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 March 2017

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***This documents is provided separately due to its size; it is available online at http://www.gov.scot/Publications/2015/10/8485/downloads**

Preface

This Scottish Independent Review (IR) of the use, safety and efficacy of transvaginal mesh implants in the treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) in women came about because of growing public concern about the number of women experiencing serious complications. This was linked with under-reporting of adverse events and a poor understanding as to why these complications had occurred.

Women felt that their voice had not been heard as they raised concerns about the side effects a number of them had suffered. Many of them eventually felt that the only way to bring this to the attention of the "powers that be" was to lodge a petition bringing the issue to the attention of the Petitions Committee of the Scottish Parliament. At that Committee the then Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, promised an independent review and asked NHSScotland to consider suspension of transvaginal mesh procedures pending the outcome of this review. A link to the Interim Report is included here:
http://www.gov.scot/About/Review/Transvaginal-Mesh-Implants

The table from Chapter 6 of the Interim Report can be found at Appendix D.

From the outset, we were charged with listening to and valuing the views of patients, both those with a good result and those with a poor result, including those living with significant impacts on their day to day life. We were asked to review the best available research evidence, statistics and both patient and expert opinion to find out the nature and scope of the problem.

We have tried to do this by involving women who have undergone such surgery; the local clinical experts in this surgery; clinical experts from around the UK; the Scottish Public Health Network for an objective review of the research literature; the Information Services Division of National Services Scotland, for an objective epidemiological review of the information from routine data; MHRA, the statutory regulatory body; the professional bodies, including the Royal College of Obstetricians and Gynaecologists (RCOG), the standard setting body for the profession; and input from the Chief Medical Officer's office and the Division of the Scottish Government Health and Social Care Directorate which deals with medical devices. We have been very ably supported throughout by a member of that latter Division.

During this IR we heard evidence from women who are disabled as a result of the surgery they had undergone. They also felt that they had not been listened to, or even believed which only increased their distress. We also heard of lives transformed and improved by the same surgery with statistical and research evidence showing poor outcomes to be in the minority of procedures done. We also acknowledged that adverse events could not be totally excluded from any surgery, as any surgery carries a risk. What we have tried to do is to take an objective view of both the results of the research and of the information review but also what they did not tell us, what was missing, what the patient stories can tell us and what the experience of clinicians in practice can tell us.

We found some concerning features about how new techniques are introduced into routine practice, how and for how long they are followed up, how women are informed of the risks and benefits so that they can give true informed consent and also how adverse events are reported and to what extent.

Our conclusions focus on the need for improved governance around both the introduction of new procedures or techniques and also of how women are assessed and treated, both initially

and in the event of any side effects following surgery. Reporting of adverse events is another area where we feel that a tighter, more explicit practice is required and we make suggestions that the government should consider to ensure this area is improved. We differentiate between the use of mesh in the treatment of SUI and when it is used in the repair of POP. We see the need for an Expert Group to oversee the implementation of an improved way of working, and of organising services. We are aware that some of our conclusions have wider implications and see the need to embed this in the Patient Safety and Clinical Governance strands of the NHS.

As Chairman, I hope that this report goes some way towards ensuring above all that patient voices continue to be heard, believed and valued and that women with these conditions can be assured that the treatment which they receive within the NHS is evidence based, audited and likely to produce a good result while keeping to a minimum the possibility of an adverse effect.

The following report sets out what we did, how we did it, what we concluded and why and what we consider should be done as a result.

This report was the work of many people and disciplines. I am extremely grateful for all their contributions. Readers of this report may notice differences in styles in the chapters arising from this collaborative process.



Lesley Wilkie

As the Chair of this important Review from November 2016 to March 2017, I am delighted to add my agreement to the words of the previous Chair. I have found the work to be detailed, professional and personal, and I commend this final report to all.

Around a year and a half has elapsed since the IR published its Interim Report. This has, however, been for very good reason, the group having awaited the publication of several key studies, including PROSPECT, published at the end of last year. All evidence, including the important new studies, is considered in detail in chapters 4, 5 and 6. Whilst the new evidence has seen those chapters revised considerably since the Interim Report, the remaining chapters remain broadly as before, brought up to date wherever necessary.

I wish to thank the previous Chair, Lesley Wilkie for her caring and thoughtful work from 2014, the previous secretary, Gillian McCallum**,** of the Scottish Government, for her exacting work bringing in the interim report to publication and the rest of the Review team for the joint effort.

The final stages of completion of the review have been marred by suggestions that evidence has been destroyed or is missing, I am confident that is not so and have written to the Cabinet Secretary for Health and Sport setting out the approach taken. The material presented by one group member and not included in the final report is available on the website with the Declarations of Interest from group members.

http://www.gov.scot/About/Review/Transvaginal-Mesh-Implants

Although three members of the group resigned prior to the completion of the final report, I am grateful to them for their contribution to the development of the report and for their final comments which have been considered in detail prior to the completion of the report.

Developing consensus is never easy and particularly in this area where the underlying clinical conditions cause reductions in their quality of life and misery for many individuals and there is no intervention which is as effective as we would wish, or without risk of complications.



Tracey Gillies

Executive Summary

This report sets out the concluding findings and recommendations of the Independent Review (IR) of the use, safety and efficacy of transvaginal mesh implants in the treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) in women.

It is the final report and supersedes the earlier interim report which was published in October 2015. As such this final report draws on new information that was not available when the interim report was published, including:

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) Opinion on "*the safety of surgical meshes used in urogynecological surgery" 3 December 2015* *http://ec.europa.eu/health/sites/health/files/scientific_committees/emerging/docs/scenihr_o_049.pdf*

"*Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials*" (PROSPECT)
http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31596-3.pdf

The Medicines and Healthcare products Regulatory Agency commissioned study "*In vivo response to polypropylene following implantation in animal models: a review of biocompatibility*"
https://www.gov.uk/government/news/interrogating-research-to-protect-public-health

The report is the product of individuals with a range of skills and interests including patients, clinicians, statisticians, public health experts, researchers, regulators, scientists and legal advisers. The deliberations of the IR have been based on the consideration of published evidence, patient stories and the opinion of clinical experts. In addition, an epidemiological study has been conducted using routinely reported Scottish hospital inpatient data, updated and published in the Lancet on 20 December 2016. From the information provided the IR has reached consensus. It is expected that the recommendations within this report will improve the quality of care in a field that crosses primary, secondary and specialist care, and will have lifelong effects on women's quality of life.

Conclusion 1

Fundamental to the treatment of patients with SUI and POP is patient-centred care which should include patient choice and shared decision making supported by robust clinical governance. To support shared decision making, management of patients must take place in the context of a multidisciplinary team (MDT), supported by a quality assurance framework. In addition, the Scottish Government should consider the alternative methods for the capture of adverse events set out in chapter 8 to determine the most effective way to ensure complete notification.

Conclusion 2

Evidence of involvement in MDT working; engagement in all relevant local and national audit activity; and the mandatory recording and reporting of adverse events, in line with GMC guidance, should be necessary parts of consultant appraisal and thus statutory revalidation of clinical staff. The Expert Group should work with Medical Directors and Responsible Officers to ensure this is included in the appraisal of all relevant staff.

Conclusion 3

Informed consent is a fundamental principle underlying all healthcare interventions. Extensive work was carried out by the Expert Group prior to the establishment of the IR, with leadership by both patients and clinicians. This has resulted in an information leaflet on Synthetic Vaginal Mesh Tape Procedure for the Surgical Treatment of Stress Urinary Incontinence in Women and consent form. Following on from this, the IR concludes that additional work is required to ensure that this work is extended to include all appropriate SUI and POP procedures and that the existing SUI leaflet is reviewed in the light of this work and other recent developments. This should be addressed by the Expert Group as a matter of urgency. Other points highlighted by the IR include the provision of adequate time for discussion and reflection. Patients should be provided with the information they need in order to make informed choices. Patients also require appropriate information, which must include device identification, to allow them to report adverse events if these occur.

Conclusion 4

The IR does not consider that current research studies on safety and effectiveness provide sufficient evidence on long-term impact of mesh surgery. The lack of long-term follow up and related outcome data, including information on quality of life and activities of daily living, should be addressed. The IR recommends the Expert Group highlights this knowledge gap to the research community and those that fund health research. Opportunities for routine audit should be explored by the Expert Group in conjunction with NHSScotland.

Conclusion 5

Good information is essential to good patient care. The experience of the IR has been that, although data on the provision of SUI and POP surgery is held both in professionally-led databases and routine NHS activity data, the information derived from such sources could be improved. It is recommended that the Expert Group works with key stakeholders to address information gaps and ensure that available information is used as effectively as possible to support safe and effective care. The IR notes that, as an important first step towards this, ISD has already secured the creation of new data codes that will allow more precise recording of mesh surgery and any subsequent mesh removal/revision within routine NHS activity data records.

Conclusion 6

The IR expressed serious concern that some women who had adverse events felt they were not believed, adding to their distress and increasing the time before any remedial intervention could take place. Improving awareness amongst clinical teams of the possible symptoms of mesh complications together with good communication skills, (including good listening and empathy) is an essential part of good clinical care. The IR concluded that the Expert Group should review the training and information available to clinical teams in primary and secondary care and find ways of incorporating patient views in MDT working. The importance of developing pathways for the treatment of complications is emphasised, ensuring involvement of clinicians with the appropriate skills to take forward the personalised and holistic care necessary in these situations.

Conclusion 7

In the case of surgical treatment for SUI, a review of the different sources of evidence has led us to recommend that women must be offered all appropriate treatments (mesh and non-mesh) as well as the information to make informed choices. Management of patients must follow agreed care pathways and the importance of multidisciplinary assessment is emphasised. When surgery involving polypropylene or other synthetic mesh tape is contemplated, a retropubic approach is recommended. The Expert Group must develop

appropriate pathways, including one for management of those suffering complications. Work with Medical Directors and Planners will be required to ensure their smooth implementation.

Conclusion 8

In the surgical treatment of POP, current evidence does not indicate any additional benefit from the use of transvaginal implants (polypropylene mesh or biological graft) over native tissue repair. Transvaginal mesh procedures must not be offered routinely. The Expert Group must develop appropriate pathways to meet clinical needs and also for the management of those suffering complications. Work with Medical Directors and Planners will be required to ensure their smooth implementation.

Chapter 1: Introduction

Update Since Interim Report

Following publication of its interim report in October 2015, the IR has continued to build on the initial findings given in that report, ultimately reaching the conclusions presented here.

As noted elsewhere in this Report, the consideration of various independent research programmes was an integral, vitally important aspect in the Group's development of its final conclusions. Delays in the publication of the reports into that research work, for example the PROSPECT Report (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials), meant that the Group was not able to fulfill its original aim of publishing this Final Report in early 2016.

In November 2016 Dr Tracey Gillies, Medical Director, NHS Lothian, was appointed Chair of the Independent Review. She replaced the previous Chair, Dr Lesley Wilkie.

1.1 Background

SUI and POP are conditions affecting a significant number of women and can result in a reduced quality of life for many.

Synthetic polypropylene mesh is an implantable medical material used in a number of operations to correct SUI and POP. Initial estimates, based on English figures, were that between 2000 and 2014, up to 1,500 women suffering from SUI and 350 suffering POP had synthetic mesh implant surgery each year in Scotland.

Concerns about the safety of mesh devices were raised by women experiencing complications. Some women adversely affected by these implants have experienced very serious complications, altering their lives forever.

The former Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, first met with a group of women adversely affected by the use of mesh to treat these conditions in May 2013. Following this meeting, the Cabinet Secretary asked that a Working Group be set-up to address the issues affecting women who have undergone transvaginal mesh surgery.

The Transvaginal Meshes Working Group (TMWG) was initiated to develop a clearer understanding of the issues affecting women who had suffered complications from mesh surgery. A review of the remit of this working group led to greater clinical representation to review current clinical practice and make recommendations for change. The Expert Group was formed in December 2013 as a development of the TMWG.

The Expert Group was established to look at ways of improving clinical practice, including developing pathways of care for women experiencing complications and to improve the consent process to ensure women are better informed of the risks and benefits of all procedures available to treat these conditions.

1.1.1 Opinion on the Safety of Mesh Devices

It is clear that a number of women have suffered serious, life changing complications following transvaginal mesh implant surgery. It is also evident that many women have benefitted from these procedures. However, due to the way these procedures are coded, it is not possible to provide accurate data on the number of mesh procedures where complications have occurred. This lack of information, allied with the fact that adverse events have been under-reported, has led to opinion being divided on the safety of transvaginal mesh procedures.

Many women have experienced a positive outcome following a transvaginal mesh implant procedure. No procedure is without risk and therefore many people, including the broad clinical community, consider that polypropylene mesh should continue to be used in some circumstances as it presents an acceptable level of risk, supported by a number of studies, including research by the UK regulator for medical devices, the Medicines and Healthcare products Regulatory Agency (MHRA).

There is broad consensus that work to improve clinical governance of these procedures is required, including improving pathways of care and the informed consent process; work which is being taken forward by the Expert Group.

The Scottish Mesh Survivors (SMS) brought together women affected by adverse events following mesh surgery to campaign to have these procedures suspended until the six points of their petition had been met. This group campaigned to suspend these procedures as they consider the severity of the complications, which can occur years after the procedure, present an unacceptable level of risk. Similar campaigns exist elsewhere, including: US, Canada, Europe, New Zealand and Australia.

Some women experiencing complications reported that they were not believed, adding considerable distress to their situation. This fact, combined with the absence of accurate data on the number and severity of complications, has led to many people concluding that these procedures should not continue.

1.1.2 The Public Petition Committee of the Scottish Parliament

On 1 May 2014, a public petition was lodged on behalf of the SMS Group. The petition called on the Scottish Parliament to urge the Scottish Government to:

1. Suspend use of polypropylene transvaginal mesh procedures;

2. Initiate a Public Inquiry and/or comprehensive independent research to evaluate the safety of mesh devices using all evidence available, including that from across the world;

3. Introduce mandatory reporting of all adverse incidents by health professionals;

4. Set up a Scottish transvaginal mesh implant register with view to linking this up with national and international registers;

5. Introduce fully informed consent with uniformity throughout Scotland's Health Boards; and

6. Write to the MHRA and ask that they reclassify transvaginal mesh devices to

heightened alert status to reflect on-going concerns worldwide.

In the light of growing public concern about the number of women experiencing complications, linked with under-reporting of adverse events and a poor understanding as to why these complications have occurred, the Scottish Government considered that an IR of transvaginal mesh surgery was necessary to establish the facts.

The former Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, announced the IR on 17 June 2014 and the acting Chief Medical Officer, Dr Aileen Keel, wrote to all Health Boards requesting that they consider suspending routine use of synthetic mesh for these procedures until the IR reported its findings.

1.2 Remit of the Independent Review

The published remit of the IR is to evaluate both the efficacy and the extent and causes of adverse incidents and complications associated with transvaginal mesh surgery for SUI and for POP. The IR recognises that these are different conditions, each managed by several different procedures and will take account of this.

The IR includes members of both the clinical and patient community and has the means of both identifying and determining the causes of issues where this is possible, and of finding and implementing solutions.

1.2.1 Purpose

1. To determine the safety of vaginal mesh implants for both SUI and POP in Scotland and to compare it to international standards. Information on how many women are experiencing complications and possible reasons for these complications will be examined.

2. To determine the relative efficacy of surgery for SUI and POP with and without the use of mesh or tapes.

1.2.2 Scope

In determining the appropriate course of action on this issue, the group is able to consider:

- the available data on procedures using mesh implants for pelvic floor surgery, including data on efficacy and complications compared to alternative surgical and non-surgical treatments;
- identifying best practice standards in management of SUI and POP;
- any issues that may lead to clinical practice not conforming to best practice standards;
- reported safety issues with devices
- including improvement in reporting adverse events;
- barriers to regular prospective auditing of results of surgical procedures;
- short, medium and long-term patient follow-up;

- identification of best practice in managing both treatment failure and complications, and resources to do so; and

- whether the information provided to patients before undergoing these procedures should be updated.

The full remit and membership of the IR is set out at Appendix B and Appendix C.

1.3 Remit of the Expert Group

The Scottish Government led Expert Group first met in February 2014 and has a remit to develop a clearer understanding of the issues affecting women who had suffered complications from mesh surgery. The working group includes clinical and patient representation, and has the purpose of reviewing current clinical practice and making recommendations for change. The areas currently being considered by the Expert Group include:

Informed Consent – a minimum standard of information to be provided to women considering surgery.

New Care Pathways –specifically for women who may require complex surgery; and for those who have suffered complications.

The Group has produced a new patient information and consent booklet for SUI,[1] which was published in June 2014 on the Scottish Government website. This booklet clearly demonstrates the risks associated with this procedure and the alternatives available before women make a decision on whether they wish to proceed.

