The Independent
MEDICINES & MEDICAL DEVICES
Safety Review

Pelvic Mesh Timeline – Key Events

July 2020

Disclaimer

The statements made and the opinions expressed in the components of the timeline do not purport to reflect the opinions, views or conclusions of the Independent Medicines and Medical Devices Safety Review's ('IMMDSR). 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.

Annex D: Mesh Timeline – Key Events

Key

Evidence Source	Colour
Regulatory, professional & public bodies	
Manufacturers	
Key Studies	
Patient Groups	
Media	
International/devolved administrations	
Significant Events	
Parliamentary Activity	

Timeline

Year	Source	Events
Mid 1950s	Ethicon Written Evidence	*'The use of various types of surgical mesh in the treatment of POP and SUI dates back to the middle of the last century as pelvic surgeons recognized the shortcomings with non-mesh native tissue repairs'*
1950s	FDA	Mersilene® (Dacron®) mesh was created during the 1950s and has been used in the United States since 1954.
February 1967	Alexander et al.	**Role of Suture Materials in the Development of Wound Infection**[1] An experimental study in domesticated rabbits, comparing several types of suture material commonly in use in their ability to resist contamination when introduced into small wounds which were contaminated with controlled numbers of staphylococci. There was no significant difference in the degree of infection which occurred with any of the nonabsorbable multifilament suture materials tested, whereas monofilament sutures withstood contamination better than multifilament sutures made of the same material. Authors conclude that the use of multifilament suture materials should be avoided in wounds having known gross bacterial contamination, with the development of infections being best prevented by the use of monofilament sutures.

[1] J. W. Alexander, J. Z. Kaplan, W. A. Altemeier, Role of suture materials in the development of wound infection. *Annals of surgery* **165**, 192-199 (1967).

		This study shows an appreciation for mesh structure (albeit sutures) with respect to infection.
January 1968	Moir, J. C.	**The Gauze-Hammock Operation. (A Modified Aldridge Sling Procedure)[2]** Description of a procedure using Ethicon's 'Mersilene' polyethylene gauze strip (cut by the surgeon) as an alternative to the 'Aldridge sling' (rectus fascial sling). The sling runs from the abdominal wall on one side, downwards to cover the bladder neck and urethra and upwards to the abdominal wall on the other side. *'The gauze appears to be non-irritating to the human tissues, and probably allows fibroblasts to make a quick penetration of the interstices of the mesh'* Seventy-one patients (having suffered from severe SUI) were followed for periods ranging from "a few months" to five years. The majority of patients had had at least one previous procedure to treat their SUI. *'Amongst Group 1, there were some remarkable successes. Two women, for example, were keen badminton players and another was a member of a bowling team; these ladies were delighted to find that they could now resume their favourite sport with impunity.'* *'If the support is too tight, the patient will experience difficulty in emptying the bladder (…) It is seldom that this difficulty persists for more than two or three weeks, but in some of the earlier cases in this series the patient complained of a "slow stream" for a much longer period. (…) With more experience, and with the realization that the hammock should not be tightened but should, in fact, be inserted with some play, there has seldom been any persisting complaint on this score.'* Thirteen of the seventy-one patients complained of increased frequency of micturition which – if not quickly relieved – led to the leakage of *'a little urine'* The author concludes that the gauze-hammock operation has the *'advantage of providing a broad support (hammock) for the bladder neck and urethra*

[2] J. C. Moir, THE GAUZE-HAMMOCK OPERATION. **75**, 1-9 (1968).

		in place of the narrow cord of fascia of the parent operation' *'This operation can be usefully employed when the patient suffers from severe stress incontinence with bladder neck descent, and previous operations have failed to bring about improvement'* *'In a series of 71 cases a cure or substantial improvement was obtained in 59, and a moderate improvement in 8 others'*
April 1969	FDA	PROLENE Polypropylene Suture (Nonabsorbable Surgical Suture, U.S.P., Type B), by Ethicon Inc., NDA 16-374 was approved followed by multiple supplements (converted from drug to PMA device in 1983 and then reclassified to class II device in 1990). Approval was granted for use in general surgery, following testing by Ethicon.
July 1972	Spencer et al.	**The gauze-hammock operation in the treatment of persistent stress incontinence[3]** Description of gauze-hammock operation, based on that described by Moir (1968) using polytheylene gauze strips (Mersilene, Ethicon). *'This gauze is relatively inert, lessening the risk of persistent infection and sinus formation, and allowing fibroblastic activity to reinforce the gauze scaffold with fibrous tissue'* *'The formation of a narrow band which could erode the urethra or bladder neck and cause fistulae is prevented by anchoring sutures which ensure the application of the gauze hammock over as wide an area as possible'* *25 patients, all of which had undergone at least one previous operation for SUI. 17 patients were completely continent at least 11 months after operation. Ten of these patients gave a clinical history of some urge incontinence, but this was confirmed by cinecystogram in 2 only. Stress incontinence was abolished in 3 other patients, but they complained post-operatively of a minor degree of frequency and*

[3] T. S. Spencer, A. M. Jequier, H. J. G. Kersey, THE GAUZE-HAMMOCK OPERATION IN THE TREATMENT OF PERSISTENT STRESS INCONTINENCE. **79**, 666-669 (1972).

		urgency. The other 5 patients showed no improvement and urge incontinence was exacerbated in 2.
January 1973	Nichols, D.H.	**The Mersilene Mesh Gauze-Hammock For Severe Urinary Stress Incontinence[4]** Description of 22 cases of Mersilene gauze-hammock procedure for SUI, performed since 1969. 'success' was reported in 21 cases. *'Of the 9 consecutive cases performed more than 2 years ago, all patients are completely relieved of their stress incontinence. Six of 8 patients operated upon between 1 and 2 years ago are currently cured and 1 partially cured. There was 1 total failure, a patient who had been subjected to transurethral resection of the bladder neck some 22 years previously, resulting in almost total incontinence'* No instances of urethra or bladder injuries were recorded, nor any evidence of mesh extrusion or sinus formation.
28th May 1976	US Congress	**Medical Device Amendments H.R.5545**[5] The FDA was given the authority to begin regulating all medical devices on May 28, 1976. This is when the President signed the Medical Device Amendments Act. Medical Devices were defined, risk-based classification introduced and regulatory process for each class of device defined. Note: Preamendments devices are those that were legally marketed in the US before May 28, 1976 **and** which have not been significantly changed since then; **and** for which a regulation requiring a PMA (premarket approval) application has not been published by FDA[6]. These devices are also known as "grandfathered" devices and do not require a 510(k)[7].

[4] D. H. NICHOLS, The Mersilene Mesh Gauze-Hammock For Severe Urinary Stress Incontinence. **41**, 88-93 (1973).

[5] US Congress, viewed 7 August 2019, summary available online at: https://www.congress.gov/bill/94th-congress/house-bill/5545?q=%7B%22search%22%3A%5B%22medical+device+amendments+1976%22%5D%7D&r=40&s=2

[6] Information on preamendment devices and the 510(k) process can be found at: https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k

[7] Note that a 510(K) is a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device.

November 1976	Liebert et al.	**Subcutaneous implants of polypropylene filaments**[8] **Experimental study performed in hamsters.** Extruded filaments of unmodified polypropylene with and without antioxidant were implanted subcutaneously in hamsters in order to determine their rate of degradation. Samples were analysed by infrared spectrometry and dynamic mechanical testing after 5 month test periods. *'The analyses show that degradation begins to occur after only a few days. Although the reaction sequence is not known, several factors suggest that the in vivo degradation process is similar to autoxidation which occurs in air or oxygen'* *'No change (…) was observed, however, for implants containing an antioxidant'* The authors conclude that *'polypropylene filaments implanted subcutaneously in hamsters degrade by an oxidation process which is retarded effectively by using an antioxidant. While the findings reported are specific to subcutaneous polypropylene implants, they suggest that degradation of other systems may involve similar processes.'* Long-term effects of polymer implantation upon tissue were not studied in this work.
October 1983	Kersey, J.	**The gauze hammock sling operation in the treatment of stress incontinence**[9] A series of 105 patients described, receiving Moir's gauze sling operation for SUI (with minor modifications). Follow-up ranged from 6 months to 9 years. Two patients lost to follow-up, of the 103 assessed, 62 were continent, 26 improved and there were 15 failures. There were 2 vesico-vaginal fistulas. The authors conclude that *'The results compare favourably with other suprapubic operations for stress incontinence'*

[8] T. C. Liebert, R. P. Chartoff, S. L. Cosgrove, R. S. McCuskey, Subcutaneous implants of polypropylene filaments. **10**, 939-951 (1976).
[9] J. Kersey, The gauze hammock sling operation in the treatment of stress incontinence. *British journal of obstetrics and gynaecology* **90**, 945-949 (1983).

July 1985	Stanton et al.	**Silastic sling for urethral sphincter incompetence in women**[10] Report on 30 Silastic (medical-grade silicone rubber reinforced with woven polyethylene terephthalate) sling procedures. Silastic sheets were chosen because of the consistent strength, lack of incorporation into surrounding tissues, local fibrous sheath response, and therefore ease of removal, if necessary. Authors report a subjective cure rate of 83% 3 months after surgery. 83% were objectively cured, although not the same 83% that were subjectively cured. Urge incontinence was seen in 18 patients before and after surgery. Frequency was reduced 3 months postoperatively (eg, from 14 preoperatively to 11 for combined nocturnal and diurnal frequency). Eight patients developed detrusor instability post-operatively. Seven patients complained of severe voiding difficulty and 4 patients required release or removal of the sling. *'The high frequency of postoperative detrusor instability is of concern'*
December 1986	Jongebloed & Worst	**Degradation of polypropylene in the human eye: a SEM-study**[11] A preliminary imaging study to characterise polypropylene degradation after implantation. A polypropylene suture was removed from the eye of a patient after 6.5 years due to breakage. After rinsing in 50% ethanol, to remove adhering debris, it was prepared for scanning electron microscopy. The suture showed cracks perpendicular to the longitudinal axis of the suture; part of the surface layer was nearly detached or completely missing; while the diameter of the suture was decreased towards both ends by over 50%. The exposed subsurface layer showed a fibrillar structure. The degradation phenomena are considered to be caused by the enzymatic action of tissue-fluids. Virgin material did not show any of the phenomena observed on the fixation suture under consideration.

[10] S. L. STANTON, G. S. BRINDLEY, D. M. HOLMES, Silastic sling for urethral sphincter incompetence in women. **92**, 747-750 (1985).
[11] W. L. Jongebloed, J. F. Worst, Degradation of polypropylene in the human eye: a SEM-study. *Doc Ophthalmol* **64**, 143-152 (1986).

February 1990	Petros & Ulmsten	**An integral theory of female urinary incontinence[12]** Petros and Ulmsten present an 'integral theory' for the cause of female urinary incontinence. In this theory paper, the interplay between anatomical structures involved in female urinary incontinence is analysed. The effects of age, hormones and iatrogenically-induced scar tissue are also discussed. This is done in the context of understanding the basis for treatment of urinary incontinence. *'According to the Theory stress and urge symptoms may both derive, for different reasons from the same anatomical defect, a lax vagina. This laxity may be caused by defects within the vaginal wall itself, or its supporting structures i.e. ligaments, muscles, and their connective tissue insertions'*
14th June 1993	EU Council	**EU Council Medical Devices Directive 93/42/EEC[13]** EU Directive 93/42/EEC was made, coming into force in July of that year and implemented on 1st July 1994. This Directive covers a wide range of devices ranging from first aid bandages, tongue depressors and blood collection bags, to hip prostheses and active (powered) devices. This included all implantable mesh devices. The directive sets out the Competent Authority, Notified Body, CE mark system for authorising medical devices for sale in the EU market. Also sets out the medical device classification system.
1993	Petros & Ulmsten	**An Integral Theory and Its Method for the Diagnosis and Management of Female Urinary Incontinence[14]** Description of the development of the 'intravaginal slingplasty' procedure for treating female urinary incontinence, based on the aforementioned 'integral theory'. This treatment is based on recreating the pubourethral ligament and strengthening the vagina. Teflon and Mersilene materials are described in this context.

[12] P. Petros, U. I. Ulmsten, An integral theory of female urinary incontinence. Experimental and clinical considerations. *Acta obstetricia et gynecologica Scandinavica. Supplement* **153**, 7-31 (1990).
[13] European Commission, Council Directive 93/42/EEC concerning medical devices, p. 1, 14th June 1993
[14] P. E. Petros, U. I. Ulmsten, An integral theory and its method for the diagnosis and management of female urinary incontinence. *Scand J Urol Nephrol Suppl* **153**, 1-93 (1993).

		'We do not consider that the actual surgical techniques are difficult to learn. The important thing will be understanding the theory and biomechanics so that proper diagnosis and surgical correction may be made' Development of the intravaginal slingplasty procedure is documented through a number of supplementary papers, listed below: **THE DEVELOPMENT OF THE INTRAVAGINAL SLINGPLASTY PROCEDURE: IVS II - (with bilateral "tucks").** **FURTHER DEVELOPMENT OF THE INTRAVAGINAL SLINGPLASTY PROCEDURE - IVS III - (with midline "tuck").** **THE FURTHER DEVELOPMENT OF THE INTRAVAGINAL SLINGPLASTY PROCEDURE: IVS IV - (with "double-breasted" unattached vaginal flap repair and "free" vaginal tapes).** **FURTHER DEVELOPMENT OF THE INTRAVAGINAL SLINGPLASTY PROCEDURE: IVS V - (with "double-breasted" unattached vaginal Flap repair and permanent sling).** **THE INTRAVAGINAL SLINGPLASTY PROCEDURE: IVS VI – further development of the "double-breasted" vaginal flap repair - attached flap.** ('tuck' refers to excision of portions of the vagina, designed to improve strength)
1985-1995	FDA (BSUG written evidence)	*'several surgical meshes, including Trelex Natural Mesh (Boston Scientific, Marlborough, MA), Supple Peri-Guard (Synovis, St Paul, MN) GORE-TEX Soft Tissue Patch (GORE, Flagstaff, AZ), Mersiline mesh (Ethicon, Somerville, NJ) and Marlex mesh (C.R. Bard, Inc., Marray Hill, NJ), were cleared by the FDA for uses including hernia repair; however, none were cleared for use as vaginal meshes'*

February 1995	Chin & Stanton	**A follow up of silastic sling for genuine stress incontinence[15]** Eighty-eight women with urodynamically proven genuine stress incontinence inserted with a sialastic sling, under minimal tension. Clinical and urodynamic data were assessed between two and three months post-surgery; thereafter clinical assessment and pad testing were performed at yearly intervals for five years. The subjective cure at three months was 81% and the objective cure was 69 %. There was a fall in success rate with increasing number of continence operations, and this was statistically significant for women with three or more previous continence operations ($P < 0.05$). Neither age, parity nor menopausal status made a statistical difference to the cure rate. Post-operatively, 29 women had detrusor instability: 22 women developed detrusor instability *de novo* and seven had detrusor instability presurgery. Urodynamic findings post-surgery showed an increase ($P < 0.001$) in outflow resistance. Four women required removal of sling for voiding difficulties. Ten women developed sling erosions: five vaginal, four bladder erosions and one urethral erosion. After removal of the sling, seven women still remained continent. The authors conclude that the procedure *'provides a good long term cure, considering that 45% of women had two or more previous failed continence operations. The high prevalence of detrusor instability and voiding difficulties post-surgery should be noted.'*
March 1995	Ulmsten & Petros	**Intravaginal slingplasty (IVS): An ambulatory surgical procedure for treatment of female urinary incontinence[16]** Description of Mersilene®, Gortex®, Teflon® and Lyodura® sling materials being used to support the urethra as treatment for SUI. Thirty-nine (78%) patients were completely cured. Six (12%) reported a considerable improvement of their SUI. Concerning urge incontinence symptoms, a

[15] Y. K. Chin, S. L. Stanton, A follow up of silastic sling for genuine stress incontinence. **102**, 143-147 (1995).
[16] U. Ulmsten, P. Petros, Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of female urinary incontinence. *Scandinavian journal of urology and nephrology* **29**, 75-82 (1995).

		significant relief of the symptoms was obtained in 6 of 12 patients. No intra- or postoperative complications were reported. The study was funded by grants from the Swedish Medical Research Council.
1996	Ulmsten et al.	**An Ambulatory Surgical Procedure Under Local Anesthesia for Treatment of Female Urinary Incontinence[17]** Postoperative study of results of a 'modified intravaginal slingplasty' (later to be known as the TVT) for the treatment of SUI. First published paper to describe this procedure. No intra- or postoperative complications and 63 patients (84 %) were completely cured throughout the 2-year follow-up period. Six patients (8%) were significantly improved, i.e. they did not lose urine apart from an occasional leakage during severe cold etc. In the remaining 6 patients (8%) no improvement was seen. The study was funded by grants from the Swedish Medical Research Council.
January 1996	Weinberger et al.	**Postoperative catheterization, urinary retention, and permanent voiding dysfunction after polytetrafluoroethylene suburethral sling placement[18]** Study to determine the incidence of permanent voiding dysfunction after polytetrafluoroethylene suburethral sling (Gore-tex Soft Tissue Patch) placement. Authors conclude that polytetrafluoroethylene suburethral sling placement commonly produces permanent voiding difficulty. Sling removal does not ensure resolution of urinary retention. The source of funding is not stated.
May 1996	Event	The Safety and Efficacy Register of New Interventional Procedures (SERNIP) set up as a three-year pilot. Run by the Academy of Medical

[17] U. Ulmsten, L. Henriksson, P. Johnson, G. Varhos, An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. *International urogynecology journal and pelvic floor dysfunction* **7**, 81-85; discussion 85-86 (1996).
[18] M. W. Weinberger, D. R. Ostergard, Postoperative catheterization, urinary retention, and permanent voiding dysfunction after polytetrafluoroethylene suburethral sling placement. *Obstetrics & Gynecology* **87**, 50-54 (1996).

		Royal Colleges, and funded by the Department of Health. DH chose to set this up as a voluntary, rather than mandatory, register against the advice of the government advisory council on science and technology.
15th November 1996	FDA	ProteGen Sling (Boston Scientific) – The first pre-shaped polyester surgical mesh product specifically designed for SUI and POP surgery, was cleared by the FDA on the basis of 510(k) equivalence to mesh devices previously approved for hernia repair (Gore-tex, Marlex and Mersilene)[19]. From this point on, many other mesh products and kits were developed by various manufacturers, many of which received 510(k) clearance based on equivalence to this device. ProteGen sling was later recalled by Boston Scientific in March 1999.
December 1996	Julian, T.M.	**The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall[20]** A study to assess the efficacy and complications of Marlex mesh in repairing severe recurrent anterior vaginal wall prolapse. Twenty-four patients with two or more postsurgical recurrences of severe anterior vaginal wall prolapse were divided equally into control and treatment groups. Transvaginal repair was similar between groups except for reinforcement of the anterior vaginal wall with synthetic mesh in the treatment group. Four patients in the control group and none in the treatment group had recurrent anterior vaginal wall prolapse ($p < 0.05$). Three patients had mesh-related complications. Author concludes that *'Repair with a synthetic mesh decreased the expected incidence of severe recurrent anterior vaginal prolapse but was associated with common complications related to synthetic mesh. Mesh reinforcement is an effective treatment for*

[19] FDA, viewed 7 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K963226

[20] T. M. Julian, The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall. *American Journal of Obstetrics & Gynecology* **175**, 1472-1475 (1996).

		severe recurrent prolapse of the anterior midvaginal wall'
Early 1998	BMJ	According to an article published in the BMJ in 2018[21], Paul Hilton (lead investigator of the 'Hilton study') said that he'd asked Ethicon to fund *'a register of TVT procedures, so that outcomes, and especially adverse outcomes, could be identified and quantified'* but *'they declined to support such a development.'* A spokesperson from Ethicon was quoted in the article as saying the company was *'not familiar'* with this request.
1998	Ulmsten et al.	**A Multicenter Study of Tension-Free Vaginal Tape (TVT) for Surgical Treatment of Stress Urinary Incontinence [22]** A prospective open multicenter study including 6 centers, each operating on approximately 20 patients. In total 131 SUI patients were included. They were followed for at least 1 year. Designed to follow the 1996 paper in which experienced urogynaecologists who had also been involved in the development of the procedure, performed the procedure. The aim was to demonstrate that the procedure had a similar safety/efficacy profile when performed by 'ordinary' surgeons. 119 (91%) of the patients were cured according to the protocol and another 9 (7%) were significantly improved. There were 3 (2%) failures. The majority of the patients (about 90%) were operated upon on a day-care basis.
8th January 1998	SERNIP	Fifth meeting of SERNIP, in which Cystourethropexy (using 'In-tac' bone anchors to secure the bladder neck sling) procedure is classified as category Cii[23]
28th January 1998	FDA	Gynecare TVT Ethicon cleared for use by FDA (K974098)[24]. Clearance was based on equivalence to ProteGen (recalled in 1999[25]).

[21] Jonathan Gornall, 2018, How mesh became a four letter, BMJ, Viewed 7 August 2019, available online at: wordhttps://www.bmj.com/content/363/bmj.k4137.full

[22] U. Ulmsten *et al.*, A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. *International urogynecology journal and pelvic floor dysfunction* **9**, 210-213 (1998).

[23] SERNIP, advisory committee minutes, provided by NICE in response to FOI request EH95323, viewed 27 August 2019, available online at: https://www.whatdotheyknow.com/request/clinical_guidance_for_polypropyl#incoming-1236732

[24] FDA, viewed 7 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K974098

		The majority of Ethicon's subsequent TVT's were approved (until 2010) based on equivalence to 'Gynecare TVT'.
1st May 1998	Wang & Lo	**Tension-free vaginal tape. A minimally invasive solution to stress urinary incontinence in women**[26] Study designed to determine safety and efficacy of the tension-free vaginal tape procedure in 70 enrolled women with SUI. Evaluation was done by a preoperative one-hour pad test, full urodynamic testing and a one-week baseline urinary diary one week before and two months after operation. Follow-up ranged from 3 to 18 months. Mean operation time was 29 minutes (20-51) and mean hospital stay 3 days (2-8). Three bladder perforations occurred intraoperatively. No patients had intraoperative bleeding > 300 mL, but 11 (16%) had blood loss > 200 mL, necessitating an indwelling catheter and vaginal tamponade. No evidence of defect healing or rejection of the tape occurred. Urine leakage observed on the pad test was significantly reduced from a mean of 63 g (10-213) before to a mean of 5 g (0-42) after surgery. The objective cure rate was 83%, and the subjective rate was 87%. The authors conclude that *'Although the follow-up period was short, the TVT procedure seemed to be a safe and effective method for the treatment of stress urinary incontinence'*
September 1998	Nicita, G.	**A New Operation for Genitourinary Prolapse**[27] Description of the use of Marlex mesh cut into a hammock shape, used to support pelvic organ prolapse. *'The approach is transvaginal and the novelties are the way in which the mesh is anchored and its considerable size'* All patients affected by some degree of incontinence were cured, according to authors. Patients with prolapse without incontinence were completely satisfied with the operation. Uterine prolapse was third degree in 6 of 20 patients and it partially recurred in 3. Cystography in all patients

[26] A. C. Wang, T. S. Lo, Tension-free vaginal tape. A minimally invasive solution to stress urinary incontinence in women. *The Journal of reproductive medicine* **43**, 429-434 (1998)
[27] G. Nicita, A new operation for genitourinary prolapse. *The Journal of urology* **160**, 741-745 (1998).

		demonstrated excellent repair of the descensus. Sexual life and menses did not change, and no pelvic fibrosis or hydroureteronephrosis occurred. Follow-up ranged from 9 to 23 months (median 13.9). Authors conclude that *'This technique has broad application and is simple to perform. Longer follow-up will prove its merits definitively'*
1998	Nilsson, C.G.	**The Tension free Vaginal Tape Procedure (TVT) for Treatment of Female Urinary Incontinence. A Minimal Invasive Surgical Procedure**[28] Study designed to test the suitability of a new surgical procedure for treatment of female urinary incontinence to be used as an ambulatory and minimal invasive operation. Of the 31 patients with proven SUI who had a tension-free tape procedure performed, all were cured from stress incontinence, according to the authors. Local anesthesia was used in all cases and additional analgetics were needed in only small doses. Seventy per cent of the patients were released from the hospital on the same day of the operation. By medical criteria 90% could have been released on the same day. No significant per- or postoperative complications occurred. Three patients needed postoperative catheterisation. All but one patient was able to empty her bladder within 24 hours from the operation. An average of 15 days sick leave was prescribed. The authors conclude that *'The tensionfree vaginal tape procedure seems to fulfil the criteria for being regarded as a minimal invasive surgical procedure for treatment of female urinary stress incontinence. It is highly effective and is associated with very few intra and postoperative side effects.'*
1998	BSUG Written evidence	TVT first marketed in the UK. *'Many surgeons did not feel that the procedure was proven to be safe and effective at the initial time that it was introduced. The TVT/Colposuspension (Ward & Hilton) trial was developed and run to address concerns from urogynaecologists in the UK. Many individuals were unhappy with the scientific evidence*

[28] C. G. Nilsson, The tensionfree vaginal tape procedure (TVT) for treatment of female urinary incontinence. A minimal invasive surgical procedure. *Acta obstetricia et gynecologica Scandinavica. Supplement* **168**, 34-37 (1998).

		regarding safety and efficacy and did not immediately introduce the technique.'[29]
December 1998	Klinge et al.	**Shrinking of polypropylene mesh *in vivo*: an experimental study in dogs**[30] A study designed to assess the extent of mesh used for hernia repair (either monofilament polypropylene (Marlex) or multifilament polypropylene/polyglactin (Soft Hernia Mesh) after implantation for 3 or 6 months in dogs. Histological examination and radiological assessment of position/area of the mesh demonstrated that after 4 weeks the area of mesh in the monofilament group was reduced from to 139 to 75 cm^2 (54%) and that of the multifilament from 116 to 77 cm^2 (66%). The multifilament mesh with the reduced amount of polypropylene showed less inflammatory response and less shrinkage. The mesh did not seem to have moved. The authors concluded that meshes that contain a lot of polypropylene shrink to about 30%-50% of their original size after 4 weeks. Reduction in the polypropylene content decreases both the inflammatory response and the shrinkage. Meshes with big pores are less likely to fold and improve compatibility.
17th March 1999	Boston Scientific	Boston Scientific recalled ProteGen due to concern regarding adverse outcomes – *'associated with a higher rate than expected of vaginal erosion and dehiscence and does not appear to function as intended'*(many of the mesh devices that had received 510(k) clearance based on equivalence to ProteGen were not recalled).
1st April 1999	NICE	NICE was set up as the National Institute for Clinical Excellence, a special health authority, to reduce variation in the availability and quality of NHS treatments and care[31].

[29] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 206, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[30] U. Klinge, B. Klosterhalfen, M. Muller, A. P. Ottinger, V. Schumpelick, Shrinking of polypropylene mesh *in vivo*: an experimental study in dogs. *Eur J Surg* **164**, 965-969 (1998).

[31] UK legislation Establishment and Constitution Order, viewed 7 August 2019, available online at: www.legislation.gov.uk/uksi/1999/220/contents/made

April 1999	Ulmsten et al.	**A three-year follow up of tension free vaginal tape for surgical treatment of female stress urinary incontinence.**[32] A prospective open study of the long-term results of TVT. Post-operative evaluation was carried out after 2 to 6, 12, 24 and 36 months. According to the protocol, 86% of the women were completely cured and another 11% were significantly improved. No signs of deterioration of the results over time were observed. No defect in healing or rejection of the tape occurred. Concludes that the TVT procedure is safe and effective for the treatment of female SUI. The technique can be considered as an ambulatory procedure performed under local anaesthesia, allowing the majority of the women to be discharged from the clinic the same day or the day after the procedure.
6th October 1999	SERNIP	Twelfth meeting of SERNIP, in which Intravaginal slingplasty (TVT) procedure was categorised as "C" (Safety and efficacy not proven), with a rider to await the results of randomised control trials that were ongoing at the time[33].
25th October 1999	Cochrane	**Surgery for complete rectal prolapse in adults**[34] Ten trials were included, with a total of 324 participants. Two trials (61 participants) compared laparoscopic with open mesh rectopexy. Data were insufficiently reported to allow any statistical analyses to be performed.
December 1999	Kobashi et al.	**Erosion of woven polyester pubovaginal sling**[35] Study retrospectively examining records of patients who had ProteGen slings removed at 5 centres during the previous 24 months. Presenting symptoms, interval between sling placement and removal, subsequent procedures and continence status following sling removal were evaluated.

[32] U. Ulmsten, P. Johnson, M. Rezapour, A three-year follow up of tension free vaginal tape for surgical treatment of female stress urinary incontinence. *British journal of obstetrics and gynaecology* **106**, 345-350 (1999).
[33] SERNIP, advisory committee minutes, provided by NICE in response to FOI request EH95323, viewed 27 August 2019, available online at: https://www.whatdotheyknow.com/request/clinical_guidance_for_polypropyl#incoming-1236732
[34] M. Brazzelli, P. Bachoo, A. Grant, Surgery for complete rectal prolapse in adults. *Cochrane Database of Systematic Reviews*, (1999).
[35] K. C. Kobashi *et al.*, Erosion of woven polyester pubovaginal sling. *J Urol* **162**, 2070-2072 (1999).

		A total of 34 women required removal of the polyester sling secondary to erosion, infection or pain. The most common presenting complaints were delayed vaginal discharge (62%), vaginal pain or pressure (62%), suprapubic pain (32%) and recurrent urinary tract infection (15%) at a mean of 7.95 months (range 1 to 22) after sling placement. Of the patients, 50% had vaginal erosion only, 20% isolated urethral erosion and 17% urethrovaginal fistulas. In 4 patients no erosion was obvious, but slings were removed secondary to vaginal pain. Before sling removal, 47% were totally dry, 38% had some degree of urinary incontinence and 8% had retention. Following sling removal, 20% remained dry and 74% had mild to severe SUI with or without urgency and urge incontinence. The authors conclude that woven polyester slings treated with pressure injected bovine collagen are prone to erosion. Although the ProteGen sling was recalled in January 1999, patients who have had the sling placed must be followed closely.
1999		Medicines Control Agency (MCA) took over control of the General Practice Research Database (GPRD) from Office for National Statistics. GPRD is a computerised database of anonymised data from the patient record.
1999	Olsson & Kroon	**A Three-Year Postoperative Evaluation of Tension-Free Vaginal Tape[36]** Study evaluating the outcome of tension-free vaginal tape procedure 3 years after surgery. 51 women with SUI underwent the procedure. All patients were evaluated 3 years postoperatively using a protocol for objective and subjective assessment of the outcome including an evaluation of quality of life related to urinary incontinence. According to the protocol, 46 women (90%) were successfully cured, another 3 patients (6%) were improved, whereas 2 patients (4%) were classified as failures. The authors conclude that *'TVT is a simple and well-accepted minimal invasive surgery for treatment of*

[36] I. Olsson, U. B. Kroon, A Three-Year Postoperative Evaluation of Tension-Free Vaginal Tape. *Gynecologic and obstetric investigation* **48**, 267-269 (1999).

		female urinary stress incontinence. The outcome 3 years after the operation showed no signs of deterioration compared to the results shortly after surgery. The cure rate of 90% is comparable with the best results of other surgical treatments for female urinary incontinence'
By late 90's	Multiple Ethicon	**Consensus on Type 1 Mesh** Consensus over macroporous polypropylene being safe for use in the human body, being supported by more clinical data than alternative mesh materials. Ethicon written evidence: *"In the 1970s, Ethicon's Prolene mesh was first used for hernia repair. This same mesh was selected in the 1990s for the Ethicon TVT device which uses a 1.1 centimeter wide strip of Prolene mesh and has been used in every synthetic midurethral SUI sling manufactured by Ethicon since.* *No material in pelvic surgical history has demonstrated higher biocompatibility than polypropylene and no polypropylene material has been used in more patients or been subject to more peer reviewed studies than Prolene"* *"Professional gynecologic and urological societies worldwide have endorsed the biocompatibility of polypropylene and have found full length mid-urethral slings such as the Ethicon TVT and TVT-O devices to be the gold standard treatment option for SUI while the use of macroporous polypropylene has been recognized as the gold standard for apical prolapse."*[37]
12th January 2000	SERNIP	Thirteenth meeting of SERNIP, in which the chairman reported that Ethicon had challenged the classification of tension free urethropexy, with their main concern being affected sales in Europe. In response to the challenge, a Review Group was set up to consider the procedure and consider further reports submitted by the company. The group comprised two members of the SERNIP Advisory

[37] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 33, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

		Committee and an independent expert from the British Association of Urological Surgeons.[38] The group's overall view was that, on the grounds of extensive usage, the categorisation of the procedure should be upgraded. Valid safety and efficacy data provided by Ethicon bought the total cases known to SERNIP to 553 and although this was all observational data, the committee thought that efficacy had been sufficiently demonstrated. Reclassification was from 'C' to 'A'.[19] Ethicon provided 4 additional papers. 2 were duplicate publications and 2 were excluded for other reasons. There were also 30 conference abstracts, most of which consisted of incomplete/uninterpretable results. Those with only subjective outcome or follow-up of less than six months were excluded, leaving 6 conference abstracts. This included 268 patients with a 86% objective cure at 6 months or more. Bladder perforation occurred in 7% and *de novo* detrusor instability in 3%.[19]
August 2000	Migliari et al.	**Tension–Free Vaginal Mesh Repair for Anterior Vaginal Wall Prolapse[39]** Study to investigate the efficacy of tension-free prolene mesh in correcting grade III anterior vaginal wall prolapse recurrence. Follow-up lasted for mean 20.5 months (15-32). Nine of 12 patients were considered cured (no cystocele recurrence) while in 3 patients a grade 1 asymptomatic cystocele was present postoperatively (asymptomatic). No significant postoperative pain was reported by the patients. The author concludes that *'in patients with moderate cystocele a tension-free mesh to support bladder base and neck effectively treats the cystocele. It is particularly recommended in the treatment of previous failure with traditional techniques and when the quality of suspending tissue is poor or defective. A long-term study on a large number of patients is still warranted to confirm and validate its clinical use'*

[38] SERNIP, advisory committee minutes, provided by NICE in response to FOI request EH95323, viewed 27 August 2019, available online at: https://www.whatdotheyknow.com/request/clinical_guidance_for_polypropyl#incoming-1236732

[39] R. Migliari, M. De Angelis, G. Madeddu, T. Verdacchi, Tension–Free Vaginal Mesh Repair for Anterior Vaginal Wall Prolapse. *European urology* **38**, 151-155 (2000).

