of pelvic organ prolapse in women updated. In this second update, 18 new trials were added, but conclusions have not changed since 2007
2009	Systematic review	Complication and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. The total reoperation rate was highest (8.5%) for vaginal mesh kits https://www.ncbi.nlm.nih.gov/pubmed/19155908
2010	Obstet Gynecol	Vaginal mesh for prolapse: a randomized controlled trial. Trial halted as at 3 months; there is a high vaginal mesh (Prolift) erosion rate (15.6%) with no difference in overall objective and subjective cure rates. https://www.ncbi.nlm.nih.gov/pubmed/20664388
2011	Int Urogynecol J	Incidence and management of graft erosion wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. 110 studies reported on erosions with an overall rate, of 10.3% (95% CI, 9.7 to 10.9%; range 0 to 30%) Dyspareunia described in 70 studies for a rate of 9.1% (95% CI 8.2 to 10.0%; range, 0 to 67%) https://www.ncbi.nlm.nih.gov/pubmed/21424785
2011	FDA	Releases review identifying serious safety concerns and adverse events. Corrects former 2008 statement that side effects are not rare. "The most common mesh-related complication experienced by patients undergoing transvaginal POP repair with mesh is vaginal mesh erosion."....."More than half of the women who experienced erosion from nonabsorbable synthetic mesh required surgical excision in the operating room. Some women required two to three additional surgeries https://www.fda.gov/downloads/medicaldevices/safety/alertsandnotices/ucm262760.pdf
2012	FDA	FDA notes a dramatic increase in complications and orders 30 manufacturers to

		conduct postmarket surveillance studies lasting at least 3 years to address safety concerns https://www.meshmedicaldevicenewsdesk.com/mesh-makers-who-received-fda-letter-requiring-follow-up-tests/
2014	CMO and MHRA	Chief Medical Officer of England asks MHRA to review evidence on vaginal mesh implants. 'MHRA's position is that, for the majority of women, the use of vaginal mesh implants is safe and effective.' In direct contrast to the FDA MHRA states: 'In line with other medical device regulators worldwide we are not aware of a robust body of evidence to suggest that these devices are unsafe if used properly as intended.....' https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/402162/Summary_of_the_evidence_on_the_benefits_and_risks_of_vaginal_mesh_implants.pdf
2014	Radar TV, Carl Heneghan	Dutch TV Exposes Farce of Pelvic Surgical Mesh Regulation Using a Tangerine Bag https://www.thetimes.co.uk/article/scandal-of-fruit-netting-approved-as-surgical-implant-dvcqd2rt9mr video: http://www.radartv.nl/uitzending/archief/detail/aflevering/01-12-2014/
2015	American Journal of Obstetrics & Gynecology	Reoperation for urinary incontinence: a nationwide cohort study, 1998–2007. Women operated with transobturator tape had a significantly higher risk of reoperation compared with retropubic mid-urethral tape. Cumulative incidence of reoperation after any surgical treatment for urinary incontinence was 10% http://www.ajog.org/article/S0002-9378(15)01017-0/abstract
2015	Cochrane review	Comparison of transvaginal grafts versus native tissue repairs published. Twelve new trials are included that were not in the previous review:
2015	NHS England	includes evaluation of both the efficacy and the extent and causes of adverse incidents and complication rates associated with these types of surgery https://www.england.nhs.uk/wp-content/uploads/2015/12/mesh-wg-interim-rep.pdf
2016	FDA	changed the approval requirements for surgical mesh from Class II to the higher risk Class III. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm479732.htm
2016	Cochrane	Transvaginal mesh or grafts compared with native tissue repair for prolapse updated. Mesh associated with lower rates of awareness of prolapse, but associated with higher rates of repeat surgery, stress urinary incontinence or mesh exposure, and higher rates of bladder injury and de novo stress urinary incontinence. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012079/full
2016	Lancet	Lancet reports women with mesh were three times more likely to suffer complications and twice as likely to need re-operation compared with traditional surgery. The study concludes mesh procedures cannot be recommended for primary prolapse repair. http://thelancet.com/journals/lancet/article/PIIS0140-6736(16)32572-7/fulltext
2016	Guardian	reports the NHS and medical devices regulator tried to limit scandal over vaginal mesh implants https://www.theguardian.com/society/2017/apr/21/nhs-vaginal-mesh-implants-scandal-suppress-media?CMP=aff_1432&awc=5795_1540227748_dad30f2a8f8134b83d8bcbc10a6