Whilst overlapping with the Expert Group, the IR has a distinct remit and constitution. The Expert Group suspended its activities during the period of the IR's main work programme and re-formed for a single meeting in late 2015 with the imminent publication of the interim report. Following the publication, the Expert Group met before again suspending its activities pending the publication of this report.

1.4 What are Medical Devices?

The official definition of a medical device is: any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease;

- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;

- investigation, replacement or modification of the anatomy or of a physiological process;

[1] http://www.gov.scot/Publications/2014/06/2806

- control of conception;

- and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

Medical devices in the UK are regulated by the MHRA, an Executive Agency of the Department of Health, and the UK's Competent Designating Authority.

MHRA regulates devices placed on the market by the manufacturer, but the healthcare services they are used in is not within its remit.

CE marking

Apart from the very lowest risk products, medical devices are certified by independent conformity assessment organisations called Notified Bodies who are designated and monitored as competent to undertake conformity assessment activities by the EU member states' Competent Authorities. A CE Mark is applied by the manufacturer and means that the device meets the relevant regulatory requirements and, when used as intended, works properly and is acceptably safe. In order to be compliant with the requirements of the Medical Device Regulations and obtain Notified Body certification, manufacturers should be able to support their safety and performance claims for the device. This involves appointing a Notified Body who oversees the process, to verify that the devices meet the relevant essential requirements laid down in the regulations including, for example, biocompatibility, toxicity, technical specifications, clinical data, sterilisation, right through to packaging and labelling and quality management systems.

Once Notified Body certification is obtained, and their other obligations under the Medical Devices Regulations are met, the manufacturer can put the CE marking on the device and place it on the EU market.

The MHRA oversees UK Notified Bodies, for example, the British Standards Institute. A list of the UK Notified Bodies can be obtained from the MHRA website at: https://www.gov.uk/government/publications/medical-devices-uk-notified- bodies/uk-notified-bodies-for-medical-devices.

The MHRA conducts regular audits of Notified Bodies, including their quality assurance processes, certification activities and compliance with the medical device regulations.

MHRA also witnesses the assessor's competency during routine assessments of manufacturers to ensure that they operate to high standards.

https://www.gov.uk/government/publications/notified-bodies-for-medical-devices/notified-bodies-for-medical-devices

Classification system

There are a vast range of products falling within the broad definition of medical devices; hence the level of conformity assessment to which a device is subjected to varies according to the degree of its inherent risk.

The aim is to balance the burden of regulatory control relative to the perceived risk whilst at

the same time protecting public safety. It is the stated intended purpose of the device, assigned by the manufacturer, which determines the class in which a device is categorised. The classification of devices is therefore a risk-based system. 'General' medical devices are grouped into four classes as follows:

- Class I - generally regarded as low risk;
- Class IIa - generally regarded as medium risk;
- Class IIb - generally regarded as medium to high risk; and
- Class III - generally regarded as high risk.

Medical devices are classified according to general specific criteria, which include duration of use, whether the device is invasive via a body orifice or surgically invasive, whether devices are implantable, and whether or not they are considered to be active (i.e. have a power source). For transvaginal use, polypropylene mesh is a class IIb device, while meshes wholly or partly consisting of biological material are Class III devices according to the Council Directive 93/42/EEC. It is anticipated the new EU Medical Device Regulations will include a change to the classification so all "surgical mesh" devices intended for "long term or permanent use" will be Class III.

Classification of medical devices varies across the world and, while there is some similarity with the United States, there is not equivalence. Therefore a direct comparison between US and EU criteria is not possible.

http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194438.htm

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm?id=otn

In Sept 2011 the FDA's Obstetrics and Gynecology Devices Panel recommended that surgical mesh for transvaginal POP be reclassified from class II to class III and require premarket approval. In January 2017 the FDA has issued new classification on surgical instrumentation for use with urogynaecological surgical mesh: from class I (general controls) to class II (special controls), and subject to premarket notification. Background information on this change can be found here:

https://www.federalregister.gov/documents/2017/01/06/2016-31862/obstetrical-and-gynecological-devices-reclassification-of-surgical-instrumentation-for-use-with

From a European perspective the current position is that reclassifying these medical devices would not confer any material difference as they are already in the medium to high risk category as non-active implantable devices.

1.5 Approach to the Independent Review: evidence, its limits and interpretation

The IR's approach was set out in the first meeting in August 2014 – "to be conducted in an atmosphere of trust and openness, where transparency would underpin open discussion in the knowledge that participants may do so in confidence".

The aim has been to discuss the scientific evidence from the literature, understand the data from Scottish information sources, hear patients' and clinicians' opinions, appreciate the work of bodies such as the Chief Scientist Office, the NHS Incident Reporting and Investigation Centre and NHS Central Legal Office, and base the conclusions on the best analysis of all the material.

As with any review of evidence and the deliberative work to gain an understanding of complex real world situations, there are limitations to this work. For the Interim Report the outputs from some important research work were not published. However, as the other evidence strands are now available, notably the Opinion of the European Commission and its Scientific Committee on Emerging and Newly Identified Health Risks Opinion (SCENIHR) and the results of the PROSPECT (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials) study, the IR is able to conclude its final report. In addition, it is expected the conclusions directed to the Expert Group and researchers will continue to improve our knowledge base. What is most important is listening to and working with patients and health professionals. In order to support understanding and transparency, this Report has included the full analysis and review of evidence so others can follow our interpretations.

Chapter 2: The clinical uses of mesh for stress urinary incontinence and pelvic organ prolapse

Update Since Interim Report

The new or updated evidence that has been published since the publication of the Interim Report is from the National Institute for Health and Care Excellence (NICE) on management of SUI in women. NICE guidelines are for information since the Scottish Intercollegiate Guidelines Network (SIGN) applies in NHSScotland. However the SIGN guideline on the management of incontinence in primary care has been withdrawn as over 10 years old. The new information on POP is considered in the evidence section in chapter 5.

NICE is reviewing all its guidance for SUI and POP. To date they have published two reports: one on the clinical guideline, and the other concerning interventional procedures. NICE clinical guidelines are for information only in NHSScotland. Scotland is a partner in the NICE Interventional Procedures Programme and therefore their guidance applies in NHSScotland.

The revised guideline for urinary incontinence in women was published in November 2015. The change in the guideline relative to the 2013 version is that there is new evidence from three randomised controlled trials that found a benefit for pelvic floor muscle training.

In October 2016 NICE published interventional procedures guidance on single-incision short sling mesh insertion for SUI in women (IPG262). This stated that, given the current evidence, the procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research. NICE encouraged further research into single-incision short sling mesh insertion for stress incontinence in women and may update the guidance on publication of further evidence.

2.1 Clinical indications

2.1.2 Stress Urinary Incontinence

SUI is the condition where urine leaks with coughing, sneezing, laughing or with lifting and exercise. A woman's bladder and urethra (water pipe/outlet of urine) are supported by pelvic floor muscles and ligaments. If the support is weakened, for example by childbirth, then SUI may occur. The problems can be mild, moderate or severe and can lead to a considerable reduction in quality of life. There are several non-surgical and surgical treatment options for women with SUI.

Non-surgical options include:

- physiotherapy, including pelvic floor exercises;
- diet;
- stopping smoking;
- pharmacological treatment;

- continence pessaries;
- absorbent products;
- catheterisation; and
- no treatment.

Surgical options include:

- colposuspension (otherwise known as bladder neck suspension);
- urethral injection therapy;
- suprapubic sling;
- retropubic mesh tapes;
- transobturator mesh tapes; and
- single incision mini-slings.

There are two main types of vaginal mesh tape procedure for SUI. They are:

Retropubic mesh tape procedure

This was the first mid-urethral tape procedure introduced, whereby the synthetic material is inserted through a small incision on the anterior vaginal wall, emerging through two small incisions in the lower abdomen above the pubic bone.

Transobturator mesh tape procedures

This procedure was developed to minimise the potential for bladder and bowel injuries. The synthetic material is inserted through a similar incision on the anterior vaginal wall, emerging through a small incision in each groin area.

Single incision mini-slings are miniature slings delivered via a single vaginal incision into the obturator muscles.

2.1.3 Pelvic Organ Prolapse

The pelvic organs (uterus, vagina, bladder and bowel) are supported by the pelvic floor muscles, fascia and ligaments. There is rarely a single cause for a prolapse, although the following are often involved: childbirth, menopause, ageing, other pelvic problems and/or surgery, long-term coughing, constipation, repeated heavy lifting or manual work and being overweight. Prolapse may arise in the front wall of the vagina (cystocele), back wall of the vagina (rectocele and enterocele) or the uterus / top of the vagina (uterine prolapse or vault in women who have had prior hysterectomy). Many women have prolapse in more than one compartment at the same time, or may experience prolapse in different compartments over a period of time. The effects can be mild, moderate or severe. There may be local discomfort with the feeling of dragging, heaviness, or a need to push the prolapse back; or there may be effects on the urinary, bowel and sexual functions for a woman.

There are several non-surgical and surgical treatment options for women with POP.

Non-surgical options include:

- physiotherapy, including pelvic floor exercises;
- diet;

- stopping smoking;
- vaginal pessary; and
- no treatment.

Surgical options include:

- anterior colporrhaphy: repair front wall without mesh;
- posterior colporrhaphy without mesh; repair posterior wall without mesh;
- anterior colporrhaphy with implant; repair of anterior wall prolapse with implant, usually mesh;
- posterior colporrhaphy with implant: repair of posterior wall prolapse with implant, usually mesh;
- vaginal hysterectomy;
- vaginal colpopexy/hysteropexy; vaginal vault support without mesh
  vaginal colpopexy/hysteropexy with implant: vaginal vault support with mesh;
  sacrocolpopexy/sacrohysteropexy: abdominal approach vaginal vault support with mesh.

2.2 Guidance for surgery (NICE and professional bodies)

As part of the surgical training for gynaecologists, urologists and urogynaecological sub-specialists there is a need to be familiar with the range of procedures to offer as treatment when discussing symptoms with patients. These procedures include the options noted above, some of which will be initially tried in General Practice before a referral to a specialist. The specialist will be aware of the range of professional advisory documents on the procedures that can be offered. In NHSScotland it is obligatory to use the guidance from the NICE Interventional Procedures Programme. This programme includes a range of procedures from 2005 to 2016 for both SUI and POP[2]. In addition NICE published a detailed clinical guideline in 2006 with updates in 2013 and 2015 on urinary incontinence management in women[3] which can be used when arranging services in NHSScotland. The professional societies including British Society of Urogynaecology (BSUG[4]), the British Association of Urological Surgeons (BAUS[5]) and the Royal College of Obstetricians and Gynaecologists (RCOG[6]) provide specialist training and professional guidance, plus a method of recording activities and patient information and consent information.

2.3 Mesh products

Several types of transvaginal implants can be used in surgery for SUI and POP, including: absorbable synthetics; biological (usually made from cow or pig tissue); non-absorbable synthetic; or a combination of the different products. Non absorbable synthetic (permanent) mesh is usually made from polypropylene. There is a range of methods for using mesh, including:

- Mesh-inlay: the mesh is cut to the desired shape and size and placed through a single incision inside the vagina.

[2] https://www.nice.org.uk/search?q=mesh+
[3] http://www.nice.org.uk/guidance/cg171
[4] http://bsug.org.uk/
[5] http://www.baus.org.uk/
[6] https://www.rcog.org.uk/

- Mesh-kit: pre-shaped mesh is placed using introduction needles or trocars that may require external skin incisions at several points.

The International Urogynecological Association (IUGA)/International Continence Society (ICS) definitions list can be accessed at the following web address:

http://c.ymcdn.com/sites/www.iuga.org/resource/resmgr/iuga_documents/iugaics_terminologyprosthese.pdf

Chapter 3: Women's experiences

Update Since Interim Report

There are two additional sources of information since the publication of the Interim Report in October 2015. The first is the October 2016 exercise by the SMS to assess the experience of women who had had a retropubic, transvaginal mesh tape (called a TVT in the survey) removed. The survey is included in this chapter.

The second additional source of information is the report by the lay member who had positive experiences as a patient and described her views on the process of the Independent Review and personal experiences, included in Appendix A.

3.1 "Telling the Story"

In Scotland, the story of those women whose experiences of mesh implant surgery was poor was first told in newspaper reports. These stories comprised: histories of painful and debilitating complications, often experienced several years after the original SUI or POP; being told by clinicians that their experiences were rare; not being believed when they sought help; further surgery; loss of quality of life; and the feelings of some women that life was no longer worth living. This review was put in place in the light of such personal experience by women for whom mesh surgery had not been a success.

However, other stories of good outcomes and everyday lives restored also came to light in the experiences of women for whom mesh surgery had been successful. It can be acknowledged that there are fewer of these, but that is perhaps not surprising when it is considered that, for many women, successful surgery is not something that they feel the need to discuss, especially when it is about a delicate subject, or because they experienced exactly what they expected to, i.e. a successful outcome, or they simply want to move on.

Without detailed, qualitative research evidence, it is hard to fully understand the differing experiences of women who have had similar mesh surgery. Such research does not – as yet – exist, and to undertake such research is beyond the scope of this review. However, at least some insight is possible into aspects of the experiences, though it does need to be understood that interpreting such data must be done with some care.

3.2 Evidence availability

As the MHRA safety review noted, what evidence exists from the personal experiences of women who have had SUI and POP surgery using mesh tends to be that which highlights the realities of long-term, life changing adverse outcomes [UK1]. Data on those women for whom their outcomes were successful, or where the surgery did not give a lasting cure are less easy to identify. In other words, what evidence does exist is presenting only one side of the overall picture.

We have been able to identify three sources of data relating to the personal experiences and reported outcomes amongst some of the Scottish women who have received mesh implants. These data are drawn from three sources: (1) from personal, written statements by women in

regard of their mesh surgery, both positive and negative, and sent either to the Cabinet Secretary for Health, Wellbeing and Sport, or directly to the IR; (2) the collected experiences of those women who are associated with the SMS; and (3) the experiences of women within the ongoing PROSPECT (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials) trial of POP surgery. Of these, only the third source of data have been collected as part of a formal research process and this means that drawing firm "scientific" conclusions from this evidence is difficult. For example, the evidence is such that we cannot be sure that we have not heard the same story more than once, captured in each of the three types of data. This is unavoidable. By not over-interpreting the evidence, such bias as could arise from this 'double-counting' should be limited.

In exploring this evidence we are not seeking to establish a rigorous set of scientific findings. Rather, we are seeking to throw some light on these patient experiences and draw out what insights they can offer.

3.3 Methods

The quality of the data available is such that a formal set of qualitative and quantitative statistical analyses would be unhelpful. Each source of data has its own limitations which has a bearing on how it can be interpreted.

Patient Stories

All written patient stories were reviewed and a sample of these, representing the balance of experiences, have been anonymised and included in this report. Whilst women were asked to tell their story, the specific content of each submission was very much left up to the women themselves. As a consequence it is not possible, for example, to know when the surgery occurred or the type of mesh used in all cases. All the women whose stories are included have given consent for this.

Analysis of SMS Data

All women in contact with the SMS were asked to complete a questionnaire concerning their experiences. All completed questionnaires were made available to the Independent Review and the data they contained was transcribed to allow a descriptive analysis to be completed. For questions which provided either "yes/no" or categorical data a simple extraction scheme was used. For more qualitative data, a coding frame was developed by the data analyst and agreed by the author.

The new exercise by the SMS to assess the experience of women who had a retropubic, transvaginal mesh tape (known as TVT in this survey) removed is also analysed in this chapter. The questions were sent out by e-mail to the 160 women in Scotland on the SMS and were also posted on the social media page of the English Sling the Mesh Group (STM). There were 31 responses in total. Of these, four responses were excluded, given that they did not concern the full removal of retropubic TVT. The remaining 27 responses were mainly drawn from the SMS (19 responses) and from women who had seen the questions on the STM social media page.

PROSPECT Trial Qualitative Data

Personal experience data from women undergoing the PROSPECT trial has been collected at one year and two years post-surgery.

3.4 Results

3.4.1 Patient stories

In total, nine patent stories were developed from those submitted. Of these, five describe adverse experiences, whilst four describe positive outcomes. These are contained in Table 3.1 at the end of this chapter.

These stories speak for themselves. However, it is clear that women have experienced both very positive outcomes as well as very negative ones. They also show a remarkable intensity associated with their experience. Irrespective of the outcome, women do feel passionately about the impact that mesh procedures have on their quality of life.