October 2000		Review of SERNIP by Department of Health concluded that responsibility for SERNIP should transfer to the National Institute of Clinical Excellence.
2001	Ethicon Written Evidence	*'Initially the TVT mesh was made using clear Prolene Mesh. In 2001, Ethicon created TVT Blue Prolene mesh, which is identical in construction to the clear Prolene mesh with the exception of the change in pigmentation with the addition of blue striping. This change enhanced the intraoperative visibility of the mesh.'* *'In 2001, the "outside-in" transobturator approach to placing a polypropylene sling to treat SUI was described (outside-in refers to initiating the tape placement through a skin incision and directing it through a periurethral incision, whereas the inside-out transobturator technique which is unique to Ethicon's TVT-O and TVT Abbrevo devices, refers to initiating the placement through the vaginal incision and then outward laterally).'*[40] *'The Ethicon TVT-O device was invented by Professor Jean De Leval, in Belgium. He used the same mesh utilized in TVT but surgically implanted it with an "inside-out" midurethral approach through the obturator space as opposed to a retropubic approach like TVT or an outside-in transobturator placement as had been previously described.'*[20] *'Prior to TVT-O's launch, Professor De Leval had studied the TVT-O procedure in 138 patients who were enrolled in a study that compared their results to 134 patients implanted with TVT. The results of this study showed similar efficacy to TVT and lower rates of bladder perforations. While it did reveal a 26% rate of thigh pain, this proved to be a transient problem resolving within 24-48 hours of surgery.'*[20]
2001	BSUG	BSUG was formed at the request of RCOG, to set and raise the profile of urogynaecology.
4th April 2001	FDA	IVS tunneller system[41] (United States Surgical) receives 510(k) clearance based on equivalence to Ethicon TVT.

[40] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 35, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[41] FDA, viewed 8 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K010035

June 2001	Falconer et al.	**Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women**[42] A study designed to investigate the influence on the paraurethral connective tissue of different sling materials (6 patients had undergone transvaginal tape procedure using Mersilene mesh, and 10 using Prolene mesh) used in incontinence surgery. Biopsies of paraurtheral connective tissue were taken intraoperatively, and at 2 years post-operatively. The authors comment that *'An obvious inflammatory reaction with a significant increase in collagen extractability by pepsin was identified in patients where Mersilene was used as the sling material. A minimal inflammatory reaction without a significant change in collagen solubility was found in the Prolene group. In the control group no inflammatory reaction was seen. Mersilene gave rise to a significant foreign-body reaction in the paraurethral connective tissue after surgery. Such a reaction was not found with Prolene'*
June 2001	Nilsson et al.	**Long-term Results of the Tension-Free Vaginal Tape (TVT) Procedure for Surgical Treatment of Female Stress Urinary Incontinence**[43] A prospective, long-term, multicentre study of 90 patients who had received tension-free vaginal tape for SUI. Patients were evaluate after approximately 5 years post-operatively (48-70 months). *'Postoperatively, the patients were regarded as cured if they had a negative stress test result, a negative 24-hour pad-weighing test result (<10 g/24 h), and if the QoL had improved 590%. To be regarded as improved the patient had to have a 575% improved QoL and a significant reduction in urine loss as measured by the 24hour pad-weighing test (>50% reduction or <15 g/24 h loss). All other patients were classified as failures even if a clear improvement from the preoperative situation had occurred'*

[42] C. Falconer, M. Soderberg, B. Blomgren, U. Ulmsten, Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. *International urogynecology journal and pelvic floor dysfunction* **12 Suppl 2**, S19-23 (2001).
[43] C. G. Nilsson, N. Kuuva, C. Falconer, M. Rezapour, U. Ulmsten, Long-term results of the tension-free vaginal tape (TVT) procedure for surgical treatment of female stress urinary incontinence. *International urogynecology journal and pelvic floor dysfunction* **12 Suppl 2**, S5-8 (2001).

		Of the 85 patients available for evaluation, 72 (84.7%) were both objectively and subjectively completely cured. Another 9 (10.6%) were significantly improved and 4 (4.7%) were regarded as failures. No patient complained of long-term voiding difficulties and there were no signs of defective healing or rejection of the tape material. All patients had suffered from primary stress incontinence, and 25 also had preoperative complaints of urge. In 14 of these (56%) the urge symptoms were relieved postoperatively. The authors conclude that *'the TVT procedure seems to fulfil the expectations of high long-term cure rates, as suggested in previous short-term reports'*
23rd June 2001	Cochrane	**Suburethral sling operations for urinary incontinence in women**[44] Twelve trials were identified including 890 women, of whom 543 were treated with suburethral slings. In respect of short-term cure, overall rates are similar (RR 0.93; 95% CI 0.68 to 1.27) in the comparison with open abdominal retropubic suspension. This mainly reflects the results of one larger trial on TVT. However, for long-term results, data are too few to give a reliable estimate. About one in 11 had a complication during TVT, most commonly bladder perforation, but none had serious consequences. Reliable evidence that suburethral slings may be better or worse than other surgical or conservative management is lacking because no trials addressed these comparisons.
1st August 2001	FDA	AMS Sparc Sling[45] receives 510(k) clearance based on equivalence to Ethicon TVT.
30th Sept 2001		Academy of Medical Royal Colleges relinquish responsibility for SERNIP, interim function managed by Department of Health, pending a final decision on future location.
2001	Ward & Hilton, based on HES data	*'by 2001 (the tension-free vaginal tape procedure) had become the most frequently performed operation for stress incontinence in the UK'*[46]

[44] C. C. B. Bezerra, H. Bruschini, D. J. Cody, J. D. Cody, Suburethral sling operations for urinary incontinence in women. *Cochrane Database of Systematic Reviews*, (2001).
[45] FDA, viewed 8 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K011251
[46] Ward KL, Hilton P. Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up. BJOG 2008;115:226-3310.1111/j.1471-0528.2007.01548.x. 10.1111/j.1471-0528.2007.01548.x 17970791

2001	Young et al.	**Mersilene mesh sling: Short- and long-term clinical and urodynamic outcomes**[47] Authors conclude that the suburethral Mersilene mesh sling has a very high long-term objective and subjective cure rate in the treatment of complicated forms of genuine stress incontinence. Frequent complications do occur but are remediable. Thirty-eight patients (19%) had a total of 43 complications directly related to the sling procedure. Ten patients (5%) had significant long-term problems: 3 (1.5%) had urinary retention beyond 1 year, one (0.5%) had failure/erosion (0.5%) that required complete sling removal, two (1%) had refractory detrusor instability, and four (2%) had recurrent urinary tract infections.
5th January 2002	Merlin et al.	**A systematic review of tension-free urethropexy for stress urinary incontinence: intravaginal slingplasty and the tension-free vaginal tape procedures**[48] A systematic review designed by the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) with the objective of assessing the safety and efficacy of tension-free urethropexy (TFU) in the treatment of SUI, compared with the pubovaginal sling and colposuspension. 17 TFU studies and 22 colposuspension studies met the inclusion criteria for the review. All studies were case series and so only provided level IV evidence of safety/efficacy, with the lack of control groups being a severely limiting factor. The authors comment that the reports reviewed on the safety and efficacy of TFU were of poor-quality, so conclusions are tentative. Based on these reports, the TVT seemed to have less infection and erosion than the intravaginal slingplasty (IVS), with lighter sedation/general anaesthetic required also. The authors comment on weak evidence that the two-stage IVS may have an effect on urge incontinence and faecal incontinence, when being used to treat SUI.

[47] S. B. Young, A. E. Howard, S. P. Baker, Mersilene mesh sling: Short- and long-term clinical and urodynamic outcomes. *American journal of obstetrics and gynecology* **185**, 32-40 (2001).
[48] T. Merlin *et al.*, A systematic review of tension-free urethropexy for stress urinary incontinence: intravaginal slingplasty and the tension-free vaginal tape procedures. *BJU international* **88**, 871-880 (2001).

		There was no published, good-quality peer-reviewed evidence to compare the safety/efficacy of TFU compared with colposuspension or pubovaginal sling. A single RCT was identified but was incomplete and had only reached 6-month follow-up. Broad comparisons between TFU and the 'gold standard' procedures showed few differences between the procedures in terms of safety. Complication rates were harder to compare due to unreliable reporting. Bladder perforation reported for TFU was thought to be due to surgeon inexperience In terms of efficacy, TFU was associated with shorter operating times, lower levels of postoperative catheterisations and shorter delays until resumption of spontaneous voiding, when compared with the 'gold standard' procedures Based on the review findings, the ASERNIP-S Review Group recommended that an RCT be conducted to compare two-stage IVS and TVT, as well as compare TVT to colposuspension. It was also recommended that: - Surgeons performing TFU should join with existing RCTs so that experience can be collated. They should also conduct an audit of the safety and efficacy outcomes associated with their practice - Longitudinal audit/prospective cohort studies be performed, examining long-term effectiveness and deteriorations in cure rate, complication rates (especially erosion) and the effect of ageing and development of prolapse on the 'tension-free' status.
8th January 2002	FDA	Gynemesh® PS, manufactured by Ethicon/Gynecare, became the first pre-configured surgical mesh product cleared for POP repair[49]. Surgical mesh products then evolved into "kits" that included tools to aid in the delivery or insertion of the mesh.
1st April 2002		**Handover from SERNIP to NICE[50]** NICE developed their own process for assessing interventional procedures. Overview documents were prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) which were based on a rapid survey of published literature,

[49] FDA, viewed 8 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K013718

[50] Based on NICE document: Proposed arrangements for the management of the safety and efficacy register of new interventional procedures.

		review of the procedure by one or more specialist advisor(s) and review of the content of the relevant SERNIP file[51]. The first NICE interventional procedures guidance was published in July 2003.
April 2002	Liapis et al.	**Burch Colposuspension and Tension-Free Vaginal Tape in the Management of Stress Urinary Incontinence in Women[52]** A study comparing efficacy and complications of tension-free vaginal tape (TVT) with Burch colposuspension in treating SUI. 35 patients underwent Burch colposuspension and 36 underwent the TVT procedure. The outcome of both operations was assessed objectively. Objective assessment included 1 h pad test, while objective cure was considered a pad weight difference <1 g, and improvement a reduction of urine loss to less than 50% of urine loss they experienced before the operation and it was based on the findings of 1 h pad test. The operative time for TVT was significantly shorter compared to colposuspension (20 min vs 58 min). The severity and duration of postoperative pain for TVT was significantly less (in terms of type/duration of analgesic, as well as self-assessed pain scale) compared to colposuspension. The necessary time for return to normal activity was 10 days for TVT and 21 days for colposuspension. The cure rate after 24 months of follow-up was as follows: TVT: 84% and colposuspension: 86%, while the improvement was 7% for TVT and 6% for colposuspension. The authors conclude that *'TVT and Burch colposuspension are equally effective in the management of female GSI at two years follow-up. TVT procedure requires much less operative time, has much shorter hospitalization time, with significantly less postoperative pain and faster return to normal daily activities than Burch colposuspension'*

[51] Additional information on NICE's consideration of inherited SERNIP procedures are available in the National Archive. Decision making options for inherited SERNIP procedures document. October 2002.
[52] A. Liapis, P. Bakas, G. Creatsas, Burch colposuspension and tension-free vaginal tape in the management of stress urinary incontinence in women. *European urology* **41**, 469-473 (2002).

July 2002	Ward & Hilton	**Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence[53]** Compares long-term outcomes of TVT and Burch colposuspension as primary treatment for SUI. Prospective multicentre randomised trial, 344 women randomly assigned to groups (TVT vs. colposuspension) No significant difference was found between the groups for cure rates:115 (66%) women in the vaginal tape group and 97 (57%) in the colposuspension group were objectively cured (95% confidence interval for difference in cure −4.7% to 21.3%). Bladder injury was more common during the vaginal tape procedure; postoperative complications, in particular delayed resumption of micturition, were more common after colposuspension. Operation time, duration of hospital stay, and return to normal activity were all longer after colposuspension than after the vaginal tape procedure. Only 63 (36%) patients in the vaginal tape arm and 48 (28%) in the colposuspension arm reported no leakage under any circumstance after surgery. The number of women reporting cure of stress leakage was 103 (59%) and 90 (53%), respectively Based on responses for the SF-36 patient questionnaire, significant differences were seen at six weeks in emotional, social, and physical function and vitality, with the colposuspension group having lower scores than the vaginal tape group. By six months, scores in the colposuspension group had shown significantly less improvement in emotional and social functioning, vitality, and mental health than those in the tape group. Operative complications were more common after the vaginal tape procedure (table 2), largely injury to the bladder and vagina. Operation times, blood loss, analgesic requirements, postoperative complications, and catheterisation were greater in the colposuspension group than the vaginal tape group.

[53] K. Ward, P. Hilton, Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. *BMJ : British Medical Journal* **325**, 67-67 (2002).

		The authors conclude that surgery with TVT is associated with more operative complications than colposuspension, but colposuspension is associated with more postoperative complications and longer recovery. Vaginal tape shows promise for the treatment of urodynamic stress incontinence because of minimal access and rapid recovery times; objective cure rates with TVT at 6-months (66%) were comparable with colposuspension (57%). Funded by Ethicon.
	Ethicon Written Evidence	With respect to the Ward & Hilton study, Ethicon state that they *"provided the products and additional support to the collaborating centers. This study was a landmark RCT that provided level 1 evidence to the medical community that TVT was set to be the new gold standard based on its benefits of providing patients with a rapid return to normal activities and shorter hospital stays compared to the Burch."*[54]
4th September 2002	Groutz et al.	**Tension-Free Vaginal Tape for Stress Urinary Incontinence: Is There a Learning Curve?**[55] Study in a single hospital of 30 incontinent women treated with TVT by a single surgeon. Five (17%) bladder perforations occurred at the beginning, due to inadvertent insertion of the applicator. Five patients had increased intraoperative bleeding, eight had immediate postoperative voiding difficulties, requiring catheterisation for 2-10 days (no long-term catheterisation). All patients subjectively cured. 80% of patients with preoperative urge syndrome, had persistent postoperative symptoms. Authors conclude that the TVT operation is a minimally invasive surgical procedure with excellent short- and medium-term cure rates. However, there is a definite learning curve, and it was believed that the operation should only be performed by experienced surgeons.
12th October 2002	Maddern et al.	**Urinary stress incontinence - Benefits of using tension-free vaginal tape remain unproved**[56]

[54] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 36, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[55] A. Groutz *et al.*, Tension-free vaginal tape for stress urinary incontinence: Is there a learning curve? *Neurourology and Urodynamics* **21**, 470-472 (2002).

[56] G. J. Maddern, P. F. Middleton, A. M. Grant, Urinary stress incontinence - Benefits of using tension-free vaginal tape remain unproved. *BMJ (Clinical research ed.)* **325**, 789 (2002).

		Editorial in the BMJ commenting on the lack of evidence on TVT, with most evidence coming from case series. The Ward et al. study published in July of that year was discussed, as the first RCT to compare TVT with colposuspension. The authors comment that claims from the above study that TVT is as effective as colposuspension may be premature, due to the researchers being unable to recruit the required number of participants and large numbers of women withdrawing, especially from the colposuspension arm. The report mentions that the women who withdrew from the colposuspension group before surgery had less severe incontinence, which may introduce bias to the study. The authors suggest that long-term cure rates are yet to be determined for TVT, recommending that more studies with greater power and longer-term follow-up should be carried out.
January 2003	NICE	**Final Appraisal Determination Tension-free vaginal tape (Gynecare TVT) for stress incontinence** [57] NICE recommend 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.'* Patients should be *'fully informed of the advantages and drawbacks'* and the procedure done *'only by surgeons who have received appropriate training in the technique, and who regularly carry out surgery for stress incontinence in women.'* NICE recommend that observational data on effectiveness and safety of TVT are collected over a period of 10 years or more, preferably nationally coordinated in the form of a registry of audit data to include both the numbers of procedures carried out and measures of outcomes and adverse events.

[57] NICE, 2003, Final Appraisal Determination – Tension-free vaginal tape (Gynecare TVT) for stress incontinence, available online at: https://www.nice.org.uk/guidance/ta56/documents/final-appraisal-determination-tension-free-vaginal-tape-gynecare-tvt-for-stress-incontinence2

20th March 2003	Ethicon Written Evidence	Gynecare Gynemesh PS received its first CE marking through the notified body BSI, allowing it to be sold in the EU. *'Gynecare Gynemesh® PS Nonabsorbable Prolene Soft Mesh (Gynemesh PS) was the first device indicated for the treatment of pelvic organ prolapse, and is made of Prolene Soft Mesh. Gynemesh PS is produced in different size sheets of mesh which are cut by the surgeon as needed for the specific POP application and patient.'*[58] This mesh has been used in other Ethicon POP transvaginal mesh devices (Gynecare Prolift (2005), Gynecare Prosima (2007)), and is the 'equivalent device' upon which Gynecare Prolift, Gynecare Prosima and Gynecare Gynemesh M were CE marked[59].
1st April 2003	MHRA	MHRA was formed in 2003 with the merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA).
August 2003	Ustün et al.	**Tension-free Vaginal Tape Compared With Laparoscopic Burch Urethropexy[60]** Randomised clinical study to compare laparoscopic Burch colposuspension and tension-free vaginal tape (TVT) procedure in women with genuine stress incontinence. Valsalva leak-point pressure increased after surgery in both groups, but TVT substantially decreased maximum urinary flow rate. Other urodynamic studies showed no statistical differences. The groups did not differ significantly with respect to intraoperative complications or objective and subjective cure rates. Operating time was significantly longer for laparoscopic Burch (p = 0.001), and three patients in this group required conversion to laparotomy. Length of hospital stay (p = 0.003) and duration of

[58] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 51, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[59] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 52, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[60] Y. Ustün, Y. Engin-Ustün, M. Güngör, S. Tezcan, Tension-free vaginal tape compared with laparoscopic Burch urethropexy. *The Journal of the American Association of Gynecologic Laparoscopists* **10**, 386-389 (2003).

		catheterization (p = 0.003) were shorter in the TVT group. The authors conclude that *'TVT holds promise in women with genuine stress incontinence, with several advantages over laparoscopic Burch'*
September 2003	Cody et al.	**Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence**[61] Aimed to evaluate the effectiveness and cost-effectiveness of TVT compared with alternatives. Concluded that despite relatively few robust comparative data, in the short to medium-term. *'Despite relatively few robust comparative data, it appears that in the short to medium term TVT's effectiveness approaches that of alternative procedures currently available, and is of lower cost'*. It warned that there was very limited information available on the long-term performance of TVT (most RCTs had only 2 year follow-up). Also noted was a lack of reassurance that TVT will have no unanticipated long-term complication related to the use of tape, such as erosion into the vagina or urinary tract. Authors set out implications for research: - Unbiased assessments of long-term performance (≥5 years) are required from follow-up of controlled trials and/or population-based registries. - There should be more data from methodologically sound RCTs. Current trials should be fully reported and include long-term follow-up. Further trials should be mounted where uncertainty persists, preferably independent of support from the manufacturers, and use standard outcome measures. - Ongoing surveillance of TVT would be enhanced by access to a regularly updated systematic summary of evidence from controlled trials, such as through the Cochrane Collaboration. - Research is needed on possible long-term complications of TVT; this would provide either

[61] Cody et al (2003) Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence, Health Technology Assessment Vol. 7: No. 21 https://doi.org/10.3310/hta7210

		reassurance of safety or earlier warning of unanticipated adverse effects. - If the indications for TVT are likely to be broadened to include women who are currently managed conservatively, this should be formally evaluated, ideally in an RCT, before widespread adoption. - As new evidence about the effectiveness, safety and costs of TVT emerges, this should be incorporated in updated cost-effectiveness analyses. - Evidence of efficacy from case series led to the rapid, widespread adoption of TVT before its relative effectiveness (its place within NHS care) and long-term safety were known. Although current evidence suggests that TVT probably is effective and safe, this approach exposed thousands of women to an incompletely evaluated procedure in a poorly controlled way. Future research to evaluate new procedures of this type could avoid this by earlier and wider use of pragmatic RCTs and rigorously organised population-based registries. Authors set out implications for patients and carers: - TVT, along with open colposuspension and traditional sling procedures, appears to be an effective method of treating urinary incontinence. Unlike these other procedures, the long-term performance of TVT is not yet known. - TVT has the advantage that it is less invasive than open colposuspension and traditional sling procedures. - Women previously considered ineligible for surgery (such as the frail elderly) may be suitable for TVT as it is less invasive. - The other less invasive surgical intervention is injectable agents and this appears to be less effective and more costly than TVT.
2nd December 2003	BAUS Written Evidence	A letter was sent to Section members from Paul Abrams, Chairman, *'reporting on meeting with NICE and MHRA to discuss BAUS's concerns about devices being marketed before an adequate body of clinical evidence of efficacy and the consequent risks to patient safety'.*[62]

[62] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 135, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

		Content: steps for better patient protection outlined (registry of trials, national audit of incontinence procedures, informing MHRA of adverse events)[63].
22nd December 2003	Ethicon Written Evidence	Gynecare TVT-O was CE marked on 22nd December 2003, through the notified body TÜV. The product was first marketed in 2004[64].
January 2004	Shah et al.	**Short-Term Outcome Analysis of Total Pelvic Reconstruction With Mesh: The Vaginal Approach[65]** Description of transvaginal total pelvic reconstruction using a prolene mesh with 4-point fixation for patients with genitourinary prolapse with/without SUI. Of the 29 patients 19 (65.5%), 7 (26.92%) and 11 (39.29%) had associated symptoms of stress urinary incontinence, urgency and frequency, respectively, and 79.31% had associated anterior and 44.8% had associated posterior prolapse. Average operative time was 175.6 minutes, blood loss was 340 cc and hospital stay was 2.46 days. Early adverse events following the procedure were perineal pain, vaginal discharge and irritative voiding symptoms. At 6 month follow-up (mean 25.14 months) mild constipation and dyspareunia were encountered in a small subset of patients. Two patients (6.89%) have genital prolapse recurrence and none has reported erosion or nonhealing. Authors conclude that this is a safe and effective procedure at 2 years.
February 2004	Ward & Hilton	**A prospective multicenter randomized trial of tension-free vaginal tape and colposuspension for primary urodynamic stress incontinence: Two-year follow-up[66]**

[63] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 139, viewed 27 August 2019, available online at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[64] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 36, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[65] D. K. Shah, E. M. Paul, A. R. Rastinehad, E. R. Eisenberg, G. H. Badlani, Short-term outcome analysis of total pelvic reconstruction with mesh: the vaginal approach. *The Journal of urology* **171**, 261-263 (2004).

[66] K. L. Ward, P. Hilton, Uk, T. V. T. T. G. Ireland, A prospective multicenter randomized trial of tension-free vaginal tape and colposuspension for primary urodynamic stress incontinence: two-year follow-up. *American journal of obstetrics and gynecology* **190**, 324-331 (2004).

		2-year follow-up from the original Ward & Hilton study. 63% of the TVT group and 51% of the colposuspension group were objectively cured (more than a 1 g decrease in weight in a 1-hour pad test). The number of women reporting cure of their stress leakage through the Bristol Female Lower Urinary Tract Symptoms (BFLUTS) questionnaire was 75 (43% - TVT) and 63 (37% - colposuspension) respectively. In terms of complications and patient-reported outcomes, the following is presented: *'The rates of re-operation for urodynamic stress incontinence did not differ significantly between the two groups. Significantly more women in the colposuspension group underwent surgery for uterovaginal prolapse during the follow-up period and a higher proportion of women in this group were still self-catheterizing at 2 years'* *'In the previous report of this study, patients reported that their return to normal activity about the home, and return to work, took longer after colposuspension than TVT. In keeping with this, the colposuspension group showed a greater deterioration in five of the eight domains of the SF-36 questionnaire at 6 weeks after surgery and retained lower scores for emotional and social functioning, vitality, and mental health at 6 months. It is perhaps surprising that differences remain between the groups in the domain scores for mental health and role limitation because of emotional problems at 2 years. This reflects greater improvement in the scores in the TVT group between 6 months and 24 months, rather than deterioration from baseline in the scores in the colposuspension group'* The authors conclude that the TVT procedure appears to be as effective as colposuspension for the treatment of urodynamic stress incontinence at 2 years.
24th February 2004	BAUS Written Evidence	Proposed Code of Good Practice for new procedures & devices for treating SUI & POP sent in letter to members of the Section of Female and Reconstructive Urology (SFRU)[67]. The letter outlined:

[67] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 142, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

		- Concern over little data supporting use - inadequacies of the EU CE marking system - *'it is possible for products to become registered with no clinical data at all, simply by claiming equivalence for the other notified devices'* Content included in code of practice: surgeons should: - participate in national audit, seek training for new procedures, - inform Trusts' clinical governance committee when using new material or device in previously established procedures - companies promoting new procedures or devices should be directed to SFRU to liase with potential 'trialists' before a surgeon agrees to participate in a company driven evaluation.
19th March 2004	BAUS Written Evidence	Members of BAUS SFRU exec and BSUG met in Bournemouth. Records of the meeting indicate that the problem of new devices / procedures being introduced with little or no supporting evidence was discussed[68]
July 2004	Valpas et al.	**Tension-free Vaginal Tape and Laparoscopic Mesh Colposuspension for Stress Urinary Incontinence[69]** A study to compare objective and subjective outcomes after the tension-free vaginal tape procedure (TVT) with laparoscopic mesh colposuspension as a primary treatment for SUI. Objective outcome measures were stress test and 48-hour pad test. When negative stress test was used as criteria for cure, 85.7% of women in the TVT group and 56.9% in the laparoscopic mesh colposuspension group were objectively cured. Subject satisfaction was *'significantly better after the TVT procedure than after laparoscopic mesh colposuspension'* The authors conclude that *'Treatment with TVT results in higher objective and subjective cure rates at 1 year than treatment by means of laparoscopic mesh colposuspension'*

[68] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 144, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[69] A. Valpas *et al.*, Tension-free vaginal tape and laparoscopic mesh colposuspension for stress urinary incontinence. *Obstetrics and gynecology* **104**, 42-49 (2004).

1st October 2004	Milani et al.	**Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh[70]** Prospective observational study designed to evaluate the effects of prolene mesh on urinary, bowel and sexual function in prolapse surgery. The study recruited 63 women (mean age 63 years) with a mean follow-up of 17 months. Anatomically, the success rate was 94%. Thirty-two women had an anterior repair. Among this group, the sexual activity rate did not alter but dyspareunia increased by 20%. Urge and stress incontinence did not change post-operatively, but urgency improved in 10% and 13% had vaginal erosion of the mesh. Thirty-one women had a posterior repair. Among this group, sexual activity decreased by 12% and dyspareunia increased in 63%. Constipation improved in 15% and anal incontinence in 4%, and 6.5% of women had vaginal erosion of the mesh and one required mesh removal for pelvic abscess. The authors conclude that '*Although this study shows good anatomical results with the use of prolene mesh for prolapse repair, there was a high rate of morbidity. We believe that the use of prolene mesh should be abandoned'*
18th October 2004	Cochrane	**Surgical management of pelvic organ prolapse in women[71]** 14 RCTs were included, involving 1004 women. Abdominal sacrocolpopexy is associated with a lower rate of recurrent vault prolapse and dyspareunia than the vaginal sacrospinous colpopexy. These benefits must be balanced against a longer operating time, longer time to return to activities of daily living and increased cost of the abdominal approach. The use of a polyglactin mesh overlay at the time of anterior vaginal wall repair may reduce the risk of recurrent cystocele.

[70] R Milani, S Salvatore, M Soligo, et al. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh. BJOG 112(1):107-111 doi:10.1111/j.1471-0528.2004.00332.x

[71] C. Maher, K. Baessler, C. M. A. Glazener, E. J. Adams, S. Hagen, Surgical management of pelvic organ prolapse in women. *Cochrane Database of Systematic Reviews*, (2004).

		Adequately powered randomised controlled clinical trials are urgently needed.
November 2004	Debodinance et al.	**[Changing attitudes on the surgical treatment of urogenital prolapse: birth of the tension-free vaginal mesh][72] (French translation)** Description of a standardised technique for the repair of urogynaecological prolapse using a one-piece synthetic mesh. A list of materials along with their respective advantages and inconveniences is reviewed and particular emphasis is put on both the tolerance and erosion issues, the latter being specific to the vaginal route. The TVM Group selected a monofilament polypropylene mesh, Prolene Soft, which seemed the most appropriate for the transvaginal approach of prolapse surgical repair. The authors note that *'The relevant literature is scarce and there is a lack of methodologically sound studies validating the materials and techniques used'* After completion of a first step of *'technique refinement and feasibility assessment involving about 300 surgical interventions'* the authors initiated a prospective multicenter study. Clinical outcome assessments using feasibility, complications, and efficacy endpoints were published after twelve months[73], three years[74], and five years[75] of follow-up (funded by Ethicon). The authors note that this research activity *'led to the development of the TVM technique of complete surgical repair of genital prolapse, which uses a synthetic materiel carefully selected after several tests. All surgeons can apply this technique after a short training period'* This work led to the development of the Prolift device

[72] P. Debodinance *et al.*, [Changing attitudes on the surgical treatment of urogenital prolapse: birth of the tension-free vaginal mesh]. *Journal de gynecologie, obstetrique et biologie de la reproduction* **33**, 577-588 (2004).
[73] M. Cosson *et al.*, Prospective clinical assessment of the total vaginal mesh (TVM) technique for treatment of pelvic organ prolapseV6 and 12 months results. *Int Urogynecol J* **17**, S139-S140 (2006)
[74] M. Cosson *et al.*, Prospective clinical assessment of the Total TransVaginal Mesh (TVM) technique for treatment of Pelvic Organ Prolapse - 3 year results. *International Urogynecology Journal* **19**, S106-S107 (2008)
[75] M. Cosson *et al.*, *TRANS-VAGINAL MESH TECHNIQUE FOR TREATMENT OF PELVIC ORGAN PROLAPSE: 5 YEARS OF PROSPECTIVE FOLLOW UP*. (2010), pp. 888-889.

December 2004	Paraiso et al.	**Laparoscopic Burch Colposuspension Versus Tension-Free Vaginal Tape: A Randomized Trial**[76] A study comparing the efficacy of the tension-free vaginal tape procedure with that of laparoscopic Burch colposuspension. Mean operative time was significantly greater in the laparoscopic Burch colposuspension group compared with the TVT (132 versus 79 min). Urodynamic studies in 32 colposuspension and 31 TVT patients showed a higher rate of urodynamic stress incontinence at 1 year in the colposuspension group, 18.8% versus 3.2%. There was a significant improvement in the number of incontinent episodes per week and in Urogenital Distress Inventory and Incontinence Impact Questionnaire scores in both groups at 1 and 2 years after surgery. However, postoperative subjective symptoms of incontinence (stress, urge, and any urinary incontinence) were reported significantly more often in the colposuspension group than in the TVT group. The authors conclude that *'The TVT procedure results in greater objective and subjective cure rates for urodynamic stress incontinence than does laparoscopic Burch colposuspension'*
December 2004	Hung et al.	**Factors That Affect Recurrence After Anterior Colporrhaphy Procedure Reinforced With Four-Corner Anchored Polypropylene Mesh**[77] A study to evaluate the effectiveness of the anterior colporrhaphy procedure reinforced with four-corner anchored polypropylene mesh in patients with severe (stage III or IV) anterior vaginal prolapse. The success rate was 87% (33/38) at a mean follow-up interval of 21 (12–29) months. A total of eight (100%) patients were also cured of concomitant stress incontinence (five overt and three occult type) with an additional tension-free vaginal tape (TVT) operation. During follow-up, there were five *de novo* stress incontinence cases (16.7%) and four vaginal erosions of mesh (10.5%).

[76] M. F. R. Paraiso, M. D. Walters, M. M. Karram, M. D. Barber, Laparoscopic Burch colposuspension versus tension-free vaginal tape: a randomized trial. *Obstetrics and gynecology* **104**, 1249-1258 (2004).

[77] M. J. Hung *et al.*, Factors that affect recurrence after anterior colporrhaphy procedure reinforced with four-corner anchored polypropylene mesh. *International urogynecology journal and pelvic floor dysfunction* **15**, 399-406 (2004).

		Authors conclude that *'the anterior colporrhaphy procedure reinforced with four-corner anchored polypropylene mesh was effective for most, but failed in some patients who had specific risk factors within short convalescence periods. Concomitant stress incontinence can be successfully treated by a TVT operation in combination with the anterior colporrhaphy procedure reinforced with four-corner anchored polypropylene mesh. However, the anterior colporrhaphy procedure may itself have adverse effects on urethral sphincter function'* The authors identify the following as risk factors for mesh failure: - co-morbidities (such as diabetes mellitus, neurological diseases, previous pelvic irradiation, previous pelvic surgery and chronic obstructive pulmonary disease) - age over 60 - previous herniorrhaphy - the size of the hernia - postoperative local complications.
2004	FDA	AMS Apogee™ System and the AMS Perigee™ System, both manufactured by American Medical Systems, Inc., were cleared. These were the first kits for POP repair. *'Attempts to establish clinical safety and effectiveness were undertaken later by the clinical community with clinical trials, published studies, and systematic reviews or meta-analyses.'* AMS Apogee Vault received 510(k) clearance based on similarity to Sparc Sling and IVS. Some of this published literature was incorporated into later 510(k) submissions to support future market clearances. Between 2002 and 2013, the FDA cleared over 100 510(k) submissions for surgical mesh with a transvaginal POP repair indication.[78]
2004	Duckett et al.	**National audit of incontinence surgery in the United Kingdom[79]** A study comprising a postal questionnaire survey that was sent to a cohort of surgeons known to be performing continence surgery in the UK. The

[78] FDA, Surgical Mesh for Transvaginal Repair of Pelvic Organ Prolapse in the Anterior Vaginal Compartment – FDA Executive Summary, Page 11, available online at: https://www.fda.gov/media/122854/download

[79] J. R. Duckett, S. Jain, A. Tamilselvi, P. A. Moran, D. Richmond, National audit of incontinence surgery in the United Kingdom. *J Obstet Gynaecol* **24**, 785-793 (2004).

		subjects addressed included the considered role of the surgeon, the total number and type of operations performed in the last year, urodynamics and physiotherapy prior to incontinence surgery, operative complications, postoperative advice and follow-up (lengths and methods). The response rate of the 1066 surgeons contacted was 54%. The number of operations performed by surgeons in the study year (year ended 1 January 2002) for women with SUI was estimated to be 16412. The most common operation was tension-free vaginal tape (45%) followed by colposuspension (27%) anterior repair (13%) periurethral injection (9%) sling procedure (4%) and needle suspension (0.05%). Twenty-six surgeons performed more than 50 TVTs each year, with a further 68 performing more than 25. Only 28 surgeons performed more than 25 colposuspensions each year. Two per cent reported patients requiring an emergency laparotomy that was not part of the original surgery. Intraoperative haemorrhage of more than 500 ml was reported by 14% of surgeons. Erosion of an artificial substance was reported by 10% of surgeons. Emergency readmission within 28 days of surgery was reported by 16%. Persistent suprapubic pain was reported by 13% of surgeons; recurrent urinary tract infections were reported as a complication by 25%; the development of urgency or urge incontinence was reported by 47%; bladder perforations were reported by 29%. Persistent voiding abnormalities for more than 6 weeks was reported by only 19% of consultants performing continence surgery in 2001. Removal of the tape/sling or sutures in response to voiding difficulties would be considered by 4% of surgeons. Among the respondents, 26% of surgeons followed patients for 6–8 weeks after the surgery. Forty-three per cent followed-up their patients routinely between 2 and 6 months and only 31% followed-up women for more than 6 months.
July 2005	BAUS Written Evidence	Section Exec Committee minutes *'NICE Guidelines – There will be a formal reappraisal of all synthetic slings. Current advice on techniques other than TVT was that the procedure should be performed within the constraints of clinical governance. Urologists*

		should follow the good practice guidelines on the SFRU website when undertaking new procedures.'[80]
20th July 2005	Cochrane	**Traditional suburethral sling operations for urinary incontinence in women**[81] Substantive amendment to 2001 review. The review was divided into two separate reviews: one on traditional sub-urethral sling operations (current review, updated) and another on sub-urethral self fixing sling operations (to include the new TVT and SPARC procedure). Five new trials were included. Authors conclude that *'the data on sub urethral sling operations remain too few to address the effects of this type of surgical treatment. Few trials are reported by authors in a complete fashion and most information came from abstracts presented in annual meetings. The broader effects of suburethral slings could not be established since trials did not include appropriate outcome measures such as general health status, health economics, pad testing, third party analysis and time to return to normal activity level. Data obtained from thirteen trials did not provide reliable estimates because of their sizes, and heterogeneity of designs, populations studied, and types of comparisons made'* *'Reliable evidence on which to judge whether or not suburethral slings are better or worse than other surgical or conservative management is currently not available'*
2006	Ethicon Written Evidence	*'In 2006, Ethicon introduced an additional way to cut the mesh for the TVT devices by using a laser instead of the traditional mechanical cutting. TVT and TVT-O are provided in either mechanical or laser cut and TVT Abbrevo and TVT Exact are laser cut.'*[82]

[80] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 135, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[81] C. A. Bezerra, H. Bruschini, D. J. Cody, Traditional suburethral sling operations for urinary incontinence in women. *The Cochrane database of systematic reviews*, Cd001754 (2005).