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2017	MHRA	MHRA response to the final report of the Mesh Oversight Group In common with other medical device regulators worldwide, none of whom have removed these devices from the market; we are not aware of a robust body of evidence which would lead to the conclusion these devices are unsafe if used as intended. https://www.gov.uk/government/news/mhra-response-to-the-final-report-of-the-mesh-oversight-group
2017	UK study	UK Study reports complications following vaginal mesh for stress urinary incontinence: 5.9% were readmitted at least once within 5 years. Complication rates were higher (9.8%) in the potentially confounded (had concomitant procedures) cohort. https://www.nature.com/articles/s41598-017-11821-w
2017	Guardian	Guardian reports 1 in 15 women with the most common type of mesh will require removal surgery https://www.theguardian.com/society/2017/aug/15/scandal-of-vaginal-mesh-removal-rates-revealed-by-nhs-records
2017	RCOG	RCOG website updates resources to support decision making https://www.rcog.org.uk/en/guidelines-research-services/patient-safety/mesh/
2017	BMJ Open	Transvaginal mesh products for pelvic organ prolapse have been approved on the basis of weak evidence over the last 20 years. Devices have inherited approval status from a few products. http://bmjopen.bmj.com/content/7/12/e017125
2017	BMJ	Carl Heneghan and colleagues in a BMJ analysis describe how failings in the process for the marketing approval of implantable transvaginal mesh devices may have exposed women to avoidable harms and how to avoid their repetition http://www.bmj.com/content/359/bmj.j5515.full?ijkey=IRhPzmSgMlC0yZc&keytype=ref
2017	Panorama	Ethicon, which markets mesh in the UK under brand name Gynecare TVT, did not update doctors with the extent of risks for its leading mesh device. https://www.independent.co.uk/news/uk/home-news/vaginal-mesh-scandal-tvt-transvaginal-sling-implant-risks-thalidomide-device-bbc-panorama-a8102726.html
2018	BMJ	Despite government guidance, it remains difficult to unpick industry funding of clinicians in the UK—and specialities in vaginal mesh treatment are no exception. Jonathan Gornall reports on the NHS surgeons, professional bodies, royal colleges, and medical conferences that benefit from corporate funding and how this financial involvement is hidden from patients https://www.bmj.com/content/363/bmj.k4164.abstract

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2. Is current legislation and regulations on safety and efficacy of mesh implants fit for purpose?

Concerns exist about the lack of premarket clinical data on the effectiveness and safety of medical devices. These concerns have previously been expressed by Susanne Ludgate of the MHRA, who stated in 2010 that she was "appalled at how many devices are brought to market with a lack of appropriate clinical data." [1]

The problems with lack of pre-market data for mesh can be summarised as:

- It is left to the discretion of the Notified Bodies (as to the extent and nature of clinical data required for the approval of even the highest-risk devices).
- Clinical data are not reviewed by Notified Bodies.
- None of the pre-market clinical data is available for independent scientific scrutiny.
- The level of clinical data required for a new device can be minimal. EU directives include as evidence for approval "a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device".
- A major problem with the current system for approving devices is the use of "equivalence" That is, if a device is similar to another manufacturer's device on the market, then there is no need for clinical trials and device manufacturers can seek regulatory approval based on a far lower level of data than devices not considered under this fast track pathway. This is unlikely to change with the new directives.
- Regulators find it incredibly difficult to judge if a device is “equivalent” to another on the market.
- Transvaginal mesh products for pelvic organ prolapse have been approved on the basis of weak evidence over the last 20 years. Devices have inherited approval status from a few products. We found (See Heneghan et al. BMJOpen [2]) 61 mesh devices whose approval ultimately relied on claimed equivalence to the Mersilene Mesh and the ProteGen Sling. We found no clinical trials evidence for these 61 devices at the time of approval.
- The concept of ‘predicate creep’ highlights a process whereby multiple submissions over time can lead to a new device that is very dissimilar to the original predicate device. As an example, one of the early devices, the ProteGen Sling made from Polyester and removed from the market, continued to be used as a predicate for more modern devices made from polypropylene. [3]
- Significant differences in evidence requirements for regulatory approval between the US and EU exist. Often the requirements in the US are far higher. As a consequence, a number of devices rejected by the FDA have been approved in the EU. [4] This list of EU approved devices rejected by the FDA includes breast implant, which spectacularly failed patients in the UK and Europe at enormous additional costs.

Trilucent breast implants

First marketed in the UK in 1995 by LipMatrix, Trilucent implants were recalled and withdrawn from the market in 1999. The filler of the implants, which was derived from soybean oil, broke down in the body and leaked through the shell, causing ruptures. The breakdown of the filler was significantly different from that predicted during preclinical testing, and many patients had to have implants removed.