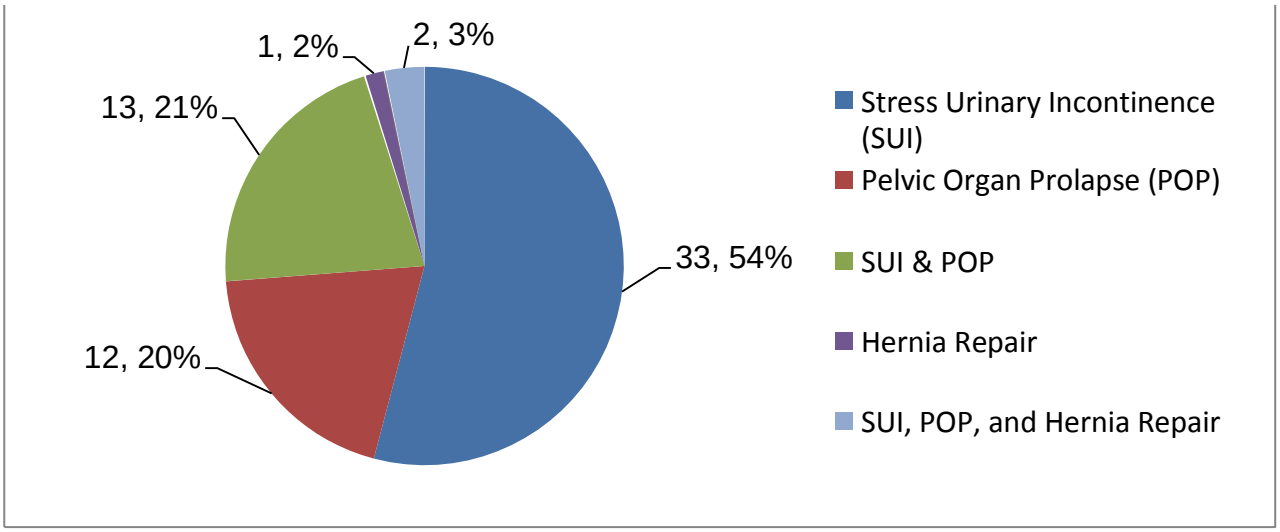
3.4.2 Analysis of Scottish Mesh Survivors Group data

The SMS questionnaire was circulated to approximately 80 women, though no precise record was made of this. The approximate response rate for completed questionnaires was 78% with the actual response rate, based on the 95% confidence interval, most likely to be between 67% and 85%. The questionnaires focused on details of the mesh procedure and the women's subsequent experiences, though they did not collect any demographic data.

The dates of the mesh procedures ranged from 1999 to 2014, with two thirds (66%) taking place between 2008 and 2012. Some 10% of women had multiple mesh implants (n=5, two procedures, n=1).

The questionnaire asked for what reason mesh was used. Data in answer to this question was provided by 61 responders (98%). These data are shown in Figure 3.1.

Figure 3.1 Reasons women reported for undergoing mesh procedures

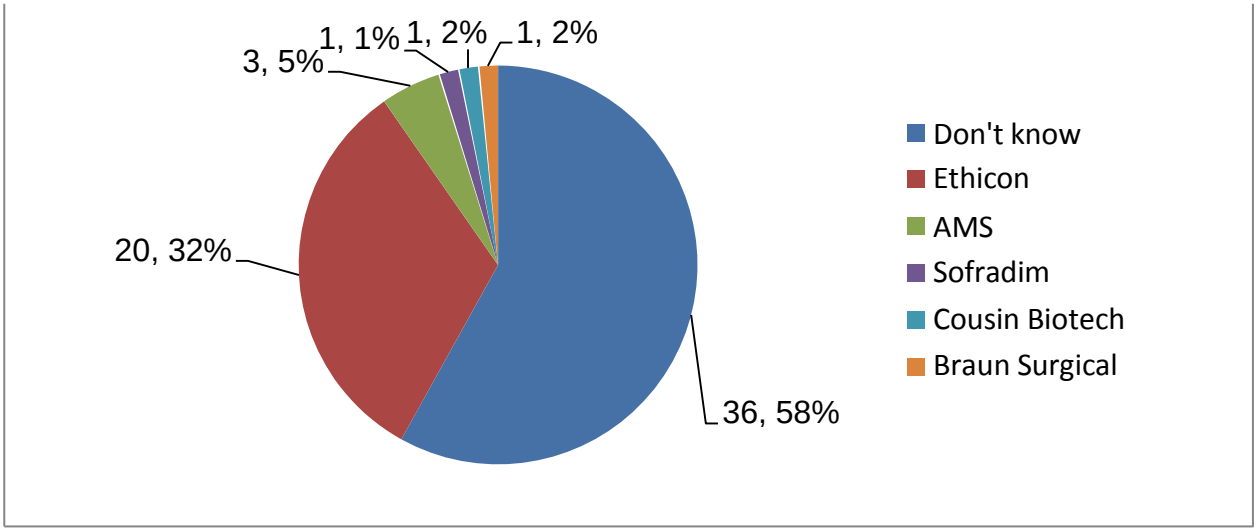


(Data labels = n of reason, % of responders)

As Figure 3.1 highlights, the largest proportion of procedures were for SUI alone (54%),

followed by SUI and POP procedures (21%). Single POP procedures accounted for one in five procedures (20%). Of the 62 responders, over half of them do not know what mesh product was fitted (58%) and just under one third are aware that they had received the Ethicon™ product. This is shown in Figure 3.2.

Figure 3.2 Types of mesh product used in the procedure



(Data labels = n of reason, % of responders)

Before the survey the women commented on the information they had received and about informed consent. Only 10 responders (i.e. 35%) answered the question concerning the information they were given about mesh before their operation. Most (n=7) said that it was inadequate, and three women said they were given no information. Almost all of the women (n=61/62, 98%) said their consent to mesh surgery was not informed. One woman said she had been denied access to her patient records by the Health Board responsible.

The questionnaire asked the women to describe how the mesh had affected them. From this it has been possible to identify the symptoms they experienced post mesh surgery. These self-reported health states are shown in Table 3.2.

Table 3.2 Self-reported health state / symptoms experienced after mesh surgery

	Number of women reporting ever experiencing	Percentage of all women surveyed (n=62)
Pain	55	89%
Impaired Mobility	31	50%
Incontinence/Frequent Urination	24	39%
Relationship/Marriage Difficulties	21	34%
Sexual Difficulty	21	34%
Loneliness/ Social Withdrawal or Exclusion	19	31%
Depression	17	27%
Recurring infection	16	26%
Lethargy	15	24%

Overall, some 74% (n=46/62) of the women reported that their symptoms were still current. Only a small proportion of these reported that their symptoms had improved / resolved over time (7%). Symptom severity was reported to have been unchanged by 72% and over a fifth reported their symptoms were getting worse (22%).

The questionnaire also asked the women about their experiences of healthcare. This question provided an opportunity for a wide range of issues to be raised. These may be summarised as:

- 65% of women described their surgeon's aftercare. Of these 70% (n=28/40) indicated that their surgeon was not open to the idea that mesh was the cause of their symptoms;
- 77% of women reported that they had repeatedly told a clinician about their symptoms or asked for a referral. Of these, 40% (n=19/48) indicated that their case had not been followed up;
- 82% of women reported on their current status. Of these, 33% (n=17/51) were not receiving ongoing care and, of the 66% who were receiving ongoing care, some 38% (n=13/34) were critical of the treatment they were currently receiving; and
- 32% of respondents made a comment indicating that they had lost faith in medical

professionals or the healthcare system.

More widely, smaller numbers of women mentioned issues including concerns over the processes of medical device manufacture and regulation, and the lack of financial support available from the public sector.

These women consider that there is no capacity in Scotland for full removal of mesh as no surgeons are trained. They also acknowledge that, for some of them, partial removal can leave some mesh and enhance erosion into organs.

The analysis of the responses to the survey shows that, of those women who indicated the time that had elapsed since the removal (14/27 responses), most had had the TVT removed within the last three years. The minimum period since removal mentioned was one week.

The key observations that can be drawn from the responses included the fact that pain after removal remained very common (20/27 responses). This was mainly associated with lower back, pelvic and leg pain. Incontinence was also reported by many women (14/27). Other problems mentioned included: multiple physical problems; recurring UTI and other infections associated with lowered immunity; and mobility issues. Factors associated with quality of life were also mentioned by several respondents, as was the lack of certainty that full removal was achieved, and a concern that ongoing problems were the result of residual parts of the mesh that could not be, or had not been, removed.

What is, perhaps, most clear from this survey is that for the majority of women who responded, following the removal of a retropubic TVT mesh, they were still having to live with a legacy of incontinence, pain and a range of other distressing symptoms that affected quality of life.

3.4.3 PROSPECT Data

As part of the PROSPECT trial, women were asked at one and two years about their personal experiences. These data were collected using a questionnaire developed specifically for inclusion in the research. Only the additional comments have been made available to the Independent Review for preliminary analysis. No demographic detail was provided and it should be noted that this study includes experiences of women from other parts of the UK.

Table 3.3 Positive and negative patient comments at one and two years within the PROSPECT trial.

	One year follow up	Two year follow up
Positive comment	16	54
Negative comment	18	53

As can be seen, whilst there is an increase in the number of comments between follow up at year one and year two, the number of positive and negative comments are roughly equal. A simple Chi^2 test shows these differences are not significant ($p = 0.844$, ns).

Clearly, a more detailed analysis of these comments, notably seeking to understand the content of them more fully, will be undertaken by the PROSPECT trial team in due course.

3.5 Interpretation

The data we have regarding the experiences of women who have undergone mesh surgery is limited and needs to be handled in a manner which does not over analyse it. We also have to be careful in interpreting the data and in framing any conclusions from it.

Ideally, it would have been helpful to be able to undertake formal research into the experiences of these women, those with both positive and adverse outcomes. This did not prove to be appropriate in the context of the IR and may have been difficult to undertake. What data we have, whilst is has been considered in a scientific manner, is not without its potential sources of bias and this has been taken into account in the analysis underlying this chapter.

Long-term, adverse outcomes in mesh surgery for SUI and POP are real and can profoundly affect the everyday lives of some women. For many of the women who have been so affected, they report that they were not able to give informed consent, were unaware of the type of mesh device implanted, and have lost confidence in medical follow up, even though some are still experiencing unpleasant and debilitating symptoms that reduce their capacity for everyday life.

However, other women have had positive outcomes. These have been experienced as strongly as have adverse outcomes. Where the data have captured something of the positive stories from women as well as those of adverse outcomes, they seem to be broadly equal in number.

Finally, it can be noted that the largest proportion of women who have had mesh surgery have not shared their personal experiences. Theirs are the silent voices, the absent evidence is the most difficult to interpret. For some, this silence is evidence for successful treatment and reflects the fact that these women have had positive outcomes. For others, it may be a sign that – at best – the surgery has not worked, but these women have chosen not to seek further intervention. Finally, this may reflect that there are women in Scotland who are still “suffering in silence”. In the absence of specific research to hear these stories, this must remain an absence of evidence for which no single interpretation is possible.

Table 3.1 Patient stories

Adverse Experiences
I watched and listened intently to [the Scottish Parliament's] Question Time this morning and heard you say that those of us who have approached our GP regarding the implant should tell what reaction we got. I would like to let you know what my experience has been. In June 2003 I received [a TVT] implant. By 2008 I was having some problems and must say that they were investigated, but was told that they did not know the cause. These problems have got worse but I never associated them with the implant until I read Marion Scott's article in Sunday Mail in April 2013. When I visited the GP to discuss her reaction was "You are just scaremongering like the mothers' who questioned the MMR Vaccine and did I not realize all the trouble we caused the Medical Profession". Reluctantly she referred me to the consultant who had performed my operation and I met with him on 8th August 2013. Only remark I took away from that appointment was "We don't know everything". On 23rd January 2014 I wrote the consultant to ask to be referred to X at Southern General in Glasgow. His reply said that he had forwarded my letter to my GP. At 3.10pm this afternoon I checked with Appointments Dept at Southern General and no request has been received. I have no way of ever finding out what, if any, damage the implant has done. If a record of how patients are treated is going to be set up I would like my experience to be added.

I am writing to inform you that I have read about your concerns surrounding the TVT mesh implant! I have had two attempts at this surgery and have been left with on-going complications. I am now in the process of being re-referred to my gynecologist! This has led to 4 separate surgical procedures with no avail and now I have been left with severe problems. I had requested after the first tape erosion to have the procedure done the old fashioned way with skin graft but was refused point blank.

I am pleased there is finally someone listening to us ladies on this matter. Let me know if I can do anything to help you with this matter or if I can do anything about it for myself. I'm only too happy to help.

I am a 51 year old female who until recently enjoyed a long career as a senior theatre nurse. That all changed, however, when in November 2013 I began to suffer pain in my groins and legs which was diagnosed as being mesh related.

I had mesh inserted in 2010 and again in 2011. The reason for this email is to make you aware of the problems I am having at the moment with the DWP. I was assessed by ATOS on 25th November 2014 as I was receiving ESA and they sent report to DWP who then decided that I was fit to work. I was then taken off ESA and put on JSA. Having never signed on in my life I have found this extremely traumatic and upsetting.

I appealed the decision and have now got to the stage where my case should go in front of a tribunal. However, another decision maker at the DWP has reassessed my claim and again taken the evidence of the ATOS assessment, basically disregarding all the evidence I produced (and there was a ton of that!!) and has recommended that the tribunal not go ahead.

I feel as if I'm fighting a losing battle with this. According to the letter I was sent I "believe that I am unfit for work". This is not my decision to make. I would love to still be working but because of this material inside me I have been declared unfit to work by medical professionals, my GP consultant gynaecologist and an NHS Occupational Health consultant. THIS IS NOT MY FAULT !!

It also states that the report "does not indicate if the Health Care Professional is familiar with X's diagnosed condition" and that she " gave an opinion that her assessment does not indicate significant functional restriction".

As it is, I am in constant pain for which I now take regular analgesia and I cannot stand or sit for any length of time without having to change position regularly.

My home life has completely changed. I do not sleep well which means my husband doesn't sleep well before doing a full day's work. My two sons see me in constant pain. I have no income and my pay off from the NHS is now finished so I have no idea how I am going to pay my mortgage and household bills from next month.

This is just a very small insight into my life with this material inside me. This email was just really to let you know how hurt and disgusted this now makes me, being treated like a scrounger and all through no fault of my own.

I am one of many women left in pain daily through mesh implant and would like to know what help is being put in place for so many injured women. I have recently lost my home after 17 years paying mortgage had to quit my job after 25 years' service fight to receive benefits after being told to visit a food bank to feed my family. I have been told I'm not entitled to PIP. I have never had benefits in my life and am struggling on a daily basis due to this. I have had to double up dose of antidepressants due to having my life taken away from me I'm only 49 and feel my life is over due to this please put some help in place for those of us crippled through no fault of our own.

I am writing to you as I recover from my 5th surgery to repair the problems left in my body by Mesh. I am now 46 years old and the last 6 years of my life have been hell since being implanted with this device after the birth of my daughter. I won't go in to all the medical intricacies of my situation, as I frankly am an emotional wreck at present, as I try to recover from a removal that was unsuccessful. I am a working mum and always have been. I am a Faculty Head in Education, a job that I love and enjoy. However, once again I have been forced to take time off from my job for another surgery that I had to wait one year for - from referral to surgery.

This isn't good enough. I am losing valuable years of my child's life, and my own. If I am unable to return to work I risk losing the home that I have worked so hard to make. This has to be dealt with now, to allow women who have been injured and left in a disgusting state a better quality of life. I am urging you to ensure that the 'right thing' is done.

Positive Experiences

Below is an email I sent supporting the continuing use of tape in urinary incontinence. He has encouraged me to copy you so that you are aware of the many lives that have been dramatically improved by this surgery.

_____

"With so much adverse publicity I just want to say how much my life was changed following insertion of a TVT. I'm running twice a week (not that far!) and could never have undertaken this before. I have never felt fitter which is a real bonus in mid 50s! There is no way I would have contemplated a colposuspension.

"I am sure for everyone who feels their life has been adversely affected; there are hundreds whose lives have been transformed for the better".

I have been advised by my Gynecologist that fitting women with tapes to support their bladder has been suspended due to a tiny amount of problems. I would like to share my experience.

I was advised there was a small chance of the procedure not being a success. Before I had these tapes inserted, I was housebound. I was wetting myself up to 20 times a day. I couldn't bend over, kneel down, carry a bag, lean over anything. it was so humiliating. Lifting or hugging my grandkids was impossible too. My life has been given back to me.. I AM 49 YEARS OLD and am far too young to have lost my dignity and freedom. I am now going to the gym, lifting weights let alone being able to carry shopping. It is the MOST AMAZING procedure.

I would ask you, for the sake of the many women looking in desperation for a cure to this awful problem, Please, please lift this suspension. I have been advised that 4 young women have been refused this simple procedure and that only from ONE surgeon. Any surgery has its risks. but we are warned beforehand. Any woman considering having this done is at her wits end and desperate for help.

You cannot deny them the chance of freedom from all the problems connected with having no bladder control.