[82] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 38, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

Annex D: Mesh Timeline – Key Events

13th February 2006	BAUS Written Evidence	Good Practice Guidelines for Urogynaecological and Female Pelvic Reconstructive surgery (based on the 2004 letter sent to section members) with particular reference to the introduction of new procedures by BAUS SFRU and BSUG[83] – sent out for consultation.
8th May 2006	Ethicon Written Evidence	Ethicon TVT Secur is the first single-incision minisling to be introduced to the market - CE marked through the notified body BSI[84]. *'TVT Secur used the same mesh as TVT and TVT-O and was designed as a single-incision sling. Unlike TVT and TVT-O, it had no exit points and was placed using inserters with fleece tips that enabled fixation of the mesh into the surrounding tissue. At 8 cm in length, TVT Secur was designed to provide the patient with an even less invasive implantation as TVT and TVT-O. TVT Secur was developed with surgeon consultants who developed the procedure which allowed for retropubic or transobturator orientation.'*[85] *'TVT Secur's components were studied, refined, and validated in human and animal cadaver studies.* Moreover, prior to launching TVT Secur, Ethicon conducted numerous cadaver labs and animal studies to evaluate pullout strength and fixation forces and holding ability of the mesh.' *'A short term trial in patients was also conducted prior to launch.* These labs and studies coupled with the decade long clinical history of TVT and TVT-O demonstrated the safety and efficacy of TVT Secur'
21st July 2006	Cochrane	**Laparoscopic colposuspension for urinary incontinence in women (Review)[86]**

[83] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 148, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[84] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 35, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[85] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 37, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[86] N. M. Dean, G. Ellis, P. D. Wilson, G. P. Herbison, Laparoscopic colposuspension for urinary incontinence in women. *The Cochrane database of systematic reviews*, Cd002239 (2006, updated in 2009).

		including 22 trials (10 laparoscopic vs. open colposuspension, 8 laprospcopic colpo vs. slings) The authors conclude that the available evidence suggests that laparoscopic colposuspension may be as good as open colposuspension at two-years post-surgery. *'However, the newer vaginal sling procedures appear to offer even greater benefits, better objective outcomes in the short term and similar subjective outcomes in the longer term (measured at 18 months).'* Mesh described as a newer 'self-fixing' sling procedures. Longer hospital time and hospital stay for colposuspension were highlighted.
25th August 2006	Kitchner et al. 'COLPO study'	**Laparoscopic versus open colposuspension—results of a prospective randomised controlled trial**[87] Women recruited from six UK gynaecology units, were randomised between open and laparoscopic colposuspension and assessed at 6, 12 and 24 months postoperatively. The intention-to-treat analysis indicated no significant difference in cure rates between open and laparoscopic surgery. The objective cure rates for open and laparoscopic were 70.1 and 79.7%, respectively. Subjective cure rates by satisfaction were lower than objective cure; 54.6 and 54.9%, respectively. The authors conclude that laparoscopic colposuspension is not inferior to open colposuspension in terms of curing stress urinary incontinence.
October 2006	NICE	**Guideline CG40: Urinary incontinence: the management of urinary incontinence in women**[88] The guidelines recommend supervised pelvic floor muscle training of at least 3 months as first-line treatment of women with SUI. Procedures using mesh should only be used when conservative management has failed, performed by surgeons who have

[87]H. C. Kitchener *et al.*, Laparoscopic versus open colposuspension--results of a prospective randomised controlled trial. *BJOG : an international journal of obstetrics and gynaecology* **113**, 1007-1013 (2006).
[88] NICE, 2006, viewed 8 August 2019, available online at: https://www.sauga.org.za/content/images/Nice%20incontinence.pdf

		appropriate training in urinary incontinence management. Laparoscopic colposuspension is not recommended as a routine procedure for the treatment of SUI in women. *'The procedure should be performed only by an experienced laparoscopic surgeon working in a multidisciplinary team with expertise in the assessment and treatment of UI'* Anterior colporrhaphy, needle suspensions, paravaginal defect repair and the Marshall–Marchetti–Krantz procedure are not recommended for the treatment of SUI.
2007	BSUG	BSUG launched BSUG.NET, the first online urogynaecology database of its kind. This launch was boosted by support from NICE in its guidance on urinary incontinence and subsequently in its guidance on any new urogynaecological interventions/procedures, particularly those involving graft insertions.
July 2007	BAUS, SFRU, BSUG	BAUS SFRU (Section of Female and Reconstructive Urology) & BSUG joint guidance on implementation of NICE Guideline is issued[89]. There is an emphasis on multidisciplinary work, followed by practical considerations regarding implementation of the NICE guidance.
18th July 2007	Cochrane	**Surgical management of pelvic organ prolapse in women[90]** Substantive update of the 2004 review, including 8 new trials. Authors conclude that *'Abdominal sacrocolpopexy is associated with a lower rate of recurrent vault prolapse and dyspareunia than the vaginal sacrospinous colpopexy. These benefits must be balanced against a longer operating time, longer time to return to activities of daily living and increased cost of the abdominal approach. The use of mesh or graft inlays at the time of anterior vaginal wall repair may reduce the risk of recurrent cystocele. Posterior vaginal wall repair may be better than transanal repair in the management of rectoceles in terms of*

[89] BAUS, 2007, viewed 8 August 2019, available online at: https://www.baus.org.uk/_userfiles/pages/files/Publications/NICEguidanceimplementationguidefinal.pdf

[90] B. K. Maher C, Glazener CM, Adams EJ, Hagen S., Surgical management of pelvic organ prolapse in women. *The Cochrane database of systematic reviews* **(3):CD004014.**, (2007).

		recurrence of prolapse. The addition of a continence procedure to a prolapse repair operation may reduce the incidence of postoperative urinary incontinence but this benefit needs to be balanced against possible differences in costs and adverse effects.' *Findings are insufficient to provide robust evidence to support current and new practice (such as whether to perform a concurrent continence operation, or to use mesh or grafts).* *Adequately powered randomised controlled clinical trials are urgently needed.*
8th November 2007	FDA	Boston Scientific Pinnacle received 510(k) clearance based on similarity to Polyform Synthetic Mesh[91]. 510(k) clearance of Pinnacle can be traced back to ProteGen.
15th May 2008	FDA	Ethicon's Gynecare Prolift Total & Gynecare Prolift M+ received 510(k) clearance based on similarity to: GYNECARE GYNEMESH PROLENE* Soft Mesh (ETHICON, Inc.) – K013718 ULTRAPRO* Mesh (ETHICON, Inc.) - K033337 AMS APOGEE Vault Suspension System (American Medical Systems, Inc.) — K040537 AMS PERIGEE System (American Medical Systems, Inc.) - K040623[92]
20th October 2008	FDA	**Public Health Notification: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence [93]** Public Health Notification (PHN) advising that complications associated with transvaginal placement of surgical mesh to treat POP and SUI - although rare - can have serious consequences. *'Over the past three years, FDA has received over 1,000 reports from nine surgical mesh manufacturers of complications that were associated with surgical*

[91] FDA, 2007, viewed 8 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K071957
[92] FDA, 2008, viewed 8 August 2019, summary available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K071512
[93] FDA, 2008, Public health notification: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence, viewed 8 August 2019, available online at: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence

		mesh devices used to repair POP and SUI. These mesh devices are usually placed transvaginally utilizing tools for minimally invasive placement' *'The most frequent complications included erosion through vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence. There were also reports of bowel, bladder, and blood vessel perforation during insertion. In some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia'* *'Treatment of the various types of complications included additional surgical procedures (some of them to remove the mesh), IV therapy, blood transfusions, and drainage of hematomas or abscesses'* *'Specific characteristics of patients at increased risk for complications have not been determined. Contributing factors may include the overall health of the patient, the mesh material, the size and shape of the mesh, the surgical technique used, concomitant procedures undertaken (e.g. hysterectomy), and possibly estrogen status'* The PHN contains recommendations that Physicians should: - Obtain specialised training for each mesh placement technique, and be aware of its risks. - Be vigilant for potential adverse events from the mesh, especially erosion and infection. - Watch for complications associated with the tools used in transvaginal placement, especially bowel, bladder and blood vessel perforations. - Inform patients that implantation of surgical mesh is permanent, and that some complications may require additional surgery that may or may not correct the complication. - Inform patients about the potential for serious complications and their effect on quality of life, including pain during sexual intercourse, scarring, and narrowing of the vaginal wall. - Provide patients with a written copy of the patient labelling from the surgical mesh manufacturer, if available.
2008	Meshies United	Patient group established.

March 2009	Elmer et al.	**Histological Inflammatory Response to Transvaginal Polypropylene Mesh for Pelvic Reconstructive Surgery[94]** A study prospectively evaluating the histological response to polypropylene transvaginal mesh used for POP surgery. Ten patients and 8 controls underwent vaginal punch biopsy sampling before surgery and patients also underwent it 1 year after pelvic reconstructive surgery using polypropylene mesh. Foreign body response to the mesh was assessed using a combination of histological, semiquantitative and computerized image based analysis. Compared to preoperative histology there was a significant postoperative increase in macrophage and mast cell counts but no significant changes in the count of cells involved primarily in the infectious cell response or collagen density and the elastin area fraction at the mesh-tissue interface. Three cases of mild granuloma formation and 2 of mild erosion were observed. There was no significant change in epithelial thickness when comparing preoperative and postoperative samples. The authors conclude that *'When used for pelvic reconstructive surgery, macroporous monofilament polypropylene mesh induces a mild but persistent foreign body reaction'*
23rd May 2009	TVT-MUM	TVT-MUM website and patient group established.
7th October 2009	Cochrane	**Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women[95]** Sixty-two trials involving 7101 women were included. The quality of evidence was moderate for most trials. Minimally invasive synthetic suburethral sling operations appeared to be as effective as traditional suburethral slings but with shorter operating time and less post-operative voiding dysfunction and *de novo* urgency symptoms.

[94] C. Elmer, B. Blomgren, C. Falconer, A. Zhang, D. Altman, Histological Inflammatory Response to Transvaginal Polypropylene Mesh for Pelvic Reconstructive Surgery. *The Journal of Urology* **181**, 1189-1195 (2009).

[95] Ogah J, Cody JD, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2009;(4):CD006375.

		Minimally invasive synthetic suburethral sling operations appeared to be as effective as open retropubic colposuspension with fewer perioperative complications, less postoperative voiding dysfunction, shorter operative time and hospital stay but significantly more bladder perforations (6% versus 1%, RR 4.24, 95% CI 1.71 to 10.52). There was conflicting evidence about the effectiveness of minimally invasive synthetic suburethral sling operations compared to laparoscopic colposuspension in the short-term. Minimally invasive synthetic suburethral sling operations had significantly less *de novo* urgency and urgency incontinence, shorter operating time, hospital stay and time to return to daily activities. A retropubic bottom-to-top route was more effective than top-to-bottom route and incurred significantly less voiding dysfunction, bladder perforations and tape erosions. Monofilament tapes had significantly higher objective cure rates compared to multifilament tapes and fewer tape erosions. The obturator route was less favourable than the retropubic route in objective cure, although there was no difference in subjective cure rates. However, there was less voiding dysfunction, blood loss, bladder perforation and shorter operating time with the obturator route. Authors conclude that *'The current evidence base suggests that minimally invasive synthetic suburethral sling operations are as effective as traditional suburethral slings, open retropubic colposuspension and laparoscopic colposuspension in the short term but with less postoperative complications. Objective cure rates are higher with retropubic tapes than with obturator tapes but retropubic tapes attract more complications. Most of the trials had short term follow up and the quality of the evidence was variable.'*

December 2009	Ross et al.	**Transobturator Tape Compared With Tension-Free Vaginal Tape for Stress Incontinence: A Randomized Controlled Trial[96]** Randomised control trial designed to compare the effectiveness of transobturator tape (TOT) with tension-free vaginal tape (TVT[97]) in terms of objective cure of stress urinary incontinence (SUI) at 12 months postoperatively. A total of 199 women participated (94 in the TOT group, 105 in the TVT group). 81% in the TOT group were cured, compared with 77% in the TVT group. On vaginal examination, the tape was palpable for 80% of women in the TOT group and for 27% in the TVT group. More women in the TOT group experienced groin pain during vaginal palpation (15% in the TOT group and 6% in the TVT group). Quality of life improved significantly from baseline in both groups (30-point improvement in IIQ-7 score for both groups). Authors conclude that at 12 months, the majority of women had minimal leakage and their quality of life had improved significantly, but differences were not observed between groups. The presence of palpable tape, particularly among the TOT group, is concerning; longer follow-up is needed to determine whether this outcome leads to extrusion or resolves over time. 5 year follow-up was published in 2016.
2009	NHS Digital (HES Data)	By 2009 the annual number of operations using polypropylene mesh tape had climbed to an all-time high of 11,365 in England.[98]
6th January 2010	Clavé et al.	**Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants[99]**

[96] S. Ross *et al.*, Transobturator tape compared with tension-free vaginal tape for stress incontinence: a randomized controlled trial. *Obstet Gynecol* **114**, 1287-1294 (2009).
[97] 'TVT' is used here as a generic term and does not imply use of an Ethicon TVT device in this trial. Indeed, Boston Scientific (Natick, MA) devices were used for all procedures in this trial. The outside-in Obtryx Halo midurethral sling system was used for transobturator tape procedures, and the Advantage retropubic midurethral sling system was used for TVT procedures.
[98] NHS Digital. Hospital Episode Statistics. Patient admitted care, England https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity
[99] A. Clave *et al.*, Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. *Int Urogynecol J* **21**, 261-270 (2010).

		A study to compare the state of alteration of different meshes commonly used in SUI or POP surgery, explanted after clinical complication, and to investigate potential causes of alteration. The study included 100 prosthetic explants surgically removed for one (or several) common complications including exposure, infection, and/or shrinkage. Morphological analysis of explants and pristine control mesh samples of the same trademark was conducted using scanning electron microscopy. Chemical analysis of 32 mesh explants was carried out to characterize the degradation of mesh materials (Fourier transform infrared spectroscopy and differential scanning calorimetry). Scanning electron microscopy revealed that 42% of the implants were degraded (observed only in samples implanted for at least 3 months). No correlation between the duration of the implant and prosthetic damage was observed. Evidences of PP degradation were more frequently observed when the surrounding tissue reaction was classified as infection, as opposed to sclerosis. Several hypotheses concerning the degradation of the polypropylene are described in the discussion. *'None of these, particularly direct oxidation, could be confirmed in this study.'* The authors conclude that polypropylene implants are altered *in vivo,* that there are classifiable histological reactions observed in standard complications of pelvic surgery with prosthetic reinforcement. There was no alteration of poly(ethylene terephthalate) (PET) implants.
4th February 2010	Health Canada	**Notice to Hospitals**[100] In the light of increased reporting of complications relating to transvaginal mesh for POP and SUI, Health Canada recommended that hospitals: - Review the labelling, especially sections concerning warnings, precautions and adverse reactions.

[100] Health Canada, 2010, Notice to Hospitals - Health Canada Issued Important Safety Information on Surgical Mesh for Stress Urinary Incontinence and Pelvic Organ Prolapse, viewed 8 August 2019,

		- Inform patients during the presurgical consultation of adverse events that may occur. Patients should be aware of the possible need for additional surgical procedures that may not always fully correct some potential complications. - Be observant both intraoperatively and postoperatively for signs of any complications. - Be aware of and/or get training on proper case selection, initial implantation procedure and management of complications.
14th April 2010	Cochrane	**Surgical management of pelvic organ prolapse in women (2007 review)** was updated[101]. In this second update, 18 new trials were added, but conclusions were unchanged.
May 2010	MHRA Written Evidence[102]	*'As part of our continuing market surveillance role, we wrote to urogynaecology mesh manufacturers known to have mesh on the UK market, stating we had received a small but increasing number of reports (…) from patients who had experienced complications such as pain, infection and erosion. We requested and examined a range of information relating to adverse events and pre and post market information. Whilst a small number of women had experienced distressing effects, the current evidence shows that when these products are used in appropriate treatment pathways, they can help with the very distressing symptoms of stress urinary incontinence (…). We found no evidence from the information provided that suggested the devices did not comply with the requirements within the Medical Device Directive. No regulatory action was taken however we continued to keep this area under review as part of ongoing post-market surveillance and took the next step.'* *'We contacted known clinical experts about our concerns with reports we had received from patients who had experienced complications with mesh asking them about their experience of using mesh in urogynaecology. Responses indicated that patient selection, training and informed patient consent were at the heart of the matter.'*

available online at: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2010/14626a-eng.php

[101] C. Maher, B. Feiner, K. Baessler, C. M. A. Glazener, Surgical management of pelvic organ prolapse in women. *Cochrane Database of Systematic Reviews*, (2010).

[102] IMMDSR written evidence, Public Bodies, Page 168, available online, at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Public%20Bodies.pdf

2nd June 2010	Ethicon Written Evidence	*'Ethicon launched the TVT Exact device. This device is the second generation of the original TVT and nearly identical to TVT. The mesh, its length and its placement are unchanged from the original TVT. The two devices, by design, provide for the placement of an identical 1.1 cm-wide sling of Prolene polypropylene mesh, using trocars with the same curvature and tip radius.'*[103] *'However, the TVT Exact has a narrower trocar (3.0 mm, and 4.2 mm when covered in the smooth plastic, closed-tip trocar sheath) designed to minimize the risk of bladder and tissue damage/perforation, along with a disposable trocar handle. TVT's twelve years of rigorous clinical study of the highest levels of evidence supported Ethicon's determination prior to its launch that TVT Exact was a safe and effective device for treating SUI. Studies have been published demonstrating equivalent efficacy and safety data with the original TVT device and the TVT Exact, suggesting no differences in continence success rates, patient satisfaction, or overall complication rates'*[62]
3rd June 2010	Richter et al.	**Retropubic versus Transobturator Midurethral Slings for Stress Incontinence**[104] A multicenter, randomised equivalence trial comparing outcomes with retropubic and transobturator midurethral slings in women with stress incontinence. The primary outcome was treatment success at 12 months according to both objective criteria (a negative stress test, a negative pad test, and no retreatment) and subjective criteria (self-reported absence of symptoms, no leakage episodes recorded, and no retreatment). Objective success at 12 months was 80.8% for retropubic sling and 77.7 in the transobturator sling group. Subjective success was achieved in 62.2% and 55.8%, respectively. The rates of voiding dysfunction requiring surgery were 2.7% in those who received retropubic slings and 0% in those who received transobturator slings. Rates of neurologic

[103] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 37, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[104] H. E. Richter *et al.*, Retropubic versus Transobturator Midurethral Slings for Stress Incontinence. *The New England journal of medicine* **362**, 2066-2076 (2010).

		symptoms were 4.0% and 9.4%, respectively. There were no significant differences between groups in postoperative urge incontinence, satisfaction with the results of the procedure, or quality of life.
27th August 2010	Ethicon Written Evidence	*'Ethicon launched the TVT Abbrevo device. Like TVT-O, this device was invented by Professor De Leval and placed the same 1.1 cm wide Prolene polypropylene mesh as TVT-O in the same manner through the obturator space using helical passers and a winged guide. Unlike TVT-O, TVT Abbrevo featured a sling that was 12 cm long'*[105] *'Unlike TVT-O, TVT Abbrevo featured a sling that was 12 cm long. In addition to the short and long term data available for TVT and TVT-O prior to the launch of TVT Abbrevo, a study by the Department of Urology at the University of Liege, Belgium*[106] *demonstrated similar efficacy for TVT Abbrevo when compared to TVT-O. This study was accepted for publication prior to the launch of TVT Abbrevo. The one and three year follow-up results confirmed that TVT Abbrevo is a safe and effective treatment option with complication rates and objective and subjective cure rates similar to TVT and TVT-O.'*[63]
August 2010	Iglesia et al.	**Vaginal mesh for prolapse: a randomized controlled trial**[107] Multicenter, double-blind RCT comparing traditional vaginal prolapse surgery without mesh with vaginal surgery with mesh. There were 5 vaginal mesh erosions. Two cystotomies and 1 blood transfusion occurred in the mesh group only. Subjective cure of bulge symptoms was noted in 93.3% of mesh patients and 100% of no-mesh patients. Subjective quality-of-life measurements did not differ between the groups at baseline or 3 months postoperatively.

[105] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh, page 37, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[106] de Leval J, Thomas A, Waltregny D. The original versus a modified inside-out transobturator procedure: 1-year results of a prospective randomized trial. Int Urogynecol J. 2011 Feb;22(2):145-56; Waltregny D, de Leval J. New surgical technique for treatment of stress urinary incontinence TVT-ABBREVO from development to clinical experience. Surg Technol Int. 2012 Dec;22:149-57.

[107] C. B. Iglesia *et al.*, Vaginal mesh for prolapse: a randomized controlled trial. *Obstet Gynecol* **116**, 293-303 (2010).

		Trial halted as at 3 months, there was a high vaginal mesh (Prolift) erosion rate (15.6%) with no difference in overall objective and subjective cure rates. *'This study questions the value of additive synthetic polypropylene mesh for vaginal prolapse repairs'* The one-year follow-up for this study was presented in January 2012 (Sokol et al.).
October 2010	BAUS Written Evidence	*'Section Exec Committee minutes record: "clinical director of MHRA, had written… expressing concerns relating to tape surgery. He said they were convening a meeting…to look at the issues." No further information or notes of such a meeting in BAUS records'*[108]
October 2010	Ostergard, D.	**Polypropylene Vaginal Mesh Grafts in Gynecology**[109] 'Current commentary' in *Obstetrics & Gynecology* which draws together basic concepts in the use of polypropylene mesh in the treatment of POP and SUI. The author discusses implantation of the mesh via a 'clean-contaminated' environment (the vagina) and the balance between the bacteria that consequently colonise the mesh and the host immune system that are recruited to defend against this bacterial invasion. The author suggests that devices with larger surface areas result in greater bacterial contamination, more polypropylene degradation, increased inflammatory response, fibrous tissue stimulation, and erosion. Non-inert polypropylene, he states, degrades into potentially toxic compounds that would be expected to stimulate a greater inflammatory reaction leading to erosion. The author warns that if the physician does not; place the mesh below full-thickness vaginal epithelium, penetrates the epithelium during insertion, or if there is hematoma formation near the vaginal incision, then defective healing and erosion may result. Scar tissue causes contraction to less than 50% of the implanted

[108] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 136, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[109] D. R. Ostergard, Polypropylene vaginal mesh grafts in gynecology. *Obstet Gynecol* **116**, 962-966 (2010).

		size. Such contraction may cause pelvic pain and subsequent erosion into adjacent organs. An individual response in fibrosis also exists, according to Ostergard, with some individuals being "high responders", with more extensive fibrosis stimulated by mesh. The author concludes that polypropylene is not inert within the human body, and that manufacturers need encouragement to develop meshes that are inert and incorporate without contraction along with routine clinical tests to detect "high responders" to avoid complications.
19th January 2011	Cochrane	**Traditional suburethral sling operations for urinary incontinence in women**[110] Update to 2005 review. 13 new RCTs added. Authors conclude that traditional slings seem to be as effective as minimally invasive slings, but had higher rates of adverse effects. Authors note that this should be interpreted with some caution however, as the quality of evidence for the studies was variable, follow-up short and populations small, particularly for identifying complication rates. Traditional sling procedures appeared to confer a similar cure rate in comparison to open retropubic colposuspension, but the long-term adverse event profile is still unclear. Reliable evidence to clarify whether or not traditional suburethral slings may be better or worse than other surgical or conservative management options is lacking.
March 2011	MHRA Written Evidence[111]	*'In response to increasing number of adverse incident reports (42 reports in 2010 from the use of slings for female Stress Urinary Incontinence (SUI) to MHRA by the public, manufacturers and users, we hosted a workshop to better understand the use of these SUI devices and complications associated with their use. Chaired by Professor Abrams (then Director of Bristol Urological Institute), representatives included the Royal College of Obstetricians and Gynaecologists (RCOG), manufacturers, and National Institute for*

[110] H. Rehman, C. C. Bezerra, H. Bruschini, J. D. Cody, Traditional suburethral sling operations for urinary incontinence in women. *The Cochrane database of systematic reviews*, Cd001754 (2011).
[111] IMMDSR written evidence, Public Bodies, Page 168, available online, at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Public%20Bodies.pdf

		Health and Care Excellence (NICE). A summary of the discussion and recommendations were published in the European Urology Journal. It concluded: *"The clinicians at the meeting concluded that all parties need to ensure that they fulfil their obligations to optimise patient safety and to ensure that patients only receive devices that are likely to produce a significant improvement in their incontinence and to deliver a satisfactory quality of life. The key points to improving the current situation when a new device is introduced into the market are as follows:* - *Adequate clinical evidence should be available to support its safety and efficacy.* - *A standard for training and mentorship for the use of a significantly new device should be produced by the professional organisations.* - *A register should be established, or a formal systematic post market surveillance programme introduced when a new device is introduced so safety and efficacy can be judged when the device is used by the wider surgical community.* - *Surgeons should be reminded of the MHRA reporting system, particularly when a new device is introduced; a "red card" system should be seriously considered"'*
June 2011	BAUS Written Evidence	BAUS response to consultation on urinary incontinence update: *'Women with persistent or recurrent SUI and women with tape complications should be treated in a specialist centre that sees an adequate number of complex cases to ensure that patients are treated effectively.'*[112]
July 2011	FDA	**Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse**[113] Update from the FDA states that serious adverse events attributed to the use of such products is **not** rare and included serious complications, such as vaginal erosions, infections, and organ perforation. Transvaginally placed mesh in POP repair does **not**

[112] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 136, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[113] FDA, 2011, Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse, available online at: http://www.fda.gov/downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf

		conclusively improve clinical outcomes over traditional non-mesh repair. 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, received from 1 January 2005 - 31 December 2010. 2874 reports were received between 1 January 2008 and 31 December 2010 and included 1,503 reports associated with POP repairs and 1,371 associated with SUI repairs. The most frequent complications from mesh POP repair included vaginal mesh erosion (35%), followed by pain (31%), infection, bleeding, dyspareunia, and organ perforation.
July 2011	MHRA Written Evidence[114]	*'At a Committee on Safety of Devices (CSD – Devices' independent expert committee) [meeting] we raised awareness of March 2011 workshop as above and plans for information to be published. They agreed further investigation was required.'*
29th July 2011	Institute of Medicine	**Medical Devices and the Public's Health – The FDA 510(k) Clearance process at 35 years[115]** The Institute of Medicine in America released a report recommending the replacement of the 510(k) clearance process for medical devices (the process by which most mesh products were cleared based on equivalence) The report concludes that the 510(k) process lacks the legal basis to be a reliable premarket screen of the safety and effectiveness of moderate-risk Class II devices and cannot be transformed into one. It is recommended that the FDA develop a new framework that uses both premarket clearance and improved post-market surveillance of device performance to provide reasonable assurance of the safety and effectiveness of Class II devices throughout the duration of their use.
August 2011	Scottish Mesh Survivors	Patient group established.

[114] IMMDSR written evidence, Public Bodies, Page 169, available online, at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Public%20Bodies.pdf

[115] Institute of Medicine, 2011, Medical Devices and the Public's Health – The FDA 510(k) Clearance process at 35 years, available online at: http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2011/Medical-Devices-and-the-Publics-Health-The-FDA-510k-Clearance-Process-at-35-Years/510k%20Clearance%20Process%202011%20Report%20Brief.pdf

September 2011	MHRA Written Evidence[116]	*'Product specific information for vaginal tapes for SUI was published on the MHRA website to provide information to patients and healthcare professionals. This included a list of questions for patients to ask their surgeon prior to surgery'*
December 2011	Abrams et al.	**Synthetic Vaginal Tapes for Stress Incontinence: Proposals for Improved Regulation of New Devices in Europe[117]** This paper reports on the issues discussed at the MHRA meeting (held 16th March 2011) under the headings of product development, clinical adoption, clinician training, the reporting of outcomes and adverse events, and finally, it lists the proposed responsibilities for manufacturers, the regulator, and clinicians. **Product Development:** Meeting attendees though that new devices should undergo clinical trials to prove safety and performance for the purpose of CE marking and comparative studies in the post-market phase to assess differences between new and existing products. The process of equivalence in CE marking was criticised as a weak point in the process. **Introducing new products into clinical practice:** It was suggested that it would be useful for BAUS and BSUG to produce a standard for training/mentorship for those surgeons wishing to implant a tape that was new to their practice. Producing and updating training manuals for new devices every 6 months was also recommended. **Reporting of patient outcome and adverse events:** Tracking of new patients with a unique sticker attached to operating notes, with a simple questionnaire to be completed by surgeon at the time of operation, used to establish a register. This would

[116] IMMDSR written evidence, Public Bodies, Page 169, available online, at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Public%20Bodies.pdf
[117] P. Abrams *et al.*, Synthetic vaginal tapes for stress incontinence: proposals for improved regulation of new devices in Europe. *European urology* **60**, 1207-1211 (2011).

		allow each tape to be tracked and adverse outcomes to be reported. All adverse events should be reported to MHRA (who believe that there is significant underreporting). **Future Research:** There is a need for RCTs at an early developmental stage for a new device – not low-quality case studies. **Responsibilities of involved parties:** Manufacturers should thoroughly test devices, ensure appropriate clinical data, ensure comprehensive, regularly updated 'Instructions for Use' with unique stickers inside for attachment to patient notes, ensure adequate training programmes and post-market surveillance programmes and report all serious AEs to the MHRA. Clinicians should choose devices with sufficient clinical data on safety/efficacy, ensure familiarity with NICE appraisal and guidelines, ensure adequate training, ensure that clinicians partake in refresher courses, ensure proper patient selection, ensure proper patient consent, that details of the device are entered into case notes, that BAUS, BSUAG and SFNUU prepare a list of adverse events and report all AEs to MHRA. MHRA should investigate all reported AEs with the manufacturer if appropriate, ensure that relevant clinical advice is developed before issuing Medical Device Alerts, promote a specific webpage for urologists on the MHRA website and ensure feedback to clinicians about AEs and outcomes at regular time intervals.
3rd January 2012	FDA	FDA orders 34 manufacturers of surgical mesh for transvaginal repair of POP to conduct new post-market safety studies (522 studies), lasting at least 3 years to address safety concerns.[118] Under s.522 of the Food, Drug and Cosmetic Act (1938), the FDA has the power to mandate manufacturers to undertake post-market surveillance studies of class II or III devices, among other criteria,

[118]FDA, 522 Postmarket Surveillance Studies Database , viewed 9 August 2019, available online at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pss.cfm

		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'. Most manufacturers elected to stop marketing surgical mesh for transvaginal repair of pelvic organ prolapse after receiving their 522 orders. There were four ongoing 522 studies for five devices.
January 2012	Sokol et al.	**One-year Objective and Functional Outcomes of a Randomized Clinical Trial of Vaginal Mesh for Prolapse**[119] 12-month outcomes of a randomised trial that compared vaginal prolapse repair with and without mesh (see Iglesia et al. 2010). Thirty-two women had mesh repair; 33 women had traditional repair. At 12 months, both groups had improvement of pelvic organ prolapse-quantification test points to similar recurrence rates. The quality of life improved and did not differ between groups: 96.2% mesh vs 90.9% no-mesh subjects reported a cure of bulge symptoms; 15.6% had mesh exposures, and reoperation rates were higher with mesh. Exposures were noted only with Prolift mesh and not with sling mesh. Of the 33 no-mesh participants, 5 women (15%) had apical Gore-tex suture exposures. Rates of dyspareunia for mesh and non-mesh procedures were reported at 6.7% and 18.8%, respectively. Authors conclude that *'Objective and subjective improvement is seen after vaginal prolapse repair with or without mesh. However, mesh resulted in a higher reoperation rate and did not improve 1-year cure'*
March 2012	MHRA Written Evidence[120]	*'We hosted a second workshop at MHRA but this time it was on POP mesh. Chaired by Prof Paul Abrams, attended by relevant leading expert clinicians in urogynaecology, including representatives of the Royal College of Obstetricians and Gynaecologists (RCOG), the British Association of Urological Surgeons (BAUS) and the British Association of Urogynaecologists (BSUG) together with*

[119] A. I. Sokol *et al.*, One-year objective and functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. *American journal of obstetrics and gynecology* **206**, 86.e81-89 (2012).
[120] IMMDSR written evidence, Public Bodies, Page 170, available online, at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Public%20Bodies.pdf

		representatives of the leading manufacturers of vaginal meshes to discuss device regulation, use and information for patients. Early draft findings from the PROSPECT trial were verbally presented to the group. Actions included: - *List of responsibilities drafted for manufacturers, Notified Bodies, MHRA. Clinicians and hospitals* - *Discussion with Bruce Keogh about a register for these devices (taken up by Department of Health led group and subsequently the NHS Mesh Working Group)* - *Writing to professional bodies about importance of reporting adverse events (facilitated by Committee of Safety of Devices (CSD) and our relationships with Royal Colleges etc)* - *Request National Institute for Health and Care Excellence (NICE) to re-look at procedures associated with these devices (taken forward by NICE)* - *Patient information leaflets be developed by clinical community* - *MHRA website pages updated to include notes of meeting and pages aimed at urology & gynaecology professionals,* - *MHRA webpage aimed at patients'*
March 2012	BAUS Written Evidence	Section Executive committee minutes record - MHRA request for notice to membership re. vaginal slings: Recent discussions with the MHRA where outlined, during which *'concerns had been raised about tape erosion. Members agreed that collecting data on this would be relevant at this time as there was not good data available on long term erosion rates. Unless there was a registry of all implants and data entry was mandatory, then it was impossible to get good base line data. Any registry would have to be financed, it was noted the national hip register was financed by the inclusion of a charge for the national registry being added to the tariff for all hip implants. It was thought a similar system should apply for all implants.*[121] *'Discussions about implant registries would be taken forward with MHRA.'*

[121] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 136, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

May 2012	Ethicon Written Evidence	Ethicon made the decision to discontinue the following products: - Gynecare Prosima Pelvic Floor Repair System - Gynecare Prolift Systems - Gynecare Gynemesh M - Gynecare Prolift +M Pelvic Floor Repair System - Gynecare TVT Secur System *'The decision to cease worldwide distribution of the products was a business decision made on the basis of commercial viability of the products and decline in the worldwide market and was not related to the safety or efficacy of the devices.'*[122] *'The precise date on which sales of the products ceased varied from market to market and within markets and depended on factors which included existing tender commitments. In general terms the de-commercialisation process in the EU (including the UK) began in Q1 2013 and was intended to be complete by the end of the year.'*[74] *'As this was not a product recall and was not driven by safety concerns, Ethicon informed customers that they were able to continue using any product(s) in their hospital(s) beyond the date of discontinuance, provided that the individual units were not expired.'*[74]
20th September 2012	BAUS Written Evidence	Letter from Adrian Joyce, then President of BAUS, to Professor Sir Bruce Keogh regarding patient complications relating to the use of mesh implants for prolapse and incontinence surgery.[123] Urologists concerns for mesh tapes outlined and letter stresses the need for a meeting with RCOG, BSUG and MHRA as soon as possible regarding mesh issues, as well as the possibility of establishing a national implant registry.