PIP breast implants

In 1991, breast implants manufactured by Poly Implant Prosthese (PIP) received a CE mark for its silicone breast implants, But in 2001 they changed the gel so that it was different from the one described in the CE marking file. This modification led to rupture rates higher than silicone implants made by other manufacturers. On 30 March 2010, the French regulator—AFSSAPS— issued a recall of all pre-filled silicone breast implants manufactured by PIP, affecting an estimated 35 000-45 000 women worldwide.

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3. **The effectiveness of the MHRA in ensuring patient safety**

On the 26th July 2017, the MHRA reported: ‘In common with other medical device regulators worldwide, none of whom have removed these devices from the market, we are not aware of a robust body of evidence which would lead to the conclusion these devices are unsafe if used as intended.’ This is despite the serious concerns being raised in the US:

- In 2011, the FDA raised concerns about the safety of some transvaginal mesh products.[5] Serious adverse events attributed to the use of such products were not rare and included serious complications, such as vaginal erosions, infections, and organ perforation.
- 'In 2011, the FDA published a systematic review of vaginal mesh studies from 1996 to 2011 and reported a number of important problems, overturning previous FDA alerts, which had stated that mesh complications were rare. Contrary to previous FDA statements, this review found that "transvaginal placed mesh in pelvic organ prolapse repair does NOT conclusively improve clinical outcomes over traditional non-mesh repair' (emphasis in the original). It concluded that "while transvaginal POP repair with mesh often restores anatomy, it has not been shown to improve clinical benefit over the traditional non-mesh repair.'[3]
- In 2011, The FDA used information reported to its Manufacturer and User Device Experience (MAUDE) database. The FDA cited 3,979 reports of serious complications associated with urogynaecological surgical mesh products. The most frequent complications included vaginal mesh erosion (35%), followed by pain (31%), infection, bleeding, dyspareunia, and organ perforation. [2]
- Transvaginal mesh devices were originally class II devices in the US, but they were reclassified in January 2016. In the 510(k) process, anyone who intends to market a new medical device has to submit a pre-marketing notification to the FDA at least 90 days before the date scheduled for marketing to begin.[6] [7]
- In 2012 the FDA asked manufacturers of surgical mesh products to conduct new safety studies. Section 522 of the Food, Drug and Cosmetic Act gives the FDA the authority to mandate manufacturers to undertake post-market surveillance studies of class II or III devices, among other criteria, when 'failure would be reasonably likely to have serious adverse health consequences … or the device is to be implanted in the body for more than one year'. [8]

In 2014 the MHRA published its assessment of the clinical effectiveness of transvaginal meshes for SUI and POP, based on data from an overview of systematic reviews and reports of adverse events. [9]

- The MHRA stated that the evidence from published reviews was insufficient to draw conclusions about the benefit to harm balance of meshes for specific procedures. [3]
- Since 2005, the MHRA had received a total of 110 reports on vaginal mesh implants used to treat pelvic organ prolapse; the most common complications reported were pain (39), extrusion/erosion (65), infection (21), relapse of conditions/urinary symptoms (20), perforation (16), and dyspareunia (18).
- In contrast to FDA findings, The MHRA concluded that the overall benefits outweighed the risks of complications. [3]
- Conflicts between reviews by the FDA and the UK MHRA are summarised in Box 1.

Box 1 reproduced from Heneghan et al. [3]

FDA summary of findings:	**UK MHRA summary findings**:
Evidence used:	
RCTs[1] , relevant systematic reviews, plus a subset of observational studies that reported data on harms associated with transvaginal repair of POP[2] using mesh between January 1996 and April 2011	A systematic review of systematic reviews and adverse incidents reported to the MHRA