I accompanied my friend to yet another appointment relating to incontinence issues, as a support. She is a young 66 years old, fit and active, takes care of herself well. She is absolutely shattered with her health situation. She has endured her incontinence for over 9 years. Was diagnosed with triple prolapse and operated on previously. Although prolapse now repaired, her incontinence continues. She was waiting for TVT surgery, but obviously this option is no longer available for time being. How long is this going to go on? What alternatives are being put in place? I can hardly believe that with the existing - and growing - number of women who are victims of this situation, there is so little help available. Her current option is to try (again) various medications. There may be some relief for her if she was able to use a newish product, some kind of tampon like insert ('vaginal rockets'- sound more exciting than they are!!) but these are not available on prescription, and are very expensive to buy privately.

First of all - Why?? If there is no surgery available currently, then why on earth are these products not being given on prescription? Second - why the terrible expense? although previously expensive enough, it seems that the producers, with an eye on the (lack of) surgery options, have latched on to the opportunity to make a few bucks, and are charging ridiculous prices for items that are desperately needed.

Thirdly - What is happening with TVS? I appreciate that some women have suffered as a result of these operations, but what is the % in comparison to the rest of the successful procedures? This situation is only going to grow and grow. You can just bet that the people making the decisions about both the surgery options, and the help available, are either men who obviously don't suffer from this, or women who don't suffer this condition at its 'full strength'. Well woe betide them!!! When they start to encounter this, I really hope it is as bad as my friend's situation. And I hope they think back and wish they had done more, fought harder! It absolutely scunners me, that this - a situation brought on mainly because of childbirth, is being side-lined. Think of the expense if all women decide they are not going to 'push' and go for C-sections? And the number of hospital beds that will impact?? And yes - this IS written on behalf of my chum - but I am also thinking of the future and the possibility of similar situation for myself.

PLEASE get this back in focus and off the subs bench!

I refer to the letter recently sent to X (of which I received a copy) in response to the concerns I raised re Transvaginal Implant procedures.

On 13 January I received an email from Y, referring to my email about these procedures “particularly how these have been reported lately." In my original letter to X two thirds of that letter concerned the present coverage of the issue by the press. I was very disappointed to see that it gave no mention whatever to the issue of press coverage, far less to the nature of that coverage. In the articles that I read I could find no vestige of any form of balanced reporting. It’s clear that there are patients who experienced very serious problems indeed. However, no mention was made of any successes.

One year ago I underwent one of these procedures because of a long standing and intractable problem. Despite the very best efforts of health professionals and myself my condition failed to respond to conservative treatments. In no way was surgery the first course of action.

I was provided with very comprehensive written and verbal information which was very straightforward and easy to understand. I was encouraged to discuss this with my family and friends. My family practitioner was able to discuss the proposed surgery in detail and to study closely all the written information.

lt was originally planned that I was to be a participant in the trial. My operation was carried out Z in a private hospital but because this hospital did not permit its premises to be used for research purposes I was no longer eligible to be part of that trial.

Media is the means by which information flows and the information that flows from certain press coverage makes no mention of any success. Certain aspects of the press continue to vilify in the most extreme terms the doctors who carry out these operations. I could imagine that these doctors may find themselves in a state of limbo, unable to respond to the allegations while their reputations and professionalism are savaged.

Confidence is a fragile commodity and in the wider medical world patient confidence in their surgeons and physicians is currently to an extent being undermined.

Survey of women who had complete removal of TVT

On 26 October 2016, we emailed 160 women living in Scotland from Scottish Mesh Survivors (SMS) group and the same questions were posted on England's Sling The Mesh (STM) Facebook page on 28 October 2016, to ask if they are cured of pain after complete removal of the retropubic mesh tape:

Dear All

Can we ask how many of you:
Q1. Have had a complete TVT mesh removal please?
Q2. If so, do you still suffer e.g. pelvic pain, autoimmune symptoms, incontinence etc?

For those who are unsure... TVT is what is known as a retropubic mesh tape/sling. It is used to treat a leaky bladder (stress urinary incontinence - SUI). It is inserted through the vagina and involves two very small incisions/cuts at the top of your pubic bone, the procedure takes approx 20 mins.

No names, names of surgeons/hospitals or personal information is required, we only want to know: How many women are still suffering after complete TVT mesh removal?

Sincere thanks in advance, your help is appreciated.

Best wishes

Elaine & Olive
http://www.scottishmeshsurvivors.com/

We received (31) responses in total. 27 of these were relevant to our questions - 19 from SMS and 8 from STM. 4 responses were irrelevant: 2 related to transobturator procedure, 1 was a partial mesh removal and 1 didn't know which procedure she had.

Serial	Pain went away?	Patients' comments
1	Yes	I had my TVT fully removed last December. Stress incontinence did return, but this has now, hopefully, been resolved by another procedure. All other symptoms disappeared immediately after removal surgery.
2	No	I'm still in pain 18 months after removal. Continued pain in left groin, hip and pelvis. Shooting, spasm like pains hit out of nowhere.
3	No	I had TVT procedure in 2015 and full removal three months later. I have been left with severe pain due to nerve damage down the whole right side of my body. It starts in my groin then radiates into my hip, side, stomach, back, buttock and then down the whole of my right leg. I have stabbing pains in my vagina, which can stop me in my tracks and have continuous UTI's. I have recently been diagnosed with fibromyalgia and am due to be tested for lupus. I have chronic fatigue, inflammation, bloating, muscle damage, digestive issues, anxiety, recurring vaginal issues, autoimmune problems, stiffness, swollen painful joints, abdominal pain and spongiotic dermatitis! I cannot bend, kneel, squat, sit on the floor or cross my legs. I take 20mg of amitriptyline per day to help....it doesn't! But.....the mesh is out....and for that I am grateful.
4	No	I'm about 18 months full TVT removal. My incontinence is worse now than ever, I used to be really fit, healthy and active. I can now barely walk any great distance because of the pain I am in, in my leg, in my pelvis, spasms, shooting pains
5	No	I year on from full TVT removal still have chronic pelvic and bladder pain. There are days when I actually wonder whether it was worth it
6	No	I'm 6 months post full TVT removal, still having some pain in lower back and buttocks and groin also a numbing in lower left leg
7	No	I've had complete mesh removal in march 2016 and at first pain seem to reduce however after a couple of months is back to the same pain pre removal. Pelvic back and leg pain and the incontinence is worse than ever.
8	No	Still suffer terrible UTIs. And incontinence - although I also suffered these symptoms with mesh. Bladder and

		lower back pain. Just constant pain. So have to manage day to day activities on a rota basis. Can't walk or stand for long periods due to nerve damage and localized area pain. Have to turn every so often in bed and move every so often when sitting. As again pain is unbearable. When suffering from UTIs it's like a flu I experience. I have earache and swollen throats on a regular basis also. Not my tonsils playing as I had them removed over 20 years ago. And now I have blood problems.
9	No	I had TVT mesh removal three years ago. Surgeon said ---- got most of it out. I wish I had asked more questions at the time. It took six months before I felt better and it was like a miracle but at the beginning of this year I started to experience problems again. I have left side constant abdominal pain day and night. Ultra sound was clear but I am really unwell and worried it's what was left behind causing problems
10	No	I've had it completely removed but still get a lot of pubic and groin pain, had the sling remade with my own tissue but I use catheters but can still dribble when am bursting.
11	No	I have autoimmune problems cannot fight anything off, lichens, I'm scared to leave house, incontinence is awful.
12	No	I have and yes still suffering
13	No	My mum said to email you she still suffers from all of these things after having the TVT mesh removed six years past there last month, still has pain every day, wears pads every day and has to be very careful with her immune system as she is open to all infections!
14	No	I haven’t a clue what I’m left with ---- did say after removal last time that no more could be removed or I would end up with a fistula. Easy for them to say they don’t have our pain.
15	No	I have had t vet mesh removal and suffer incontinence the recently offered me a further operation but I refused for the time being I also have pelvic and lower back pain all the time and other problems
16	No	Mesh removal , horrific pain all day all night , still leaking , worse than what I went for . Smell disgusting. Pins and needles up and down legs . Headaches Migraines burning feet and hands I have to stand on a stone floor my legs ache all day all night vibrations in my legs forgetfulness so bad lately. Always have a cold ,take whites like car sickness or travel sickness

		Even when I'm not traveling soup helps no nervy fatigue for days on end mood swings frustration painful pelvis and all my organs feel so tender
17	No	I apparently had full OR as close as all removed, although they will not guarantee that. No incision was made through my tum and I have asked about the ends/anchors but have received NO reply to that question. I do have incontinence which is intermittent, if I go to sleep on my front then through the night I leak, if I overfill my bladder I leak when I get up from a sitting position OR if I was to run really fast of sneeze without warning I would leak. I will now have incontinence pads for the rest of my life as I have made up my mind I do not want any further operations. Giving it further thought, I would also say that I still have a lot if internal inflammation going on, i.e. never have felt truly well since my body was fighting the Mesh. I most certainly cannot eat or drink like I used to without suffering the consequences. Body is sore and I am very lethargic. Whether that's a consequence of getting older or my foreign body granuloma, I don't know.
18	No	I had this done 16 years ago. I was not aware of it until quite recently. I have more than one meshes and many removal ops. I don’t have a clue where it is now
19	No	I had a removal last October at first the pain was manageable, now it’s worse than ever, I still suffer from stress incontinence worse than I ever did before tape was inserted, autoimmune symptoms. I wish I didn't need to work as I'm really struggling big time.
20	No	I had TVT removal 2015 it was all removed however and am still in pain please add my name to list
21	No	Complete removal but I have doubts. Felt better initially but back to pain, incontinence and UTIs.
22	No, but improved	I am still in pain after full removal! Not as bad as before but still needing eight solpadol a day and eight nortriptyline at night
23	No, but improved	After total removal I was able to pee in a straight line and it felt as though I could empty fully. The pulling sensation/ pain had subsided. Still left leg is still troubling me (nerve impingement and strangulated area - according to Physiotherapist. difficult to: walk for a long time - pain and leaking after about 20 minutes (despite emptying beforehand), climbing stairs, lifting my left leg (exercising - at work), I cannot do any other exercise - only swimming, I now leak – cannot make the loo in time – once my bladder contains 300ml, I still have difficulty stretching my left leg fully in bed and still sleep with a pillow under my knee/knees, Sitting for a

		long time is difficult, I still have to raise both my legs when resting, as they have swollen straight after the operation, I still have this feeling of a "Lump" in my left side - especially after overdoing things, Leaking to the extent that I now do is distressing - but I am not considering any more interventions, I have used Betmiga tablets while on holidays - this gave me the peace of mind of not having to worry about finding a loo or leaking. However Betmiga does make my legs swell up (the fluids have to go somewhere in my tissues in the body?) if I use it for more than a day or two. No sex since 2010, which strains our relationship as I do feel "unloved" as the physical side is missing. I am grateful for having been able to have the tape removed fully. I consider myself lucky and blessed.
24	No, but improved	I had my mesh removed in corrective surgery 2015 – seven months after it was first put in. The pain has pretty much subsided and I am off all the medication which I relied on. However I will never go back to what I was. I can now no longer put any impact on my legs – so activities like running or skipping are gone, forever. I also find if I overstretch my legs in activities like yoga then the leg pain returns. Kneeling down or doing squats also sets off the leg pain. Because I am so determined I still go boxing but make sure I don't bounce on my legs in any way. I swim and go on long dog walks - but every day I am mindful of all of my movements to make sure I do not do anything that could trigger the horrific leg pain.
25	Not sure	2015 full TVT removal incontinence 10 times worse and so is the urgency! LFT's back to normal auto immune also back to normal, but left its mark in arthritis in my feet!
26	Not sure	I have only just had TVT 1st removal and although only just over two weeks on, and on full medication, I am pleased to say that my leg pain is definitely better than it was pre op. The TVT had been incorrectly inserted
27	Not sure	officially my mesh has all been removed but I'm not convinced the on-going bladder problems are not connected with some small amount still there

Chapter 4: Assessing the safety and effectiveness of vaginal mesh surgery for stress urinary incontinence and pelvic organ prolapse in Scotland, using nationally available NHS data

Update Since Interim Report

The Information Services Division (ISD), part of NHSScotland, undertook an analysis of nationally available hospital discharge records on behalf of the Scottish Government's Independent Review of Transvaginal Mesh Implants over 2015 and 2016.

The analysis examined how many women undergo operations for SUI and POP, and how many go on to develop immediate or later complications, or require further surgery.

This chapter provides a summary of the final results. Full details of methods and results are available in the Lancet, as published on 20 December 2016:

http://www.isdscotland.org/whats-new/Stress-Urinary-Incontinence-and-Pelvic-Organ-Prolapse/

Preliminary results of this analysis were included in the interim report of the IR, published in October 2015. These final results differ from those published in the Interim Report, the main reasons being:

- The study period has been extended from 1997-98-2013-14 to 1997-98-2015-16.
- Enterocele procedures (OPCS4 code P23.4) are now counted in the posterior (rather than anterior) non-mesh colporrhaphy group.
- Vaginal vault prolapse repair procedures involving transvaginal placement of mesh (OPCS4 code P24.6) are now labelled 'Vaginal mesh vault repair' (rather than 'Infracoccygeal colpopexy').
- Further incontinence and prolapse surgery occurring after the index procedure are now considered as two separate outcomes (rather than a single composite outcome).
- The secondary outcomes initially examined (for example all readmissions, referrals to pain clinics, and prescriptions for pain relief) added little to the main outcomes (complications and further surgery) so have not been included in the final analyses.
- Analysis errors have been corrected, in particular:
    - Previously procedures were excluded if the woman had undergone prior incontinence or prolapse surgery in the five years up to 1997/98. Now they are excluded if the woman had undergone prior incontinence or prolapse surgery in the five years up to the procedure being considered. This means that repeat procedures are now more effectively excluded from the analysis as intended.

- Previously vault prolapse repair procedures were excluded if the woman's prior surgery had involved any incontinence or prolapse procedure. Now vault procedures are excluded if the woman's prior surgery involved any incontinence or prolapse procedure except hysterectomy. In addition, vault procedures were previously included regardless of any other incontinence or prolapse procedures done at the same time. Now vault procedures are only included if done as a single procedure or in combination with a standard (non-mesh) anterior and/or posterior colporrhaphy. This means that 'first, single' vault repair procedures are now included as intended.

- Previously only a certain subtype of immediate complications (procedure related) was counted in the total number of immediate complications. Now all subtypes (haemorrhage, infection, pain, procedure related) are included as intended. This means that our results now show a higher proportion of women experiencing immediate complications.

4.1 Operations provided in Scotland for stress urinary incontinence and pelvic organ prolapse

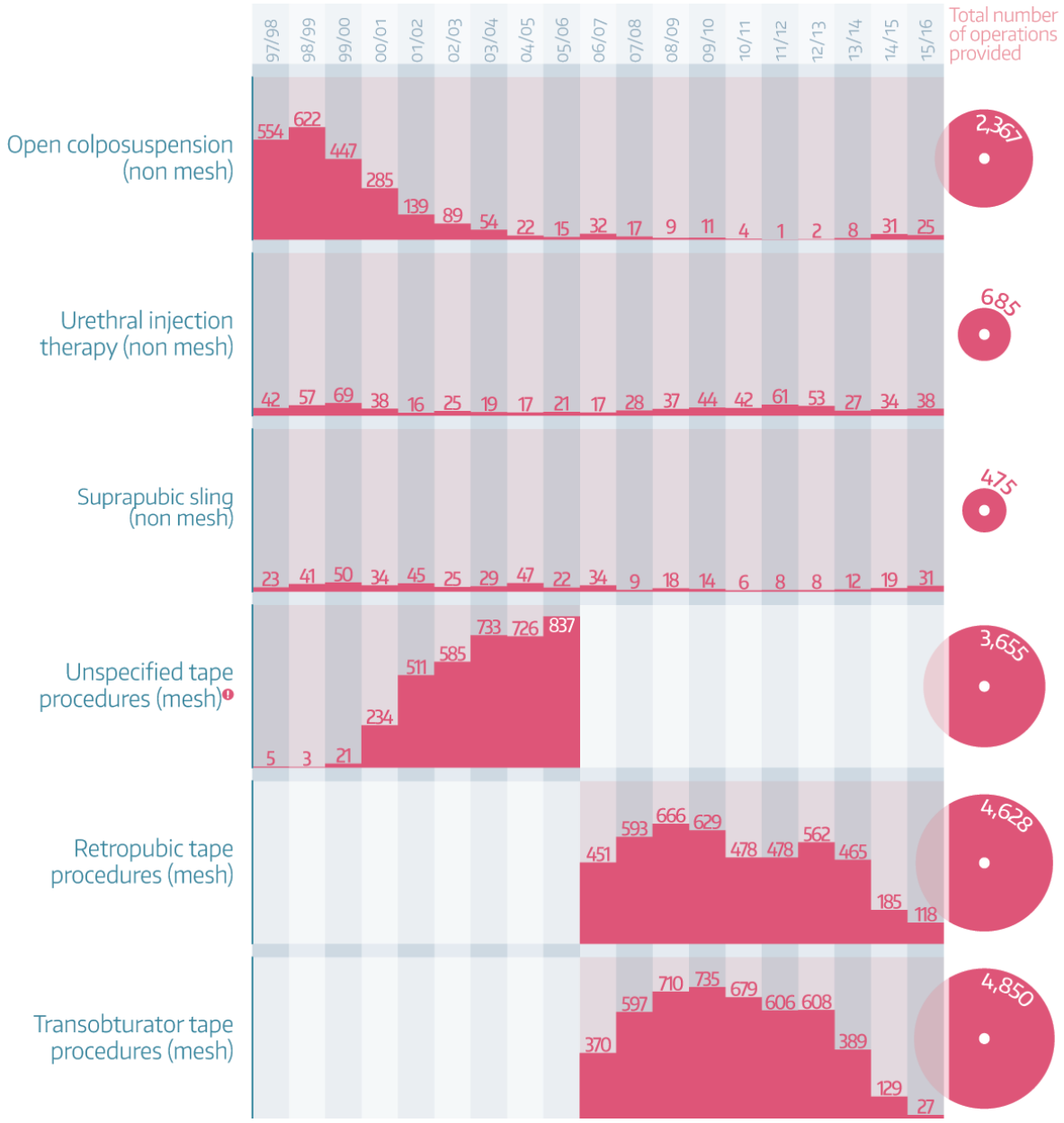
For this study, ISD used routine hospital discharge records to identify the different operations provided for SUI and POP in Scotland between 1997/98 and 2015/16. Specific types of operation that were provided in reasonably high numbers were included in the analysis.