[122] IMMDS Review, Written Evidence, Manufacturers of Pelvic Mesh page 20, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Manufacturers%20of%20Pelvic%20Mesh.pdf

[123] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 153, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

November 2012	York Economics Consortium for MHRA	**Summaries of the Safety/Adverse Effects of Vaginal Tapes/Slings/Meshes for Stress Urinary Incontinence and Prolapse – final report**[124] Reviewed published literature on adverse events. Key findings: • Vaginal tapes for SUI: adverse events generally in the range 1-3% (0% postoperative pain/discomfort after 6 months in some studies but as high as 9% for deterioration in sexual function after 6 months for one technique); • Vaginal meshes for POP: adverse events are in the range 2-6% for most outcomes, but 14-15% for deterioration in sexual function after 6 months following prolapse surgery in some studies.
November 2012	BAUS Written Evidence	Section Executive minutes record[125] Slings and complications of mid-urethral tapes data: *'It was reported that this had been launched at BAUS 2012 following some changes to the dataset. There had been 63 returns from 13 centres, but it was noted only 50% had completed the Quality of Life form from patients. As revalidation comes on stream people would be required to enter data in compliance with audits for revalidation'* *'BAUS audit of SUI launched in June 2012, BAUS members advised that data collected in 2014 would be published in 2015 as part of the consultants' outcome project.'* In November 2012, the Department of Health published a press notice to coincide with the publication of the York report in which they announced The Department of Health, the NHS Commissioning Board, NHS surgeons (urologists and gynaecologists), and the Medicines and Healthcare products Regulatory Agency (MHRA) were taking action to help reduce the side effects after surgery using vaginal tape for stress incontinence and vaginal

[124] J. Mahon, M. Cikalo, D. Varley, J. Glanville, *Medicines and Healthcare Products Regulatory Agency - Summaries of the Safety/Adverse Effects of Vaginal Tapes/Slings/Meshes for Stress Urinary Incontinence and Prolapse - Final Report*, York Health Economics Consortium (2012)
[125] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 137, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

		meshes for pelvic organ prolapse. They included an outline action plan to address the issues raised by the report. *'There had been a rush to pull this together but following publication BAUS heard nothing further from NHS England until it received an email on 5 August 2013 inviting BAUS to take part in a teleconference on 24 September 2013. The teleconference on 24 September was chaired by Catherine Calderwood, then National Clinical Director, Maternity and Women's Health, it was agreed there needed to be further discussion'*
21st November 2012	NHS England	Letter from NHS England (still known then as the NHS Commissioning Board) to NHS Medical Directors: **Vaginal Tapes and Meshes**[126] which draws attention to a report on the rates of common adverse events associated with vaginal tapes (the 'York study') and action plan agreed by DH, NHSE, MHRA and professional associations. The key elements were: • To develop proposals for a single registry of vaginal implants, building on the existing registries maintained by the professional associations; • To develop and issue professional guidance for surgery using vaginal meshes, complementing existing NICE guidance, on aspects such as selection of patients, choice of device, and processes for informed patient consent; • To develop and issue guidance to commissioners to enable them to commission services from providers which maintain high standards of training and clinical audit; • To develop and issue professional guidance on those centres competent to carry out surgery for women with recurrent problems from incontinence or prolapse, or women needing further surgery as a result of complications.
22nd November 2012	Department of Health and Social Care	Press release published, stating that the *'Department of Health, clinical groups and the MHRA are working together to make sure that surgeons have all the necessary guidance and support to carry out these*

[126] Letter from Sir Bruce Keogh to NHS medical directors, 2012, viewed 9 August 2019, available online at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/213189/Vaginal-tapes-and-meshes-letter-to-NHS-final1.pdf

		operations as safely and effectively as possible, and that women feel reassured before making decisions about undergoing surgery . These measures will include developing proposals for a registry for implanted vaginal tapes and meshes to help surgeons to compare the outcomes of their treatment.'
December 2012	Albo et al.	**Treatment Success of Retropubic and Transobturator Mid Urethral Slings at 24 Months**[127] Continence rates, complications and symptom outco mes from a randomised equivalence trial. Primary outcomes were objective (negative stress test, negative pad test and no re-treatment for stress urinary incontinence) and subjective (no self-report of stress urinary incontinence symptoms, no leakage episodes on 3-day bladder diary and no re-treatment for stress urinary incontinence) success at 24 months. Objective success rates for retropubic and transobturator mid urethral slings were 77.3% and 72.3%, respectively, and subjective success rates were 55.7% and 48.3%, respectively. Patient satisfaction rates for retropubic and transobturator midurethral slings were 86.3% and 88.1% respectively. Authors conclude that *'Objective success rates met the criteria for equivalence at 12 months but no longer met these criteria at 24 months. Subjective success rates remained inconclusive for equivalence. Patient satisfaction remained high and symptom severity remained markedly improved. Continued surveillance is important in women undergoing mid urethral sling surgery'*
28th February 2013	Cochrane	**Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery in women**[128] Twelve studies were identified, but all were excluded because they did not meet the eligibility criteria.

[127] M. E. Albo *et al.*, Treatment success of retropubic and transobturator mid urethral slings at 24 months. *J Urol* **188**, 2281-2287 (2012).
[128] E. Bakali, B. S. Buckley, P. Hilton, D. G. Tincello, Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery in women. *The Cochrane database of systematic reviews*, Cd009407 (2013).

		Authors conclude that there were no data to recommend or refute any of the different management strategies for recurrent or persistent stress incontinence after failed suburethral tape surgery. Evidence is urgently required to address this deficiency, ideally from RCTs.
27th March 2013	FDA	FDA updated the Urogynecologic Surgical Mesh Implant website to include more information for patients about stress urinary incontinence (SUI). This update provides the FDA's current thinking about the use of surgical mesh for repair of SUI and is based on an analysis of adverse events reported to the FDA, findings reported in the scientific literature and input received from the Sept. 9, 2011 meeting of the Obstetrics and Gynecology Devices Panel of the Medical Device Advisory Committee.[129]
April 2013		NICE was established in primary legislation, as set out in the Health and Social Care Act 2012[130]. NICE took on responsibility for developing guidance and quality standards in social care.
April 2013		Review of Regulation of Cosmetic Interventions discussed recommendations for a register of breast implants, but not for all high-impact medical devices as suggested in the NHS England letter of 2012[131].
6th April 2013	Nilsson et al.	**Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence**[132] 90 women operated on with TVT were followed for 17 years. 58 women were included in the final evaluation. Seventy-eight percent of the potentially assessable women were evaluated either by a clinic visit or by a telephone interview. One case of a minimal, symptom-free tape extrusion was seen. No other tape complications occurred. Over 90% of the women were objectively continent (stress test). Eighty-seven per cent were subjectively cured or significantly improved.

[129] FDA website, viewed 17 March 2020, available online at: https://www.fda.gov/medical-devices/urogynecologic-surgical-mesh-implants/fdas-activities-urogynecologic-surgical-mesh
[130] UK government legislation, national archives, 2012, viewed 9 August 2019, available online at: http://www.legislation.gov.uk/ukpga/2012/7/part/8/enacted
[131] https://www.gov.uk/government/publications/review-of-the-regulation-of-cosmetic-interventions
[132] C. G. Nilsson, K. Palva, R. Aarnio, E. Morcos, C. Falconer, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J* **24**, 1265-1269 (2013).

May 2013	Wai et al.	**Patient Satisfaction After Midurethral Sling Surgery for Stress Urinary Incontinence**[133] Study designed to identify factors that may contribute to patient satisfaction with outcome in women who received retropubic and transobturator midurethral slings. Satisfaction was assessed 12 months postoperatively in women taking part in the TOMUS trial (see Richter et al. 2010) using the Incontinence Surgery Satisfaction Questionnaire. Both treatment groups experienced high levels of satisfaction, with 85.9% in the retropubic and 90.0% in the transobturator group reporting that they were either "mostly" or "completely" satisfied with respect to urine leakage, with no significant difference between the two routes of surgery. The majority of patients were highly satisfied with respect to other measures on the questionnaire, specifically with urgency to urinate, frequency of urination, capability of physical activity, social activity, ability to engage in sexual activity, and from an emotional standpoint, with no significant difference between the two procedures. Additionally, more than 95% of participants in both sling groups indicated that they would still choose to have the surgery or recommend it to a family member or friend if they could go back in time with the knowledge and experience they acquired after the surgery. Authors conclude that *'The high level of satisfaction seen after midurethral sling procedures is associated with greater objective and patient-perceived improvement of stress incontinence and fewer complications'*
25th June 2013	Welsh Mesh Survivors	Patient group established.
July 2013	Senapati et al.	**PROSPER: a randomised comparison of surgical treatments for rectal prolapse**[134] A systematic review on the surgical treatment of constipation. It had been hoped that the PROSPER trial would provide an evidence base for surgery in this field. This was not the case. No significant differences were seen in any of the randomised

[133] C. Y. Wai *et al.*, Patient satisfaction after midurethral sling surgery for stress urinary incontinence. *Obstet Gynecol* **121**, 1009-1016 (2013).
[134] Senapati et al (2013) PROSPER: a randomised comparison of surgical treatments for rectal prolapse doi: 10.1111/codi.12177

		comparisons, although substantial improvements from baseline in quality of life were noted following all procedures.
August 2013	Svenningsen et al.	**Long-term Follow-Up of the Retropubic Tension-Free Vaginal Tape Procedure**[135] Population-based prospective study of 483 women who had undergone a retropubic TVT procedure, designed to evaluate the long-term objective and subjective outcomes 10 years postoperatively. Objective cure rate was 89.9 %, subjective cure rate was 76.1 %, and 82.6 % of the patients stated they were "very satisfied" with their surgery (treatment satisfaction rate). Only 2.3 % of the women had undergone repeat SUI surgery. Subjective voiding difficulties were reported by 22.8 %, the majority describing slow stream or intermittency. *De novo* urgency incontinence increased significantly from 4.1 % 6–12 months after surgery to 14.9 % at the 10-year follow-up. Authors conclude that *'Long-term objective and subjective outcome after retropubic TVT is excellent with a low number of reoperations even in a non-selected cohort of patients.'*
11th September 2013	NICE	NICE guideline CG40 is updated to **CG171 - Urinary incontinence: The management of urinary incontinence in women**[136]. There is a focus on MDT working, as well as new guidance to: - Offer invasive therapy for SUI only after MDT review. - If women are offered a procedure involving the transobturator approach, make them aware of the lack of long-term outcome data. - Use 'top-down' retropubic tape approach only as part of a clinical trial. - Refer women to an alternative surgeon if their chosen procedure is not available from the consulting surgeon.

[135] R. Svenningsen, A. C. Staff, H. A. Schiøtz, K. Western, S. Kulseng-Hanssen, Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int Urogynecol J* **24**, 1271-1278 (2013).
[136] NICE, The National Archives, 2013, viewed 9 August 2019, available online at: https://webarchive.nationalarchives.gov.uk/20150506071149/https://www.nice.org.uk/guidance/CG171/chapter/1-Recommendations#the-multidisciplinary-team-mdt-2

		When offering a synthetic mid-urethral tape procedure, surgeons should: - use procedures and devices for which there is current high-quality evidence of efficacy and safety - only use a device that they have been trained to use - use a device manufactured from type 1 macroporous polypropylene tape - consider using a tape coloured for high visibility, for ease of insertion and revision. The guideline only recommends the use of tapes with proven efficacy based on robust RCT evidence. However, *'technological advances are frequent, therefore the choice of tape should include devices that are shown in future clinical trials to have equal or improved efficacy at equal or lower cost'* At the time of publication, the following met the Guideline Development Group criteria: - TVT or Advantage for a 'bottom-up' retropubic approach - TVT-O for an 'inside-out' transobturator approach - Monarc and obtryx halo for an 'outside-in' transobturator approach.
24th September 2013	European Commission	Commission recommendation on the audits and assessments performed by notified bodies in the field of medical devices is published.[137] The recommendation focusses on the Notified Body's duty to employ audits and assessments to ensure conformity of products to design dossiers as part of manufacturer applications for CE marks, as well as conformity of quality systems with EU Directive requirements. It is also recommended that, to verify the day-to-day compliance with legal obligations, notified bodies should, in addition to the initial, surveillance or renewal audits, visit the manufacturer or, if this is likely to ensure more efficient control, one of its subcontractors in charge of processes which are essential for ensuring compliance with legal requirements.

[137] Commission Recommendation on the audits and assessments performed by notified bodies in the field of medical devices, Official Journal of the European Union, viewed 05/11/19, available online at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:253:0027:0035:EN:PDF

December 2013	BAUS Written Evidence	*'Letter from Bruce Keogh sent to the Health Service, BAUS President was a co-signatory. BAUS drew this to the attention of all members, updated information on website and included link to MHRA.'*[138] Although this letter refers to centres for removal of mesh which are recognised by Commissioners or via Specialised Commissioning processes, BAUS state that *'it would be fair to say that these processes are still in development. Following this letter BAUS wrote to members inviting centres to self-nominate and subsequently published a list of centres, jointly with BSUG, each organisation included the list on its website'* see: https://www.baus.org.uk/patients/sui_mesh_complications.aspx
December 2013	SIMS Trial	**Adjustable Anchored Single-Incision Mini-Slings Versus Standard Tension-Free Mid-Urethral Slings in the Surgical Management Of Female Stress Urinary Incontinence; A Pragmatic Multicentre Non–Inferiority Randomised Controlled Trial**[139] The SIMS RCT began. The trial is still ongoing. The aim of this pragmatic multicentre RCT is to determine the clinical effectiveness and cost-effectiveness of adjustable anchored Single Incision MIni-Slings (SIMS) compares to tension-free Standard Mid-Urethral Slings (SMUS) in the surgical management of female stress urinary incontinence (SUI). The hypothesis being tested is that patient-reported success rate following surgical treatment with adjustable anchored SIMS procedures is non-inferior to tension-free SMUS while the former is associated with less post-operative pain, shorter hospital stay, earlier recovery and consequently earlier return to usual activities/work and is more cost effective than SMUS.
January 2014		In January 2014, the European Commission asked the SCENIHR to provide an opinion on the safety of

[138] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 138, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[139] Trial website viewed 05/11/19, available online: https://w3.abdn.ac.uk/hsru/sims/

		surgical meshes used in urogynaecological surgery.[140]
February 2014	Mostafa et al.[141]	**Single-Incision Mini-Slings Versus Standard Midurethral Slings in Surgical Management of Female Stress Urinary Incontinence: An Updated Systematic Review and Meta-analysis of Effectiveness and Complications[142]** This meta-analysis shows that, excluding TVT-Secur, there was no evidence of significant differences in patient-reported and objective cure between currently used single-incision minislings and standard midurethral slings at mid-term follow-up while associated with more favourable recovery time. Results should be interpreted with caution due to the heterogeneity of the trials included.
20th March 2014	MHRA	**Patient Safety Alert – Improving medical device incident reporting and learning[143]** Patient Safety Alert regarding the joint efforts of NHS England and the MHRA to simplify and increase reporting, improve data quality, maximise learning and guide practice to minimise harm from medical devices by: - sharing incident data between the MHRA and NHS England, reducing the need for duplicate data entry by frontline staff by developing a new integrated National Learning and Reporting System (NRLS). Separate reporting to the MHRA will then no longer be necessary; - giving new types of feedback from the NRLS and the MHRA to improve learning at local level; - clarifying medical device safety roles and identifying key safety contacts to allow better

[140] NHS England, 2015, Mesh Working Group - Interim Report, viewed 9 August 2019, available online at: https://www.england.nhs.uk/wp-content/uploads/2015/12/mesh-wg-interim-rep.pdf

[141] Initially this article did not contain a full declaration of funding. This was subsequently corrected see ***Corrigendum re "Prospective Randomised Controlled Trial of Transobturator Tapes in Management of Urodynamic Stress Incontinence in Women: 3-Year Outcomes from the Evaluation of Transobturator Tapes Study" [Eur Urol 2012;62:843–51]*** *Abdel-fattah, Mohamed et al. European Urology, Volume 75, Issue 4, e119*

[142] A. Mostafa, C. P. Lim, L. Hopper, P. Madhuvrata, M. Abdel-Fattah, Single-Incision Mini-Slings Versus Standard Midurethral Slings in Surgical Management of Female Stress Urinary Incontinence: An Updated Systematic Review and Meta-analysis of Effectiveness and Complications. *European urology* **65**, 402-427 (2014).

[143] MHRA, Patient Safety Alert – Improving medical device incident reporting and learning, Alert number NHS/PSA/D/2014/006, 2014, viewed 18/10/2019, available online at: https://www.england.nhs.uk/wp-content/uploads/2014/03/psa-med-device-inci.pdf Via

		communication between local and national level; - setting up a National Medical Devices Safety Network as a new forum for discussing potential and recognised safety issues, identifying trends and actions to improve the safe use of medical devices. Instructions are given to continue reporting separately to the MHRA and the NRLS until the integrated reporting system becomes operational.
30th April 2014	Scottish Mesh Survivors	Elaine Holmes and Olive McIlroy on behalf of Scottish Mesh Survivors - "Hear Our Voice" campaign launched a petition[144] calling for a reclassification and suspension of transvaginal mesh procedures, a public enquiry, mandated reporting of adverse events, a Scottish mesh implant register and improved informed consent from the Scottish Government.
13th May 2014	Health Canada	Health Canada issued safety information to hospitals regarding the use of mesh placed transvaginally to treat POP and SUI[145]. Regarding mesh placed transvaginally to treat POP, Health Canada stated that these procedures have a higher risk of complications compared to native tissue repair and mesh placed abdominally. complications associated with these procedures (as well as mesh used to treat SUI) may require additional surgery to repair which may not fully correct the complications, and surgeons placing these devices should have adequate training and be familiar with the device labelling. For mesh used to treat SUI, Health Canada state that *'traditional mid-urethral sling procedures for the treatment of SUI have been extensively studied, and are commonly performed for SUI repair.'* Single-incision mini sling procedures are novel and may carry a higher risk of complications than traditional midureth eal slings.

[144] The Scottish Parliament, Petitions, PE01517: Polypropylene Mesh Medical Devices, viewed 9 August 2019, available online at: http://www.parliament.scot/GettingInvolved/Petitions/scottishmeshsurvivors

[145] Health Canada, Recalls and safety alerts, 2014, Surgical Mesh – Complications Associated with Transvaginal Implantation for the Treatment of Stress Urinary Incontinence and Pelvic organ Prolapse – Notice to Hospitals, viewed 9 August 2019, available online at: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/39475a-eng.php

28th May 2014	Therapeutic Goods Administration (TGA) – Australia Review	Review into urogynaecological surgical mesh implants (based on TGA monitoring of surgical meshes since 2008) publishes outcomes[146]. The review found that the use of urogynaecological surgical mesh devices for the surgical treatment of SUI and abdominal POP repair is adequately supported by the evidence. However, due to the poor-quality of the studies undertaken, the evidence to support the use of these meshes for transvaginal POP repair, particularly, posterior repair, is not well established. The TGA review also found that, while adverse events involving these devices are likely under-reported, the reported complication rate remains low. From July 2012 to 3 April 2014, the TGA received 32 adverse events reports involving urogynaecological surgical meshes. The most frequently reported adverse events were pain and erosion. The TGA review identified inadequate training/experience for implanting surgeons as a factor in increasing the risk of complications. Certain patients, including those who smoked or were obese, were found to be at higher risk of adverse events and repeated procedures. Each mesh product was reassessed for clinical effectiveness and safety and those not found not to be compliant, faced regulatory action, such as cancellation or suspension from the Australian register of therapeutic goods (ARTG).
1st June 2014	Cochrane	**Single-incision sling operations for urinary incontinence in women[147]** The review includes 31 trials involving 3290 women. The authors conclude that TVT-Secur is inferior to standard mid-urethral slings for the treatment of women with stress incontinence. Indeed, it had already been withdrawn from clinical use. They concluced that there was not enough evidence on

[146] TGA, Australian Government Department of Health, 2014, Results of review into urogynaecological surgical mesh implants, viewed 8 August 2019, available online at: https://www.tga.gov.au/behind-news/review-urogynaecological-surgical-mesh-implants

[147] A. Nambiar, J. D. Cody, S. T. Jeffery, Single-incision sling operations for urinary incontinence in women. *The Cochrane database of systematic reviews*, Cd008709 (2014).

		other single-incision slings compared with retropubic or transobturator slings to allow reliable comparisons. Additional adequately powered and high-quality trials with longer-term follow-up are required. Trials should clearly describe the fixation mechanism of these single-incisions slings.
4th June 2014	BAUS Written Evidence	BAUS was invited to join NHS England working group chaired by Professor Keith Willett.[148]
10th June 2014	House of Commons	Short debate in response to question from MP Graeme Morris regarding a review of the safety of polypropylene transvaginal mesh implants. The Parliamentary under-Secretary of State for Health (Dr Daniel Poulter) replied that *'The Department of Health, NHS England and the Medicines and Healthcare Products Regulatory Agency—the MHRA—have been working collaboratively with the clinical community to address the serious concerns that have been raised about transvaginal mesh implants. A working group, chaired by NHS England, has been set up to identify ways to address them. The group will also have patient representation.'*[149]. He states that an *'NHS England-funded audit on urogynaecological procedures for stress urinary incontinence is currently taking place, which covers all procedures, not just mesh implants.'*
17th June 2014	Scottish Cabinet Secretary for Health and Wellbeing	The former Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, announced the Transvaginal mesh implants independent review. The acting Chief Medical Officer, Dr Aileen Keel, wrote to all Health Boards requesting that they consider suspending use of synthetic mesh for these procedures until the independent review reported its findings[150].
24th June 2014	Khan et al.	**Long-term follow-up of a multicentre randomised controlled trial comparing tension-free vaginal tape, xenograft and autologous fascial slings for**

[148] IMMDS Review, Written Evidence, Professional and Trade Bodies, page 139, viewed 27 August 2019, available online at: http://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20-%20Professional%20and%20Trade%20Bodies.pdf

[149]Hansard, House of Commons, Oral Answers to Questions, 10 June 2014, viewed 9 August 2019, available online at: https://hansard.parliament.uk/Commons/2014-06-10/debates/14061052000013/PolypropyleneTransvaginalMeshImplants

[150] Scottish Government, Department of Health and Social Care, 2017, Transvaginal mesh implants independent review: final report, Chapter 1, viewed 9 August 2019, available online at: https://www.gov.scot/publications/scottish-independent-review-use-safety-efficacy-transvaginal-mesh-implants-treatment-9781786528711/pages/3/

		the treatment of stress urinary incontinence in women[151] A multicentre randomised controlled trial carried out in four UK centres from 2001 to 2006 involving 201 women requiring primary surgery for SUI. Designed to compare the long-term outcomes of TVT, autologous fascial sling (AFS) and xenograft sling. Authors conclude that there is not enough evidence to suggest a difference in long-term success rates between AFS and TVT. However, there is some evidence that cure (dry) rates for AFS may be more durable than TVT.
June 2014	Laurikainen et al.	**Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence**[152] Study designed to compare the efficacy and safety of retropubic tension-free vaginal tape (TVT) and transobturator tension-free vaginal tape (TVT-O) procedures, 5 years after intervention. Objective success criteria were a negative stress test, a negative 24hr pad test, and no retreatment for SUI. Patient satisfaction was assessed by condition-specific quality-of-life questionnaires. The objective cure rate was 84.7% in the TVT group and 86.2% in the TVT-O group, with no statistical difference between the groups. Subjective treatment satisfaction was 94.2% in the TVT group and 91.7% in the TVT-O group, with no difference between groups. Complication rates were low, with no difference between groups. *"No woman had any sign of tissue reaction, erosion, or tape protrusion at their 5-yr follow-up. During the course of the study, two women experienced tape problems, both in the TVT-O group. One woman had a tape extrusion 1 yr postoperatively. The midline visible part of the tape was excised, resulting in incontinence, and she later had a TVT operation. One woman had retention problems, and the tape was cut*

[151] Z. A. Khan *et al.*, Long-term follow-up of a multicentre randomised controlled trial comparing tension-free vaginal tape, xenograft and autologous fascial slings for the treatment of stress urinary incontinence in women. *BJU international* **115**, 968-977 (2015).
[152] E. Laurikainen *et al.*, Five-year results of a randomized trial comparing retropubic and transobturator midurethral slings for stress incontinence. *European urology* **65**, 1109-1114 (2014).

		in the midline twice, which resolved the retention, but she experienced urgency symptoms" *De novo* urgency incontinence was exerinced by 3.1% in the TVT group and 2.4% in the TVT-O group at 5 years. At least one UTI requiring antibiotic treatment was experienced in 20.6% of the TVT group and 22.1% of the TVT-O group.
2014	CMO and MHRA	Chief Medical Officer of England asks the MHRA to review the evidence on the benefits and risk of vaginal mesh implants.
1st July 2014	Khan et al.	**Outcomes and complications of trans-vaginal mesh repair using the Prolift™ kit for pelvic organ prolapse at 4 years median follow-up in a tertiary referral centre[153]** A single-centre observational study of 106 successive patients, who underwent Prolift™ mesh repair (POP) with a median follow-up of 4 years. Mesh exposure was noted in 6 (5.6 %) women throughout the entire study period. 5.6% needed surgery for stress urinary incontinence (SUI), two for new onset and 4 for worsening SUI. 2.8% were reoperated on due to prolapse recurrence in the operated compartment, 13.2% in the non-operated compartment. Vaginal/groin pain was noted in 5.6%. Vaginal adhesions were experienced in 1.9% of patients, granulation tissue was seen in 1.9%. Authors conclude that the study demonstrates that Prolift™ vaginal mesh surgery offers anatomical cure rates of 89.9 %. A higher rate of *de novo* recurrence in the non-operated compartment was noted suggesting that surgical correction in one compartment may exacerbate recurrence in other compartments.
July 2014	Schimpf et al.	**Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis[154]** Systematic review of randomised controlled trials from 1990 to April 2013 with a minimum 12-month follow-up comparing sling procedures and Burch urethropexy.

[153] Z. A. Khan, L. Thomas, S. J. Emery, Outcomes and complications of trans-vaginal mesh repair using the Prolift kit for pelvic organ prolapse at 4 years median follow-up in a tertiary referral centre. *Archives of gynecology and obstetrics* **290**, 1151-1157 (2014).
[154] M. O. Schimpf *et al.*, Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *American journal of obstetrics and gynecology* **211**, 71.e71-71.e27 (2014).

		For MUS vs Burch, meta-analysis of objective cure showed no significant difference. For pubovaginal sling vs Burch, the evidence favoured slings for both subjective and objective cure. For pubovaginal slings vs MUS, meta- analysis of subjective cure favoured MUS. For obturator slings vs retropubic MUS, meta analyses for both objective and subjective cure favoured retropubic slings but were not significant. Meta-analysis of satisfaction outcomes favoured obturator slings but was not significant. Meta analyses of objective and subjective cure both significantly favoured full-length slings over mini-slings. Adverse events were variable between slings; meta-analysis showed overactive bladder symptoms were more common following retropubic slings.
23rd August 2014	Kenton et al.	**5-Year Longitudinal Follow-up after Retropubic and Transobturator Midurethral Slings**[155] 404 women were enrolled into the study. Treatment success decreased during 5 years for retropubic and transobturator slings, and did not meet the prespecified criteria for equivalence, with retropubic demonstrating a slight benefit. However, satisfaction remained high in both arms. Women undergoing a transobturator sling procedure reported more sustained improvement in urinary symptoms and sexual function. New mesh erosions occurred in both arms over time, although at a similarly low rate.
28th October 2014	MHRA	**'Summary of the Evidence of the Benefits and Risks of Vaginal Mesh Implants**[156]**'** is published by the MHRA based on data from an overview of systematic reviews and reports of adverse events. This report concluded that pelvic mesh is safe when used for the treatment of SUI, but that more caution was needed when using mesh for treating POP. It is noted that MHRA attended BAUS and RCOG conferences in 2013. *'there was much discussion about the use of vaginal mesh implants, and*

[155] K. Kenton *et al.*, 5-Year Longitudinal Followup after Retropubic and Transobturator Mid Urethral Slings. *The Journal of Urology* **193**, 203-210 (2015).

[156]MHRA, 2014, A summary of the evidence on the benefits and risks of vaginal mesh implants, viewed 9 August 2019, available online at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/402162/Summary_of_the_evidence_on_the_benefits_and_risks_of_vaginal_mesh_implants.pdf

		knowledge of patient concerns. However, there were no indications of vaginal mesh implants being unsafe.'. *'Benefits outweigh the risks'* for transvaginal mesh used to treat both SUI and POP although *'evidence is inadequate in quantity and quality'.* MHRA's position was that, for the majority of women, the use of vaginal mesh implants is safe and effective. However, as with all surgery, there is an element of risk to the individual patient. This conclusion is entirely dependent on compliance with NICE and other sources of guidance, which emphasise the caution that should be exercised prior to surgery being considered. The current evidence shows that when these products are used correctly, they can help alleviate the symptoms of SUI and POP and as such the benefits still outweigh the risks.
2015	Mesh Working Group	Mesh Working Group[157] is established by NHS England to address concerns raised by patient organisations and some clinicians around the safety and efficacy of surgery for stress urinary incontinence and pelvic organ prolapse, using mesh devices. One of the main objectives of the working group was to identify the evidence around use of vaginal mesh and understand other pertinent information from regulatory agencies. Stakeholders included: BSUG, MHRA, BAUS, DHSC, and patient groups. The role of NHSE in the Mesh working group (chaired by Keith Willett) was to act as broker to open and honest debate between patients, clinicians, policy makers and regulators.
2015	Devices Expert Advisory Committee	The Devices Expert Advisory Committee (DEAC) replaces the Committee on Safety of Devices and is responsible for providing independent, external expert input and advice on a wide range of aspects relating to medical devices to help the MHRA in the execution of its role in ensuring the safe introduction and management of medical devices.[158] DEAC was formed following an independent review on Medicines and Healthcare products Regulatory Agency's (MHRA) access to clinical advice and engagement with the clinical community.

[157] Webpage available online at: https://www.england.nhs.uk/mesh/
[158] Viewed 05/11/19, available online at: https://www.gov.uk/government/groups/devices-expert-advisory-committee

29th January 2015	Hansen et al.	**Reoperation for urinary incontinence: a nationwide cohort study, 1998–2007**[159] The Danish National Patient Registry was used to identify women who had surgery for urinary incontinence from 1998 through 2007 for whom the outcome was a reoperation within 5 years. 8671 women were identified. 67% received a synthetic midurethral sling. The lowest rate of reoperation was seen among women having pubovaginal slings (6%), retropubic midurethral tape (6%) and Burch colposuspension (6%) followed by transobturator tape (9%), and miscellaneous operations (12%), whereas the highest observed risk was for urethral injection therapy (44%). Authors conclude that women who were operated with transobturator tape had a significantly higher risk of reoperation compared with retropubic midurethral tape.
13th March 2015	ACC (Accident Compensation Corporation) – New Zealand	**ACC Surgical Mesh Review: Analysis of Treatment Injury Claims - 1 July 2005 to 30 June 2014**[160] A retrospective audit review undertaken in response to a private petition that was sent to the New Zealand Health Committee on 20th March 2014. This resulted in 466 treatment injury claims being included. Data is limited to treatment injury claims lodged with the ACC from 1st July 2005 to 30th June 2014. Key findings on post-surgery complications & claims: - The claim rate is 5 times higher in using mesh for POP repair than SUI or hernia repair. - The most common claims for urogynaecological procedures using mesh was mesh erosion/exposure (65%). - The most common postoperative complication for hernia repair was infection or fistulae (51%). - In the majority of cases where the surgical mesh failed, subsequent surgery was required.

[159] M. Foss Hansen, G. Lose, U. S. Kesmodel, K. O. Gradel, Reoperation for urinary incontinence: a nationwide cohort study, 1998–2007. *American journal of obstetrics and gynecology* **214**, 263.e261-263.e268 (2016).

[160] ACC, 2015, ACC Surgical Mesh Review: Analysis of Treatment Injury Claims - 1 July 2005 to 30 June 2014, viewed 12 August 2019, available online at: https://www.acc.co.nz/assets/provider/surgical-mesh-report.pdf

		- 56,508 mesh devices were sold in New Zealand between 1st January 2005 and 31st October 2014, 58% of mesh devices were sold for hernia repair, 30% for POP repair and 11% for SUI repair. - 48% of the mesh was made of synthetic material, while less than 2% was biological mesh, and 21% was composite mesh. 29% of the device-related information was not documented.
June 2015	SCENIHR	SCENIHR preliminary opinion is published
June 2015	Sling The Mesh	Patient group established.
12th June 2015	SCENIHR	Launched a public consultation on the draft report on the website of the Scientific Committees from 12th June to 19th July 2015. *'Information about the public consultation was broadly communicated to national authorities, international organisations and other stakeholders. 52 organisations and individuals (providing in total 178 comments) participated in the public consultation providing input to different chapters and subchapters of the Opinion. Among the organisations participating in the consultation, there were universities, professional associations, institutes of public health, industry representatives and NGOs.'*[161]
1st July 2015	Cochrane	**Mid-urethral sling operations for stress urinary incontinence in women**[162] Update on 'Minimally invasive synthetic suburethral operations for stress urinary incontinence in women' (2009). 19 new trials added. the quality of most outcomes was moderate Review of 81 trials, including 12,113 women. MUS procedures performed using the retropubic route had higher morbidity when compared to transobturator route, though the overall rate of adverse events remained low. The overall rate of vaginal tape erosion/exposure/extrusion was low in both groups:

[161] SCENIHR, 2015, Opinion on The safety of surgical meshes used in urogynecological surgery, available online at: https://ec.europa.eu/health/sites/health/files/scientific_committees/emerging/docs/scenihr_o_049.pdf

[162] A. A. Ford, L. Rogerson, J. D. Cody, J. Ogah, Mid-urethral sling operations for stress urinary incontinence in women. *The Cochrane database of systematic reviews*, Cd006375 (2015).