Based on data from 110 studies including 11,785 women.	Unclear. Used data from RCTs of included systematic reviews; however, the results were not pooled across included reviews, and the number of included reviews was not specified
Results reported for mesh versus native tissue repair.	The results presented do not compare intervention effects for mesh versus native tissue repair
Complications	
"Patients who undergo POP repair with mesh are subject to mesh-related complications that are not experienced by patients who undergo traditional surgery without mesh."	"Adverse event rates for POP repair are in the range 2-6% for most outcomes and 14-15% for deterioration in sexual function." However, there was no comparable information about pain after prolapse surgery without mesh.
"Mesh-associated complications are not rare. The most common mesh-related complication experienced by patients undergoing transvaginal POP repair with mesh is vaginal mesh erosion."	Mesh erosion may occur in around 1 in 15 women, "but may be less common if a biological graft is used rather than a non-absorbable synthetic mesh."
"Approximately 10% of women undergoing transvaginal POP repair with mesh experienced mesh erosion within 12 months of surgery." "Mesh contraction, resulting in vaginal shortening, tightening, and/or vaginal pain in association with transvaginal POP repair with mesh, is increasingly reported." "More than half of the women who experienced erosion from non-absorbable synthetic mesh required surgical excision in the operating room. Some women required two to three additional surgeries."	Around around 1 in 20 or fewer women required further surgery for mesh erosions. Organ damage because of mesh exposure occurs in 2% of cases. It was unclear whether pain before surgery was accounted for in women exposed to mesh surgery, and data on the number of women whose sexual function or pain improved after surgery were not reported.
Quality of evidence	
Adverse events in clinical trials "are inconsistently defined and reported", and very few studies have lasted 2 years or more Many trials have been poorly designed and/or conducted, have been largely underpowered, have inadequately reported inclusion/exclusion criteria, have inadequate blinding techniques, and have failed to account for variations in the duration of patient follow-up	Difficult to draw specific conclusions about actual rates of adverse events and subjective cure rates Overall, the quality of the systematic reviews was good; however, the quality of the RCTs in the systematic reviews was variable

4 The MHRA's approach to gathering evidence on patient safety

The MHRA has previously reported it relies on a "statutory vigilance or voluntary adverse incident reporting system" to regulate—in other words, governmental regulation really starts when devices are already on the market. [10];

It is not mandatory for manufacturers to present their final report to the Competent Authority.' [11]

Minutes of a meeting of the MHRA's safety of devices committee in 2009 stated: 'It was also noted that MHRA does not see the clinical data that is generated from a clinical trial prior to it being submitted to a Notified Body as part of a conformity assessment process.

The MHRA itself has reported that "*Long term outcomes of implanted devices are a particular concern."*
(http://www.mhra.gov.uk/home/groups/clin/documents/websiteresources/con082076.pdf)

The MHRA's current systems are insufficient to detect early warning systems or for spotting new problems as they emerge. For example, registers often only include patients who have had revision surgery, which may be many years after symptoms first occur. [12]

There is currently no formal system for post market surveillance of medical devices in the UK and many vested interest's disincentive manufacturers and clinicians from highlighting problems as they arise.

As a consequence, there is currently no way of knowing which patients in the UK have had a mesh device implanted, since this information is not available on GP records, and is not routinely noted on hospital records (or discharge summaries). Therefore, if a device is found to be faulty, there is no way of notifying GPs or their patients.

The lack of data does not help clinical decision making. Indeed, the lack of clinical studies or trials makes it an almost impossible task for health technology appraisal. In the worst-case scenarios, patients are subjected to an intervention that is inappropriate for them. Also, the lack of clinical data means it is difficult if not impossible for commissioners of health care to understand the true cost of interventions.

Information about the number of recalled devices, voluntary recalls, market withdrawals and the risk of harms to patients is not forthcoming. The manufacturer and the Notified Body hold these data. Information held by the Notified Bodies is confidential and not available for scrutiny.

The MHRA ultimately relies on a flawed approach to gathering evidence to inform patient safety because of the regulatory environment, its reactive approach to data gathering and the extensive problems with publication bias and under-reporting.

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4. **How effective is NICE at ensuring patient safety**

In 2003 NICE approved TVT for the treatment of stress urinary incontinence but did so with a number. of recommendation that never came into force. Perhaps the most damming of these is the recommendation 'that observational data on effectiveness and safety of the procedure should be collected over at least 10 years,' that never was acted upon.

NICE guidance has a significant impact on practitioner behaviour. However, its lack of legislative powers can present a barrier to the safe adoption of technologies in the NHS. As a consequence, NICE's recommendation that adds extra burden and costs, but aims to ensure patient safety, are often largely ignored.

NICE production of evidence to meet the safety needs of patients is burdensome and often slow to react. When NHS England's Mesh Oversight group report was published in July 2017, they stated the combined SUI and POP guideline update was planned for publication in 2019.

NICE Medical Technologies Evaluation Panel requires that medical devices should be cost saving or resource releasing to be recommended for use in the NHS. However, how this can be determined in the absence of long-term data for life-long implants, is unclear. This problem is further compounded as the evidence used in the appraisal of medical devices is often poor quality (that is when any is forthcoming) and often does not address the essential questions for implementation in the NHS.

5. **The effectiveness of NHS statistics in informing patient safety matters**

In 2017 NHS Digital published a retrospective review of surgery for prolapse and stress urinary incontinence using tape or mesh. The review included women who had surgical procedures for prolapse and stress urinary incontinence using mesh and or tape between 2008/09 and 2016/17.