In general, only single operations were included in the analysis. 'Single' means that the woman did not have any additional/second operation for incontinence or prolapse at the same time as the operation being examined. It is quite common for women to have more than one operation at the same time. However, if complications subsequently develop it can be difficult to know which operation caused the problem. Only single operations were included so that the study could focus on the risks of each particular operation separately.

In general, only first operations were included in the analysis. 'First' means that the woman had not had any other operation for incontinence or prolapse in the previous five years. In addition, only the first potentially eligible operation provided within the study period was included for any individual woman. Only first operations were included because the risk of complications may be quite different for a woman having a repeat operation. It was important that the study did not mix operations with different levels of risk.

4.2 Operations provided for stress urinary incontinence

In the late 1990s open colposuspension was the main operation provided in Scotland for SUI (around 500 first single procedures per year). Tape (mesh) procedures were introduced in the UK from 1998 and quickly replaced colposuspension as the most common operation type for this condition. However, the number of tape procedures fell substantially in the most recent years included in the analysis. First single urethral injection therapy and suprapubic sling operations have been provided in moderate numbers (fewer than 100 per year) throughout the time period included in the analysis.



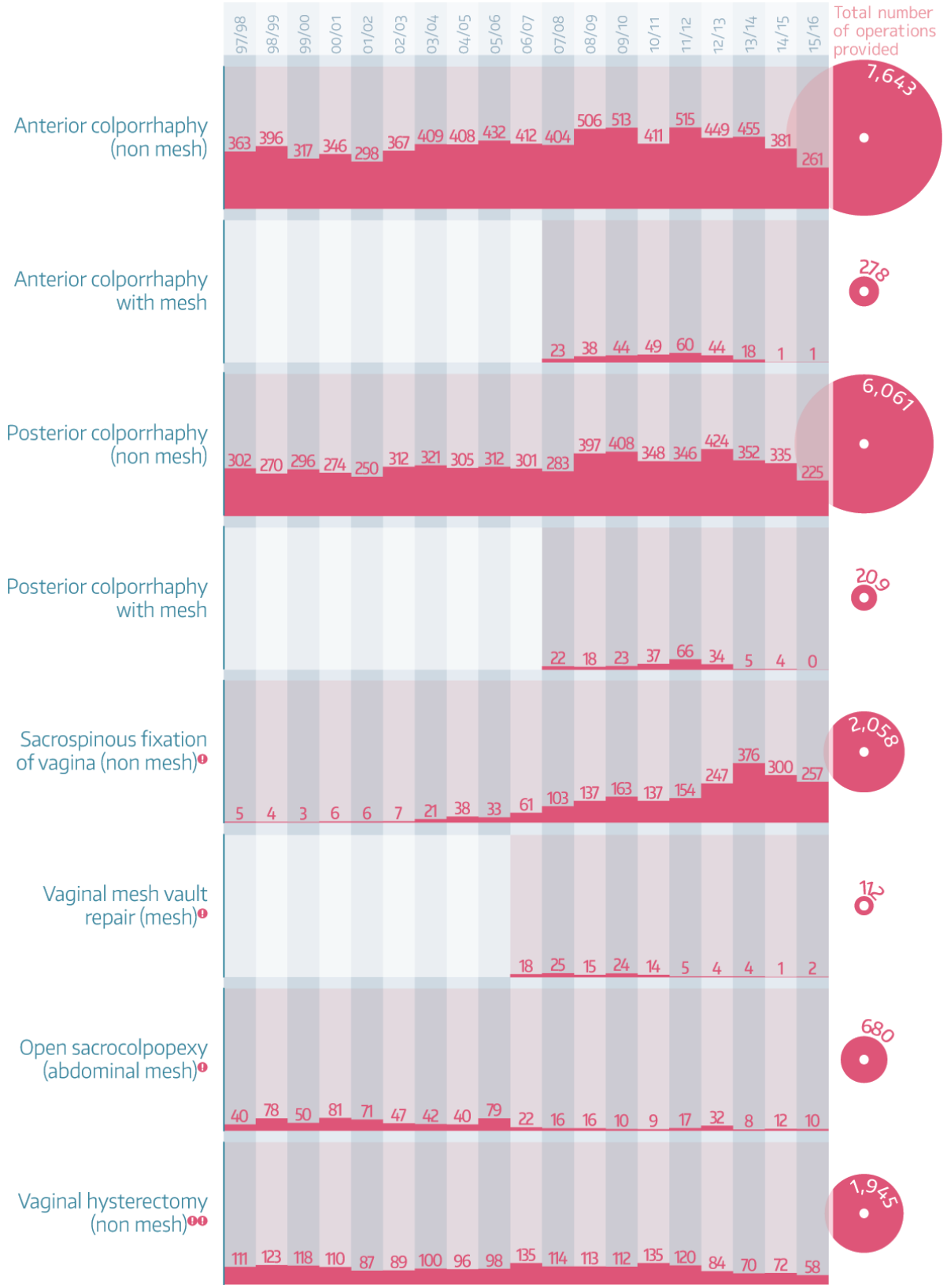
Operations provided during a patient's admission to hospital are recorded on routine hospital discharge records using OPCS Classification of Interventions and Procedures codes. Between 1997- 98 and 2005-06, the codes available did not specify which kind of mesh tape operation had been provided. After April 2006, new codes allowed the particular type of mesh tape operation (retropubic or transobturator) to be recorded.

4.3 Operations provided for pelvic organ prolapse

Anterior and posterior non-mesh colporrhaphies (first, single operations) have been commonly provided (up to around 500 per year) throughout the study period. Anterior and posterior mesh colporrhaphies can be identified in hospital discharge records from 2007/08 onwards. Relatively small numbers of mesh colporrhaphies have been provided in Scotland since then, and numbers provided have fallen in the most recent years.

Sacrospinous fixation operations have increased markedly over recent years (to around 300 first single procedures per year). Vaginal mesh vault prolapse repair procedures can be identified in hospital discharge records from 2006/07 onwards. Relatively small numbers have been provided since then, and numbers provided have fallen in the most recent years. Mesh open sacrocolpopexies have been provided in moderate numbers (fewer than 100 per year) over the time period included in the analysis. Moderate numbers (around 100 per year) of

vaginal hysterectomies for POP have also been provided over the time period included in the analysis.



Sacrospinous fixation, vaginal mesh vault repair, and open sacrocolpopexy are provided for prolapse of the top of the vagina following a hysterectomy. These operations were therefore included if the woman had had a previous hysterectomy (but no other operation for incontinence or prolapse in the previous five years). In addition, these operations are rarely done as single operations so ISD included them if they were done at the same time as a traditional (non-mesh) colporrhaphy (but no other incontinence or prolapse operation).

Vaginal hysterectomy can be done for prolapse or other problems such as heavy periods. Only vaginal hysterectomies done for prolapse were included in the analysis.

4.4 Problems after surgery for stress urinary incontinence or pelvic organ prolapse

Main problems

ISD looked at four main categories of problem that can develop after an operation for SUI or POP. These were:

- immediate complications;
- later complications;
- further incontinence surgery; and
- further prolapse surgery.

Immediate complications

'Immediate complications' means that at least one complication was recorded on the same hospital discharge record as the operation being examined; in other words, the woman developed a complication when she was still in hospital following her first operation.

Later complications

'Later complications' means that at least one complication was recorded on a subsequent hospital discharge record; in other words, the woman had been discharged home then readmitted for a complication at a later date. In general, readmissions for later complications were counted if they happened within five years of the operation being examined. Complications that would be expected to develop quickly after an operation were only counted if the readmission was within three months of the operation.

Further incontinence or prolapse surgery

'Further incontinence or prolapse surgery' means that at least one operation for either of these conditions was recorded on a subsequent hospital discharge record; in other words, the woman had been discharged home after her first operation then readmitted for another SUI or POP operation at a later date. All readmissions for further surgery were counted if they happened within five years of the operation being examined.

What is a 'complication'?

'Complications' included the following:

- problems directly related to the operation, such as damage to the bladder or difficulty passing urine;
- excessive bleeding;
- infection;
- pain; and
- partial or total removal of mesh (later complications only).

Only complications that were treated in hospital were included in the analysis.

Complications treated in outpatient clinics or in general practice were not included because this information was not available to us.

The risk of developing problems after an operation

The risk of developing problems after an operation for SUI or POP depends on the type of operation done and on a number of other factors such as:

- the age of the woman;
- how many additional health problems she has; and
- how experienced the surgeon doing the operation is.

To compare the risks specifically associated with different types of operation, it is important to take account of these other factors that may be influencing the number of problems seen. For example, if older women with a lot of additional health problems tend to have mesh colporrhaphies rather than standard (non-mesh) colporrhaphies, we would expect to see more problems after mesh operations even if mesh colporrhaphy did not in itself carry any more risk than standard colporrhaphy.

Statistical methods can be used to take account of other factors that may influence the number of problems seen after different types of operation and allow us to focus on the differences that are due specifically to the type of operation that was provided.

4.5 Problems following operations for stress urinary incontinence

The risk of developing problems after the different types of SUI operation included in the analysis is shown below.



This is the total number of readmissions that would occur on average if 200 women were each monitored for five years after having their SUI operation.

The increase or decrease in risk of the various problems following each type of operation compared to that experienced by women undergoing open colposuspension, the commonest non-mesh operation, is shown below.

These final results have used statistical methods to take account of various factors that may influence the level of problems seen after operations as discussed above. The factors that have been accounted for are women's age, deprivation level, and additional health problems; the experience of the surgeon; and the type of hospital providing the operation.

Taking these factors into account means that the remaining differences in risk are not due to those factors and are likely to reflect genuine differences in risk associated with the different types of operation.

To help interpret these figures, a 50% decrease in risk is the same as the risk being halved, and a 100% increase in risk is the same as the risk being doubled.



Green indicates significantly lower risk than that seen after open colposuspension
Red indicates significantly higher risk than that seen after open colposuspension

4.6 Summary of findings for stress urinary incontinence operations

Mesh tape procedures for SUI carried a lower risk of immediate complications than open colposuspension (a non-mesh procedure). Infections and problems directly related to the operation were the most common immediate complications following all types of SUI operations.

Mesh tape procedures carried a similar risk of being readmitted for a later complication compared to open colposuspension.

The relatively high risk of later complications seen after urethral injection therapy (a non-mesh procedure) may be due to the very high risk of needing another incontinence operation after this type of surgery (see below).

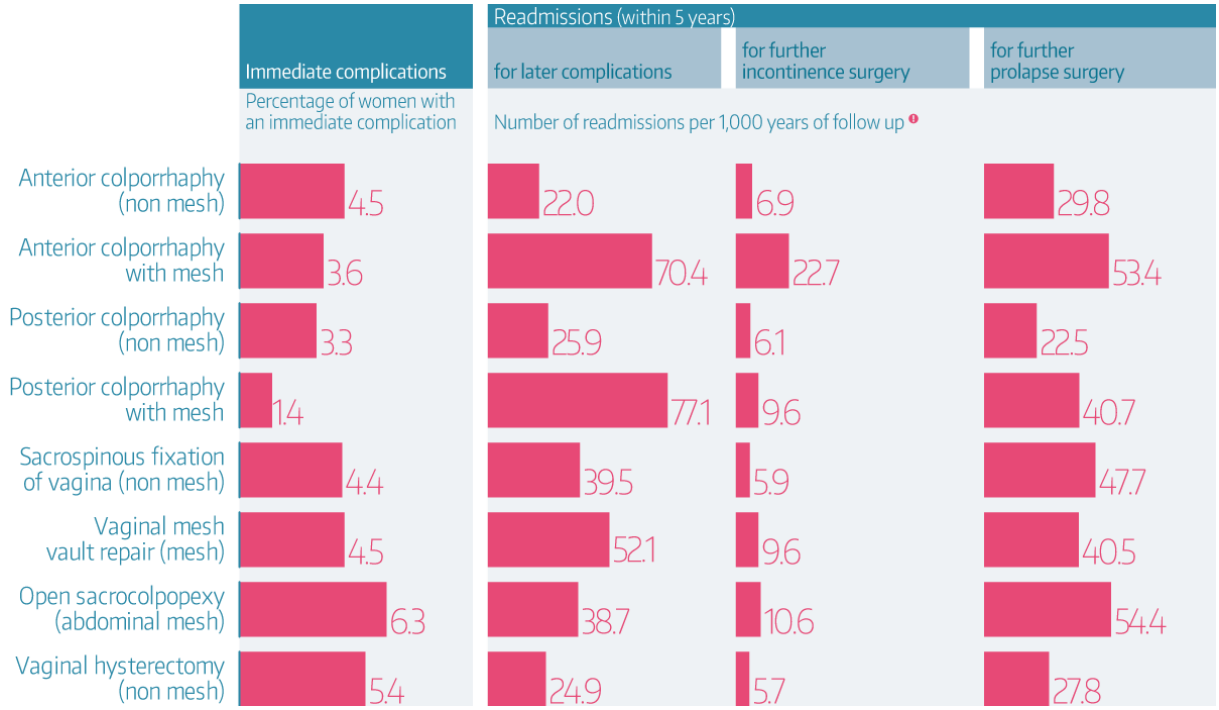
Problems directly related to the operation, infections, and (for mesh operations) further surgery to remove the mesh, were the most common later complications seen after operations to treat SUI.

Mesh tape procedures carried a similar risk of being readmitted for repeat incontinence surgery compared to open colposuspension. By contrast, urethral injection therapy carried a much higher risk of being readmitted for further incontinence surgery than open colposuspension.

All the procedure types examined carried a lower risk of being readmitted for subsequent prolapse surgery compared to open colposuspension.

4.7 Problems following operations for pelvic organ prolapse

The risk of developing problems after the different types of POP operation included in the analysis is shown below.



This is the total number of readmissions that would occur on average if 200 women were each monitored for five years after having their POP operation.

The increase or decrease in risk of the various problems following each type of operation compared to that experienced by women undergoing anterior colporrhaphy (the commonest non-mesh operation) is shown below.

As described earlier, these final results have used statistical methods to take account of the various other factors that may influence the level of problems seen after these operations. The differences shown are likely to reflect genuine differences in risk associated with the different types of operation.



Green indicates significantly lower risk than that seen after anterior colporrhaphy (non-mesh)
Red indicates significantly higher risk than that seen after anterior colporrhaphy (non-mesh)

4.8 Summary of findings for pelvic organ prolapse operations

Among the POP operations included in the analysis, open sacrocolpopexy and vaginal hysterectomy carried the highest risk of immediate complications. In general, infections and problems directly related to the operation were the most common immediate complications following prolapse operations. Excessive bleeding was also relatively common after open sacrocolpopexy and vaginal hysterectomy.

Mesh colporrhaphies (anterior and posterior) carried considerably higher risk of being readmitted for a complication over the five years following the initial operation than the equivalent operations carried out without mesh.

All procedures for vaginal vault prolapse (sacrospinous fixation, vaginal mesh vault repair, and open sacrocolpopexy) carried a higher risk of later complications than non-mesh anterior colporrhaphy; however complication rates were similar between the three different vault repair procedures.