		24/1000 instances with transobturator route compared with 21/1000 for retropubic route. A retropubic bottom-to-top route was more effective than top-to-bottom route for subjective cure, it incurred significantly less voiding dysfunction, and led to fewer bladder perforations and vaginal tape erosions. Analysis of the trials showed that over 80% of women with SUI were cured, or have significant improvement in their symptoms, with either operation (retropubic or transobturator) for up to five years after surgery. The information that was available for quality of life *'shows that it improves as a result of these operations, though there is no clear difference between the two procedures'* *'There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes'* Author concludes that *'Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI'*. The authors note that *'a bottom-to-top route was more effective than top-to-bottom route for retropubic tapes'* and also note the need for reporting of longer-term outcome data from the numerous existing trials.
September 2015	Blaivas et al.	**Safety considerations for synthetic sling surgery[163]** Nature Review of safety considerations for synthetic midurethral slings (SMUS) for treating incontinence. The authors state that the effectiveness of the SMUS

[163] J. G. Blaivas *et al.*, Safety considerations for synthetic sling surgery. *Nature Reviews Urology* **12**, 481 (2015).

		is comparable to that of the historical gold standards—autologous fascial slings and the Burch colposuspension, but that the quality of the studies with respect to assessing risks of SMUS-associated complications is currently poor. *'Of the thousands of published studies, only a few were even designed to track complications in any meaningful way. The short follow-up duration of most of these studies and the lack of accounting for those lost to follow up are additional confounders.'* The authors state that the most common risks in patients with SMUS include urethral obstruction requiring surgery (2.3% of patients with SMUS), vaginal, bladder and/ or urethral erosion requiring surgery (1.8%) and refractory chronic pain (4.1%); these data likely represent the minimum risks. In addition, the failure rate of SMUS implantation surgery is probably at least 5% in patients with stress urinary incontinence (SUI). Furthermore, at least one-third of patients undergoing sling excision surgery develop recurrent SUI. Considering the additional risks of refractory overactive bladder, fistulas and bowel perforations, among others, the overall risk of a negative outcome after SMUS implantation surgery is ≥15%. *'Considerable evidence exists that SMUS complications are underreported. Discrepancies exist between the SMUS complication rates reported by urologists from individual institutions, those reported in the literature, the (unreported) experience of tertiary care practices and those in the MAUDE (Manufacturer and User Facility Device Experience) database'* In terms of women who may be at risk of mesh erosion, the authors state that oestrogen-deficient states, genital atrophy, surgical scarring, concurrent prolapse surgery, type 1 or type 2 diabetes mellitus, steroid use, concurrent anticholinergic use and smoking have been reported as risk factors. *'Published reports on long-term outcomes of patients after mesh removal surgery are limited. All published studies are retrospective chart or database reviews and substantial heterogeneity exists in terms of both methodology and outcome measures. Most authors of studies in this area commented on the technical*

		difficulties encountered during mesh excision surgery and the fact that many (in some series, most) patients require two or more surgeries; thus, even in the short term, outcomes are often suboptimal'
September 2015	Tommaselli et al.	**Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis[164]** A systematic review and metanalysis of the literature, designed to evaluate the long-term outcomes of retropubic midurethral sling (RP-MUS) procedures and the medium-term outcomes of transobturator midurethral sling (TO-MUS) procedures. Studies with a follow-up of 36 months for TO-MUS and 60 months for RP-MUS were searched. Only studies comparing a RP-MUS or TO-MUS with another synthetic sling were included. Data from 49 studies were included. 49 studies were included in the review (11 RCTs and 38 nonrandomised studies, including prospective, retrospective, and cohort studies) with a total of 6,406 patients (1,200 in RCTs and 5,206 in nonrandomised studies) aged 19 – 89 years. RP-MUS had similar objective cure rates, but higher subjective cure rates than TO-MUS. No differences were observed between outside-in (TOT) and inside-out (TVT-O) and between TO-MUS and minisling. Bladder injuries were more frequent and vaginal erosions were less frequent for RP-MUS. Vaginal injuries were more common with TOT than with TVT-O. Pain-related complications were more common with TO-MUS than with minimally invasive tapes. Authors conclude that *'this meta-analysis showed that RPMUS and TO-MUS have similar objective cure rates in the long-term and medium-term but TOTs have a lower subjective cure rate than TVT. This efficacy is backed by a high safety profile, and by a limited number of complications which were seldom severe. More randomized trials comparing TVT-O and TOT investigating objective cure rates and with a longer follow-up are needed, and further data are*

[164] G. A. Tommaselli, C. Di Carlo, C. Formisano, A. Fabozzi, C. Nappi, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. *Int Urogynecol J* **26**, 1253-1268 (2015).

		needed regarding minimally invasive slings to be able to draw more accurate conclusions.'
2nd October 2015	Scottish Independent Review	**Interim Report of the Scottish Independent Review of the Use, Safety and Efficacy of Transvaginal Mesh Implants in the Treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse in Women Interim Report**[165] **Authors' Conclusions** - No significant differences were found in the risk of adverse effects between retropubic and transobturator, mid-urethral mesh tape procedures. - Mid-urethral mesh tape procedures were not found to be associated with greater risk of adverse outcomes than laparoscopic colposuspension, though long-term, data was not collected. - Mid-urethral mesh tape procedures were associated with lower complication rates than traditional suburethral sling operations. - The clinical importance of these adverse outcomes does differ: bladder perforation (more common in retropubic procedures) is of little or no clinical importance, whilst groin pain (more common for transobturator procedures) is of greater importance clinically. Recommendations made including the need for robust clinical governance around treatment, MDT working, audit activity, reporting of adverse events, improved consent procedure, greater evidence on long-term safety/efficacy of mesh, including outcome date (with quality of life and daily living inclusion). Improvement in information handling is recommended, as well as improved clinician communication skills. Concern is expressed about the use of the transobturator rather than the retropubic approach for routine surgery for SUI using mesh, as well as the use of transvaginal mesh for POP surgery.

[165] Health Performance and Delivery Directorate, Department of Health and Social Care, Scottish Government, 2015, Transvaginal mesh implants independent review: interim report, viewed 12 August 2019, available online at: https://www.gov.scot/publications/scottish-independent-review-use-safety-efficacy-transvaginal-mesh-implants-treatment-stress-urinary-incontinence-pelvic-organ-prolapse-women-interim-report/

November 2015	NICE	**Urinary incontinence in women: management [CG171 – update][166]** Deleted recommendation 1.1.14 (regarding referral) and replaced it with a link to updated guidance in suspected cancer: recognition and referral (NICE guideline NG12).
3rd December 2015	Mesh Working Group	**Mesh Working Group – Interim Report[167]** The interim report includes evaluation of both the efficacy and adverse incidents and complications associated with mesh used to treat POP/SUI. Sub-groups were set up for each of the following areas, made up of members from the working group and selected others with relevant expertise or experience (Clinical Quality, Data and Information, Informed Consent). **Recommendations:** Clinical Quality: - Use trust appraisal system to ensure that surgeons are appropriately trained, adhere to clinical guidance, comply with national data requirements and report complications. - NICE should produce guidance that holistically describe care for women with POP, and review the guidance for urinary incontinence (CG171). - A nurse helpline for mesh-injured women should be set up. - GP awareness should be improved through an e-learning package. Data and information: - HES OPCS codes should be developed to reflect complications which result from mesh removal. - A better understanding of the true nature and extent of complications needs to be established - Cost/benefit analysis of establishing a registry of procedures should be taken. Informed Consent: - Consistent information about procedures should be given to women through leaflets that have been developed in line with national guidance in

[166] NICE, Urinary incontinence in women: management, updated November 2015, available online at: https://webarchive.nationalarchives.gov.uk/20161104213627/https://www.nice.org.uk/guidance/cg171
[167] Mesh Working Group, NHS England, 2015, Mesh Working Group – Interim Report, Viewed 12 August 2019, available online at: https://www.england.nhs.uk/wp-content/uploads/2015/12/mesh-wg-interim-rep.pdf

		collaboration with clinicians, professional bodies and patient support groups. - The consent discussion should be recorded, and reasonable time given to ask questions before signing the consent form. GMC guidance on obtaining consent should be followed. - RCOG, BSUG and BAUS should recommend the use of the SUI and POP leaflets (once finalised) to their members, including those in the private sector. - Professional bodies should review the leaflets every 2 years, taking into account new information.
3rd December 2015	SCENIHR (EU)	**Opinion on the safety of surgical meshes used in urogynecological surgery**[168] The SCENIHR state that mesh exposure rates for vaginal POP surgery with mesh range from 4 to 19%. The use of absorbable mesh inserted either via a transabdominal or transvaginal route is associated with a high failure rate. Transvaginal surgery using non-absorbable synthetic mesh for POP is associated with a higher risk of mesh-related morbidity than seen with transabdominal insertion of mesh. Sacrocolpopexy is associated with greater surgical morbidity compared to vaginal repair. *'In sling surgery, there is evidence that absorbable biological materials have a high failure rate while sling surgery with non-absorbable synthetic mesh was effective with an approximately mesh exposure rate of 4% (Brubaker et al., 2011). Autologous slings are a more invasive alternative (because of the need to harvest native tissue), but they also can be inserted using a minimally invasive approach. The traditional surgical approach of colposuspension is associated with greater morbidity compared to sling surgery with mesh'* *'However, synthetic sling SUI surgery is an accepted procedure with proven efficacy and the safety of surgical meshes used in urogynecological surgery 5 safety in the majority of patients with moderate to severe SUI, when used by an experienced and appropriately trained surgeon. Therefore, the SCENIHR supports continuing synthetic sling use for*

[168] Scientific Committee on Emerging and Newly Identified Health Risks, 2015, *Opinion on the safety of surgical meshes used in urogynecological surgery*, viewed 12 August 2019, available online at: http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_049.pdf

		SUI, but emphasises the importance of appropriately trained surgeons and detailed counselling of patients about the associated risk/benefits' The authors suggested, based on current evidence: − Type 1 (macroporous, monofilament) is considered to be the most appropriate synthetic mesh for insertion via the vaginal route. − Type 1 (macroporous, monofilament) and Type 3 (microporous, multifilament) are the most appropriate synthetic meshes for insertion via the abdominal route. Attention is drawn to the effectiveness of the consent procedure in the executive summary *'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. Information given to practitioners by the manufacturers regarding the 'proven' safety of these products and the 510k clearance loophole needs to be addressed before true informed consent can be made'* Based on the available scientific evidence, the SCENIHR recommends: - The implantation of any mesh for the treatment of POP via the vaginal route should be only considered in complex cases in particular after failed primary repair surgery, - That due to increased risks associated with the use of synthetic mesh for POP repair via a transvaginal route, this option should only be used when other surgical procedures have already failed or are expected to fail. - Limiting the amount of mesh for all procedures where possible. However, there is a need for further improvement in the composition and design of synthetic meshes, in particular for POP surgery. - The introduction of a certification system for surgeons based on existing international

		guidelines and established in cooperation with the relevant European Surgical Associations. - • Appropriate patient selection and counselling, which is of paramount importance for the optimal outcome for all surgical procedures, particularly for the indications discussed. This should be based on the results of further clinical evidence, which should be collected in a systematic fashion for all of these devices.
15th December 2015	Ross et al.	**Transobturator tape versus retropubic tension-free vaginal tape for stress urinary incontinence: 5-year safety and effectiveness outcomes following a randomised trial[169]** 5 year follow-up to 2009 randomised trial comparing retropubic tension-free vaginal tape (TVT[170]) and transobturator tape (TOT) for treatment of SUI. Consenting women from the original trail had a vaginal examination, a pad test for urinary incontinence (UI) and completed Health-related Quality of Life Questionnaires (HRQOL). One hundred and seventy-six (88.4 %) women participated in the 5-year follow-up (83 TOT, 93 TVT). The primary composite outcome (mesh exposure or other serious adverse outcomes) occurred in 21.8 % of the TOT and 27.6 % of the TVT groups. Vaginal examination found more women with palpable tapes in the TOT versus the TVT group (48.5 % versus 22.4 %). There were no other significant differences between groups. The authors conclude that the outcomes for TOT patients at 5 years after initial SUI surgery may be generally more favourable than for TVT patients. However, more women in the TOT group continue to have tapes that remain palpable on vaginal exam and may proceed to experience adverse events.
December 2015	Imel et al.	***In vivo* oxidative degradation of polypropylene pelvic mesh[171]**

[169] S. Ross *et al.*, Transobturator tape versus retropubic tension-free vaginal tape for stress urinary incontinence: 5-year safety and effectiveness outcomes following a randomised trial. *Int Urogynecol J* **27**, 879-886 (2016).
[170] 'TVT' is used here as a generic term and does not imply use of an Ethicon TVT device in this trial. Indeed, Boston Scientific (Natick, MA) devices were used for all procedures: the outside-in Obtryx Halo midurethral sling system was used for transobturator tape procedures, and the Advantage retropubic midurethral sling system was used for TVT procedures.
[171] A. Imel, T. Malmgren, M. Dadmun, S. Gido, J. Mays, *In vivo* oxidative degradation of polypropylene pelvic mesh. *Biomaterials* **73**, 131-141 (2015).

		Commercial polypropylene pelvic mesh products were characterized in terms of their chemical compositions and molecular weight characteristics before and after implantation. Polypropylene mesh materials showed clear signs of oxidation by both Fourier-transform infrared spectroscopy and scanning electron microscopy with energy dispersive X-ray spectroscopy. The oxidation was accompanied by a decrease in molecular weight. Scanning electron microscopy revealed the formation of transverse cracking of the fibers which generally increased with implantation time. The authors conclude that these results, as well as the loss of flexibility and embrittlement of polypropylene upon implantation as reported by other workers, is evidence of *in vivo* oxidative degradation of polypropylene.
4th January 2016	FDA	Changed the approval requirements for transvaginal mesh (for POP repair) from Class II to the higher risk Class III and required submission of premarket approval (PMA) applications, the agency's most stringent device review pathway.[172] This reclassification did not include mesh products used for transabdominal POP repair, or those used for SUI treatment, which remained class II. As a result of the FDA's actions, manufacturers began to stop marketing surgical mesh intended for transvaginal repair of posterior compartment prolapse.
9th February 2016	Cochrane	**Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse**[173] A comparison of transvaginal grafts versus native tissue repair for vaginal prolapse published. 37 RCTs (4,023 women) were included, 12 new trials not included in the previous review. The quality of the evidence ranged from very low to moderate. Transvaginal mesh or grafts compared with native tissue repair for prolapse updated. Mesh associated with lower rates of awareness of prolapse at one to

[172] FDA, 2016, FDA strengthens requirements for surgical mesh for the transvaginal repair of pelvic organ prolapse to address safety risks, viewed 12 August 2019, available online at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm479732.htm

[173] C. Maher *et al.*, Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. *Cochrane Database of Systematic Reviews*, (2016).

		three years but associated with higher rates of repeat surgery for prolapse, stress urinary incontinence or mesh exposure, and higher rates of bladder injury and *de novo* stress urinary incontinence. There was no evidence of a difference between the groups in rates of repeat surgery for continence. Recurrent prolapse on examination was less likely after mesh repair than after native tissue repair. Surgery for mesh exposure was required in 8% of women. There was no evidence of a difference between the groups in rates of *de novo* dyspareunia. Limited evidence suggests that absorbable mesh may reduce rates of recurrent prolapse on examination compared to native tissue repair, but there was insufficient evidence on absorbable mesh for conclusions on other outcomes to be drawn. There was also insufficient evidence to draw conclusions regarding biological grafts compared to native tissue repair.
23rd May 2016	Kelly et al.	***In vivo* response to polypropylene following implantation in animal models: a review of biocompatibility[174]** A review of the *in vivo* response to polypropylene following implantation in animal models. The specific areas explored are material selection, impact of anatomical location, and the structure, weight and size of polypropylene mesh types. Based on the evidence reviewed, the authors conclude that *'polypropylene evokes a less inflammatory or similar host response when compared with other materials used in mesh devices'*
August 2016	Nolfi et al.	**Host response to synthetic mesh in women with mesh complications[175]** A study characterising the macrophage response in patients who undergo mesh excision for pain or mesh exposure. On histologic examination, macrophages surrounded each mesh fibre, with predominance of the M1

[174] M. Kelly, K. Macdougall, O. Olabisi, N. McGuire, *In vivo* response to polypropylene following implantation in animal models: a review of biocompatibility. *International urogynecology journal* **28**, 171-180 (2017).
[175] A. L. Nolfi *et al.*, Host response to synthetic mesh in women with mesh complications. *American journal of obstetrics and gynecology* **215**, 206 e201-208 (2016).

		macrophage subtype (known to elicit a pro-inflammatory response). Cytokines/chemokines typically produced by M1 and M2 macrophages, as well as matrix metalloproteinases MMP-9 and MMP-2 were increased significantly in mesh-vagina explants, as compared with vagina without mesh. A positive correlation was observed between the profibrotic cytokine interleukin-10 and the percentage of M2 cells in the pain group. Authors conclude that in those with complications, mesh induces a proinflammatory response, characterised by chronic M1 macrophage activation. The increase in MMP-9 in mesh explants indicates tissue degradation; the positive association between interleukin-10 and M2 macrophages in mesh explants that are removed for pain is consistent with overzealous tissue remodelling as part of the foreign body response, resulting in fibrosis.
September 2016	Linder et al.	**Evaluation of the Local Carcinogenic Potential of Mesh Used in the Treatment of Female Stress Urinary Incontinence[176]** Study designed to evaluate the carcinogenic potential of implanted synthetic mesh midurethral slings in the treatment of female SUI. During the study period, 2,474 patients underwent polypropylene midurethral sling placement. The median age was 57 years and the median follow-up was 60 months. Overall, 51 patients also had a cancer diagnosis (8 bladder cancers, 7 vaginal malignancies, 8 ovarian carcinomas, 26 endometrial cancers, 2 cervical malignancies); however, only 2 cancers (0.08 %) developed following sling placement (a vaginal melanoma 3 years after sling placement and an ovarian tumour 1 year after sling placement). No cases of sarcoma formation, bladder, urethral or squamous cell carcinomas were identified. Authors conclude that the development if pelvic malignancy was rare, and unlikely to be secondary to foreign body reaction from the implanted material.

[176] B. J. Linder *et al.*, Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. *Int Urogynecol J* **27**, 1333-1336 (2016).

November 2016	Northern Irish Mesh Sufferers	Patient group established. Name changed to 'Sling The Mesh Northern Ireland' in November 2017.
6th December 2016	Duckett et al.	**Mesh removal after vaginal surgery: what happens in the UK?**[177] An electronic questionnaire was sent to all members of the RCOG and members of the Section of Female Neurological and Urodynamic Urology of the BAUS. The questionnaire aimed to identify the number of procedures performed for mesh complications and whether they were reported to the MHRA and the patterns of referral and treatment. Overall 359 surgeons completed the survey. Referral to a colleague in the same hospital was common practice (69 %). Only 27 % of respondents stated that they reported all removals to the MHRA. The numbers of surgical procedures were low, with most respondents performing between one and three procedures each year and many not performing any surgery for a specific mesh complication in the previous year. 59 % of respondents performed 5 – 150 procedures per year (median 32). Of those surgeons who performed MUS insertion, 21 % performed fewer than 20 procedures per year. MUS removal from the bladder was performed by 23 % of the respondents, but 21 % had not performed the procedure in the last year, and 13 % had performed 4 or more procedures (maximum 8). Urethral erosion was seen in 17 % of removals, and 4 or more removals (maximum 11) had been performed at 3 centres in the last year. Overall 15 % of respondents reported inserting a mesh during prolapse surgery, with a median of 8 procedures per year. Of those who performed mesh insertion, 31 % reported removal due to mesh complications related to prolapse surgery. There is no denominator for this surgery, so it is impossible to estimate the incidence of complications of mesh surgery. *'It is very difficult to assess competence and the levels of training and care for mesh removal when most surgeons perform only a small number of surgical procedures each year. It could be argued that*

[177] Duckett, J., Morley, R., Monga, A. et al. Int Urogynecol J (2017) 28: 989. https://doi.org/10.1007/s00192-016-3217-z

		all significant mesh erosions should be managed in a tertiary centre to maintain and increase expertise as well as to allow meaningful audit of results. A contrary argument for local management of minor complications could also be made. All cases should be discussed at a multidisciplinary team meeting' Authors conclude that *'A variety of surgeons in the National Health Service perform a low number of mesh removal procedures. Whilst this survey provided evidence of who is performing these procedures and where they are being done, it did not provide information regarding success (objective or subjective). All outcomes should be audited via national recognized databases. The rate of reporting of complications to the MHRA is poor. The requirement for adverse event reporting via surgical databases and to the MHRA should be encouraged, and in future may be mandated through hospital governance systems. The results of this survey have led to a commitment of the RCOG, BAUS and BSUG to set national standards for the management of mesh complications and identify those units that conform to these standards so that in the future women with mesh complications will be able to access appropriate levels of care and expertise.'*
December 2016	Glazener et al. (PROSPECT)	**Clinical effectiveness and cost-effectiveness of surgical options for the management of anterior and/or posterior vaginal wall prolapse: two randomised controlled trials within a comprehensive cohort study – results from the PROSPECT Study[178]** PROSPECT study comprises a panel of pragmatic, parallel-group RCTs set within a comprehensive cohort design. The aim was primarily to compare the clinical effectiveness and cost-effectiveness of three treatment modalities (synthetic non-absorbable mesh inlay, biological graft and mesh kit using similar material) compared with a standard repair in women with POP of the anterior or posterior vaginal walls. 3,087 women who were having prolapse surgery in 35 UK centres were consented between January 2010 and August 2013.

[178] C. Glazener *et al.*, Clinical effectiveness and cost-effectiveness of surgical options for the management of anterior and/or posterior vaginal wall prolapse: two randomised controlled trials within a comprehensive cohort study - results from the PROSPECT Study. *Health technology assessment (Winchester, England)* **20**, 1-452 (2016).

		The mean score on the 'POP Symptom Scale' was similar for each comparison. There was also no statistically significant difference in the prolapse-related 'quality of life' score. The number of women with serious non-mesh adverse effects, such as infection, pain, urinary retention and dyspareunia, was similar between the groups in the first year. There were no statistically significant differences between the groups for any adverse effect measure at any time period. The cumulative mesh complication rates over 2 years were 0.5% for standard repair, 10.6% for mesh inlay and 0.5% for biological graft. In the first year, 2 of 430 women in the standard group and 32 of 435 in the mesh inlay group had mesh complications, with a further 2 out 368 mesh complications in the biological group. Both women in the standard group, and 23 in the mesh inlay group, had surgery to remove or overlay the mesh. In the second year, 1 of 430 in the standard group and 25 of 435 in the mesh inlay group had a mesh complication. Of these, 17 in the mesh inlay group required surgical correction of the exposure, the remainder received conservative/no treatment. Compared with standard repair, using a synthetic mesh cost an additional £363 per woman and biological graft an extra £565. A decision-analytic model to extrapolate results of RCT1 over a longer time shows that at 5 years there is no evidence that either mesh strategy would be a cost-effective use of NHS resources. Standard repair was, on average, the most cost-effective because of lower intervention costs, lower costs of treating mesh-related complications and similar rates of surgical failure at 2 years. However, further long-term follow-up is required to validate the extrapolation models used. Authors conclude that *'unless there is a significant decrease in reoperation rates for failure in the medium or long term, it is unlikely that any type of mesh or graft would be cost-effective, given the excess cost over standard repair and the excess cost of treatments for mesh complications'*

20th December 2016	Glazener et al. (PROSPECT)	**Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT)[179]** Two parallel-group, multicentre, randomised, controlled trials of mesh, graft or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery. 13521,352 women randomly allocated to treatment, of whom 13481,348 were included in the analysis. 865 women were included in the mesh trial (430 to standard repair alone, 435 to mesh augmentation) and 735 were included in the graft trial (367 to standard repair alone, 368 to graft augmentation). For the mesh trial, at 2 years, the rate of symptomatic prolapse were 82% and 85% for standard repair and synthetic mesh repair, respectively. 31% and 34% respectively reported 'something coming down' and severe urinary incontinence was seen in 6% and 9%, respectively. Faecal incontinence was seen in 26% and 27%, respectively and severe dyspareunia was seen in 5% and 3%, respectively. For the graft trial, at 2 years, the rate of symptomatic prolapse were 81% and 82% for standard repair and Biological graft repair, respectively. 31% and 40% respectively reported 'something coming down' and severe urinary incontinence was seen in 7% and 7% for both procedures. Faecal incontinence was seen in 27% and 26%, respectively and severe dyspareunia was seen in 4% for both procedures. In the second year of the mesh trial, 'any mesh complications' were reported as <1% and 6% for standard repair and synthetic mesh repair, respectively In the second year of the graft trial, 'any mesh complications' were reported as <1% for both standard repair and biological graft repair.

[179] PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials. Glazener CMA et al (on behalf of the PROSPECT Group), (2016). Mesh, graft, or standard repair for women having primary anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT). Lancet. DOI: http://dx.doi.org/10.1016/S0140-6736(16)31596-3.

		The study found no improvement to outcomes (reported at 1 and 2 years: effectiveness, quality of life, adverse effects, or any other short-term outcome) with treatment via mesh or graft. However, more than 1/10 women had a mesh complication, although most were asymptomatic. Restricting the data to women who actually received synthetic mesh either as part of their anterior or prolapse repair or as a concomitant vault, uterine, or continence procedure, the number of women with a mesh complication in the first two years was 51 (12%) of whom 37 required a surgical removal. Although no evidence was apparent of differences between standard, mesh, or graft repair in other adverse effects up to 2 years after surgery, mesh use did result in the need for additional surgical procedures for exposures and extrusion in the first 2 years. The authors recommend more long-term follow-up. Of note is the fact that less than 1% of women received treatment using mesh kits, defined as synthetic mesh inserted using trochars. The other synthetic mesh procedures would have been cut to size by the surgeon.
13th January 2017	Talley et al.	**Oxidation and degradation of polypropylene transvaginal mesh.[180]** Polypropylene degradation as a result of the foreign body reaction (FBR) has been proposed as a contributing factor to mesh complications. Test of whether polypropylene oxidises under *in vitro* conditions simulating the FBR, resulting in degradation. Test specimens were incubated in an oxidative medium for up to 5 weeks. Oxidation was assessed by infrared spectroscopy, and degradation by scanning electron microscopy. Found evidence of polypropylene oxidation. SEM images at 5 weeks showed evidence of surface degradation, including pitting and flaking.

[180] A. D. Talley, B. R. Rogers, V. Iakovlev, R. F. Dunn, S. A. Guelcher, Oxidation and degradation of polypropylene transvaginal mesh. *J Biomater Sci Polym Ed* **28**, 444-458 (2017).

		To assess changes in polypropylene surface chemistry *in vivo*, fibres were recovered from mesh explanted from a single patient without formalin fixation, untreated or scraped to remove tissue, and analysed by X-ray photoelectron spectroscopy. Mechanical scraping removed adherent tissue, revealing an underlying layer of oxidised polypropylene. The authors highlight the need for further research into the relative contribution of oxidative degradation to complications associated with polypropylene mesh devices in larger cohorts of patients.
17th January 2017	Karmakar et al.	**Long-term outcomes of transobturator tapes in women with stress urinary incontinence: E-TOT randomised controlled trial[181]** 341 women were randomised to receive either 'inside-out' TVT-O or 'outside-in' TOT-ARIS. Long-term follow-up (median 9 years) using validated symptom severity and quality-of-life questionnaires. The overall patient-reported success rate was 71.6%, with a further 14% reporting 'improvement', and there was no significant difference between inside-out and outside-in groups. The success rate showed a significant reduction compared with 1-year results (71.6% versus 80%). 7.96% underwent further continence surgery, the tape extrusion/erosion rate was 4.5%, and groin pain/discomfort was reported in 4.32%, with only 1.4% requiring treatment.
10th February 2017	Barski et al.	**Transvaginal PVDF-mesh for cystocele repair: A cohort study[182]** First report of safety and efficacy of transvaginal application of (polyvinylidene fluoride) PVDF mesh. Authors recommend that meshes probably shouldn't be used as first line treatment. Authors comment that a standardised approach for market approval of an innovation or new device is needed. A prospective long-term evaluation in a registry is justified, according to the authors. Authors also state that PVDF is more resistant to hydrolysis and degradation, and that ageing does not increase the stiffness, as seen in polypropylene.

[181] Karmaker DK, Mostafa A, Abdel-Fattah M, BJOG; DOI: 10.1111/1471-0528. 14561
[182] D. Barski *et al.*, Transvaginal PVDF-mesh for cystocele repair: A cohort study. *International journal of surgery (London, England)* **39**, 249-254 (2017).

11th February 2017	Morling et al.	**Adverse events after first, single, mesh and non-mesh surgical procedures for stress urinary incontinence and pelvic organ prolapse in Scotland, 1997–2016: a population-based cohort study**[183] Between 1st April 1997, and 31st March 2016, 16,660 women underwent a first, single incontinence procedure, 79% of which used mesh. Compared with colposuspension, mesh procedures had a lower risk of immediate complications and subsequent prolapse surgery, and a similar risk of further incontinence surgery and later complications. During the same time period, 18,986 women underwent a first, single prolapse procedure, 7% of which used mesh. Compared with non-mesh repair, mesh repair of anterior compartment prolapse was associated with a similar risk of immediate complications, an increased risk of further incontinence and prolapse surgery, and a substantially increased risk of later complications. Compared with non-mesh repair, mesh repair of posterior compartment prolapse was associated with a similarly increased risk of repeat prolapse surgery and later complications. No difference in any outcome was observed between vaginal or abdominal mesh repair of vaginal vault prolapse compared with vaginal non-mesh repair. Authors support the use of mesh procedures for incontinence, although further research on longer-term outcomes would be beneficial. Mesh procedures for anterior and posterior compartment prolapse were not recommended for primary prolapse repair.
22nd February 2017	Mesh UK Charitable Trust	Patient Group established.
February 2017	Thames et al.	**The Myth: *In Vivo* Degradation of Polypropylene-Based Meshes**[184] A non-destructive, hydrolytic cleaning process, supplemented with light microscopy (LM), Fourier transform infrared spectroscopy (FTIR), and scanning electron microscopy (SEM) data, was used to

[183] Morling JR, McAllister DA, Agur W et al, The Lancet, 389, No. 10069, 629-640, Feb 2017
[184] S. F. Thames, J. B. White, K. L. Ong, The myth: *in vivo* degradation of polypropylene-based meshes. *Int Urogynecol J* **28**, 285-297 (2017).

		evaluate 78 explanted Prolene meshes (with duration of implantation ranging from 0.4 to 11.7 years). The cleaning process exposed clean, unoxidized, nondegraded Prolene fibers with smooth surfaces and with no visible evidence of gradient-type or ductile damage. LM showed identical translucent and sometimes clear, cracked/flaking material on both blue and clear fibers, instead of clear cracked/flaking material on the clear fibers and blue cracked/flaking material on the blue fibers. FTIR confirmed progressive protein removal and loss of protein absorption intensity after each cleaning step. Authors conclude that *'Our effective cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo, confirming the in vivo stability of properly formulated polypropylene. Instead, the cracked layer that some researchers have identified as degraded Prolene is an adsorbed protein–formaldehyde coating, resulting from the well-established formalin–protein fixation process, which occurs immediately upon placing an explant in formalin'* While the study was not directly funded by any company, the manuscript was based on findings by medicolegal experts paid by Ethicon in the defense of polypropylene mesh litigation
February 2017	Iakovlev et al.	**Degradation of polypropylene *in vivo*: A microscopic analysis of meshes explanted from patients**[185] A study using a range of microscopy techniques to visualise explanted mesh. A cross-sectional approach was used to show a degradation layer on the mesh fibre - like tree bark – which was confirmed as degraded polypropylene, with this degradation occurring *in vivo*. Histologically, adherent macrophages were seen at the polypropylene surface, suggesting a chronic immune reaction, which is thought to be the source of the degradation, through the release of reactive oxygen species (indeed, strong staining for macrophage-derived myeloperoxidase – an oxidative

[185] V. V. Iakovlev, S. A. Guelcher, R. Bendavid, Degradation of polypropylene *in vivo*: A microscopic analysis of meshes explanted from patients. *Journal of biomedical materials research. Part B, Applied biomaterials* **105**, 237-248 (2017).

		enzyme - was seen at the tissue surrounding the mesh fibres). Increased brittleness and bacterial colonisation of fissures after degradation are suggested as pathological mechanisms.
27th March 2017	The Scottish Independent Review	**Scottish Independent Review of the use, safety and efficacy of transvaginal mesh implants in the treatment of stress urinary incontinence and pelvic organ prolapse in women - Final Report**[186] Recommendations: - Patient management in the context of an MDT - Alternative methods of adverse event capture, mandatory reporting of adverse events - Local and national audit activity - SUI patient leaflet to be improved and more time allocated for discussion, for better-informed consent procedure. - Women must be offered all appropriate treatments (mesh and non-mesh) as well as the information to make informed choices. - Lack of long-term follow-up and related outcome data, including information on quality of life and activities of daily living, to be addressed. - When mesh is used, a retropubic approach is recommended. - Transvaginal mesh not to be used routinely in the treatment of POP as evidence of additional benefit over native tissue repair is not present.
5th April 2017	European Parliament and the council of the European Union	European Parliament directive moves mesh from a class IIb to class III device. To be adopted by 26th May 2020[187]
May 2017	Chughtai et al.	**Is vaginal mesh a stimulus of autoimmune disease?**[188] Reterospective cohort study designed to investigate a potential link between the development of

[186] *The Scottish Independent Review of the use, safety and efficacy of transvaginal mesh implants in the treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse in women Final Report* Final Report March 2017, available online at: http://www.gov.scot/Resource/0051/00515856.pdf

[187] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

[188] B. Chughtai *et al.*, Is vaginal mesh a stimulus of autoimmune disease? *American journal of obstetrics and gynecology* **216**, 495.e491-495.e497 (2017).

		systemic/autoimmune disorders and synthetic polypropylene mesh repairs. A total of 2,102 patients underwent mesh-based POP surgery from January 2008 through December 2009. In the control cohorts, 37,298 patients underwent colonoscopy and 7,338 underwent vaginal hysterectomy. When patients were matched based on demographics, comorbidities, and procedure time, mesh-based surgery was not associated with an increased risk of developing autoimmune disease at any of the evaluated time periods. Authors conclude that *'Mesh-based vaginal surgery was not associated with the development of systemic/autoimmune diseases. These data refute claims against mesh as a cause of systemic disease.'*
2nd June 2017	Tincello et al.	**Surgery for recurrent stress urinary incontinence: the views of surgeons and women[189]** Study exploring the views of women with recurrent SUI with regard to treatment preferences, as well as the views of UK specialists on treatment preferences and equipoise regarding different treatment alternatives. 256 survey replies were received. Single-incision tapes were not offered by many respondents (7.8%). Urogynaecologists were more likely to offer pelvic floor muscle exercises than urologists, and also much more likely to offer a repeat MUT. Among those offering repeat MUT, there was a clear preference for retropubic tape as second surgery in all cases, with more urologists being willing to consider a transobturator tape in either scenario. It was noticeable that for repeat tape vs colposuspension or fascial sling that urologists were more likely to be in favour of the major surgery and were overall more in equipoise about these two comparisons. Also, when dealing with an existing (failed) MUT, there was a clear preference (78%) for leaving this in position (remove tape 20: no preference 13: leave tape 116) with no significant difference between specialities. Among the 40 respondents who offered single-incision tapes, most preferred this to a colposuspension (57.5%) and

[189] D. G. Tincello, N. Armstrong, P. Hilton, B. Buckley, C. Mayne, Surgery for recurrent stress urinary incontinence: the views of surgeons and women. *Int Urogynecol J* **29**, 45-54 (2018).

		fascial sling (57.5%), with no difference between specialities. The overall preference for a repeat tape observed in the survey was explained by both those who expressed this preference and those commenting on others' practice – during interviews - as being primarily due to this being a relatively easy and readily available option with which people were experienced and comfortable. The declining expertise in the more invasive procedures was commonly discussed as an important factor underlying the preference for repeat tapes. As regards a future RCT, there was general agreement that this is an important research topic, as evidence is needed. The authors comment on *'the dominant effect of repeat MUT in every comparison in which it was included, a finding that was confirmed from the interviews as being a consequence of training and experience rather than an actual preference. It appeared that many respondents were unable to offer alternative procedures because they had not received training in procedures such as colposuspension or fascial sling'* *'it is clear from the data that the treatments women may be offered may depend largely upon the discipline and training of the surgeon, and that the choice of treatments offered depends upon the surgeon's skills, experience and opinion rather than any evidence. This highlights the importance of comprehensive and appropriate training, in addition to the need for research addressing the specific issue of failed continence surgery'*
25th July 2017	Mesh Oversight Group	**Mesh Oversight Group Report**[190] Mesh Oversight Group report follows on from the interim report (2015). The report sets out the actions that had been taken to implement the recommendations made in the interim report.