NHS digital data has several limitations that prevent useful inferences to be drawn:

- results do not include procedures before the audit review period or those that occurred in hospitals outside England or in a private setting;
- reporting of the primary diagnosis is not mandatory in Hospital Episode Outpatient data, only 4.9% of attended appointments had a main diagnosis recorded.
- There is also no General Practice data that reflects the work and morbidity in primary care
- NHS statistics for mesh are described as experimental and are therefore subject to significant uncertainty in terms of their accuracy

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6. How do conflicts of interest affect patient safety

Financial and non-financial conflicts of interests are a widespread phenomenon amongst academic institutions, researchers and clinicians and are associated with pro-industry findings, withholding of results and provider preferences. Conflicts also overtly influence guidelines [13]

One quarter of investigators have industry ties, and about 2/3rds of academic institutions hold equity in start-up companies that sponsor research performed at the same institutions. Industry sponsorship is significantly associated with positive conclusions and often with restrictions on publication, lack of investigator access to research results and a shift in research emphasis.[14]

Jonathan Gornall BMJ investigation states that despite government guidance, it remains difficult to unpick industry funding of clinicians in the UK—and specialists in vaginal mesh treatment are no exception. NHS surgeons, professional bodies, royal colleges, and medical conferences benefit from corporate funding, and this financial involvement is largely hidden from patients

'In September 2017 a joint meeting of the European Urology Association and the European Urogynaecological Association published a consensus statement on the use of implanted materials to treat pelvic organ prolapse and stress urinary incontinence. Of the 24 co-authors of the paper, 17 declared financial relations of some sort—as consultants, speakers, researchers, etc.—with a total of

34 companies. All three UK co-authors declared links with industry: two with five companies and the other with six.' [15]

Current recording of employees' conflicts of interest by NHS trusts is poor. An analysis of 185 Trusts found that only 31 registers contained enough information to assess employees' conflicts of interest. Despite obligations to disclose conflicts of interest, and organisations to record these. [16]

There is currently no public register that allows individuals to assess the nature of the impact of the conflict, particularly with regard to informing decision making.

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7. What further measures are warranted?

- A robust approach to registering conflicts of interest of doctors is required that informs decision making, ensures patient safety and restores public trust. (The GMC have consulted on changes to the medical register that might require a change in the law. However, they have not chosen to consult on statutory declarations).

Questions to ask the GMC: why have they not initiated a conflict of interest register?
Questions to ask the Health Select committee: why is there no conflict of interest policy across the NHS?

- There is a need to define the responsibilities across multiple agencies involved in patient safety. It is currently not clear who has responsibility for what, for whom in what contexts and who has the legislative capacity to ensure recommendations that enact patient safety are enforced.

  Questions to ask the MHRA: why has the MHRA differed so much in its recommendations to the FDA?
  Questions to ask NICE: what is the purpose of patient safety recommendations that are not monitored or implemented? Whose role is it to enact NICE safety recommendations?

- It is not clear what evidence (including study types, length of follow up and relevant outcomes) is required by NICE to inform cost saving or resource releasing recommendation for the use of lifelong implanted devices in the NHS.

  Questions to ask NICE: what are the evidence requirements to ensure patient safety?

- A National registry (funded partly by the government) for surgical mesh (and for all implantable devices) to protect patients, improve outcomes, and identify best practice is warranted. International initiatives should inform the development of a registry and based on best practices. A national registry requires a robust approach to informing who has had what device, in what setting. Updated EU legislation with the Unique Identifier offers an opportunity to develop and set standards for an NHS wide procedural database.

Questions to ask NHS Digital: what Is required to ensure that every device procedure (including the unique identification) is recorded across all UK health care settings (NHS and private)?
Questions to ask the Health Select committee: who should fund a national register?
Question to ask of the NHS: why is there no mandatory device registry in the NHS?

- An independent assessment unit is required that has the skills, the impartiality and the know how to evaluate evidence for patient safety. Assessment should occur for multiple sources

of evidence and consider investigative powers to review evidence when there are public safety issues to hand

Further questions to ask: who currently has responsibility for evaluating the safety of devices on an ongoing basis? Whoever has had the responsibility, why have they so spectacularly failed in the case of mesh, and what lessons can be learnt?

References

1 Website. (http://www.guardian.co.uk/science/2011/may/16/medical-devices-lack-clinical-data) (accessed 22 Oct 2018).

2 Heneghan CJ, Goldacre B, Onakpoya I, *et al.* Trials of transvaginal mesh devices for pelvic organ prolapse: a systematic database review of the US FDA approval process. *BMJ Open* 2017;**7**:e017125.