Problems directly related to the operation, infections, and (for mesh operations) further surgery to remove the mesh were the most common later complications seen after operations to treat POP.

Mesh anterior colporrhaphy carried a higher risk of being readmitted for further incontinence surgery over the five years following the initial operation than non-mesh anterior colporrhaphy. Mesh colporrhaphies (anterior and posterior) also carried a higher risk of being readmitted for further prolapse surgery.

Procedures for vaginal vault prolapse (sacrospinous fixation, vaginal mesh vault repair, and open sacrocolpopexy) generally carried a higher risk of further incontinence and prolapse surgery than non-mesh anterior colporrhaphy; however further surgery rates were similar between the three different vault repair procedures.

4.9 How to interpret our findings

This study has used routinely available health information to look at:

- the number of operations provided in Scotland for SUI and POP; and
- how often women having the different types of operation develop problems after their surgery.

The study has several strengths. It includes all relevant operations provided in Scotland over a long time period. It uses high quality NHS information to assess how often women develop significant problems requiring further treatment up to five years following their initial operation.

The study also has some limitations. We only included first, single procedures so we cannot comment on outcomes following combined or repeat surgery. We only measured problems that required inpatient hospital treatment: problems that were dealt with in primary care or outpatient departments have not been included. We only described the number of problems seen so we cannot comment on the impact of these problems on patients' quality of life. In addition, it is possible that individuals with the most severe disease receive particular types of operation: this would then tend to make the results of those operations seem relatively poor.

4.10 Key Messages

- No operation is without risk. It is important for women and doctors to have clear information about the different risks associated with different types of operation. This will help them decide which operation will be best for an individual woman.
- The risk of immediate complications, later complications, and further surgery for SUI or POP differs between the different types of operation examined. An operation can carry

a relatively high risk of one of these problems (for example immediate complications) but a relatively low risk of a different problem (for example longer term complications).

- More extensive operations, for example those involving operating through the abdomen or a hysterectomy, tend to carry the highest risk of immediate complications.

- Compared to open colposuspension, mesh tape operations for SUI tend to carry a lower risk of immediate complications, a lower risk of requiring subsequent prolapse surgery, and a similar risk of requiring repeat incontinence surgery. Mesh tape procedures carry a similar risk of longer term complications as open colposuspension (at least up to five years following the initial surgery), although the profile of later complications differs between the different operations, with subsequent mesh removal surgery only seen following mesh procedures. Our results currently support the use of mesh procedures for incontinence, although further research on longer term outcomes would be beneficial.

- Mesh colporrhaphies for the treatment of POP carry a substantially higher risk of later complications than non-mesh colporrhaphies. Mesh colporrhaphies also carry a higher risk of the woman needing further surgery for incontinence or prolapse than non-mesh colporrhaphies. Our results do not support the use of mesh colporrhaphies for primary prolapse repair.

- Procedures for vaginal vault prolapse repair in general carry higher risk than non-mesh anterior colporrhaphy, however rates of later complications and further incontinence and prolapse surgery are similar between vault repair procedures that do not involve mesh (sacrospinous fixation of the vagina) and those involving mesh inserted vaginally (vaginal mesh vault repair) or abdominally (open sacrocolpopexy). Our results do not clearly favour any particular vault repair procedure.

Chapter 5: Review of the evidence from safety reviews and systematic reviews

Update Since Interim Report

Background

Since publication of the IR's Interim Report in October 2015, six further reports have been published which are within the scope of the review. These comprise two reports which are concerned with the Safety Reviews:

- Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). *Opinion on the safety of surgical meshes used in urogynecological surgery*. December 2015; and

- Kelly M, Macdougall K, Olabisi O, & McGuire N (2016). *In vivo response to polypropylene following implantation in animal models: a review of biocompatibility.* International Urogynecological Journal. DOI:10.1007/s00192-016-3029-1.

In addition there have been three updated Cochrane Reviews which focused on the effectiveness of mesh implants. These are:

- Lapitan MCM, Cody JD, (2016). *Open retropubic colposuspension for urinary incontinence in women.* Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD002912.

- Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J, (2016a). *Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse.* Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD012079;

- Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J, (2016b). *Surgery for women with apical vaginal prolapse.* Cochrane Database of Systematic Reviews 2016. DOI:10.1002/14651858.CD012376;

Finally, an update on the final report from the PROSPECT trial is included:

- Glazener CMA, Breeman S, Elders A, Hemming C, Cooper CG, Freeman RM, Smith ARB, Reid F, Hagen S, Montgomery I, Kilonzo M, Boyers D, McDonald A, McPherson G, MacLennan G, Norrie J (on behalf of the PROSPECT Group), (2016). *Mesh, graft, or standard repair for women having primary transvaginal 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.

This chapter provides an update on these documents and the impact they have on the conclusions of the interim report. The tabulated results from the interim report remain available on the website here http://www.gov.scot/Publications/2015/10/8485/downloads.

5.1 Evidence availability

This section of the IR was undertaken in line with a modified form of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline[7].

This review considered systematic review evidence of two sorts. The first were the reviews of evidence undertaken by those agencies responsible for the safety of medical devices on a national and international basis. The second were the published, peer-reviewed Cochrane systematic reviews and health technology assessments undertaken in relation to mesh devices for SUI and POP.

5.1.1 Safety reviews

Safety reviews of medical devices seek to determine if the device can continue to be used safely and how best to ensure that both patient safety and device effectiveness is maintained. One reviewed the evidence relating to adverse outcomes following mesh implantation; the other examined the toxicology of the product.

Safety reviews are most likely to focus mainly on the nature, severity and frequency of any surgical complications and adverse outcomes. They are also likely to consider aspects of efficiency and effectiveness in the delivery of care. Finally, they may consider whether there has been any failure in the regulatory system that was used to determine the original safety of the device as “safe" for health care use.

Different reviews may use varying methods. In most cases, the reviews use a “narrative” method, reporting on available evidence.

5.1.2 Cochrane Systematic reviews

Cochrane systematic reviews are produced by the Cochrane Collaboration. This is a global, independent network of researchers, professionals, patients, carers and people interested in health. It is formed as a not-for-profit organisation which spans contributors from more than 120 countries. Its work is always free from commercial sponsorship and other conflicts of interest.

Cochrane Collaborators produce reviews that summarise the best available evidence generated through research to inform decisions about health and health care. These Cochrane Reviews are a systematic synthesis of primary research in human health care and health policy. They are internationally accepted as providing health care evidence of the highest standard. Cochrane Reviews are updated as needed, ensuring the most up-to-date and reliable evidence is available.

The full text of Cochrane Review and Protocol are published online in the Cochrane Database of Systematic Reviews in the Cochrane Library[8]. In the UK, Cochrane Reviews are used to inform the National Institute for Health and Care Excellence (NICE) and the Scottish Intercollegiate Guidelines, Network (SIGN) guidelines, as well as informing policy and decision making in health care commissioning and development.

[7] http://www.prisma-statement.org/
[8] http://www.cochranelibrary.com/

5.1.3 Randomised controlled trials

A randomized controlled trial is a clinical-epidemiological experiment in which subjects are randomly allocated into groups, usually called test and control groups, to receive or not to receive a preventive or a therapeutic procedure or intervention. The results are assessed by comparison of rates of disease, death, recovery, or other appropriate outcome in the study groups.

Randomised controlled trials are generally regarded as the most scientifically rigorous method of hypothesis testing available in epidemiology and medicine. Nonetheless, they may have limitations. These typically include a limitation of the trials findings being applied elsewhere due, for example, to the non-representativeness of patients who participate.[9]

5.2 Methods of reviewing evidence

Following discussions with both patients and clinicians, a number of key outcome areas were identified to provide a data extraction framework. These were:

- Effectiveness of SUI or POP procedure(s):
  - effectiveness in terms of objective SUI / POP cure at one year or more;
  - effectiveness in terms of subjective SUI / POP cure at one year or more;
  - need for repeat SUI or POP surgery; or
  - further conservative treatment for SUI.

- Reported safety issues with SUI or POP procedure;
  - mesh technology; or
  - proprietary brand of mesh.

- Patient-focussed outcomes: Quality of Life (QoL):
  - measurable QoL at one year or more post procedure, specific to SUI or POP.

- Patient-focussed outcomes: adverse outcomes:
  - Short-term/postoperative complications;
  - long-term disability due to adverse effects;
  - surgical treatment for adverse effects.

- Relative efficacy of alternative therapy to mesh.

- Systems efficacy:
  - surgical capacity and competency issues;
  - service capacity and feasibility; and
  - other factors.

Data were extracted and tabulated for further interpretation. The overall quality of the evidence reviewed was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) on grades of evidence [SIGN 50 reference].

[9] http://irea.ir/files/site1/pages/dictionary.pdf

5.3 Safety Reviews

5.3.1 The Scientific Committee on Emerging and Newly Identified Health Risks Safety Review

5.3.1.1 Aims

The SCENIHR report is the European Safety Review commissioned by the Commission of the European Union. The report aims to answer a series of specific questions. In this case the review's scope was to consider the:

- risks associated with the use of surgical meshes for treating SUI and POP;
- identification of high-risk patient groups;
- risks associated with mesh use for non-urogynecological surgery;
- need for further assessment in this field; and
- scientific rationale for the use of synthetic surgical mesh for the management of urinary incontinence, POP and colorectal functional disorders.

The scope of the European Review is slightly broader than that of the Independent Review (IR), which is limited to the use of surgical mesh in SUI and POP.

5.3.1.2 Update since interim report

The IR included evidence derived from the earlier, preliminary opinion from SCENIHR published in June 2015. This preliminary opinion document was subsequently subject to a formal consultation by the SCENIHR before the final version was published in December 2015.

5.3.1.3 Describe included studies

The surgical mesh component of the safety review considered 24 studies. Four studies were in humans (n= 64 in total), and the rest were in animals.

5.3.1.4 Outcomes

For this evidence update, a comparison between the conclusions reached in the preliminary and the final versions of the European Review has been undertaken for those areas which were included into the IR. The text below provides a narrative between the relevant conclusions and recommendations of the preliminary and final version of the European Review.

5.3.1.5 Follow up period

The follow up period of all studies included in the surgical mesh element of the this safety review varied from 14 days to 3 years.

5.3.1.6 Quality of evidence

The quality of this evidence has been assessed as very good.

5.3.1.7 Findings

In the main differences between the preliminary opinion of the SCENIHR and the final opinion are in the wording and there is no substantive difference in the underlying meaning of the opinion. Additional detail has been added to improve clarity of the opinion made in several cases.

There are differences between the preliminary and final opinion regarding the specific sub-groups of women who are identified as having greater risk of adverse outcomes in the use of synthetic mesh. The final report has removed mention of both an association between smoking and mesh exposure and the potential need for greater consideration prior to mesh use in younger age groups. The final report highlights an increased risk associated with age and obesity.

5.3.1.8 Conclusions

Risks associated with the use of surgical meshes for treating SUI and POP include various complications of poor tissue integration, such as tissue extrusion, exposure of the mesh and shrinkage of the mesh. High-risk patient groups are associated with age and obesity. There is insufficient evidence to comment on the risk of meshes other than for urogynecological surgery.

The factors influencing the surgical outcomes are mesh properties (biocompatibility, tissue integration, long-term stability, and mechanical performance over time which includes flexibility, elasticity, aging and resistance to deformation) product design (e.g. physical characteristics of the mesh, size of the pore as a predisposing factor to infection in particular with a pore size less than 75 microns) overall mesh size (which is greater for POP than for SUI), route of implantation, (e.g., vaginal or transabdominal), patient characteristics (e.g., age, obesity, smoking), associated procedures (e.g., hysterectomy) and surgeon's experience.

5.3.2 Kelly et al (2016). In vivo response to polypropylene following implantation in animal models: a review of biocompatibility.

5.3.2.1 Aims

This paper reports on a Literature Review undertaken by staff within the MHRA. The focus of the review is research on polypropylene devices after implantation in the body.

5.3.2.2 Update since interim report

This safety review has been published since the interim report.

5.3.2.3 Description of included evidence

46 articles investigating the response of mesh in live subjects were reviewed.

5.3.2.4 Outcomes

The specific areas considered were: the type of material selected; the impact of anatomical location; and the structure, weight and size of polypropylene mesh types. In all cases the studies focussed on animal models.

5.3.2.5 Follow up period

The studies included have a limited follow up period, with few long-term studies possible.

5.3.2.6 Quality of evidence

The quality of this evidence has been assessed as very good.

5.3.2.7 Findings

While this review only focusses on research evidence drawn from animal studies, the findings are consistent with other safety reviews. Specifically, the review concluded:

- polypropylene meshes are less likely to evoke an inflammatory or similar host response than other synthetic materials and polypropylene composite meshes;
- using a light-weight mesh with large pores results in fewer complications; and
- current evidence, although limited, suggests that mesh implants in the pelvic region are more susceptible to complications than the abdominal region.

There are limitations of applying data from animal studies to humans, and the review itself acknowledges this shortcoming. However, the use of animal models in such situations is well-accepted in research literature.

5.3.2.8 Conclusions

In summary, this review concludes that the biocompatibility of synthetic polypropylene mesh for use in SUI and POP is comparable with or better than other synthetic meshes, composite meshes and biologically-derived meshes when examining complication rates. While more research is indicated, the overall findings from the animal studies are consistent with existing evidence, suggesting that mesh type, size and location of implantation are all risk factors for complications.

5.4 Systemic Review – Stress Urinary Incontinence

5.4.1 Lapitan & Cody (2016). Open retropubic colposuspension for urinary incontinence in women

5.4.1.1 Aims

This systematic review considers the effectiveness of surgical techniques for retropubic colposuspension as a treatment for SUI or SUI mixed with other urinary symptoms in women.

5.4.1.2 Update since interim report

This review adds new evidence since the interim report was published regarding the comparison of open retropubic colposuspension (ORC) with self-fixing sling procedures using either retropubic or transobturator mesh tapes.

5.4.1.3 Description of included trials

Overall, the review found 22 trials that compared ORC with sling procedures; of which 12 related to retropubic and 4 to transobturator mesh tape procedures.

5.4.1.4 Outcomes

Across all studies there were 27 different outcomes considered, these varied considerably between the studies that consider mesh procedures. Those reported were:

- reported cure;
- incontinence rate;
- outcomes associated with surgical characteristics (e.g. length of stay);
- quality of life measures;
- health economic outcomes; and
- adverse outcomes.

5.4.1.5 Follow up period

Less than one year to more than five years.

5.4.1.6 Quality of Evidence

The overall quality of the evidence included was not well described and the potential bias in the included trials was generally assessed as "uncertain". The additional evidence of interest to the IR, may be of low quality at best. The review's authors comment on the *",,,urgent need for further trials of adequate power to assess the effectiveness, safety and cost-effectiveness of open retropubic colposuspension in comparison with (a) suburethral slings, using both traditional and minimally invasive approaches, and (b)the laparoscopic technique. In addition, the long-term outcomes of existing trials could and should be reported"*. (Lapitan & Cody (2016). Pg 26).

The data from one trial, which considered the use of the Gynecare TVT™ procedure, was sufficiently large to dominate the analysis relating to retropubic mesh tapes. This may be a potential bias.

5.4.1.7 Findings

The summarised results from the individual comparisons made in this systematic review are included below.

5.4.1.8 Conclusions

Open retropubic colposuspension is an effective treatment modality for stress urinary incontinence, especially in the long-term. Within the first year of treatment, the overall continence rate is approximately 85% to 90%. After five years, approximately 70% of women can expect to be dry. Newer minimal access sling procedures look promising in comparison with open colposuspension but more evidence is required. Open colposuspension is associated with a higher risk of pelvic organ prolapse compared to sling operations and anterior colporrhaphy, but with a lower risk of voiding dysfunction compared to traditional sling surgery. Laparoscopic colposuspension should allow faster recovery but its relative safety and long-term effectiveness is not yet known.

Table 5.1 Summary overview of Systematic Review on Stress Urinary Continence by Lapitan & Cody 2016.

Author(s) (Year) & Title	Effects	Colposuspension	Mesh Tape	RR, 95%CI, number of studies and participants
Lapitan MCM & Cody JD (2016) Open retropubic colposuspension for urinary incontinence in women	Short-term efficacy (1 year)	Subjective: 75.4%	71.1%	0.88 [0.67, 1.16], 5 RCTs, 547 participants
		Objective: 82.4%	83.4%	1.08 [0.74, 1.57], 4 RCTs, 515 participants
	Medium term efficacy (1-5 year)	Subjective: 74.0%	70.0%	0.91 [0.68, 1.22], 4 RCTs, 427 participants
		Objective: 84.0%	85.9%	1.14 [0.69, 1.88], 3 RCTs, 348 participants
	Long-term efficacy (>5 year)	Subjective: 69.7%	63.3%	0.83 [0.54, 1.26], 1 RCT, 177 participants
		Objective: 89.8%	80.6%	0.52 [0.20, 1.36], 1 RCTs, 121 participants
	Repeat continence surgery	3.4%	2.4%	1.46 [0.40, 5.32], 1 RCTs, 316 participants

Table 5.2 Extracted Data from Systematic Review on Stress Urinary Incontinence by Lapitan & Cody 2016.