[190] Mesh Oversight Group, NHS England, 2017, Mesh Oversight Group Report, viewed 12 August 2019, available online at: https://www.england.nhs.uk/wp-content/uploads/2017/07/mesh-oversight-group-report.pdf

		The report states that mesh is safe and effective for SUI and POP, but should not be first line surgery for POP. Surgeons performing POP procedures should complete a minimum number of procedures per year. Recommendations: • NICE guidelines should be followed. More information, support, specialised commissioned hospital services and development of a registry. • Reporting of adverse events by the clinician must occur and the Yellow Card system allows for patient reporting. Future implementation of barcode tracking of mesh. • All appropriate treatments (nonsurgical, mesh and non-mesh) should be offered to patients in fully informed consultations. • Care should be delivered by a multidisciplinary team of appropriately trained and experienced specialists. All cases should be registered on an appropriate database such as those provided by BSUG and BAUS.
25th July 2017	RCOG, BSUG	**RCOG and BSUG response to the Mesh Oversight Group Report[191]** In response to the Mesh Oversight Group Report, the Vice President of RCOG (Eddie Morris) supported the fact that women with mesh complications would be referred to specialist units with MDTs. Vice Chair of BSUG (Prof Jonathan Duckett) highlighted that mesh complications may surface after many years, with primary care being their first contact point for complications. He praised the creation of the GP learning resource, which might allow women with mesh complications to receive appropriate support and be quickly referred to specialist centres. He praised the new patient leaflets in their role to strengthen the informed consent process through consistent and accurate information. He highlighted the need to report to the BSUG database as well as the MHRA.

[191] Royal College of Obstetricians & Gynaecologists, 2017, RCOG and BSUG response to NHS Mesh report, viewed 12 August 2019, available online at: https://www.rcog.org.uk/en/news/rcog-and-bsug-response-to-nhs-england-mesh-report/

26th July 2017	MHRA	**MHRA response to the Mesh Oversight Group Report[192]** Director of Devices (John Wilkinson) stated that evidence supports the use of mesh devices in the UK for treatment of SUI and POP in appropriate circumstances. This is supported by the greater proportion of the clinical community and patients, according to the written response. He also encouraged reporting of complications to the MHRA through the Yellow Card Scheme. *'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.'*
19th September 2017	Pelvic Floor Society	**Position Statement by The Pelvic Floor Society on behalf of the Association of Coloproctology of Great Britain and Ireland on the use of mesh in ventral mesh rectopexy (VMR)[193]** Response to the current concerns regarding use of mesh to perform rectal prolapse surgery. - Evidence suggests that mesh morbidity for VMR is far lower than that seen in transvaginal procedures. - VMR should be performed by adequately trained surgeons who work within an MDT. - Clinical outcomes/any complications resulting from surgery should be recorded in the PFS - hosted national database (registry). - Accreditation of UK units performing VMR will improve performance and outcomes in the long-term. - An enhanced program of training including staged porcine, cadaveric and preceptorship will ensure competency of surgeons. - Enhanced consent forms/patient information booklets will help both surgeons and patients.

[192] Medicines and Healthcare products Regulatory Agency, 2017, MHRA response to the final report of the Mesh Oversight Group, viewed 12 August 2019, available online at: https://www.gov.uk/government/news/mhra-response-to-the-final-report-of-the-mesh-oversight-group

[193] M. A. Mercer-Jones, S. R. Brown, C. H. Knowles, A. B. Williams, Position Statement by The Pelvic Floor Society on behalf of The Association of Coloproctology of Great Britain and Ireland on the use of mesh in ventral mesh rectopexy (VMR). *Colorectal Disease* **0**.

		- There is weak observational evidence that technical aspects of the procedure can be optimised to reduce morbidity rates. Suture material choice may contribute towards morbidity. The available evidence is insufficient to support the use of one mesh over another (biologic versus synthetic), however the use of polyester mesh is associated with increased morbidity.
20th September 2017	Keltie et al.	**Complications following vaginal mesh procedures for stress urinary incontinence: an 8 year study of 92,246 women**[194] Retrospective cohort study of first-time TVT, TOT or suprapubic sling (SS) surgical mesh procedures between April 2007 and March 2015. Cases identified from HES database. 92,246 first-time surgical mesh procedures (56,648 TVT, 34,704 TOT, 834 suprapubic sling and 60 combinations) were identified, including 68,002 unconfounded procedures. Peri-procedural and 30-day complication rates in the unconfounded cohort were 2.4% and 1.7% respectively; 5.9% were readmitted at least once within 5 years for further mesh intervention or symptoms of complications, the highest risk being within the first 2 years. The complication rate within 5 years of the mesh procedure was 9.8%.
September 2017		**Consensus Statement of the European Urology Association and the European Urogynaecological Association on the Use of Implanted Materials for Treating Pelvic Organ Prolapse and Stress Urinary Incontinence**[195] A document summarising the deliberations of a consensus group meeting convened by the European Association of Urology (EAU) and the European Urogynecological Association, to explore the current evidence relating to the use of polypropylene (PP) materials used for the treatment of SUI and POP. *'Current data suggest that the use of non-autologous durable materials in surgery has well-established benefits but significant risks, which are specific to the*

[194] K. Keltie *et al.*, Complications following vaginal mesh procedures for stress urinary incontinence: an 8 year study of 92,246 women. *Scientific Reports* **7**, 12015 (2017).
[195] C. R. Chapple *et al.*, Consensus Statement of the European Urology Association and the European Urogynaecological Association on the Use of Implanted Materials for Treating Pelvic Organ Prolapse and Stress Urinary Incontinence. *European urology* **72**, 424-431 (2017).

		condition and location they are used for. Various graft-related complications have been described—such as infection, chronic pain including dyspareunia, exposure in the vagina, shrinkage, erosion into other organs of xenografts, synthetic PP tapes (used in SUI), and meshes (used in POP)—which differ from the complications seen with abdominal herniae' Midurethral sling procedure (MUS) *'using synthetic PP tape is the recommended method of surgical approach for the correction of SUI in the 2016 EAU guidelines. Both retropubic and transobturator (TO) approaches are well-established standard MUSs within clinical practice. The 2015 Cochrane review and the recent SCENIHR report concluded that synthetic MUSs are the most extensively researched surgical treatment for SUI, with over 200 published clinical trials establishing its effectiveness and good safety profile. Long-term outcomes for the TO approach have since been published. In recent years, some surgeons used single-incision mini-slings in clinical practice; however, no long-term data exist on their efficacy. One systematic review have shown that excluding TVT-Secur, there was no evidence of significant differences in patient-reported and objective cure compared with MUSs at 18-mo follow-up, while they were associated with more favourable recovery'* *'Abdominal sacrocolpopexy (ASC) is the most durable operation for advanced POP and serves as the criterion standard with which other operations are compared. ASC involves attaching the vaginal apex to the sacral anterior longitudinal ligament reinforced with a graft, usually synthetic mesh'.* Authors conclude that: *'the use of synthetic MUSs for surgical treatment of SUI in both male and female patients has good efficacy and acceptable morbidity. However, synthetic mesh for POP should be used only in complex cases with recurrent prolapse in the same compartment and restricted to those surgeons with appropriate training who are working in multidisciplinary referral centres. Patients should be adequately informed regarding the potential success rates and mesh-related adverse events compared with nonmeshnon-mesh alternatives, and should be engaged in the decision-making process'*

		The following recommendations are made as *'essential for the future'* - Design implants specifically for their application, rather than extrapolate from indications in abdominal wall repair. - Establish accurate and complete databases registering the numerator and denominator, patient profile and surgical experience. - Establish long-term assessment in high-quality RCTs and mandatory postmarketingpost-marketing registries. - Research new materials that should be introduced into clinical practice according to a cautious and rigorous process. - Follow the evidence-based EAU and EUGA guidelines. - Support and register the specialist training of surgeons in urology and urogynaecology. - Encourage multidisciplinary team working. - Develop appropriate information for patients. - Collaborate with patient advocacy groups. - Encourage premarketing safety and efficacy data before using a product in routine clinical practice. - Establish reference centres for reinterventions (complicated cases). - Use condition-specific patient-reported outcome measures wherever possible.
1st October 2017	Chughtai et al.	**Challenging the Myth: Transvaginal Mesh is Not Associated with Carcinogenesis**[196] Study to determine if there is a link between polypropylene mesh implantation for POP/SUI and carcinogenesis. 2,229 patients who underwent mesh POP surgery and 10,401 who underwent sling surgery for SUI between January 2008 and December 2009 were included in the study. Mean follow-up was 6 years (range 5-7). Transvaginal mesh implantation was not associated with an increased risk of a cancer diagnosis (pelvic/local cancers or any cancer) at 1 year and during the entire follow-up of up to 7 years.
10th October 2017	Hansard	House of Commons oral response to a question from Paul Masterson, MP about conversations with the MHRA in relation to transvaginal mesh. Jackie Doyle-Price (Parliamentary Under-Secretary of State for

[196] B. Chughtai *et al.*, Challenging the Myth: Transvaginal Mesh is Not Associated with Carcinogenesis. *J Urol* **198**, 884-889 (2017).

		Health) commented that *'we do not currently have enough evidence to warrant our asking the MHRA to reclassify these procedures, and this is a view shared by other regulators across the world. …the National Institute for Health and Care Excellence strongly recommends that mesh implants not be routinely offered for the first surgical intervention on prolapse. That guidance is being updated—publication is due at the start of the new year—and will include an overarching document that looks in depth at the devices and the conditions surrounding the need for them, as well as the treatment of complications, to support better health outcomes.'*[197]
18th October 2017	Hansard	Debate lead by Emma Hardy, MP, Vice Chair of APPG on Surgical mesh implants, in which she calls for the government to commit to a full retrospective and mandatory audit of all interventions that involved mesh, followed by a full public inquiry. She also called for the suspension of prolapse and incontinence mesh operations while the audit is being carried out. Thirdly, she calls for NICE to bring forward their guidelines for mesh in stress-related urinary incontinence from 2019 to 2018. Fourthly, raised awareness among the general public and GPs is called for[198]. The parliamentary under-secretary of state for health (Jackie Doyle-Price) made the following pertinent remarks, in conclusion: *'Obviously, many hon. Members would like an immediate ban on mesh products. From my perspective, the issue is not with the product but with clinical practice. That is what is going wrong. That is where we need to be much clearer, ensuring that women are treated properly by their clinicians, given proper advice and risk assessments, and given the opportunity to report any complications and the ability to complain and challenge. The Government also need to ensure that all clinicians have the most up-to-date and appropriate advice.'*

[197] Hansard, House of Commons, Oral Answers to Questions, 10 October 2017, Transvaginal Mesh Implants, Volume 629, viewed 12 August 2019, available online at: https://hansard.parliament.uk/Commons/2017-10-10/debates/1F9D4DC2-5571-4319-8166-7393B9931AB9/TransvaginalMeshImplants

[198] Hansard, House of Commons, 18 October 2017, Volume 629, Debate on Surgical Mesh Implants, viewed 12 August 2019, available online at: https://hansard.parliament.uk/Commons/2017-10-18/debates/B546B1F1-099F-442C-AD71-0185D1B3F69C/SurgicalMeshImplants

		'The advice I have received from the MHRA is that mesh is still the best product for treating stress incontinence, but the evidence regarding prolapse is more mixed. I can give that advice to hon. Members today, but we await the NICE guidelines before the end of the year.' *'we need to continue to draw on emerging evidence.'* *'It is still important that we listen to the concerns of women, and I encourage all hon. Members who speak to their constituents suffering with the consequences, to make sure that they report those complaints through the MHRA yellow card scheme, so that we can build a body of evidence about where things have gone wrong.'*[124]
1st November 2017	Mesh Ireland	Patient Group established.
20th November 2017	Balsamo et al.	**Sacrocolpopexy with polyvinylidene fluoride mesh for pelvic organ prolapse: Mid term comparative outcomes with polypropylene mesh[199]** First study to compare surgical, anatomical and functional outcomes of POP repair (in this case, sacrocolpopexy) using polyvinylidene fluoride (PVDF) and polypropylene (PP) mesh. The mean follow-up was 94± 17.31 months for the PP and 25.6± 13.8 months for the PVDF group. *'Only 1 patient in PP group and 2 in PVDF group (p = 0.47) presented a mesh exposure'* Study findings suggest that both meshes can be safely and effectively used with good anatomical outcomes. PVDF use was associated with significantly less urinary storage dysfunction symptoms and sexual dysfunction.
28th November 2017	TGA (Australia)	Removal of transvaginal mesh products whose sole use is the treatment of POP via transvaginal implantation from the Australian Register of Therapeutic Goods (ARTG).

[199] R. Balsamo *et al.*, Sacrocolpopexy with polyvinylidene fluoride mesh for pelvic organ prolapse: Mid term comparative outcomes with polypropylene mesh. *European journal of obstetrics, gynecology, and reproductive biology* **220**, 74-78 (2018).

		Following TGA review of clinical evidence and international studies, TGA was of the belief that the benefits of using transvaginal mesh products in the treatment of POP did not outweigh the risks. TGA also considered that the risks associated with mesh products as single incision mini-slings for SUI were not outweighed by benefits. These products were removed from the ARTG. Mid-urethral slings were not removed from the ARTG[200].
December 2017	NICE	Guidance IPG599 **Transvaginal mesh repair of anterior or posterior vaginal wall prolapse**[201] Current evidence on the safety of transvaginal mesh repair of anterior or posterior vaginal wall prolapse shows there are serious but well-recognised safety concerns. Evidence of long-term efficacy is inadequate in quality and quantity. Therefore, this procedure should only be used in the context of research. All adverse events should be reported to the MHRA. Further research should include details of patient selection, long-term outcomes including complications, type of mesh used and method of fixation, and quality of life.
6th December 2017	Heneghan et al.	**Trials of transvaginal mesh devices for pelvic organ prolapse: a systematic database review of the US FDA approval process.**[202] Used FDA databases to determine the evidence for approval of transvaginal mesh. A 'family tree' of device equivalence was created also (see Appendix 1). The study found 61 devices whose approval ultimately relied on claimed equivalence to the Mersilene Mesh and the ProteGen Sling. There was no clinical trials evidence for these 61 devices at the

[200] TGA, Safety information, 17 May 2019, TGA undertakes regulatory actions after review into urogynaecological surgical mesh implants, viewed 12 August 2019, available online at: https://www.tga.gov.au/alert/tga-actions-after-review-urogynaecological-surgical-mesh-implants
[201] NICE, Guidance December 2017, Transvaginal mesh repair of anterior or posterior vaginal wall prolapse Interventional procedures guidance [IPG599] viewed 12 August 2019, available online at: https://www.nice.org.uk/guidance/ipg599/chapter/1-Recommendations
[202] C. J. Heneghan *et al.*, Trials of transvaginal mesh devices for pelvic organ prolapse: a systematic database review of the US FDA approval process. *BMJ Open* **7**, (2017).

		time of approval. Publication of RCTs occurred at a median of 5 years after device approval (range 1-14 years). Analysis of 119 FDA 522 orders revealed that in 79 (66%) the manufacturer ceased market distribution of the device, and in 26 (22%) the manufacturer had changed the indication. Only seven studies (six cohorts and new randomised controlled trial) covering 11 orders were recruiting participants (none had reported outcomes).
7th December 2017	BMJ	**Transvaginal mesh failure: lessons for regulation of implantable devices**[203] 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.
2017	RCOG	RCOG website updates resources to support decision making, including patient information leaflets.[204]
2017	Cochrane	**Single-incision sling operations for urinary incontinence in women (Review)**[205] 31 trials identified involving 3290 women. Found that women were more likely to remain incontinent after surgery with single-incision slings than with retropubic slings such as TVT. The adverse event profile was significantly worse, specifically consisting of higher risks of vaginal mesh exposure and operative blood loss. Postoperative pain was less common with single-incision slings and rates of long-term pain were marginally lower. Overall results show that TVT-Secur is considerably inferior to retropubic and inside-out TOT, but additional evidence is required to allow any reasonable comparison of other single-incision slings versus TOT.

[203] C. Heneghan *et al.*, Transvaginal mesh failure: lessons for regulation of implantable devices. *BMJ (Clinical research ed.)* **359**, (2017).
[204] Available online: https://www.rcog.org.uk/en/guidelines-research-services/patient-safety/mesh/
[205] A. Nambiar, J. D. Cody, S. T. Jeffery, P. Aluko, Single-incision sling operations for urinary incontinence in women. *The Cochrane database of systematic reviews* **7**, Cd008709 (2017).

13th January 2018	Song et al.	**The efficacy and safety comparison of surgical treatments for stress urinary incontinence: A network meta - analysis**[206] 44 studies which reported objective cure rate (7117 patients) were included in the meta-analysis. Compared to TVT, TOT (and Adjust) had no significant difference in objective cure rate (whist TVTO and TVT-S had lower objective cure rates). - 18 studies described subjective cure rate (2,490 patients). There were no significant differences between TVT, TOT, and TVT-O. - 20 studies (3,200 patients) reported the number of postoperative complications. Results from network meta-analysis suggested that there were no statistically significant differences between TVT and TOT (TVTO, Adjust and TVT-S) - 16 studies described the adverse event of the bladder perforation. TOT (TVTO and TVT-S) had a statistically lower bladder perforation rate compared with TVT. - 13 studies reported tape erosion - there were no significant differences between TVT and TOT. - 22 studies analysed postoperative urinary retention. The method of TVT-O appeared to exhibit less postoperative retention compared with TVT. The other surgeries of TVT-S, TOT, and Ajust had no significant difference with each other. - 22 studies described postoperative pain. No significant difference was observed between TVT and TOT. TVT-S had the lowest pain risk. Authors conclude that TOT is the optimal regimen for SUI with high efficacy and moderate safety when compared with TVT, TVT-O, TVT-S, and Ajust interventions. However, the study had limitations (only 5 procedures looked at, inconsistent description of blinding and allocation concealment in studies, not all endpoints looked at) and additional high-quality studies are needed to further evaluate the outcomes.

[206] Song P, Wen Y, Huang C et al Neurourol Urodyn. 2018 Apr;37(4):1199-1211.

17th January 2018	TGA (Australia)	New additions to Instructions For Use (IFU) for mid-urethral slings for SUI[207]
18th January 2018	RCOG, BSUG	**RCOG and BSUG response to NICE guidance on transvaginal mesh repair for prolapse**[208] It is noted that *'current evidence does not recommend the routine use of mesh to treat prolapse as the first surgical intervention, due to higher complication rates when compared to non-mesh repairs. Therefore, this guidance is consistent with the majority of UK current clinical practice'.* Concern was acknowledged that there is a small subset of women for whom other surgical interventions are not appropriate and the use of mesh may be of benefit to them, provided they have appropriate information and counselling about the risks and benefits, and have explored all other treatment options. Concern was raised that the guidance may leave these women without an effective option to manage their condition. It was also a concern that the recommendation would halt research into vaginal placement of mesh for POP. The societies suggested that NICE recommend this as a priority area in order to ensure we have the optimal surgical approach to care for women with prolapse. Incomplete recording of long-term outcome and complication incidence was raised as an issue, with the recommendation for increased reporting to the BSUG database and the MHRA Yellow Card scheme.
31st January 2018	MedSafe (New Zealand)	Announcement on the outcomes of regulatory action on surgical mesh products in New Zealand.[209] In December 2017, Medsafe used the provisions in the Medicines Act 1981 to request safety information from four suppliers of surgical mesh products in New

[207] TGA, Safety information, 17 January 2018, Update – Stress Urinary Incontinence (SUI) mid-urethral slings, viewed 12 August 2019, available online at: https://www.tga.gov.au/alert/tga-actions-after-review-urogynaecological-surgical-mesh-implants#actions

[208] BSUG, 2018, RCOG and BSUG response to NICE guidance on transvaginal mesh repair for prolapse, viewed 12 August 2019, available online at: https://bsug.org.uk/news-details/rcog-and-bsug-response-to-nice-guidance-on-transvaginal-mesh-repair-for-prolapse/72/0/0

[209] Medsafe – New Zealand Medicines and Medical Devices Safety Authority, Safety Information, 2018, Surgical Mesh Implants – Regulatory action on surgical mesh products, viewed 12 August 2019, available online at: https://www.medsafe.govt.nz/hot/alerts/UrogynaecologicaSurgicalMeshImplants.asp

		Zealand. All four companies responded to confirm that all products removed from Australian register are no longer supplied in New Zealand Following TGA lead, no transvaginal mesh products for POP supplied in New Zealand and info added to IFU for mid-urethral slings. This action relates to use of surgical mesh in POP via transvaginal implantation and one single type of mesh for SUI. This action does not affect the supply of surgical mesh products for hernia repair or SUI.
January 2018	Souders et al.	**The Truth Behind Transvaginal Mesh Litigation: Devices, Timelines, and Provider Characteristics**[210] Evaluated a 1% random sample from the Bloomberg Law Database: 2000 to 2014 and associated legal documents. Outcomes and measures used included annual rate of claim, mesh type, time interval between surgery and claim, defendants, and surgeon training. Of 739 claims, 63.3% involved slings for SUI, 13.3% mesh for POP, and 165 (23.2%) involved both. The mesh named most often in claims was retropubic slings at 30.3% and transobturator slings at 27.1%. The number of cases filed increased significantly from 730 in 2011 to 11,798 in 2012 (perhaps as a result of 2011 FDA communication about mesh for POP) which then almost tripled in 2013 to 34,017. The interval from surgery to claim filing ranged from 4.8 to 5.3 years. Only 12% of implanting surgeons were or became board certified in Female Pelvic Medicine and Reconstructive Surgery. Only 4 cases named providers as co-defendants.
6th February 2018	Hansard	House of Lords - In response to a question from Lord Hunt of Kings Heath regarding a review of the safety of pelvic mesh implants, Lord O'Shaughnessy (Parliamentary Under Secretary of State at the Department of Health) stated that:

[210] C. P. Souders *et al.*, The Truth Behind Transvaginal Mesh Litigation: Devices, Timelines, and Provider Characteristics. *Female pelvic medicine & reconstructive surgery* **24**, 21-25 (2018).

		'…we have asked the MHRA, NICE and NHS England to have a look at the correct use of this kind of mesh. They have all concluded that they do not support a complete ban. They propose a range of restrictions on usage. Indeed, the most recent interventional procedure from NICE on prolapse said that it should be used only for research purposes and not as a front-line treatment. However, I am aware that Australia and New Zealand are implementing bans for particular usage. I have asked NICE and MHRA to investigate why they have done that and to report to me urgently so that I can see the grounds for the ban.'[211].
12th February 2018	Luo et al.	**Long term Follow-up of Transvaginal Anatomical Implant of Mesh in Pelvic organ prolapse**[212] A study designed to assess the safety and long-term outcomes of transvaginal mesh to treat POP, through retrospective review of the medical records of 175 consecutive patients who underwent transvaginal mesh implantation for POP at a single centre from April 2007 to December 2012. The 'anatomical implant technique' is described and the authors sate that their '*anatomical implant technique for correcting POP is feasible in TVM procedures, which lead to favourable subjective and objective outcomes with the lowest rates of mesh exposure (1.1%) in published data'* The anatomical implant technique was applied in all patient operations. 36 cases of Prolift A, 114 cases of Prolift T, 4 cases of Prolift P, 3 cases of Prosima A and 18 cases of Prosima C were performed; 25 cases of Tension-free Vaginal Tape Obturator (TVT-O) and 4 cases of Tension-free Vaginal Tape (TVT) were performed at the same period of surgery. Authors report that *'In average of 8 years (ranging from 4 to 10 years), the objective cure ratio reached 99.4%; and the subjective success rate of the TVM operation was 91.4%. Only 2 cases (1.1%) were identified as having mesh exposure. The reoperation rate was 4.0% (95% CI, 1.1–6.9%). No patients abstained from sex due to the operation or postoperative discomfort.'.* Seventeen patients

[211]Hansard, House of Lords, Health: Pelvic Mesh Implants, 06 February 2018, Volume 788, viewed 12 August 2019, available online at: https://hansard.parliament.uk/Lords/2018-02-06/debates/D175ADBF-5215-441A-AD04-727CA8A5C7AB/HealthPelvicMeshImplants

[212] D.-Y. Luo, T.-X. Yang, H. Shen, Long term Follow-up of Transvaginal Anatomical Implant of Mesh in Pelvic organ prolapse. *Scientific reports* **8**, 2829-2829 (2018).

		reported chronic pain and discomfort on the perineum, operative incision or puncture area. Ninety-six PFDI-20 questionnaires (54.9%) were effectively completed. When the patients were asked whether they would have the operation again with the clear knowledge of their postoperative life state, the responses were all positive; and they would recommend this operation to other patients.
21st Feb 2018	Hansard	House of Commons - The Secretary of State for Health and Social Care (Jeremy Hunt) announced an Independent Medicines and Medical Devices Safety Review (IMMDS Review). One of the interventions the Review was tasked with considering was the use of mesh in pelvic surgery.[213] *'I have asked Baroness Julia Cumberlege to conduct a review into what happened in each of these three cases, including whether the processes pursued to date have been sufficient and satisfactory, and to make recommendations on what should happen in future. She will assess, first, the robustness and speed the of processes followed by the relevant authorities and clinical bodies to ensure that appropriate processes were followed when safety concerns were raised; secondly, whether the regulators and NHS bodies did enough to engage with those affected to ensure their concerns were escalated and acted upon; thirdly, whether there has been sufficient co-ordination between relevant bodies and the groups raising concerns; and fourthly, whether we need an independent system to decide what further action may be required either in these cases or in the future.'* 'On vaginal mesh. I asked the chief medical officer for advice in the light of calls for a full ban. She has been clear that clinical experts here and abroad agree that, when used appropriately, many women gain benefit from this intervention, hence a full ban is not the right answer in the light of the current evidence available. However, this is not to minimise the suffering many women have experienced, which is why today I can announce that we will be publishing a retrospective audit to investigate the links between patient-level data to explore outcomes, and investing £1.1 million

[213] Hansard, House of Commons, 21 February 2018, Volume 636, Medicines and Medical Devices Safety Review, viewed 12 August 2019, available online at: https://hansard.parliament.uk/Commons/2018-02-21/debates/7DA2E2F3-E1E6-40CB-8061-680E0399CA97/MedicinesAndMedicalDevicesSafetyReview

		to develop a comprehensive database for vaginal mesh to improve clinical practice and identify issues.' 'When it comes to mesh, no EU country has banned its use. In my understanding, Australia and New Zealand have not introduced a full ban. We have taken very clear advice. We obviously have a responsibility to all patients, and the medical advice from the chief medical officer is clear that some women benefit from mesh, if it is appropriately used, so we are following that advice. However, the review will look at all the processes around mesh. We will publish NICE guidelines on persistent pain and ventral meshes—it is also important to say that meshes are used in men as well as women—and we absolutely have to get this right.'
February 2018	American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) joint position statement	Updated position statement on mesh MUS for SUI[214], in response to FDA white paper and safety communication published in 2011, regarding safety and efficacy of transvaginal mesh of surgical mesh for POP as well as increased media reporting of mesh litigation. The societies were *'concerned that the multimedia attention has resulted in confusion, fear, and an unbalanced negative perception regarding the midurethral sling as a treatment for SUI. This negative perception of the MUS is not shared by the international medical community and the overwhelming majority of women who have been satisfied with their MUS'* The statement posits that Polypropylene material is safe and effective as a surgical implant, the monofilament polypropylene mesh MUS is the most extensively studied anti- incontinence procedure in history, Polypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients, The FDA has clearly stated that the polypropylene MUS is safe and effective in the treatment of SUI and the European Commission enquiry on the safety of surgical meshes supports continuing synthetic sling use for SUI.

[214] AUGS, SUFU, 2018, Position Statement – Mesh Midurethral Slings for Stress Urinary Incontinence, viewed 12 August 2019, available online at: https://www.augs.org/assets/1/6/AUGS-SUFU_MUS_Position_Statement.pdf

		The statement concludes that *'This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.'* The statement was supported by the American Association of Gynecologic Laparoscopists (AAGL) the National Association For Continence (NAFC) the International Urogynecological Association (IUGA) and the American College of Obstetricians and Gynecologists (ACOG).
28th March 2018	Mashed Up By Mesh	Patient Group set up.
March 2018	Altman et al.	**Cancer Risk After Midurethral Sling Surgery Using Polypropylene Mesh[215]** Nationwide (Sweden) cohort study designed to assess whether there is any association between the implantation of synthetic polypropylene mesh slings for the treatment of SUI and risk of cancer. The final study population included 5,385,186 women, including 20,905 with mesh sling insertions. Other than an inverse association with rectal cancer, there were no significant differences in risk between mesh-inserted patients and non-mesh patients for pelvic organ cancers including ovarian, endometrial, cervical, bladder, and urethra. No significant association was observed between mesh-inserted patients and primary cancer in any organ system when compared with non-mesh patients. The relative risk for cancer after exposure showed little variation over time except for an inverse overall correlation within the first 4 years of surgery. The incidence rates per 100,000 person-years (95% CIs) for mesh-inserted vs non-mesh patients were 20.5 (14.3-29.5) vs 21.0 (20.6-21.5) for rectal cancer, 25.5 (18.4-35.3) vs 19.8 (19.4-20.2) for ovarian cancer, 65.0 (53.0-79.8) vs 33.1 (32.6-33.7) for endometrial cancer, 5.7 (2.8-11.3) vs 11.9 (11.6-12.2) for cervical cancer, and 19.1 (13.1-27.8) vs 13.3 (13.0-13.7) for bladder and urethra cancer.

[215] D. Altman *et al.*, Cancer Risk After Midurethral Sling Surgery Using Polypropylene Mesh. *Obstet Gynecol* **131**, 469-474 (2018).

		Authors conclude that their results *'suggest that midurethral polypropylene sling surgery for SUI is not associated with an increased cancer risk later in life'*
17th April 2018	NHS Digital	**Retrospective Review of Surgery for Urogynaecological Prolapse and Stress Urinary Incontinence using Tape or Mesh: Hospital Episode Statistics (HES), Experimental Statistics, April 2008 - March 2017**[216] The HES data warehouse contains details of all admissions, outpatient appointments and accident and emergency (A&E) attendances at NHS hospitals in England. 100,516 patients reviewed. The statistics are classified as experimental and should be used with caution. Experimental statistics are new official statistics undergoing evaluation. In this case, the statistics are marked as 'experimental' because the pseudonymised patient key is used to count the number of patients, rather than 'episode attendances' which is achieved normally from HES data. *'such information is now being published by NHS Digital as experimental statistics whilst further development work on establishing a robust methodology for aggregating patient level HES data is undertaken'* **Key Facts:** Between April 2008 and March 2017: - 194,107 patients had urogynaecological procedures of which 96,286 were for

[216]NHS Digital, 2018, Retrospective Review of Surgery for Urogynaecological Prolapse and Stress Urinary Incontinence using Tape or Mesh: Hospital Episode Statistics (HES), Experimental Statistics, April 2008 - March 2017 [PAS], viewed 12 August 2019, available online at: https://digital.nhs.uk/data-and-information/publications/statistical/mesh/apr08-mar17/retrospective-review-of-surgery-for-vaginal-prolapse-and-stress-urinary-incontinence-using-tape-or-mesh-copy

		urogynaecological prolapse and 101,538 were for stress urinary incontinence. - 100,516 patients had a reported tape insertion procedure for stress urinary incontinence. - 1,195 patients had a reported non-tape procedure for stress urinary incontinence. - 27,016 patients had a reported mesh insertion procedure for urogynaecological prolapse. - 71,350 patients had a reported a non-mesh procedure for urogynaecological prolapse. From April 2016 to March 2017: - 7,245 patients had a tape insertion for SUI (a reduction of 48% from the period April 2008 to March 2009 when 13,990 patients were recorded). - 133 patients had an initial non-tape procedure for SUI (a reduction of 6% from April 2008 to March 2009 when 141 patients were recorded). - 2,680 patients had a mesh insertion for urogynaelogical prolapse (a reduction of 13% from April 2008 to March 2009 when 3,073 patients were recorded). - 7,334 patients had a non-mesh procedure for urogynaelogical prolapse (a reduction of 12% from April 2008 to March 2009 when 8,338 patients were recorded). Readmission for removal: 1.2-1.7 per 1,000 Removal post 30 days: 10.2 per 1,000 but dropping to 7.2
19th April 2018	Hansard	House of Commons - Debate on Surgical Mesh, led by Emma Hardy, MP, Vice Chair of APPG on Surgical Mesh Implants. She called for the Government to suspend prolapse and incontinence mesh operations while the audit is being carried out, to bring forward the NICE guidelines for mesh in SUI from 2019 to 2018, and to commit to a full public inquiry into mesh if the audit suggests that this is the best course of action.[217] The parliamentary under-secretary of state for health (Jackie Doyle-Price) made the following pertinent remarks, in conclusion:

[217] Hansard, House of Commons, 19 April 2018, Volume 639, Surgical Mesh, viewed 12 August 2019, available online at: https://hansard.parliament.uk/Commons/2018-04-19/debates/C5B94EB2-2398-4F0E-BE9E-D502ACEBFA62/SurgicalMesh

		'It is very clear from the clinical guidance on these products that they should not be used as a first intervention, and should be used only in very extreme cases. We are to be very concerned about the extent to which this has been adopted.' *'I have been horrified in this debate to hear how many women did not understand the treatment that they were getting. That is clearly unacceptable.'* *'We need to do more to change the culture of our health service and the way in which medical professionals interact with women.'*
4th May 2018	Welsh Task and Finish Group	**Report of the Welsh Task and Finish Group to Review the Use of Vaginal Synthetic Mesh Tape and Sheets for Stress Urinary Incontinence and Pelvic Organ Prolapse[218]** Recommendations include: - Scottish decision-making tool and BAUS info leaflets should be modified for use in Wales, a series of FAQs to be produced also. - Enhanced physiotherapy service - NICE guidelines to be followed - Improvements to informed consent procedure for SUI procedures. - Colorectal surgeons to adopt a suitable shared decision tool - Establishment of more MDTs in Wales, with at least one accredited mesh removal centre also. - Improved GP access to specialist advice, such as the GP resource produced by the English Oversight Group. - Improved recording of procedures/implants, linked to patient record, with improved clinical coding and the implementation of barcode scanning. Any system developed should allow clinicians to add 'soft data' such as decision-making tools or patient questionnaires.