3 Heneghan C, Aronson JK, Goldacre B, *et al.* Transvaginal mesh failure: lessons for regulation of implantable devices. *BMJ* 2017;**359**:j5515.

4 Cohen D, Billingsley M. Europeans are left to their own devices. *BMJ* 2011;**342**:d2748.

5 Urogynecologic Surgical Mesh. http://www.fda.gov/downloads/medicaldevices/safety/alertsandnotices/UCM262760.pdf (accessed 7 Mar 2017).

6 Website. US Food and Drug Administration. The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications - Final Guidance. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080189.pdf (accessed 7 Mar 2017).

7 Heneghan C, Thompson M, Billingsley M, *et al.* Medical-device recalls in the UK and the device-regulation process: retrospective review of safety notices and alerts. *BMJ Open* 2011;**1**:e000155.

8 Devices CF, Health R. 522 Postmarket Surveillance Studies - 522 Postmarket Surveillance Studies – Frequently Asked Questions (FAQs). http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/PostmarketSurveillance/ucm134497.htm (accessed 7 Mar 2017).

9 UK Medicines and Healthcare products Regulatory Agency (MHRA). October 2014. A summary of the evidence on the benefits and risks of vaginal mesh implants. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/402162/Summary_of_the_evidence_on_the_benefits_and_risks_of_vaginal_mesh_implants.pdf (accessed 26 Jul 2017).

10 Cohen D. Revision rates for metal on metal hip joints are double that of other materials. *BMJ* 2011;**343**:d5977.

11 Cohen D. How safe are metal-on-metal hip implants? *BMJ* 2012;**344**:e1410.

12 Cohen D. US regulator seeks advice on health risks of metal on metal hip implants. *BMJ* 2012;**344**:e2460.

13 Rose SL, Highland J, Karafa MT, *et al.* Patient Advocacy Organizations, Industry Funding, and Conflicts of Interest. *JAMA Intern Med* 2017;**177**:344–50.

14 Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA* 2003;**289**:454–65.

15 Gornall Jonathan. Vaginal mesh implants: putting the relations between UK doctors and industry in plain sight BMJ 2018; 363 :k4164

16 Feldman HR, DeVito NJ, Mendel J, et al A cross-sectional study of all clinicians' conflict of interest disclosures to NHS hospital employers in England 2015-2016 BMJOpen 2018;8:e019952. doi:10.1136/bmjopen-2017-019952

Submission from Matthew Hill

BBC Health Correspondent West

COI:

I do not have any 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.

Submission:

Shared two documentaries on the use of surgical mesh, which were aired as follows:

- Inside Out West October 16 2017
- Inside Out West March 12 2018

These are no longer available to view, however you can read the supporting BBC News articles:

- **16 October 2017 Mesh surgeon investigated by NHS trust in Bristol**
  https://www.bbc.co.uk/news/uk-england-bristol-41596436
- 12 March 2018 Mesh surgeon removed ovaries without prior consent
  https://www.bbc.co.uk/news/uk-england-bristol-42961195

Submission from Myra Robson

Senior Pelvic Health Physiotherapist at Lewisham and Greenwich NHS Trust

COI:

I am the physiotherapist involved in Squeezy app and work with the company Living With Ltd on this. I receive no income from Squeezy sales or work on Squeezy but I do receive payment from the company for other consultancy services for their healthcare products such as the "Living With Pelvic Health" platform. They also sponsor some of my travel and accommodation costs for conferences.

I am one of three physios involved in the campaign group "#pelvicroar". We receive no income but have received sponsorship for some of our activities and campaigns. More details can be found on our website www.pelvicroar.org.

Submission:

Explanatory note: I met Baroness Cumberlege and Valerie Brasse in August and took these notes with me for the meeting. I was asked to add some of the points we discussed on the day and resubmit, which I did. I am therefore using these same notes, with a few amendments, for my written evidence submission.

Myra Robson

Senior Pelvic Health Physiotherapist at Lewisham and Greenwich NHS Trust

Member of POGP (Pelvic, Obstetric and Gynaecological Physiotherapists)

Physiotherapist behind Squeezy App

One of the three physiotherapists who established the campaign group “#pelvicroar”

My involvement in mesh issues:

- I work with a uro-gynaecologist closely involved with Ms Elneil and my awareness of the mesh controversy started there. I met the mesh campaigner Kath Sansom online (via Squeezy) and joined “Sling the Mesh” around two years ago
- I have been offering the group clinical advice informally and have been attempting to build bridges between the group and the medical community. It took around 18 months to be fully trusted by the group as a whole
- I have recently joined a different group called “Mesh UK”, which has been an altogether more challenging experience

Key problems:

- There is a lack of Trust in the medical profession and the entire healthcare system. This ranges in severity and presentation

- There are very few trusted and accepted health care professionals and individuals – these include the review team (who have made a very good impression), Ms Elneil, Mr Agur, Dr Veronikis, Ms Ward and myself. The extended team at UCLH are beginning to gain acceptance also
- The belief is widespread that there has been much more going on than lack of evidence, mistakes, poor judgement etc – anything from poor to absent consent, deliberate harm, surgery for financial incentives, incentives from Pharma companies, cruelty….
- There is anger that more people were not offered conservative options prior to surgery
- There is widespread general anger and fear. Many of those joining the groups have no current mesh-related symptoms but are panicking that they will develop them. They are often advised by the group to consider removal of mesh to prevent these problems from occurring
- There are many cases of complex and persistent pelvic pain in the individuals in the groups – I believe this could lead to significantly more presenting with these issues and requiring multi-disciplinary treatment
- The list of symptoms connected with mesh is wide and varied, and increasing on almost a daily basis
- Group members offer each other advice on everything from accessing treatment to managing symptoms – often the suggestions are inappropriate and may be harmful but I have learnt to be extremely selective in the replies I offer
- The consensus is that patients should wait to see one of the mesh experts, yet waiting times are increasingly lengthening and this creates yet more anger. The call is for more "experts" to be trained but in general, no-one wants to see new mesh removal surgeons!
- The Uro-gynaecologist I work closely with has been training in mesh removal under Ms Elneil, yet is reluctant to take it on due to the pressure around it. Complications are common and the risk to a surgeon's reputation if complications arise is very high
- There is much heated debate around the non-surgical management of women with vaginal/gynae mesh complications and post-removal. Dr Veronikis and some campaigners are strong in their promotion that physiotherapy causes pain and harm. This is leading to women not accessing treatment that may be helpful and may prevent further surgery in the future
- Some campaigners have publicly bullied and named individual therapists and surgeons and I have had to step in several times to control the situation and protect individuals
- I have spoken to consultants who have received significant episodes of online bullying and been in situations where a single comment has been misconstrued and used against an individual with an alarming speed and level of consequence
- A further complication with physiotherapy is that individuals with mesh complications (such as groin pain) may be sent to a musculo-skeletal physiotherapist by an unsuspecting GP, with neither being fully aware of the complexities around mesh. This fuels the distrust within the group when shared online. It is proving very difficult to support people in understanding that specialist pelvic physiotherapy is different from mainstream physiotherapy

What next?

- The review will go a long way to building bridges
- We need to find a way to improve the awareness and training of GP's and non-mesh specialists eg physiotherapists. This can be through conference talks, discussions and articles in journals and newsletters, social media etc
- An example of the excellent work that is going on includes a course on mesh and its effect on pelvic pain in November - (www.baus.org.uk/professionals/events/3052/implanted_pelvic_materials_and_chronic_pain_the_full_story), including a talk by Kath Sansom
- I keep the specialist physiotherapy groups updated, I spoke at our annual conference in October and I am writing an article but more time is required to make sure everyone is up to speed. This is scratching the surface….All of this is done in my limited spare time and I am probably the most knowledgeable physiotherapist on mesh in the UK!
- It is vital that we develop some guidelines for health care professionals on how to manage people with mesh concerns, mesh complications and post mesh removal or related surgeries. The new advice hotline has been well received
- I have made arrangements with Dr Veronikis, Mr Agur, Ms Elneil and the lead physiotherapist at UCLH to draft some international guidelines relating to the rehabilitation of these patients. However, this is again all being done in my own time which is a challenge - we need to support more funded time as quickly as possible! It is key to have some simple guidelines that are approved by the clinicians who hold the trust and respect of the mesh-injured community
- I believe that we also need these guidelines to support healthcare professionals who are in very vulnerable positions at the moment, when managing these patients

Physiotherapy and related treatments

- There is a need to look at how we provide specialist services to support patients and to manage the increased awareness and demand for the conservative management of pelvic health conditions in particular. There are only around 800 pelvic health physiotherapists in the UK and the need to be innovative in our approach is clear. There are a number of possibilities that I can imagine working
- Improving public awareness of pelvic health conditions, in particular stress incontinence and pelvic organ prolapse, and the treatments available. This could include a patient decision aid for surgery and could include a similar pathway for hernias. Mr Agur has an excellent plan, as yet unfunded, for supporting patient decisions in stress incontinence surgery
- Ensuring that the designated mesh removal centres have clear policies, holistic treatment pathways and recognised expertise rather than being self-appointed. Holistic packages could include a number of elements such as specialist pelvic health physiotherapy, acupuncture, specialist pain management teams, counselling….
- Look at the conservative management of pelvic health conditions for individuals without mesh, with mesh complications and post removal (many of the original symptoms will return at this stage). Specialist pelvic physiotherapy has a key role and my colleagues within POGP would also be delighted to support any work in this area. The new NICE guidelines on stress

incontinence and pelvic organ prolapse (out for consultation) have been welcomed as they have a much greater emphasis on conservative therapies