Author(s) & Title	**Aim Review type, Evidence quality**	**Level of evidence & Description of studies**	**Findings** • **Surgical** • **Adverse** • **QoL**	**Conclusions**
Lapitan MCM & Cody JD (2016) Open retropubic colposuspension for urinary incontinence in women. Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD002912.pub6 Last assessed as complete at 12th February 2016	To assess the effects of open retropubic colposuspension for the treatment of urinary incontinence. Cochrane Systematic Review. This is a full search update to Lapitan & Cody (2012). In this table,	Systematic Review based on evidence ranging from SIGN 1++ (High quality meta-analysis, systematic reviews of Randomised Controlled Trials (RCTs) ,or RCTs with a very low risk of bias) to SIGN 1+.(Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias) In total 55 studies which were either randomised or quasi-randomised controlled trials which involved ORC in at least one arm of the trial In total these 22	All results refer to comparisons between ORC and Mesh self-fixing slings. Where possible TVT or TOT procedures as comparators are shown. Outcomes are described using the terms adopted in the update review. **1. Women's' Observations (Subjective cure)** • Short-term (<1y). Comparisons including five trials (n=547) showed no differences between OTC and TVT (RR = 0.88; 95% CI.67 to 1.16) for any short-term women's outcomes; • Mid-term (1-5y). Analysis for ORC v TVT for subjective incontinence (five trials) (RR = 1.18; 95% CI 1.01 to 139) and for improvement in incontinence (two trials) (RR = 1.11; 95% CI 0.64 to 1.91) were inconclusive. The significant finding of superior subjective cure with TVT being a consequence of 1 large trail in that comparison. • Long-term (>5y). Pooled data from three trials showed no significant differences between ORC and TVT (RR = 1.11; 95% CI 0.97 to 1.27). **2. Clinician's Observations** • Data for: Short-term (<1y) (RR = 1.11; 95% CI 0.97 to 1.27, four trials); Mid-term (1-5y). (RR = 1.14; 95% CI 0.69 to 1.88, three trials); Long-term (>5y). (RR = 0.52; 95% CI 0.20 to 1.36, 1 trial**)** showed no significant differences in objective cure.	*"… [There is an] urgent need for further trials of adequate power to assess the effectiveness, safety and cost-effectiveness of open retropubic colposuspension in comparison with (a) suburethral slings, using both traditional and minimally invasive approaches, and (b)the laparoscopic technique. In addition, the long-term outcomes of existing trials could and should be reported".* (Pg. 26).

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • Surgical • Adverse • QoL	Conclusions
	only the comparison of surgical open retropubic colposuspension (ORC) with self-fixing sling procedures using either tension-free vaginal tape (TVT) or transobturator tape (TOT) forms of mesh implants are considered. The potential bias in the included trials was generally assessed as "uncertain". The quality of the relevant evidence may be assumed to be low at best.	trials randomised 2343 women to surgical interventions. Data from one of the new trials could not be included in pooled data analyses as there was insufficient information.	• Surgical outcomes showed that Mesh procedures were superior to ORC for length of operative time (RR = 18.06; 95% CI 14.67 to 21.46, 3 trials); length of hospital stay of 4 days (MD=3.99; 95% CI 3.71 to 4.28, 6 trials); and time to catheter removal (MD = 4.51; 95% CI 3.05 to 5.97, 1 trial). **3. Adverse outcomes** • No significant differences were found between ORC and TVT procedures in relation to: ○ perioperative (7d) surgical complications (RR = RR 1.11; 95% CI 0.66 to 1.87, 4 trials); (n= ○ voiding dysfunction (RR = 0.85; CI 0.47 to 1.53, 6 trials); or ○ repeat incontinence surgery (RR = 1.46; 95% CI 0.40 to 5.32, 1 trial); • TVT procedures were found to be superior to ORC in relation to: ○ the rate of new or recurrent prolapse post-surgery (RR = 1.85; 95% CI 1.25 to 2.75, three trials), though this superiority was not observed if only symptomatic prolapse was analysed; ○ bladder perforation (RR=0.20; 95% CI 0.08 to 0.49, 7 trials); and ○ other complications (RR =0.24 95% CI 0.09 to 0.62, 4 trials); • There was insufficient pooled data to assess if there were differences between TVT and ORC procedures relating: ○ to de novo symptoms of urgency (RR = 1.28; 95% CI 0.51 to 3.16, 2 trials); or ○ de novo detrusor over-activity (RR = 1.28 95% CI 0.71 to 2.32). 3 trials). • One trial reported a case of vascular injury associated with TVT procedure.	*"The minimally invasive sling procedures confer similar success rates in comparison to open colposuspension. However, traditional slings provide better cure rates at the expense of more voiding dysfunction in the short-term. The long-term adverse event profile of the sling procedures, in particular with the use of the TVT, is still unclear."* (Pg. 26).

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • Surgical • Adverse • QoL	Conclusions
			4. Quality of Life Outcomes • Two trials included formal assessment of QoL using standardised instruments. All showed no differences between ORC and TVT surgery safe for one trial that showed a significant improvement in the emotional and social functioning sub-scale of the SF36 associated with TVT.	

5.5 Systematic Reviews – Pelvic Organ Prolapse

5.5.1 Maher et al (2016a). Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse.

5.5.1.1 Aim

This Cochrane systematic review provides a partial update on the initial Cochrane systematic review by Maher C et al (2013): "*Surgical management of POP in women".* The update focusses only on studies that consider transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse.

5.5.1.2 Update since interim report

Twelve new trials were included in the systematic review and data from the three year follow up of a study previously included in the 2013 review.

5.5.1.3 Description of included trials

In total, 37 trials were included, representing data from 4,023 adult women who had sought treatment for symptomatic POP (either primary or recurrent). Of these 1,986 had been treated with colporrhaphy augmented with transvaginal implant (synthetic mesh or biological graft) and 2,037 with traditional native tissue repair (colporrhaphy).

5.5.1.4 Outcomes

The studies included a range of primary and secondary outcomes. These can be summarised as:

- Primary outcomes:
  - subjective awareness of prolapse;
  - repeat surgery – for prolapse, SUI; or composite; and
  - recurrent prolapse.

- Secondary outcomes:
  - adverse events: death (related to surgery); mesh exposure; bladder or bowel; surgery for mesh exposure;
  - prolapse outcomes: objective failure by compartment) objective failure by POPQ score; total vaginal length;
  - bladder function: recurrent or SUI; recurrent or de novo overactive or urge incontinence;
  - bowel function: de novo faecal incontinence or obstructed defecation;
  - sexual function: de novo dyspareunia; PISQ-12;
  - quality of life and satisfaction measured by questionnaire (PG1-1, PQOL, PFDI-20, or PFIQ-7); and
    measures associated with surgery: operating time; blood transfusion; length of hospital stay.

5.5.1.5 Follow up period

The trials varied in their follow up periods. While one only reported a six month follow up, there were 25 reporting after one year, eight with after two years and three after three years.

5.5.1.6 Quality of evidence

Overall the quality of evidence was assessed to be:

- permanent transvaginal mesh compared with native tissue: was low to moderate for most outcomes;

- absorbable mesh compared with native tissue repairs: was generally very low to low, reflecting smaller, older studies; and

- biological grafts compared with native tissue repairs: was very low to low, reflecting poor reporting of study methods, lack of clarity with regard to blinding of assessors, and imprecision.

The main limitations were poor reporting of study methods, inconsistency, and imprecision.

The risk of bias in the main studies was considered to be low.

5.5.1.7 Findings

The summarised results from the individual comparisons made in this systematic review are shown below.

5.5.1.8 Conclusions

The general conclusions from this systematic review are:

1. Permanent transvaginal mesh surgery is associated with lower rates of awareness of prolapse and prolapse on examination than native tissue repair. However, it is also associated with increased morbidity. There is a complex risk-benefit profile which suggests that transvaginal mesh has limited utility in primary surgery. In cases where there is a high risk of recurrence, some women and their clinical team may feel that the benefits may outweigh the risks. This systematic review, however, has no evidence to support this position.

2. There is limited evidence that absorbable mesh may reduce the risk of recurrent prolapse on examination compared with native tissue repair. Existing evidence from trials using absorbable mesh was insufficient to allow any further conclusions to be drawn.

3. Many of the permanent transvaginal mesh devices reviewed have now been removed from clinical use by their manufacturers. This review does not include RCT data for any of the more recently introduced, lightweight transvaginal meshes for permanent insertion. Until such RCT data become available, these newer transvaginal meshes should be utilised under the discretion of the ethics committee. Unfortunately, at least two such ethically approved trials have been terminated due to difficulty in recruitment or funding.

4. Other urgent research needs include: an updated cost-benefit analysis of transvaginal mesh surgery; and long-term outcome studies should be undertaken for existing mesh procedures.

Table 5.3 Summary Table of Systematic Review on Pelvic Organ Prolapse by Maher et al 2016 (a)

Author(s) (Year) & Title	Effects	Native Tissue Repair	Mesh Repair	RR (95%CI, number of studies and participants
Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J.(2016) Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse.	Short-term efficacy (1-3 years)	Subjective: 81%	85-90%	0.66 (0.54-0.81), 12 RCTs, 1614 participants
		Objective: 62%	80-89%	0.40 (0.30-0.53), 21 RCTs, 2494 participants
	Need for further POP surgery after 1 year	3.2%	1.7%	0.53 (0.31-0.88), 12 RCTs, 1674 participants
	Development of de novo SUI	9.6%	13.3%	1.39 (1.06-1.82), 12 RCTs, 1512 participants
	Need for SUI surgery after 1 year	2.6%	2.8%	1.07 (0.62 to 1.83), 9 RCTs, 1284 participants
	Combined need for further surgery (POP, SUI or mesh removal) at 1 year	4.8%	11.4%	2.40 (1.51-3.81), 7 RCTs, 867 participants
	Development of de novo dyspareunia	9.5%	8.8%	0.92 (0.58-1.47), 11 RCTs, 764 participants
	Bladder injury	0.5%	2.1%	3.92 (1.62-9.50), 11 RCTs, 1514 participants
	Length of hospital stay			0.06 days (0.03-0.18),7 RCTs, 953 participants
	Blood transfusion			1.55 (0.88-2.72), 6 RCTs, 723 participants

Table 5.4 Extracted Data from Systematic Review on Pelvic Organ Prolapse by Maher et al 2016 (a)

Author(s) & Title	**Aim Review type, Evidence quality**	**Level of evidence & Description of studies**	**Findings** • **Surgical** • **Adverse** • **QoL**	**Conclusions**
Maher C et al. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. Cochrane Database of Systematic Reviews 2016 DOI: 10.1002/14651858.CD012079.pub2 Last assessed as complete at 6th July 2015.	To determine the safety and effectiveness of transvaginal mesh (TM) or biological grafts compared to native tissue repair (NTR) for vaginal prolapse Cochrane Systematic Review This is a full search update on Maher et al (2013). The comparison of TM repairs versus NTR for vaginal prolapse are relevant. Overall the	Systematic Review based on evidence ranging from SIGN 1++ (High quality meta-analysis, systematic reviews of Randomised Controlled Trials (RCTs) ,or RCTs with a very low risk of bias) to SIGN 1+.(Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias) In total 37 trials	All results refer to comparisons between NTR and TM repairs. Where possible permanent (pTM) or absorbable (aTM) Mesh procedures are shown. **1. NTR v pTM** • Primary Outcomes ○ Awareness of prolapse – no significant differences were found at mid-term review (1-3y) (RR = 0.66; 95% CI 0.54 to 0.81, 12 trials); ○ Surgery for prolapse – rate of repeat surgery was lower for pTM (RR = 0.53; 95% CI 0.31 to 0.88, 12 trials); ○ Surgery for SUI – rate of repeat surgery was not significantly different between pTM and NTR (RR = 1.07; 95% CI 0.62 to 1.83, 9 trials); ○ Surgery for prolapse, SUI or pTM erosion –repeat surgery was less likely in NTR than pTM (RR = 2.40; 95% CI 1.51 to 3.81, 7 trials); ○ Recurrent prolapse at mid-term review (1-3y) –was less likely for pTM versus NTR (RR = 0.40; 95% CI 0.30 to 0.53, 21 trials). Sub analysis suggested this benefit of pTM was maintained for both anterior repairs alone (RR = 0.33; 95% CI 0.26 to UL+0.40, 15 trial) or multi-compartment repairs (RR = 0.59; 95% CI 0.40 to 0.87, 6 trials).	"… while permanent transvaginal mesh is associated with a greater reduction in prolapse on examination, awareness of prolapse and reoperation for prolapse than native tissue repairs, it is associated with increased morbidity, including a higher rate of bladder injury, de novo stress urinary incontinence, and reoperation rates for prolapse, stress urinary incontinence, and/or mesh exposure. The rate of mesh exposure was 12%, and surgery for mesh exposure was required in 8%, accounting for most of the reoperations for mesh complications."

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • Surgical • Adverse • QoL	Conclusions
	quality of evidence was assessed to be: • permanent transvaginal mesh compared with native tissue – low to moderate; and • absorbable mesh or biological grafts compared with native tissue repairs – very low to low. The main limitations were poor reporting of study methods, inconsistency, and imprecision. The risk of bias in the main studies was	were included with data from 4,023 women who had sought treatment for symptomatic pelvic organ prolapse (either primary or recurrent). Of these 1,986 had been treated with transvaginal graft repairs and 2,037 with traditional NTR (colporrhaphy). Twelve new trials were include in this 2016 systematic review and data from the three year follow up of a study previously included in the 2013 systematic review was included.	• Secondary (Adverse) Outcomes o POPQ scores –pTM repairs at the mid-anterior vaginal wall were superior to NTR (MD = -0.93; 95% CI -1.27 to -0.59, 10 trials). No differences were found between procedures at other vaginal sites; o Mesh exposure at mid-term review (1-3y) –was reported in 10% of anterior repairs and 17% of multi-compartment repairs; o Surgery for mesh exposure at mid-term review (1-3y) – the rate was 8% for all pTM procedures; o Prolapse at mid-term review (1-3y) –less in pTM repair vs NTR (RR = 0.45; 95% CI 0.36 to UK=0.55, 13 trials). Sub-analysis associated this with anterior repairs (RR = 0.36; 95% CI 0.28 to 0.47, 9 trial), but not multi-compartment repairs (RR = 0.73; 95% CI 0.51 to 1.06, 4 trials); o Prolapse in the posterior vaginal compartment – no significant differences in procedures (RR = 0.64; 95% CI 0.29 to 1.42, 3 trials); o Bladder or bowel injury – Bladder injury was more likely with pTM and NTR (RR = 3.92; 95% CI 1.62 to 9.50, 11 trials). No significant differences were reported in one trial that reported on bowel injury; o De novo bladder voiding problems – no differences between procedures were found (RR = 0.75; 95% CI 0.35 to 1.63, 3 trials); o De novo dyspareunia - there was no evidence of a difference between the procedures (RR = 0.92; 95% CI 0.58 to 1.47, 11 trials); • Secondary (Surgical) Outcomes	(pg. 17)

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • **Surgical** • **Adverse** • **QoL**	Conclusions
	considered to be low.		○ Operating times – only data relating to multi-compartment repairs were suitable for analysis. The mean operating time was shorter for pTM procedures (MD = 7.48m; 95% CI -10.87 to UL = -4.08, 3 trials); ○ No differences were found in relation to blood transfusion use during the procedure (RR = 1.55; 95% CI 0.88 to 2.72, 6 trials) or length of hospital stay (MD = -0.06d; 95% CI -0.03 to UL = 0.18, 7 trials). • Secondary (QoL) Outcomes ○ No significant differences in either the PSSFQ scores (MD= -0.13, 95% CI -0.40 to 0.13, 7 trials), or combined scores from the PQLQ (3 trials) and the PFIQ (4 trials) (Standard MD = 0.05; 95% CI -0.20 to 0.30). **2. NTR v aTM** • Primary Outcomes ○ Awareness of prolapse (2y review) –no evidence of a difference between NTR and aTM repair (RR = 1.05,;95% CI 0 .77 to 1.44, 1 trial); ○ Repeat surgery (2y review) –no evidence of differences for prolapse (RR = 0.47; 95% CI 0.09 to 2.40, 1 trial); ○ Recurrent prolapse (3m to 2y review) –rates at review were lower for aTM (RR = 0.71, 95% CI 0.52 to 0.96, 3 trials) However, this finding was sensitive to statistical analysis, if a random-effects model was used the difference was not significant (RR = 0.74, 95% CI 0.51	

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • **Surgical** • **Adverse** • **QoL**	**Conclusions**
			to 1.06); • Secondary (Adverse) Outcomes ○ Death – none reported; ○ Post-operative SUI – there was no evidence of a difference between aTM and NTR (RR = 1.38; 95% CI 0.95 to 2.00, 1 trial). • Secondary (Surgical) Outcomes ○ No differences in NTR and aTM, at 1-2 yr review, in failure of anterior compartment (RR = 0.72; 95% CI 0.53 to 0.98, 2 trials) or failure of posterior compartment (RR = 1.13; 95% CI 0.40 to 3.19, 1 trial); • Secondary (QoL) Outcomes ○ Prolapse Quality of Life Questionnaire (2y review) –no difference between aTM and NTR (MD = 0.00, 95% CI -2.82 to 2.82, 1 trial).	