[218] Report of the Welsh Task and Finish Group to Review the Use of Vaginal Synthetic Mesh Tape and Sheets for Stress Urinary Incontinence and Pelvic Organ Prolapse May 2018 https://gov.wales/docs/dhss/publications/180504reporten.pdf

May 2018	Welsh Minister for Health and Social Services	Announcement of the establishment of the Women's Health Implementation Group (WHIG) to oversee specific areas of women's health requiring urgent attention and improvement. The first priority of the WHIG would be to oversee the implementation of recommendations from the vaginal mesh and tape review.[219] £1 million a year was pledged to support the work of WHIG.
7th July 2018	Bakas et al.	**Assessment of the long-term outcome of TVT procedure for stress urinary incontinence in a female population: results at 17 years' follow-up[220]** A prospective study designed to assess the outcome of the tension-free vaginal tape (TVT) procedure in female patients with urodynamic SUI at 17 years follow-up. Out of the 61 initial patients, 56 were available for follow-up. Objective cure rate was 83.9% at 17 years follow-up. Subjective cure rate was 78.6%, subjective improvement was 8.9%, and failure rate was 12.5%. Frequency was present in 39.3% of patients, overactive bladder symptoms were present in 30.3% of patients and urge urinary incontinence was reported by 12.5% of patients. Difficulty emptying the bladder was reported by 17.8% of patients and recurrent UTI was seen in 3.5% of patients. There was one case of TVT erosion to the vaginal mucosa, which was managed conservatively. Authors conclude that the TVT procedure for the management of SUI in women maintains its efficacy in the long-term, with a very low complication rate.
10th July 2018	IMMDS Review	IMMDS Review calls for immediate pause in the use of surgical mesh for stress urinary incontinence. Baroness Julia Cumberlege, Chair of the Review, has advised the Department of Health and Social Care and NHS England that surgical mesh should not be used for the treatment of stress urinary incontinence

[219] Written Statement, Welsh Government, viewed 05/11/19, available online at: https://gov.wales/written-statement-update-progress-being-made-womens-health-implementation-group

[220] P. Bakas *et al.*, Assessment of the long-term outcome of TVT procedure for stress urinary incontinence in a female population: results at 17 years' follow-up. *Int Urogynecol J* **30**, 265-269 (2019).

		until a set of conditions to mitigate the risks of injury are met. Baroness Cumberlege has said that these conditions should be met by March 2019. The Department and NHS England have accepted the recommendation. The conditions of lifting the pause in the use of surgical mesh, which should be met by March 2019, are as follows: i. Surgeons should only undertake operations for SUI if they are appropriately trained, and only if they undertake operations regularly; ii. They report every operation to a national database; iii. A register of operations is maintained to ensure every procedure is notified and the woman identified who has undergone the surgery; iv. Reporting of complications via the MHRA is linked to the register; v. Identification and accreditation of specialist centres for SUI mesh procedures, for removal procedures and other aspects of care for those adversely affected by surgical mesh. vi. NICE guidelines on the use of mesh for SUI are published[221]
10th July 2018		Following a recommendation by the Independent Medicines and Medical Devices Safety Review, the government and NHS paused the use of vaginally inserted surgical mesh for SUI. A letter is sent from NHS England to Acute Trust CEOs and Medical Directors 'VAGINAL MESH: HIGH VIGILANCE RESTRICTION PERIOD: Immediate action required, all cases should be postponed if it is clinically safe to do so'

[221] NICE, April 2019, Urinary incontinence and pelvic organ prolapse in women: management NICE guideline [NG123], available online at: https://www.nice.org.uk/guidance/ng123

		The letter also announces the commissioning of specialised centres which will provide a new multidisciplinary team management and complex vaginal mesh removal surgery for women who have complex vaginal mesh complications.[222]
10th July 2018	BSUG	The British Society of Urogynaecologists (BSUG) made a statement following the mesh pause. '*The British Society of Urogynaecologists (BSUG) does not agree with and strongly opposes the decision to pause/suspend the use of surgical mesh for stress urinary incontinence recommended by the APPG (All Party Parliamentary Group).'* *'This decision is not based on any scientific logic or thinking'.*[223]
11th July 2018	CMO Northern Ireland	Instigation of a pause in the use by the HSC of surgical mesh/tape to treat stress urinary incontinence (SUI) and for urogynaecological prolapse where the mesh is inserted through the vaginal wall[224]. The pause will continue until the following conditions are met: - surgeons should only undertake operations for SUI if they are appropriately trained, and only if they undertake operations regularly - surgeons report every procedure to a national database; - a register of operations is maintained to ensure every procedure is notified and the woman identified who has undergone the surgery; - reporting of complications via MHRA is linked to the register; - identification and accreditation of specialist centres for SUI mesh procedures, for removal procedures and other aspects of care for those adversely affected by surgical mesh; - NICE guidelines on the use of mesh for SUI are published.

[222] Letter from Prof Stephen Powis and Dr Kathy McLean to Acute trust CEOs and medical directors, 2018, VAGINAL MESH: HIGH VIGILANCE RESTRICTION PERIOD: Immediate action required, all cases should be postponed if it is clinically safe to do so, viewed 12 August 2019, available online at: https://i.emlfiles4.com/cmpdoc/9/7/2/8/1/1/files/47633_mesh-letter-to-acute-ceos-and-mds.pdf
[223] https://bsug.org.uk/news-details/vaginal-mesh-high-vigilance-restriction-period/76/0/0
[224] Letter from Dr Michael McBride, 11 July 2018, viewed 12 August 2019, available online at: http://www.hscbusiness.hscni.net/pdf/HSS(MD)12%202018_IMMEDIATE%20ACTION%20REQUIRED.pdf

11th July 2018	Welsh Cabinet Secretary for Health and Social Services	In a written statement in response to the IMMDS Review's announcement of the UK mesh pause, Vaughan Gething wrote that the principle of high vigilance and mesh restriction until conditions are met should also apply in Wales, noting consistency with the recommendations made by the Welsh Task and Finish Group. It was noted that the Welsh CMO had written to medical directors to draw their attention to the IMMDS Review recommendations and that the Women's Health Implementation Group (WHIG) would meet to oversee implementation of the recommendations.[225]
11th July 2018	BSUG	**National BSUG audit of stress urinary incontinence surgery in England[226]** Supported by HQIP and NHS England, this was a national clinical audit looking at the intra- and postoperative complications and outcomes for stress urinary incontinence procedures. Data were collected for all continence procedures performed in 2013 through the BSUG database. 4993 urinary incontinence procedures were recorded from 177 consultants at 110 centres in England: 94.6% were midurethral slings; 86.7% were submitted by BSUG members. Postoperative follow-up data were available for 80% of patients: 92.3% were very much better/much better postoperatively, and 96.3% proceeded with no reported complications. There were 3.7% of cases in which a perioperative complication was recorded. Pain persisting >30 days was reported in 1.9% of all patients. National BSUG audit of stress urinary incontinence surgery in England Midurethral synthetic slings were shown to be safe and effective as a treatment option, with >90% being very much/much better at their postoperative follow-up.

[225] Vaughan Gething, 2018, Written Statement - Baroness Cumberlege's announcement on the use of surgical mesh, viewed 12 August 2019, available online at: https://gov.wales/written-statement-baroness-cumberleges-announcement-use-surgical-mesh

[226] S. Jha, T. Hillard, A. Monga, J. Duckett, National BSUG audit of stress urinary incontinence surgery in England. *Int Urogynecol J*, (2018).

12th July 2018	British Pain Society	**Press statement on suspension of mesh surgery in NHS hospitals**[227] In response to the mesh pause, the society, and Dr Andrew Baranowski (President) raise the issue of limited NHS resources for those with chronic pelvic pain. It is unclear how many mesh-inserted women go on to develop chronic pain (some estimates are as high as 40%) – more research is required to understand extent of the problem. The statement supports the careful and responsible use of pelvic mesh surgery by expert surgeons but recommends support by trained pain specialists at all levels.
13th July 2018	FDA	FDA ordered the manufacturer of the last mesh surgical products on the market for the transvaginal repair of pelvic organ prolapse in the posterior compartment (rectocele) to stop selling and distributing their products. The company withdrew their product from the market.[228]
17th July 2018	MHRA	Statement on 'pause', accepting the recommendation made by the IMMDS Review.[229] *'These procedures have not been banned and during this pause, they will continue to be used when there is no viable alternative and after close and comprehensive consultation between patient and clinician.'* *'There has not been any new evidence which would prompt regulatory action and the position of MHRA remains the same on these medical devices. We continue to work with other regulators in the EU and wider, as well as colleagues across the health sector, to monitor and examine evidence as it becomes available.'*
18th July 2018		**Review letter to Keith Willett (cc'd to DHSC) regarding how 'high vigilance, restrictive practice' is being interpreted in practice**:

[227] The British Pain Society, 2018, Press Statement on suspension of mesh surgery in NHS Hospitals, viewed 12 August 2019, available online at: https://www.britishpainsociety.org/static/uploads/resources/files/Press_statement_on_suspension_of_mesh_surgery_in_NHS_Hospitals.pdf

[228] FDA, 2019, FDA's Activities: Urogynecologic Surgical Mesh, viewed 12 August 2019, available online at: https://www.fda.gov/medical-devices/urogynecologic-surgical-mesh-implants/fdas-activities-urogynecologic-surgical-mesh

[229] MHRA, 2018, Pause on the use of vaginally inserted surgical mesh for stress urinary incontinence, viewed 12 August 2019, available online at: https://www.gov.uk/government/news/pause-on-the-use-of-vaginally-inserted-surgical-mesh-for-stress-urinary-incontinence

		- the means and the frequency with which NHSE proposes to monitor the number and nature of the 'exceptions' to the 'pause' on a Trust by Trust basis; - the evidence medical Directors will be asked to supply in order to attest to the competence of the surgeons undertaking these mesh procedures by exception and - the process by which we can be satisfied that where such procedures by exception are undertaken they are based on fully informed patient choice and consent.
20th July 2018	NHS England, NHS Improvement	**Letter sent from NHS England (Keith Willett) and NHS Improvement (Kathy McLean) to Regional Directors, Trust Medical Directors**, and clinicians involved in the care of patients with stress urinary incontinence and pelvic organ prolapse, regarding the pause, including Clinical Advisory Group (CAG) guidance[230]. The recommendations of the mesh pause CAG are summarised below: **Recommendation A: The mesh and tape procedures to be included in the restriction of use** 1) The restricted practice should apply only to: 2) Insertion of synthetic tape as a surgical intervention in SUI. 3) Vaginally inserted synthetic mesh as a treatment for prolapse. **Recommendation B: Mesh procedures that should be excluded from the restriction but should be subject to high vigilance scrutiny** 4) Abdominally-inserted mesh for prolapse (such as for sacrocolpopexy, hysteropexy, and rectopexy) should be excluded from the restriction but included in the high vigilance scrutiny. Clinical advice is that there are few viable alternatives.

[230] Letter from Prof Kieth Willet and Dr Kathy McLean, with guidance, 20th July 2018, viewed 12 August 2019, available online at: https://www.rcog.org.uk/globalassets/documents/guidelines/safety-alerts/lettertotrusts.pdfhttps://improvement.nhs.uk/documents/5122/MESH_letter_-_Extension_of_pause_on_the_use_of_vaginal_mesh_29_March_2019.pdf

		Recommendation C: Alternative non-mesh procedures that should also be subject to increased vigilance given the change in practice that may result from the restriction of synthetic mesh and tape use. 5) The restriction in practice should not apply to non-tape/mesh alternative procedures for SUI – periurethral injectables, colposuspension and fascial sling procedures. 6) However, it must be recognised that few surgeons now have the skills for open or laparoscopic colposuspension 7) It will therefore be essential to mitigate this by including non-tape procedures for SUI in the high vigilance scrutiny: e.g. colposuspension, fascial sling procedures, and periurethral injectable treatments. 8) Biological mesh should not be used as a substitute for synthetic mesh **Recommendation D: The high vigilance process must ensure the necessity and appropriateness of any procedure, and ensure that all appropriate treatment and surgical options have been fully explained and offered, including where secondary referral would be required.** 9)This includes MDT decision making, assurance of surgeon competence and ensuring that appropriate information is used during the consent process, as well as ensuring that a process for documenting and registering procedures is in place. **Recommendation E: Trusts/hospitals and GPs should support patients with advice, including patients newly referred or diagnosed, patients already on the waiting list, and patients who have had previous mesh surgery who may have concerns.**
23rd July 2018		**Excellence in Continence Care** is published by NHS England[231] This document gives practical guidance for commissioners, providers, health and social care staff

[231] https://www.england.nhs.uk/publication/excellence-in-continence-care/ (published 23 July 2018)

		to help ensure people receive excellent continence care consideration.
24th July 2018	Republic of Ireland Minister for Health	Statement made in response to the English mesh pause. The Department's CMO requested the Health Service Executive (HSE) to pause the use of all procedures involving transvaginal mesh devices for the management of SUI or POP in HSE funded hospitals, in cases where it is clinically appropriate and safe to do so.[232]
July 2018	Braga et al.	**Tension-free Vaginal Tape for Treatment of Pure Urodynamic Stress Urinary Incontinence: Efficacy and Adverse Effects at 17-year Follow-Up[233]** A prospective study conducted in two centres across two countries, designed to assess the efficacy and safety of retropubic tension-free vaginal tape (TVT) 17 years after implantation for the treatment of female pure stress urinary incontinence (SUI). A total of 52 women underwent TVT implantation. At 17-year follow-up, 46 women were available for the evaluation. At 17 years after surgery, 89.1% of the 46 women declared themselves cured, 91.4% were objectively cured. No significant deterioration in objective cure rates was observed over time. 32.6% of women reported the onset of *de novo* overactive bladder at 17-year follow-up. No other late complications were reported. Authors conclude that *"The 17-year results of this study showed that TVT is a highly effective and safe option for the treatment of SUI".*
16th August 2018	NHS England	Consultation Guide: Specialised gynaecology surgery and complex urogynaecology conditions service specifications (including service specification for complications of mesh inserted for urinary incontinence and vaginal prolapse) – opened for consultation[234]

[232] Minister for Health, 2018, Press Release: Minister for Health Simon Harris Announces Pause in the Use of Transvaginal Mesh Devices, viewed 12 August 2019, available online at: https://health.gov.ie/blog/press-release/minister-for-health-simon-harris-announces-pause-in-the-use-of-transvaginal-mesh-devices/

[233] A. Braga *et al.*, Tension-free vaginal tape for treatment of pure urodynamic stress urinary incontinence: efficacy and adverse effects at 17-year follow-up. *BJU international* **122**, 113-117 (2018).

[234] NHS England, 2018, Specialised gynaecology surgery and complex urogynaecology conditions service specifications, viewed 12 August 2019, available online at: https://www.engage.england.nhs.uk/consultation/gynaecology-surgery-and-complex-urogynecology/

21st August 2018	Scottish Parliament	**Public Petitions Committee PE1517 - Polypropylene Mesh Medical Devices Report**[235] In response to petition PE1517, which was lodged in April 2014. The committee calls into question the credibility of the final report as a basis for informing both clinicians and patients to make fully informed decisions. Concern that the final report didn't go far enough and could be used to justify lifting of mesh bans in other jurisdictions. The Committee's preference is for the use of mesh devices to treat SUI and POP to cease in Scotland. It is emphasised that any information made available regarding mesh procedures must highlight the non-mesh alternatives. Due to international concerns around the use of mesh, there may be merit in an international summit/meeting being held in Scotland. Issue of patients being believed was raised throughout the petition process. It was recommended that the independent review be investigated and disregarded/repeated if it is found to lack credibility.
12th September 2018	Cabinet Secretary for Health & Sports – Scottish Government	Statement made in parliament[236], requesting that the use of transvaginal mesh in the treatment of both SUI and POP is immediately halted in Scotland, until: 1. Publication of revised NICE guidance on treatment of both SUI and POP 2. Introduction of a restricted use protocol to assure all surgical interventions *'are carried out only in the most exceptional circumstances and subject to a robust process of approval and fully informed consent'* ***'**Such a halt in use will not affect other uses of mesh—for example, transabdominal and in hernia repair—but we will continue to keep those areas under review.'*

[235] Public Petitions Committee, Scottish Parliament, 2018, PE1517 - Polypropylene Mesh Medical Devices, viewed 12 August 2019, available online at: http://external.parliament.scot/S5_PublicPetitionsCommittee/Reports/PE1517Report.pdf

[236] Cabinet Secretary for Health and Sport Jeane Freeman, Scottish Parliament, 12th September 2018, Debate on Transvaginal Mesh, viewed 12 August 2019, available online at: https://www.theyworkforyou.com/sp/?id=2018-09-12.14.0

12th September 2018	RCOG, BSUG	In response to the Scottish CMO's announcement on the restricted use of transvaginal mesh, the societies supported the CMO's commitment to a UK-wide registry in order to prospectively collect information on the use and outcomes of transvaginal mesh.[237]
October 2018	NICE	**Public consultation on NICE Draft Guideline: Urinary incontinence and pelvic organ prolapse in women: management[238].** This update is intended to include pelvic organ prolapse following the concerns raised.
9th October 2018	Australian Government	Australian Health Minister – Greg Hunt issues a national apology to mesh patients, for the *'historic agony and pain that has come from mesh implantation which have led to horrific outcomes'*
10th October 2018	BMJ	**Vaginal mesh implants: putting the relations between UK doctors and industry in plain sight**[239] Report 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.
10th October 2018	BMJ	**The trial that launched millions of mesh implant procedures: did money compromise the outcome?** [240] Report on potential conflicts of interest in the original two reports produced by Ulmsten et al.[*(1, 2)*] demonstrating safety and efficacy of the TVT procedure. The first showed a promising safety and efficacy profile, but was only performed by urogynaecologists who had developed the procedure. The second study included a further five centres but in the intervening years, Ethicon had agreed to pay Ulmsten $1mil pending a report that showed similar safety and efficacy to his first (which it did) – accusation of potential 'wallet-driven research'.

[237]RCOG, 2018, RCOG/BSUG statement in response to the Scottish CMO's announcement on the restricted use of transvaginal mesh, viewed 12 August 2019, available online at: https://www.rcog.org.uk/en/news/rcogbsug-statement-in-response-to-the-scottish-cmos-announcement-on-the-restricted-use-of-transvaginal-mesh/

[238]NICE, October 2018, Urinary incontinence and pelvic organ prolapse in women: management – Draft for consultation, viewed 12 August 2019, available online at: https://www.nice.org.uk/guidance/ng123/documents/draft-guideline

[239] J. Gornall, Vaginal mesh implants: putting the relations between UK doctors and industry in plain sight. *BMJ (Clinical research ed.)* **363**, (2018).

[240] J. Gornall, The trial that launched millions of mesh implant procedures: did money compromise the outcome? *BMJ (Clinical research ed.)* **363**, (2018).

	Ethicon Written Evidence	Ethicon state[241] that Prof. Ulmsten *'conducted a study on TVT on his own group of 75 patients and published the two-year data in 1996. As part of Ethicon's due diligence in licensing the TVT product in 1997, Ethicon was interested in evaluating evidence that the TVT device would be safe and effective and that Prof. Ulmsten's results could be replicated in the hands of other surgeons in other institutions. To this end, there was a milestone payment of $400,000 included in the TVT License and Supply Agreement which was payable if other surgeons had similar results to that published by Prof. Ulmsten. This type of milestone payment is common where the intellectual property at issue (here the TVT) shows an increased value and utility. While it was impressive that TVT was revolutionary and worked in Prof. Ulmsten's hands, Ethicon wanted to see if the device would be helpful to other surgeons and their patients. Otherwise Ethicon would not want to overpay for intellectual property that had limited use. As a result, several surgeons from six different medical institutions participated in the Scandinavian multicenter trial that was the subject of the 1998 study. Prof. Ulmsten's center was just one of the study centers. None of the trial centers received any financial support from Ethicon for conducting this study. The results of the work of those surgeons were consistent with Prof. Ulmsten's initial findings and demonstrated that the TVT device and the procedure to implant it held immense value to the broader medical community separate and apart from the surgical skills of its inventor. Both studies were published in the International Urogynecology Journal, which is a peer reviewed journal that is one of the preeminent journals in this field. In the twenty years that have passed since the study was published in 1998, hundreds of clinical studies, systematic reviews and metaanalyses with no connection to Prof. Ulmsten or Ethicon have evaluated the clinical performance of TVT, further validating its safety, effectiveness, broad utility, and value'*
11th October 2018	BMJ	**How mesh became a four letter word[242]** Jonathan Gornall charts the use of vaginal mesh as well as the rise and fall of its usage

[241] IMMDSR, Written Evidence, page 112, available online at: https://immdsreview.org.uk/downloads/Evidence/FOR%20PUBLICATION%20Evidence%20submitted%20to%20the%20Review%20following%20its%20Oral%20Hearings%20-%20October%20update.pdf

[242] J. Gornall, How mesh became a four letter word. *BMJ (Clinical research ed.)* **363**, (2018).

23rd October 2018	Gurol-Urganci et al.	**Long-term Rate of Mesh Sling Removal Following Midurethral Mesh Sling Insertion Among Women With Stress Urinary Incontinence**[243] Population-based retrospective cohort study of 95,057 women who underwent midurethral mesh sling insertion for SUI (60,194 with retropubic insertion and 34,863 with transobturator insertion) using HES data. Median follow-up rime was 5.5 years. The rate of sling removal was 1.4% at 1 year, 2.7% at 5 years and 3.3% at 9 years. The 9-year removal risk after transobturator insertion was lower than the risk after retropubic insertion. The rate of reoperation for stress urinary incontinence was 1.3% at 1 year, 3.5% at 5 years, and 4.5% at 9 years.
26th October 2018	Scottish Government Independent Report	**An Investigative Review into the process of establishing, managing and supporting Independent Reviews in Scotland**[244] In response to criticism of the Scottish mesh review, the government ordered an inquiry into the way the review was conducted. The report concluded that the Mesh Review was ill-conceived, thoughtlessly structured and poorly executed. Negative factors including irreconcilable differences of opinion of Review members, lack of agreement on the interpretation of evidence, unhelpful political and media influences and pressure to complete the report. The investigation also identified a number of problems with how the Mesh review solicited, monitored and reported relevant declarations and conflicts of interests by members of the Review Group.

[243] Gurol-Urganci et al. (2018) Long-term Rate of Mesh Sling Removal Following Midurethral Mesh Sling Insertion Among Women With Stress Urinary Incontinence doi: 10.1001/jama.2018.14997
[244] Investigative Review, Department of Health and social care, Scottish government, 2018, An Investigative Review into the process of establishing, managing and supporting Independent Reviews in Scotland, viewed 12 August 2019, available online at: https://www.gov.scot/publications/investigative-review-process-establishing-managing-supporting-independent-reviews-scotland/pages/2/

October 2018	BSUG	BSUG release first national report from the audit and database committee on SUI surgery in the UK from 2008-2017[245]. It is approximated that the database captured approximately 40% of continence procedures between 2008-2017. 26,765 Retropubic MUT procedures were performed in this period and 9,411 transobturator MUT procedures were performed. Note: a total complication rate (postoperative and intraoperative) of 15% for retropubic MUT, 8.5% for transobturator MUT. The total complication rate for colposuspension was 22.4% and that for fascial (native tissue) slings was 29.5%.
27th November 2018	TGA (Australia)	In response to the Expert Review of Medicines and Medical Devices Regulation (MMDR) the TGA attempted to align (wherever possible) the Australian classification of medical devices with the European Union framework. Reclassifying all mesh medical devices from Class IIb to Class III (high risk)[246]. The decision to reclassify ahead of Europe was made due to the serious concerns about risks associated with the use of these devices.
December 2018	Taylor, D.	**The failure of polypropylene surgical mesh *in vivo*[247]** Review of current knowledge on polypropylene mesh, with additional biomechanical analysis. The author comments on the variability of published failure rates from 110 studies; some reported no failures, whilst the highest rate reported was 29.7%. This implies that some other factor(s) may be involved, such as the competence of individual surgeons or the choice of operative procedure in different clinical centres.

[245] BSUG audit and database committee, 2018, Stress urinary incontinence surgery in the UK 2008-2017, viewed 12 August 2019, available online at: https://bsug.org.uk/budcms/includes/kcfinder/upload/files/BSUG%20National%20Report%20-%20Stress%20%20Incontinence%20Surgery%20in%20the%20UK%20(2008-2017).pdf

[246] TGA, Australian Government, 2018, Reclassification of surgical mesh devices, viewed 13 August 2019, available online at: https://www.tga.gov.au/publication/reclassification-surgical-mesh-devices?fbclid=IwAR0HBnoh0JXePmNyrRpa6w-8WYCnzep5HqFV5Gx7yn4qziJuPI1MqDzExNw

[247] D. Taylor, The failure of polypropylene surgical mesh *in vivo*. *Journal of the mechanical behavior of biomedical materials* **88**, 370-376 (2018).

		The author comments that there is no reliable figure for the rate of mesh fracture, but erosion and fracture seem to be linked. Fracture will create sharp edges which are much more likely to abrade tissue. Taylor examines the mechanical forces/loads placed on mesh used for pelvic procedures, he concludes that it is difficult to imagine how the mesh could be loaded sufficiently to cause fracture, even given the most severe conditions. The author concludes/recommends the following: 1. In the case of POP procedures, the rate of mesh failure is so high, and its consequences so severe, that products used for this purpose can be regarded as defective and should not be used. 2. In the case of mesh products for SUI, the rate of mesh failure is lower, but the potential consequences are still severe and long-lasting. So the decision to undergo this kind of operation is one that the patient should make, only after being fully informed of the risks involved. 3. A biomechanics analysis considering various forms of loading, suggests – albeit tentatively - that failure is unlikely by purely mechanical means. It is difficult to estimate the loadings for pelvic mesh operations, compared with hernia mesh. 4. In the case of mesh products for SUI, the rate of mesh failure is lower, but the potential consequences are still severe and long-lasting. So the decision to undergo this kind of operation is one that the patient should make, only after being fully informed of the risks involved. 5. A biomechanics analysis considering various forms of loading, suggests – albeit tentatively - that failure is unlikely by purely mechanical means. It is difficult to estimate the loadings for pelvic mesh operations, compared with hernia mesh. 6. Stress corrosion failure may be occurring in PP mesh *in vivo*. Currently, the evidence is inconclusive, and more work needs to be done. In particular, mechanical tests should be carried out on samples of mesh which have spent periods of time *in vivo*, both in human patients and in animal models. 7. Further work is also needed to quantify the mechanical behaviour of surgical mesh materials,

		especially their defect tolerance, fatigue, creep and stress-corrosion behaviour.
1st January 2019	Pécheux et al.	**Long-term (8.5 years) analysis of the type and rate of reoperation after transvaginal mesh repair (Prolift®) in 349 patients[248]** Study following up 349 patients from a single hospital (via phone calls) at a medium time of 8.5 years. Designed to determine the long-term reoperation rates and type in our patients after transvaginal mesh repair and to study their risk factors. The global reoperation rate at median 8.5 years (including mesh complications, prolapse recurrence and urinary incontinence) was 14.5%. The mesh-related complication rate (including mesh exposures, infections, and retractions requiring surgery) was 4.3%, the urinary incontinence rate was 5.7%. The prolapse recurrence rate was 7.2%; mainly found with posterior mesh only (18.5% of reoperations). For total Prolift, the reoperation rate for prolapse recurrence was 4%. 86.7% of the patients who had an anterior Prolift only or a posterior Prolift only and who were re-operated for prolapse recurrence showed recurrence exclusively in another compartment. Only the posterior mesh type was significantly associated with prolapse recurrence versus total meshes. Authors conclude that *"despite their market withdrawal, the transvaginal meshes are a safe and efficient option for pelvic organ prolapse surgical management. Low rates of mesh complications can be achieved with cautious dissection and adequate training of surgeons."* Two of the authors state conflicts of interest concerning Boston Scientific.
9th January 2019	Welk et al.	**Association of Transvaginal Mesh Complications With the Risk of New-Onset Depression or Self-harm in Women With a Midurethral Sling[249]**

[248] O. Pécheux *et al.*, Long-term (8.5 years) analysis of the type and rate of reoperation after transvaginal mesh repair (Prolift(®)) in 349 patients. *European journal of obstetrics, gynecology, and reproductive biology* **232**, 33-39 (2019).
[249] B. Welk, J. Reid, E. Kelly, Y. M. Wu, Association of Transvaginal Mesh Complications With the Risk of New-Onset Depression or Self-harm in Women With a Midurethral Sling. *JAMA Surg*, (2019).

		Study to determine whether the risk of depression or self-harm behaviour is greater among women with transvaginal mesh complications that required surgical intervention compared with women who did not undergo such surgical correction. 57,611 women met the inclusion criteria and underwent a midurethral mesh sling procedure during the 12-year study period. Of these, 1,586 underwent a surgical correction for a transvaginal mesh complication. The authors identified a statistically significant increased risk of depression among women who required surgical correction. Because of a statistically significant interaction between age and a transvaginal mesh complication, we stratified the study cohort by age groups. A statistically significant increased risk of depression was found only in women younger than 46 years of age. Similar models were created for the secondary outcome of self-harm, and a statistically significant increased adjusted hazard ratio was found for self-harm among women younger than 46 years and those between 46 and 66 years of age. The authors conclude that women can be profoundly affected by complications from a midurethral mesh sling procedure. The age-dependent interaction is potentially a result of a stronger association between transvaginal mesh complications and intimacy among younger women. When managing women with complications, the authors advise that surgeons should be aware of the potential serious psychological implications of these complications.
12th February 2019	Hansard	House of Commons - Debate lead by Owen Smith (chair of APPG on Surgical Mesh Implants) on the licensing of medical devices. Mesh was used as a primary illustrative example of the regulatory system for medical devices in the UK and Europe being unfit and requiring reform.[250] Jackie Doyle-Price (Parliamentary Under-Secretary of State for Health and Social Care) made the following comments in summary: *'It is fair to say that perhaps in the past regulation has focused excessively on what is in the commercial*

[250] Hansard, House of Commons, 12 February 2019, Volume 654, Licensing of Medical Devices, viewed 13 August 2019, available online at: Licensing of Medical Devices - Hansard

		interests of businesses to maintain competition, rather than having patient safety at its heart' *'…it is becoming clear that mesh was deployed far too insensibly—far too many women were given this treatment, often at comparatively young ages, given that this was going to stay in their body for a long time.'* *'I say to those women who have suffered badly at the hands of mesh treatment that there are clear medical criteria relating to that product and, if they have any complaint about the treatment they have received, they should be pursuing claims for clinical negligence against their practitioners.'* *'…medical devices are regulated in an entirely different way from medicines, and we need to make sure that regulation remains fit for purpose and that it responds to technological innovation. We also need to make sure that we have sufficient pre-market assessment, so that in assessing their efficacy we can really give evidence of how these devices are used by patients. That is why manufacturers, notified bodies and the MHRA conduct ongoing post-market surveillance.'* *'…we will implement the regulatory improvements currently being taken through the EU, even though we are now leaving the EU institutions. We are confident that the regulation will drive system-wide improvement, including to the levels of clinical data mandated before products can be placed on the market. That will establish a strong and improved baseline for any system we implement after our departure from the EU'* *'…there has been a historic lack of transparency in the current system. It has not always been easy for patients to investigate and find more data about the things being put in their bodies. That is why the Government have prioritised the issue in negotiations on the new EU legislation'*
28th February 2019	Hansard	House of Lords - Members of the House of Lords

		debated the steps being taken to improve the safety of medicine and medical devices, including vaginal mesh. [251] Lord O'Shaughnessy (former Parliamentary Under Secretary of State for Health and Social Care) summarised with the following comments: *'…patient safety is paramount but must be balanced with innovation; not to give someone a potentially effective treatment is also an issue of safety, because they could be harmed."* *"The importance of data was mentioned, to make sure that treatment is more targeted but also for better reporting and mandatory reporting'* *'…as our medical knowledge expands, complications will only grow. We will need a different, better and more sophisticated system for dealing with those complications.'* *'I finish by reflecting on three things that my noble friend Lady Cumberlege said, which are the lessons for today: we need to be better at listening, better at learning and better at caring. We owe patients in this country better on all those fronts, and I am sure that as a result of today's debate we will do so.'*
1st March 2019	Jan Willem Cohen Tervaert	**Autoinflammatory/autoimmunity syndrome induced by adjuvants (Shoenfeld's syndrome) in patients after a polypropylene mesh implantation**[252] First study linking polypropylene mesh to autoimmune manifestations. Study of 40 patients with mesh implants referred to an Autoimmunity Clinic between January 2014 and December 2017. The study concludes that 40 patients developed symptoms of a systemic illness after a mesh operation. All patients fulfilled the diagnostic criteria for autoinflammatory/autoimmunity syndrome induced by adjuvants (ASIA). One quarter of the patients had

[251] Hansard, House of Lords, 28 February 2019, Volume 796, Safety of Medicines and Medical Devices, viewed 13 August 2019, available online at: https://hansard.parliament.uk/lords/2019-02-28/debates/5C15EA5D-06A3-4F43-90BE-A3FBE6225E54/SafetyOfMedicinesAndMedicalDevices

[252] J. W. Cohen Tervaert, Autoinflammatory/autoimmunity syndrome induced by adjuvants (ASIA; Shoenfeld's syndrome): A new flame. *Autoimmunity Reviews* **17**, 1259-1264 (2018).

		an immunodeficiency, whereas in approximately half of the patients, an autoimmune disease developed. It is postulated that polypropylene mesh implants may increase the risk of developing (auto)immune diseases by acting as an adjuvant.
7th March 2019	C.R. Bard	All urogynaecological mesh manufactured by C.R. Bard designed for the treatment of POP and SUI was voluntarily withdrawn from the market in the UK. The decision was part of a business strategy to stop production rather than continuing to invest in clinical data to support additional EU requirements.[253]
15th March 2019	FDA	Statement issued on efforts to evaluate materials in medical devices to address potential safety questions. The FDA state that the current evidence, although limited, suggests some individuals may be predisposed to develop an immune/inflammatory reaction when exposed to select materials. Pelvic mesh is not directly referenced in this statement, although it demonstrates a growing appreciation of the risks associated with medical devices, especially in relation to potential immune/inflammatory manifestations.[254]
29th March 2019	NHS England, NHS Improvement	The conditions set by the IMMDS Review for resumption of mesh use had not been met. A letter issued to all acute trusts to extend the period of high vigilance restriction on the use of vaginal mesh, with the same restrictions in place.[255]
1st April 2019	NICE	NICE releases patient decision aid for SUI surgery[256] The decision aid carries the logos of The British Association of Urological Surgeons, Royal College of Obstetricians & Gynaecologists and BSUG.