- Digital support for conservative treatments such as Squeezy App and the clinician platform that can work alongside it (www. livingwith.health/products/living-with-pelvic-health) are also tools worth considering
- Investment in vaginal pessary services would offer another evidence-based and very low-risk treatment option for both pelvic organ prolapse and stress incontinence. This service is usually limited and poorly managed and is another area that I am working on at the moment
- Utilise the power of social media to build bridges and spread messages about what is being done – again, the time required to do it well is key. My campaign group, #pelvicroar, is already working in this area and it is through this that I have set up the group to look at rehabilitation guidelines. We would be delighted to help…

Specific recommendations following our meeting:

- In my opinion, there is no need to consider mesh as an option for stress urinary incontinence as there is no actual medical need to treat it. The important issues are symptom control and quality of life, which can very effectively be managed by pelvic health physiotherapy, vaginal pessaries and non-mesh surgical interventions. The NICE guidelines for SUI recommend three months of specialist, supervised physiotherapy as the first line treatment
- In my opinion, there will be a very small minority of cases where mesh needs to be considered for pelvic organ prolapse, rectal prolapse and possibly hernias (this is not my area of expertise). Pelvic organ prolapse surgery has a recurrence rate of 20-30% and mesh is one way to try reduce this, especially in women with connective tissue disorders such as hypermobility. I think there needs to be a small number of specialised mesh centres where any mesh implantation is carried out – or at least some form of MDT with a mesh specialist (could be by video/Skype) where such cases are discussed
- Rectal prolapse and related bowel issues can also be effectively managed conservatively by simple lifestyle factors, physiotherapy and gadgets such as the SquattyPotty and Femmeze, in many cases
- Ideally the vast majority (if not all) women with pelvic health issues such as bladder and bowel dysfunction, pelvic pain, mesh complications and pelvic organ prolapse will have access to pelvic health specialist physiotherapists as a first-line treatment. An MDT approach is essential and the majority of patients should only see a surgeon once conservative treatments have been explored
- It is clear that there are not enough pelvic health physiotherapists currently to meet the demand. Along with redirecting resources (such as work within my Trust to make a specialist physio the first contact for most pelvic health patients) it is possible to be creative with the resources we do have such as Squeezy app, the POGP website, NHS Choices website and related information, media links, education for healthcare

professionals etc. It is key that some of the most basic strategies such as weight loss, good bowel and bladder habits and pelvic floor exercises are effectively communicated as this can make a significant difference to a variety of conditions and symptoms

- I am involved currently with establishing an excellent on-line consultation service for pelvic floor physiotherapists, based on a model used by a colleague in the North of England (www.stressfreewoman.com). It is being designed by the team behind Squeezy App (www.livingwith.health) and will include options for patients to pay for brief question and answer sessions or longer consultation sessions, with the option also to find specialist physiotherapy services around the country. I believe this model has enormous value for supporting the mesh community

Key Mesh groups:

Sling the Mesh (over 6,000 members) led by Kath Sansom

Mesh UK Charitable Trust led by Ophelia Payne (also known as Candia McCullough) and Ann Boni

Mashed up by Mesh – Yvette Greenway

Mesh SOS – Cat Lee

There are some other very small groups such as Meshed Up Mum, Mesh Awareness Wales, TVT Mum, Mesh Awareness Australia, Mesh Injured Australia, Meshies United, Original Australian Mesh Support, ……and many single campaigners.

I have no other contact details but they can all be found on Twitter and usually on Facebook.

Myra Robson


Pain
Sex-impossible
Groin-pain
Reduced-mobility
Infection
Erosion
Fibromyalgia
Persistent-pain
Bladder-perforation
Interstitial-cystitis
Pelvic-floor-pain
Painful-sex
Back-pain
Depression
Leg-pain
Urine-retention
Hip-pain
Joint-pain
Nausea
Anxiety
Cystitis
Night-sweats
Fatty-liver
Hair-loss
Adhesions
Insomnia
Smears-impossible
Nerve-pain
Restless-legs
Sepsis
Tinnitus
Appendicitis
Low-libido
Thrush
High-cholesterol
Bowel-perforation
Psoriasis
Auto-immune-disease