[253] MHRA, 2019, Medical Device alert issued for urogynaecological mesh manufactured by C.R. Bard, viewed 13 August, available online at: https://www.gov.uk/government/news/medical-device-alert-issued-for-urogynaecological-mesh-manufactured-by-cr-bard

[254] FDA, Press Announcement, 2019, Statement from FDA Commissioner Scott Gottlieb, M.D. and Jeff Shuren, M.D., Director of the Center for Devices and Radiological Health, on efforts to evaluate materials in medical devices to address potential safety questions, viewed 13 August 2019, available online at: https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-jeff-shuren-md-director-center-devices-and-3?fbclid=IwAR0-Jp0-3VhiwBT2vq0byTEcOQDxvyGf6CroInGxngVEA5c9eYKH91DnqN4

[255] Letter from Stephen Powis and Kathy McLean to Regional Directors, Trust Medical Directors and clinicians, 29 March 2019, Extension of pause to the use of vaginal mesh, viewed 13 August 2019, Letter from Stephen Powis and Kathy McLean to Regional Directors, Trust Medical Directors and clinicians involved in the care of patients with stress urinary incontinence and pelvic organ prolapse, 2019, available online at: https://www.rcog.org.uk/globalassets/documents/guidelines/safety-alerts/nhs-mesh-letter-extension-of-pause-on-the-use-of-vaginal-mesh-29-march-2019.pdf

[256] NICE, 2019, Surgery for stress urinary incontinence – Patient decision aid, viewed 13 August 2019, available online at: https://www.nice.org.uk/guidance/ng123/resources/surgery-for-stress-urinary-incontinence-patient-decision-aid-pdf-6725286110

2nd April 2019	NICE	NICE published updated guidelines for **Urinary incontinence and pelvic organ prolapse in women: management [NG123]**[257] The guidelines describe MDT setups for the organisation of specialist services, data to be collected from patients, as well as follow-up activity in a registry. Recommendations were made on assessing and managing mesh complications also. If non-surgical management for stress urinary incontinence has failed, and the woman wishes to think about a surgical procedure, offer her the choice of: -colposuspension (open or laparoscopic) or -an autologous rectus fascial sling. Also include the option of a retropubic mid-urethral mesh sling in this choice but see recommendations 1.5.7 to 1.5.11 for additional guidance on the use of mid-urethral mesh sling procedures for stress urinary incontinence. For Mid-urethral mesh sling procedures, NICE recommends not offering TOT unless clinical circumstances prevent use of the retropubic approach. The guidelines also recommend against using the 'top-down' retropubic sling approach, or single-incision mini slings, apart from in clinical trials. For anterior prolapse, recommendation 1.8.21 stated that clinicians should consider synthetic polypropylene or biological mesh insertion for women with recurrent anterior vaginal wall prolapse only after: - regional MDT review and - discussion with the woman about the risks of mesh insertion (see recommendation 1.8.2) and if: - apical support is adequate or - an abdominal approach is contraindicated. This was taken by many to mean that the relegation of transvaginal mesh for POP to 'research only' had been reversed.
2nd April 2019	RCOG, BSUG	In response to the NICE guidance on SUI and POP management, these professional bodies fully endorse the patient decision aids published by NICE. They

[257] NICE, 2019, Urinary incontinence and pelvic organ prolapse in women: management, viewed 13 August 2019, available online at: https://www.nice.org.uk/guidance/ng123

		highlighted that the high vigilance restriction remains in place for the use of mesh and state that they are *'firmly committed to meeting the conditions set out by the Independent Medicines and Medical Devices Safety Review to ensure women receive the safest and most effective treatments'*[258].
16th April 2019	FDA	FDA ordered all manufacturers of surgical mesh intended for transvaginal repair of anterior compartment prolapse (cystocele) to stop selling and distributing their products immediately. Based on the fact that the manufacturers (Boston Scientific and Coloplast) had not demonstrated reasonable assurance of safety and effectiveness for these devices[259]
22nd April 2019	Washington State – Office of the Attorney General	Attorney General Bob Ferguson's announced that Johnson & Johnson will pay $9.9 million to avoid going to trial for misrepresentations and failure to include serious risks in the instructions and marketing materials for surgical mesh devices. Ferguson is the first state attorney general to file a lawsuit against Johnson & Johnson regarding surgical mesh devices[260].
29th April 2019	Boston Scientific	After being instructed to cease sales of surgical mesh intended for transvaginal repair of anterior compartment prolapse (cystocele) in the USA by the FDA, Boston Scientific chose to voluntarily withdraw all products indicated for the transvaginal repair of pelvic organ prolapse worldwide[261].
17th May 2019	TGA (Australia)	A recall was issued by Boston Scientific Corporation Pty Ltd on 2nd May 2019, to remove any remaining stockroom product from the Australian market for: - Pinnacle LITE Pelvic Floor Repair Kit, Posterior

[258] RCOG, 2019, RCOG/BSUG response to NICE guidance on stress urinary incontinence and pelvic organ prolapse, viewed 13 August 2019, available online at: https://www.rcog.org.uk/en/news/rcogbsug-response-to-nice-guidance-on-stress-urinary-incontinence-and-pelvic-organ-prolapse/

[259] FDA, 2019, Urogynecologic Surgical Mesh Implants, viewed 13 August 2019, available online at: https://www.fda.gov/medical-devices/implants-and-prosthetics/urogynecologic-surgical-mesh-implants

[260] Washington State Office of the Attorney General, 2019, Johnson & Johnson will pay $9.9 million for failing to disclose the risk of its surgical mesh devices, viewed 13 August 2019, available online at: https://www.atg.wa.gov/news/news-releases/johnson-johnson-will-pay-99-million-failing-disclose-risk-its-surgical-mesh?fbclid=IwAR0e18KEOEEW-jBUmU7KTsR4-ze0uAP68ed4SZ92ozX6l8eQYX-7vwF1C8Y

[261] Boston Scientific, Letter to Hospitals, 29 April 2019, Urgent Field Safety Notice - Medical Device Withdrawal Xenform™ Soft Tissue Repair Matrix Uphold™ Lite with Capio SLIM Vaginal Support System Polyform™ Synthetic Mesh Pinnacle™ LITE Pelvic Floor Repair Kit, Posterior, viewed 13 August 2019, available online at: https://laegemiddelstyrelsen.dk/da/udstyr/sikkerhedsmeddelelser/uphold-lite-vaginal-support-system-og-xenform-soft-tissue-repair-system-/~/media/51EA230CE6D348F8B63CD00CBA909E32.ashx

		- Xenform Soft Tissue Repair Matrix, with the indication for transvaginal placement of POP.[262]
May 2019	Liao et al.	**Changes in Female Sexual Function After Vaginal Mesh Repair Versus Native Tissue Repair for Pelvic Organ Prolapse: A Meta-Analysis of Randomized Controlled Trials[263]** Meta-analysis of 17 trials including 2,976 patients (1,488 with TVM repair and 1,488 with native tissue repair). Designed to evaluate changes in female sexual function after transvaginal mesh (TVM) repair versus native tissue repair for pelvic organ prolapse. There was no significant difference in postoperative dyspareunia after TVM repair versus native tissue repair. Likewise, there was no significant difference in *de novo* dyspareunia after TVM (10.3% overall) repair versus native tissue repair (9.4% overall). There was also no significant difference in the short form Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire score after TVM mesh repair versus native tissue repair. Authors conclude that *'sexual function and de novo and postoperative dyspareunia were similar between the patients who underwent TVM repair and those who underwent native tissue repair.'*
5th June 2019	Imamura et al.	**Surgical interventions for women with stress urinary incontinence: systematic review and network meta-analysis of randomised controlled trials[264]** Meta-analysis comparing the effectiveness and safety of surgical interventions for women with SUI. 175 randomised controlled trials assessing a total of 21 598 women were included (147 from Cochrane reviews). Network meta-analyses were based on data

[262] TGA, 2019, TGA actions after review into urogynaecological surgical mesh implants: Update – Boston Scientific mesh recall, viewed 13 August 2019, available online at: https://www.tga.gov.au/alert/tga-actions-after-review-urogynaecological-surgical-mesh-implants
[263] S. C. Liao, W. C. Huang, T. H. Su, H. H. Lau, Changes in Female Sexual Function After Vaginal Mesh Repair Versus Native Tissue Repair for Pelvic Organ Prolapse: A Meta-Analysis of Randomized Controlled Trials. *The journal of sexual medicine* **16**, 633-639 (2019).
[264] M. Imamura *et al.*, Surgical interventions for women with stress urinary incontinence: systematic review and network meta-analysis of randomised controlled trials. *BMJ (Clinical research ed.)* **365**, l1842 (2019).

		from 105 trials that reported cure and 120 trials that reported improvement of incontinence symptoms. Sample sizes were generally small (median 91). Most studies had a short duration of follow-up (median 12 months) with only 41 studies having a mean follow-up of three years or longer. The type and definition of complications reported were not consistent across Cochrane reviews Results showed that the interventions with highest cure rates were traditional sling, retropubic MUS, open colposuspension, and transobturator MUS, with rankings of 89.4%, 89.1%, 76.7%, and 64.1%, respectively. Women were also more likely to experience an improvement in their incontinence symptoms after receiving retropubic MUS or transobturator MUS compared with other surgical procedures. Quality of evidence was moderate for retropubic MUS versus transobturator MUS and low or very low for retropubic MUS versus the other two interventions. Data on adverse events were available mainly for mesh procedures, indicating a higher rate of repeat surgery and groin pain but a lower rate of suprapubic pain, vascular complications, bladder or urethral perforation, and voiding difficulties after transobturator MUS compared with retropubic MUS. Data on adverse events for non-MUS procedures were sparse and showed wide confidence intervals. Long-term data were limited. Authors conclude that retropubic MUS, transobturator MUS, traditional sling, and open colposuspension are more effective than other procedures for stress urinary incontinence in the short to medium-term. Data on long-term effectiveness and adverse events are limited, especially around the comparative adverse events profiles of MUS and non-MUS procedures. A better understanding of complications after surgery for SUI is imperative.
10th June 2019	Ong et al.	**Management of Pelvic Mesh Complications in Scotland**

		Preliminary Results of a Service Evaluation - Co-designed by Patients and Clinicians[265] Data collected via an anonymised evaluation form co-designed by clinicians and patient representatives, distributed by patient group. 51 respondents. Average duration from implant surgery to the onset of mesh-related adverse event was 0.9 years (0-11). Prior to surgery, only 10 (38.5%) women felt they had enough time to discuss removal surgery with their surgeon. Eleven women (44%) were offered postoperative physiotherapy / pain clinic review. Initially, seven out of 24 (29.1%) felt better, however, only one maintained improvement long-term. The other six currently feel 'much worse' or 'very much worse'. Only one patient felt worse initially, but now feels 'much better'. No patient who indicated partial removal stated that they feel better currently. Nineteen women rated their current general health at 50 or less. Majority of women had persistent chronic pain (48/51) and dyspareunia (43/51) after receiving a partial removal. Partial explant surgery does not appear to be highly effective in addressing these complications.
14th June 2019	Scottish Mesh Survivors & Agur, W.	**Views of the Scottish Mesh Survivors Group on the Service provided to the Mesh-injured Women in Scotland[266]** Situational background assessment and recommendation (SBAR) document presented to the Scottish Government Accountable Officers Short-Life Working Group. Comments on lack of established care pathway, lack of skill in full removal (behind the skill of US

[265] H. Ong, E. Homes, O. McIlroy, W. Agur, V. Granitsiotis, 2019, Management of Pelvic Mesh Complications in Scotland - Preliminary Results of a Service Evaluation Co-designed ny Patients and Clinicians. Published on Scottish Parliament website, available online at: https://www.parliament.scot/S5_PublicPetitionsCommittee/Submissions%202019/PE1517_HHHH_Comb.pdf

[266] Elaine Holmes & Olive McIlroy, on behalf of The Scottish Mesh Survivors Group, 2019, Views of the Scottish Mesh Survivors Group on the Service provided to the Mesh-injured Women in Scotland, available online at: http://www.scottishmeshsurvivors.com/pdf/SBAR_SMS_for_Publication_230619.pdf

		surgeons), the need for total, not partial removals and the need for the social support system to recognise pelvic mesh complications as a source of serious physical disability/psychological suffering. There is a call to allow US surgeons (namely, Dr Veronikis) to share knowledge/technique with Scottish surgeons. There is a short mention of the benefits of translabial ultrasound for imaging of vaginally-placed mesh to treat SUI. Recommendations: - Consider postponing non-urgent total mesh removals until surgeon technique has met US surgeons. - Stop partial removals in local units. - Facilitate second opinions from other units in the UK/overseas. - Mandate a photograph of mesh explant. - Patient follow-up at 6 months. - Mandate national database. - Facilitate psychological support and raise awareness within the social support setting. Develop a national treatment pathway, including physio/pain clinic interventions, translabial ultrasounds, rheumatologist MDT involvement and the development of PDAs.

19th June 2019	Scottish Government	**Press release – 'Improving services for mesh complications'[267]** Announcement of the establishment of a complex case review unit to ensure that women with mesh complications receive the best care possible. The release also states that steps are being taken to engage with international experts to see how mesh complication services - including mesh removal - can be improved. The Scottish Health Secretary spoke of establishing *'a national complex case review unit within the NHS in Scotland. This will be taken forward through our service design processes, with a view to being established as soon as is practicable'* *'Work is underway to enhance care pathways for patients with complications within individual boards, with each board tasked with setting out how this will be achieved – including the need for improved co-ordination with primary care services'*
24th June 2019	NICE	**Urinary incontinence and pelvic organ prolapse in women: management [NG123][268]** Recommendations 1.8.21 and 1.8.22 regarding synthetic polypropylene or biological mesh insertion for women with recurrent anterior vaginal wall prolapse were withdrawn. Instead, the reader is directed to NICE interventional procedures guidance 599, which clarifies the relegation of this mesh to 'research only'. *'The replacement of the guideline recommendation with a cross-reference to IPG599 is to provide clarity regarding the relation of NG123 and IPG599 and to take account of a material change since* publication in the availability of products CE-marked for the indication which was referred to in the guideline recommendations.'

[267] Scottish Government, Improving services for mesh complications, 19 June 2019, viewed on 22 October 2019, available to view online: https://www.gov.scot/news/improving-services-for-mesh-complications/

[268] NICE, 2019, Urinary incontinence and pelvic organ prolapse in women: management, viewed 13 August 2019, available online at: https://www.nice.org.uk/guidance/ng123

16th July 2019	HQIP	**Interim Surgical Mesh Database Feasibility Report[269]** HQIP was commissioned by the DHSC to undertake a short-term feasibility study to investigate surgical mesh data requirements. Specifically, the current sources of mesh, SUI or POP data maintained by three professional societies (BAUS, BSUG and The PFS), and whether these current data collections could address the data reporting recommendations from the IMMDSR report as an interim measure before a full clinical national registry could be established. A series of interim recommendations were suggested: - Establishment of governance group. - Include devolved nations, NHS/private sector - Inclusion of mesh and non-mesh procedures (as a comparator) including complication procedures. - Work toward mandating data collection. - Ensure that interim database is capable of linking to other national datasets, performing an implant track/trace function, linking to MHRA Yellow Card system and processing third party data access requests. - Report results at the level of individual surgeons, hospital, region and nationally. Publish national reports annually. Produce a summary extract for patients.
26th July 2019	Health Canada	Health Canada's safety review found that compared to other treatment options, transvaginal implantation of non-absorbable synthetic surgical mesh to treat posterior compartment prolapse (such as the rectum) has greater risk of complications including pain, repeated infections, and erosion. The use of non-absorbable synthetic mesh for the transvaginal repair of anterior (bladder) and/or apical (uterus) prolapse should only be used for patients who have significant risk factors for recurrence of POP or recurrent POP, or for whom alternative surgical treatments are not appropriate.[270]

[269] HQIP, 2019, Interim Database Feasibility Report – Uroynaecological Surgical Mesh, viewed 13 August 2019, available online at: https://www.hqip.org.uk/wp-content/uploads/2019/07/Interim-Surgical-Mesh-Database-Feasibility-Report-FINAL.pdf

[270] Health Canada, 2019, Status of non-absorbable synthetic surgical mesh for the transvaginal repair of pelvic organ prolapse in Canada, viewed 13 August 2019, available online at: https://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/70563a-eng.php

3rd August 2019	Ong et al.	**Development, Validation and Initial Evaluation of Patient-Decision Aid (SUI-PDA©) for Women Considering Stress Urinary Incontinence Surgery**[271] Investigation of a novel validated Patient Decision Aid (PDA) for women considering SUI surgery in Scotland. The PDA was drafted and face-validated by members of NHS Ayrshire & Arran Continence MDT, later reviewed by the Scottish expert group, including patient representatives. Plain English guidelines were followed to give clear/concise information. The PDA has 4 components: 'What matters to me', 'Care Pathway', 'Procedure Comparison' and 'Request for Treatment'. 40 women completed the PDA, 20 completed the Decisional Conflict Scale (DCS) - which measures uncertainty in choosing options and the factors contributing to this uncertainty. Bulking agent injections were the most common choice of procedure (40%), and its most common acceptance theme was 'recovery', followed by colposuspension (35%) and autologous sling (25%). While the option of using the mesh remained on the PDA, no patient had chosen this option. The most common reason for decline conformed to the theme 'safety'. The total DCS score was 9.29 (range 0.0 – 29.69), suggesting an overall usefulness of the SUI PDA to women considering surgery.
5th September 2019	Taylor & Barton	***In vitro* characterisation of the erosion of soft tissues by surgical mesh** [272] The first published study to investigate mesh erosion in *in vitro* laboratory experiments. 'Sutulene' polypropylene mesh was used and tested on porcine muscle, due to its similarity in mechanical properties when compared with pelvic organ tissue.

[271] H. L. Ong *et al.*, Development, validation and initial evaluation of patient-decision aid (SUI-PDA©) for women considering stress urinary incontinence surgery. *International Urogynecology Journal*, (2019).
[272] D. Taylor, E. Barton, *In vitro* characterisation of the erosion of soft tissues by surgical mesh. *Journal of the mechanical behavior of biomedical materials* **101**, 103420 (2019).

		Force applied and movement distance of the mesh relative to the tissue were chosen to reflect likely conditions *in vivo*. The authors demonstrated erosion of tissue in this simple laboratory experiment. Erosion rate was seen to be greater when the mesh was orientated perpendicular with respect to the direction of muscle fibres. Overall the measured rates of erosion were *'consistent with the clinical experience that mesh can erode completely through the walls of organs such as the bladder and vagina in a few weeks or months. In our opinion, the phenomenon of mesh erosion should be more extensively investigated and different mesh products characterised in order to prevent future clinical complications.'* Further testing - including animal models - is called for.
17th October 2019	Multi-state settlement (USA)	Johnson & Johnson and Ethicon were alleged of violating Unfair Trade Practices and Consumer Protection laws in the USA[273]. J&J/Ethicon chose to settle (payment of $116,860,000 to be divided between each attorney general of the multistate working group) without admission of liability or wrongdoing. The 'consent decree' - which lays out the terms that the defendants must follow as part of the settlement - focusses on device labelling (warnings and precautions, adverse reactions) promotion, clinician training, sponsorship and payment. IFUs must not represent *in vivo* elasticity of mesh, suggest that the mesh remains supple or pliable after implantation, suggest that inflammatory/foreign body reactions are transient/minimal or that they 'may occur'. Risks must be fully documented, including fistula, inflammation, extrusion, exposure, erosion, voiding dysfunction/obstruction (temp. or permanent), contraction/shrinkage of surrounding tissue, pain with intercourse, loss of sexual function, requirement for

[273] Commonwealth of Pennsylvania, Attorney General Josh Shapiro, Consent Decree, 17/10/19, viewed 05/11/19, available online at: https://www.attorneygeneral.gov/wp-content/uploads/2019/10/2019-10-17-JJ-Transvaginal-Mesh_Consent-Decree-Only.pdf

		one/more revision surgeries (which may not resolve complications), urge incontinence, infection and vaginal scarring. Additions/removals from the IFU must be kept up to date and follow valid scientific evidence. Promotional material should not contradict the IFU, should not make claims that risks can be eliminated with surgical experience/technique alone, misrepresent the commonality of risks, compare safety and efficacy to other surgeries unless supported by valid scientific evidence, or present surgical mesh as 'FDA approved' or that it has undergone the PMA process, unless this is the case. FDA communications/warnings about mesh shall not be miscommunicated and communications shall provide a full list of risks, consistent with the IFU. Any training for Healthcare providers that Ethicon sponsors for mesh procedures will inform the clinician about all risks in the IFU. Ethicon sponsorship should be fully disclosed when submitting a clinical study/data/preclinical data regarding mesh for publication and in all contracts for consulting services regarding mesh between Ethicon and any Healthcare provider. The Healthcare provider must also declare this sponsorship in any publication/public presentation, following relevant COI requirements. Ethicon will present a fair/balanced presentation of clinical studies/data/pre-clinical data regarding surgical mesh. Ethicon provided the following response to the IMMDSR: *'While Ethicon is confident that the instructions for use (IFUs), patient brochures, professional education materials, and sales documents fairly represented the risks and benefits of transvaginal surgery using mesh, Ethicon agreed to the settlement to avoid unnecessary expense and a prolonged and uncertain legal process.'*

21st November 2019	Australian Class Action Lawsuit	**Gill v Ethicon Sàrl (No 5) [2019] FCA 1905**[274, 275] Judge Katzmann made the following conclusions about mesh properties, based on available evidence[276]: *'The changes to pore sizes in vivo are significant'* *'The Amid system of mesh classification is of limited utility, certainly in relation to meshes in the pelvic floor, although many of the observations made by Professor Amid remain important'* *'The data derived from the Aachen Group's pelvis data pool is not unreliable. In any case, it was only one resource from which the opinions of Professors Klosterhalfen and Klinge were derived'* *'Bridging fibrosis can occur with any of the Ethicon devices and is of clinical significance'* *'Mesh contraction is of clinical significance. It can cause complications such as mesh exposure/erosion and chronic pain, including at rest and with sexual intercourse'* *'Since it is uncontentious that all the Ethicon devices may cause pain, including chronic pain, and that there are various mechanisms that may be responsible for it, it is unnecessary to choose between them'* *'Prolene undergoes oxidative degradation in vivo but the evidence is not sufficient to demonstrate that the degradation is clinically significant'* The following conclusion was made about risk warnings: *'The respondents did provide warnings about some risks but the warnings they gave did not extend to all known risks or to all the pleaded complications. No information was provided about the probability of the risks and next to no information*

[274] Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905
[275] It is not known at the time of writing whether this judgment will be appealed.
[276] All conclusions from paragraph 787 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905

		about their severity. Nor did the respondents disclose the manner in which the risks were established'[277] With regard to SUI devices, Judge Katzmann concluded: *'Having regard to the nature and extent of the risks associated with all the devices, the deficiencies of the respondents' warnings and the other information they provided, the repeated failure to comply with the requirements for CE marking, and the way in which the devices were marketed, at no relevant time was the safety of any of the SUI devices such as persons generally were entitled to expect. Accordingly, each SUI device had a "defect" or "a safety defect'*[278] With regard to POP devices, Judge Katzmann concluded *'that at all relevant times the safety of all the POP devices was below the level that persons generally were entitled to expect. Notwithstanding the differences in the various devices, each of them exposed women to significant risks of injury against which inadequate warnings were given and in respect of which misleading representations were made. The respondents were not candid with the public about the risks of, and contradictions for, use of the devices or the limitations of the available data. The respondents represented that the benefits of using the POP devices outweighed the risks for women with any level of prolapse when the evidence did not support that. None of the POP devices was the subject of an adequately powered clinical trial, before it was released to market. The respondents represented that the devices met the essential requirements for CE marking when the material upon which they relied to affix and maintain the CE mark was insufficient to satisfy those requirements'*[279] In terms of complication risk, Katzmann stated that *'the evidence established that implantation of all the Ethicon devices could cause serious injury and that most of the pleaded complications are not rare.*

[277] Paragraph 3033 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905
[278] Paragraph 3458 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905
[279] Paragraph 3496 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905

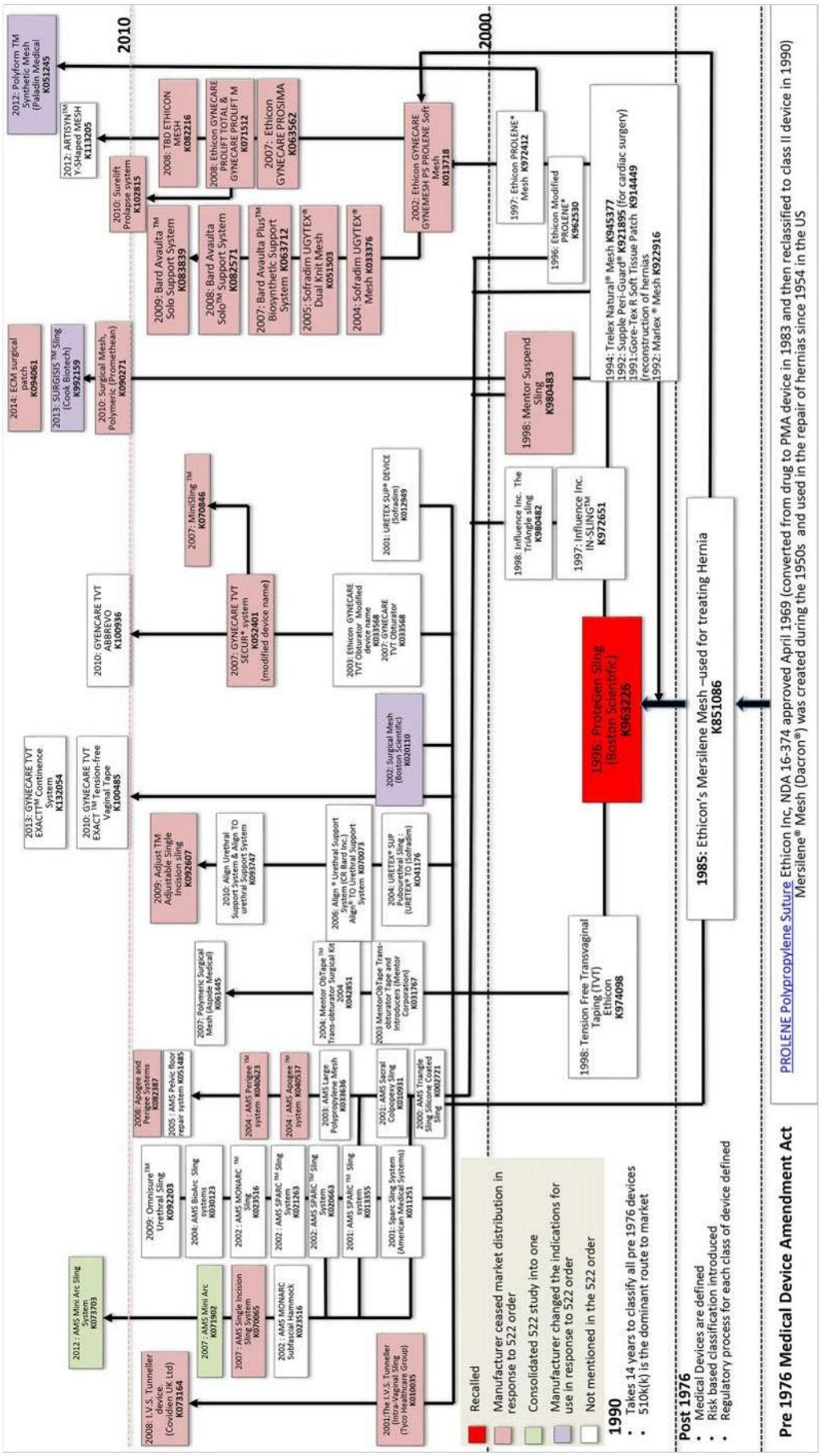
		Indeed, many are common or at least not uncommon'[280] Katzmann also concluded that each *of the respondents was negligent. The risks were known, not insignificant, and on Ethicon's own admission, serious harm could ensue if they eventuated. A far more cautious approach was warranted than the respondents took'*[281]
20th January 2020	Superior Court of the State of California County of San Diego, Central Branch	**The People of the State of California v. Johnson & Johnson, a New Jersey Corporation; Ethicon, Inc., a New Jersey Corporation, and Does 1 through 100, inclusive - Statement of decision**[282, 283] Action filed 24th May 2016 Trial date: 12th July 2019 *'The Court concludes that the People of the State of California ("Plaintiff") have proven by a preponderance of the evidence that Defendants deceptively marketed their pelvic mesh products in the state of California and that their marketing was likely to deceive reasonable doctors and reasonable lay consumers, including potential patients and their friends and family, about the risks and dangers of these products. The Court therefore finds in favor for Plaintiff and awards civil penalties in the amount of $343,993,750'*
4th March 2020	NICE	**Bilateral cervicosacropexy (CESA) or vaginosacropexy (VASA) using mesh for pelvic organ prolapse - Interventional procedures guidance [IPG669]**[284] Based on a rapid review of the published literature on the safety and efficacy of the procedure, NICE made the following recommendations: - Evidence on the safety and efficacy of bilateral cervicosacropexy (CESA) or vaginosacropexy (VASA) using mesh for pelvic organ prolapse is

[280] Paragraph 3675 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905
[281] Paragraph 3879 of Gill v Ethicon Sàrl (No 5) [2019] FCA 1905 available online at: https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2019/2019fca1905
[282] Superior Court of the state of California County of San Diego, Central Branch, The people of the state of California v. Johnson & Johnson, Ethicon. Statement of decision, 30th January 2020. Available online at: https://oag.ca.gov/system/files/attachments/press-docs/Statement%20of%20Decision.pdf
[283] It is not known at the time of writing whether this judgment will be appealed.
[284] NICE, 2020, Bilateral cervicosacropexy (CESA) or vaginosacropexy (VASA) using mesh for pelvic organ prolapse, viewed 11 March 202, available online at: https://www.nice.org.uk/guidance/IPG669

		inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. - Further research should include randomised controlled trials, and report details of patient selection, technique, improvement in the prolapse, procedure-related adverse events and patient-reported outcome measures.

Annex D: Mesh Timeline – Key Events

Appendix 1



Annex D: Mesh Timeline – Key Events

Key to Abbreviations

A&E	Accident & Emergency
AAGL	Association of Gynecologic Laparoscopists
ACC	Accident Compensation Corporation
ACOG	American College of Obstetricians and Gynecologists
AE	Adverse Event
AFS	Autologous Fascial Sling
APPG	All-Party Parliamentary Group
ARTG	Australian Register of Therapeutic Goods
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
ASIA	Autoinflammatory/Autoimmunity Syndrome Induced by Adjuvants
AUGS	American Urogynecologic Society
BAUS	British Association of Urological Surgeons
BFLUTS	Bristol Female Lower Urinary Tract Symptoms
BSUG	British Society of Urogynaecology
CAG	Clinical Advisory Group
CAM	Chorioallantoic membrane
CE	Conformité Européene
CI	Confidence Interval
CMO	Chief Medical Officer
DCS	Decision Conflict Scale
DEAC	Devices Expert Advisory Committee
DH	Department of Health and Social Care
DHSC	Department of Health and Social Care
ECM	Extracellular Matrix
E-TOT	Evaluation of TransObturator Tension free vaginal tapes
EU	European Union
FAQ	Frequently Asked Questions
FBR	Foreign Body Reaction
FDA	Food and Drug Administration
GMC	General Medical Council
GP	General Practitioner
GPRD	General Practice Research Database
HES	Hospital Episode Statistics
HQIP	Healthcare Quality Improvement Partnership
HRQOL	Health-related Quality of Life
HSE	Health Service Executive
IFU	Instructions For use
IIQ-7	Incontinence Impact Questionnaire - Short Form
IMMDSR	Independent Medicines & Medical Devices Safety Review
IPAC	Interventional Procedures Advisory Committee
IUGA	International Urogynecological Association
IVS	Intravaginal Slingplasty

Annex D: Mesh Timeline – Key Events

MAUDE	Manufacturer and User Facility Device Experience
MCA	Medicines Control Agency
MDA	Medical Devices Agency
MDT	Multidisciplinary Team
MHRA	Medicines and Healthcare products Reguatory Agency
MMDR	Medicines and Medical Devices Regulation
MMP	Matrix Metalloproteinase
MP	Member of Parliament
MUS	Midurethral Sling
MUT	Midurethral Tape
NAFC	National Association For Continence
NGO	Non-governmental Organisation
NHS	National Health Service
NHSE	National Health Service England
NICE	National Institute for Health and Care Excellence
NRLS	National Learning and Reporting System
OPCS	Office of Population Censuses and Surveys
PDA	Patient Decision Aid
PET	poly(ethylene terephthalate)
PFS	Pelvic Floor Scoiety
PHN	Public Health Notification
PMA	Premarket Approval
POP	Pelvic Organ Prolapse
PP	Polypropylene
PVDF	Polyvinylidene fluoride
Q1	Quarter 1
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised Control Trial
RR	Relative Risk or Risk Ratio
SBAR	Situational Background Assessment and Recommendation
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SEM	Scanning Electron Microscopy
SERNIP	Safety and Efficacy Register for New Interventional Procedures
SFNUU	Section of Female, Neurological & Urodynamic Urology
SFRU	Section of Female and Reconstructive Urology
SMUS	Synthetic Midurethral Sling
SS	Suprapubic Sling
SUFU	Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
(S)UI	(Stress) Urinary Incontinence
TFU	Tension-free Urethropexy
TGA	Therapeutic Goods Administration
TOT	Transobturator Tape
TVT	Trans-vaginal tape

Annex D: Mesh Timeline – Key Events

TVT-O	Trans-vaginal Tape - Obturator
TVT-S	TVT-Secur
VMR	Ventral Mesh Rectopexy
WHIG	Women's Health Implementation Group