5.5.2 Maher et al (2016b). Surgery for women with apical vaginal prolapse

5.5.2.1 Aim

This second Cochrane systematic review by Maher et al focusses on apical vaginal prolapse, included cases which occurred post-hysterectomy.

5.5.2.2 Update since interim report

As such, it also provides updated evidence alongside studies previously considered in the Maher C et al (2013) review.

5.5.2.3 Description of included trials

52 papers from 30 trials were included in the review, though only six trials that compared vaginal surgery with or without mesh were included. In total these trials included 598 women: 297 had a sacrospinous colpopexy as a native tissue repair, and 301 a mesh repair. In all trials polypropylene mesh was used, with monofilament mesh used in four trials and multi-filament mesh in the remaining two. Of the six studies, two included only those with post-hysterectomy prolapse and four included those with both uterine and vaginal apical prolapse.

5.5.2.4 Outcomes

As with Maher et al (2016a), a range of primary and secondary outcomes were considered (see section 3.1 above).

5.5.2.5 Follow up

Follow up periods were between 1 and 3 years post-surgery.

5.5.2.6 Quality of evidence

The quality of the evidence contained within the six trials included in this review was assessed as very low to moderate, though the risk of bias in the six trials was assessed at being mainly low or uncertain.

5.5.2.7 Findings

Overall the review found little or no difference between native tissue repairs and mesh repairs in relation to the primary outcomes of:

- awareness of prolapse;
- the need for repeat surgery for prolapse;
- an increased need for repeat surgery for SUI following mesh repair; or
- a decrease in recurrent prolapse following mesh surgery.

No significant differences were noted in any of the secondary outcomes except that the rate of mesh exposure after transvaginal mesh was 18% and rate associated with the need for further surgery for mesh exposure was 9.5%.

5.5.2.8 Conclusions

Sacral colpopexy is associated with lower risk of awareness of prolapse, recurrent prolapse on examination, repeat surgery for prolapse, postoperative SUI and dyspareunia than a variety of vaginal interventions. The limited evidence does not support use of transvaginal mesh compared to native tissue repair for apical vaginal prolapse. Most of the evaluated transvaginal meshes are no longer available and others currently lack evidence of safety. The evidence was inconclusive when comparing access routes for sacral colpopexy and comparing uterine preserving surgery versus vaginal hysterectomy for uterine prolapse.

Table 5.5 Summary of Systematic review on Pelvic Organ Prolapse by Maher et al 2016 (b)

Author(s) (Year) & Title	Effects	Native Tissue Repair	Biological Graft Repair	RR, 95%CI, number of studies and participants
Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J. (2016) Surgery for women with apical vaginal prolapse.	Short-term efficacy (1-3 years)	Subjective: 89.5%	89.8%	0.97 (0.65-1.43), 7 RCTs, 777 participants
		Objective: 70.5%	72.3%	0.94 (0.60-1.47), 7 RCTs, 587 participants
	Need for further POP surgery at 1-2 years	4.3%	5.2%	1.22 (0.61-2.44), 5 RCTs, 306 participants
	Development of de novo dyspareunia (1-3 years)	17.7%	15.0% (3.5-64.8%)	0.85 (0.20-3.67), 1 RCTs, 37 participants

Table 5.6 Extract data from Systematic review on Pelvic Organ Prolapse by Maher et al 2016 (b)

Author(s) & Title	**Aim Review type, Evidence quality**	**Level of evidence & Description of studies**	**Findings** • **Surgical** • **Adverse** • **QoL**	**Conclusions**
Maher C et al. Surgery for women with apical vaginal prolapse. Cochrane Database of Systematic Reviews 2016, DOI: 10.1002/14651858.CD012376.pub10 Last assessed as being up to date at 6th July 2016.	To evaluate the safety and efficacy of any surgical intervention compared to another intervention for the management of apical vaginal prolapse. Cochrane Systematic Review This is a full search update on Maher et al (2013). In this table only the analysis of the comparison of vaginal surgery with or without transvaginal mesh is considered.	Systematic Review based on evidence ranging from SIGN 1++ (High quality meta-analysis, systematic reviews of Randomised Controlled Trials (RCTs) ,or RCTs with a very low risk of bias) to SIGN 1+.(Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias) In total 30 trials	All results relate to the comparisons between NTR and TM repairs at one to two year review. • Primary Outcomes ○ No significant differences were found between TM and NTR in relation to: ▪ Awareness of prolapse (3y review) – (RR = 1.08; 95% CI 0.35 to 3.30, 1 trial); ▪ Repeat surgery for prolapse (1-3y review) – (RR = 0.69; 95% CI 0.3 to 1.60, 5 trials); ▪ Repeat surgery for SUI (2y review) – (RR = 4.91; 95% CI 0.86 to 27.94, 2 trials); ○ There was possible, marginal evidence rates of recurrent prolapse (1-3y) were lower for TM repairs – (RR = 0.36; 95% Ci 0.09 to 1.40, 3 trials) • Secondary Outcomes ○ Mesh exposure – rates for mesh exposure associated with TM repairs were 18%. Of these 9.5% required surgical intervention; ○ No significant differences were found for: ▪ Bladder injury – RR 3.00 (0.91 to 9.89) (4 studies) ▪ De novo SUI (1-3y) – (1.37 (0.94 to 1.99) (4 studies) ▪ De novo dyspareunia (1 to 3y) – (RR = 1.21; 95% CI 0.55 to 2.66, 5 trials).	"In those not suitable for sacral colpopexy and in those with uterine prolapse, we were unable to detect an advantage to utilising transvaginal mesh as compared to vaginal colpopexy, and the transvaginal mesh was associated with a one in 10 risk of a sub-sequent surgical intervention for the management of mesh exposure. All the transvaginal mesh kits that have been evaluated in this review have been voluntarily removed from the market following transvaginal mesh alert issued by the American Food and Drug Administration. The principal concern raised by the FDA related to vaginal pain and dyspareunia that

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of studies	Findings • Surgical • Adverse • QoL	Conclusions
	The quality of the evidence contained within the trials included in these comparisons was considered very low to moderate. The risk of bias was assessed as being mainly low or uncertain.	were included with data from 3414 women who had sought apical vaginal prolapse. Of these, 6 trials representing 598 women who had been treated with either transvaginal mesh (TM) repairs or varying approaches to native tissue repairs (NTR).		accounted for36% of adverse events reported to the FDA. These concerns have not been realised in this analysis with the rate of dyspareunia and sexual function scores on the validated Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire (PISQ) being the same between native tissue and transvaginal mesh interventions. There were no reports of mesh being removed in any of these trials except for the management of mesh exposure." (pg. 38)

5.6 Pelvic surgery : PROSPECT Trial

5.6.1 Glazener et al (2016). Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT)

5.6.1.1 Aim

The PROSPECT study aimed to compare the outcomes of prolapse repair involving either synthetic mesh inlays or biological grafts against standard repair in women.

5.6.1.2 Update since interim report

The interim report included some early data from the PROSPECT trial relating to the experiences of women who had undergone POP repair using mesh implants. In December 2016 the final report from the trial was published in The Lancet.

5.6.1.3 Description of trials

The PROSPECT study comprised two randomised controlled trials that were undertaken in 35 UK hospitals, including both secondary (General) and tertiary (Regional Specialist) Hospitals. Women undergoing primary transvaginal anterior or posterior compartment prolapse surgery were recruited and randomly assigned one of the two trials. The first trial compared native tissue repair alone with standard repair augmented with synthetic mesh (the Mesh Trial - MT). The second compared native tissue repair alone with biological graft (the Graft Trial – GT). In total 65 surgeons participated. These were either surgeons who were subspecialist urogynaecologists or general gynaecologists with a special interest in the field; all had experience of transvaginal anterior and posterior prolapse repair. The trial standardised the types of mesh and biological grafts used for augmented repairs.

5.6.1.4 Outcomes

Primary outcomes assessed were women's report of prolapse symptoms and a measure of quality of life. Secondary outcomes assessed using patient reports included generic quality of life, adverse events/complications, and bladder, bowel and sexual function. In all cases validated approaches were used. In addition objective assessment of prolapse stage was undertaken. Were possible, adverse event reports were verified from a secondary source.

5.6.1.5 Follow up

Trial follow up continued for two years post-surgery. and was found to be robust, with high levels of patient participation at six month (93% native tissue, 88% mesh), one year (92%, 89%), and two year (81%, 79%) reviews.

5.6.1.6 Quality of evidence

Overall, the authors considered that the study produced high quality evidence; "….pragmatic effectiveness design allowed PROSPECT to generate, using a well done study, high quality evidence for the real-world comparison of these surgical options." (Glazener et al (2016) pg 10) This would seem to be the case as the quality of the data is markedly better than many trials included in systematic reviews.

5.6.1.7 Findings

For the purposes of this update, the results of the MT are considered. The summarised results from the individual analyses made are shown below. Overall, however, the results of the MT can be summarised as:

- no significant differences were found between standard native tissue repairs and repairs augmented by mesh in any of the primary outcomes (at one year) or secondary outcomes (at one and two years) formally analysed;

- overall the rate of mesh complications was 12% amongst women in the MT or who had mesh as an additional procedure. In the MT, surgical mesh removal occurred for 25 women during the first year and 17 women between one to two years. In the GT, a further three women needed surgical mesh removal during the first year following concomitant use of mesh; and

- most of the mesh complications were reported as asymptomatic by the women involved and most mesh exposures were small, requiring only partial removal in all but one case.

5.6.1.8 Conclusions

Augmentation of a vaginal repair with mesh or graft material did not improve women's outcomes in terms of effectiveness, quality of life, adverse effects, or any other outcome in the short-term, but more than one in ten women had a mesh complication. Therefore, follow-up is vital to identify any longer-term potential benefits and serious adverse effects of mesh or graft reinforcement in vaginal prolapse surgery.

Table 5.7 Extracted Data from the Randomised Controlled tRial by Glazener et al(on behalf of the PROSPECT group) (2016)

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of study	Findings • Surgical • Adverse • QoL	Conclusions
Glazener CMA et al. (on behalf of the PROSPECT Group) Mesh, graft, or standard repair for women having primary transvaginal 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.	To compare the outcomes of prolapse repair involving either synthetic mesh inlays or biological grafts against standard repair in women. Pragmatic, parallel-group, multicentre, randomised controlled trials. The authors state that the evidence generated was of a high quality. The potential for bias was considered to be low.	The trial is of a standard that would be suitable for inclusion in a Systematic Review based on evidence ranging from SIGN 1++ (High quality meta-analysis, systematic reviews of Randomised Controlled Trials (RCTs) ,or RCTs with a very low risk of bias) to SIGN 1+.(Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias).	In this table, only the analyses which compared TM v NTR are presented. **Objective Prolapse Outcomes (1y review)** • Assessment by Pelvic Organ Prolapse Questionnaire (by site of repair, mean treatment effect). – No significant differences between NTR and TM at : ○ Anterior edge – (Mean = 0·06; 95% CI –0·17 to 0·29); ○ Cervix/vault – (Mean = –0·03; 95% CI –0·36 to 0·31); ○ Posterior edge – (Mean = –0·03; 95% CI –0·21 to 0·15); ○ Total vaginal length – (Mean = 0·12; 95% CI –0·07 to 0·30). • Overall POP-Q stage (by stage, mean treatment effect) – No significant differences between procedures were found: ○ Stage 0 (no prolapse) – (Mean = 1·11; 95% CI 0·83 to 1·47); ○ Stage 2b,3 or4 - (prolapse) – (Mean = 1·12; 95% CI 0·79 to 1·60) ; **Clinical Outcomes** • 6 month outcomes – no difference was found for clinical symptoms: ○ POP-SS – (Mean = 0·57, 95% CI (–0·12 to 1·26); ○ Symptomatic prolapse – (Mean = 1·07, 95% CI 1 to 1·14);	"The PROSPECT study showed that augmenting a primary transvaginal anterior or posterior prolapse repair with non-absorbable synthetic mesh or biological graft confers no symptomatic or anatomical benefit to women in the short term. More than one in ten women had a mesh complication, but most were asymptomatic, and most of the mesh exposures measured less than 1 cm^2. 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

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of study	Findings • Surgical • Adverse • QoL	Conclusions
		The trial ran from 2010 to 2013, with follow up for 2 years post-surgery. In total 1,348 women were included in the trial, with 856 allocated to the transvaginal mesh (TM) versus native tissue repair (NTR). Follow up was found to be robust the trial 79% or women followed up at two year review.	○ 'Something coming down' (SCD) – (Mean = 1·09, 95% CI 0·90 to 1·34). • 1 year outcomes – no differences were found between procedures: ○ POP-SS – (Mean = 0·00, 95% CI –0·70 to 0·71); ○ Symptomatic prolapse – (Mean = 1·01, 95% CI 0·95 to 1·08); ○ Women with any report of SCD – (Mean = 0·98, 95% CI 0·82 to 1·18); ○ Severe urinary incontinence – (Mean = 1·34, 95% CI 0·79 to 2·26); ○ Faecal incontinence – (Mean = 0·92, 95% CI 0·74 to 1·13); ○ ICI Vaginal Symptoms Score – (Mean = 0·52, 95% CI – 0·64 to 1·68); ○ Severe dyspareunia – (Mean = 1·73, 95% CI 0·52 to 5·78). • 2 year outcomes – No significant differences found between NTR and TM: ○ POP-SS – (Mean 0·32, 95% CI –0·39 to 1·03); ○ Symptomatic prolapse – (Mean = 1·04, 95% CI 0·97 to 1·11); ○ Women with any report of SCD – (Mean = 1·06, 95% CI (0·85 to 1·32); ○ Severe urinary incontinence – (Mean = 1·01, 95% CI (0·51 to 1·99); ○ Faecal incontinence – (Mean = 1·13, 95% CI 0·92 to 1·41); ○ ICI Vaginal Symptoms Score- (Mean = –0·18, 95% CI – 1·34 to 0·98);	years, which might be considered to be an unnecessary risk. This additional risk suggests that in the future mesh should only be used in the context of trials aimed at identifying benefit from modifying mesh type or insertion techniques, or in defined categories of high-risk women." (pg. 11-12).

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of study	Findings • Surgical • Adverse • QoL	Conclusions
			○ Severe dyspareunia – (Mean = 0·49, 95% CI 0·15 to 1·55). **Adverse Outcomes** • 6 month outcomes – no differences were found: ○ Number readmitted (0–6 m – (Mean = 1·15; 95% CI 0·51 to 2·57); • 1 year outcomes – no differences between procedures were found: ○ Number readmitted (6–12m) – (Mean = 1·32; 95% CI 0·36 to 4·81); ○ New prolapse operation – (Mean = 1·99 ; 95% CI 0·76 to 5·24); ▪ Same compartment (Mean = 2·55; 95% CI 0·68 to 9·53); ▪ Different compartment – (Mean = 1·35; 95% CI 0·31 to 5·96); ○ New continence operation – (Mean = 0·40; 95% CI 0·08 to 2·04); • Adverse effects in year 1 – no differences between NTR and TM were found: ○ Serious adverse effects (exc. TM) – (Mean = 1·08; 95% CI 0·68 to 1·72); ○ Any mesh complications (NTR <1% v TM 7%); ○ Surgical removal (NTR <1% v TM 5%); ○ Conservative treatment (NTR 0% v TM 2%); ○ No treatment (NTR 0% v TM <1%); ○ De novo mesh procedure (NTR <1% v TM 6·2%); ○ Concomitant mesh procedure (NTR <1% v TM 1%);	

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of study	Findings • **Surgical** • **Adverse** • **QoL**	Conclusions

			• 2 year outcomes – no differences were found:
			  ○ Number readmitted (12–24m) – (NTR <1% v TM 0%);
			  ○ New prolapse operation – (Mean = 0·94; 95% CI 0·47 to 1·88);
			  ▪ Same compartment – t(Mean = 0·79; 95% CI 0·30 to 2·11);
			  ▪ Different compartment – (Mean = 1·14; 95% CI 0·42 to 3·10);
			  ○ New continence operation – (Mean = 1·28; 95% CI 0·35 to 4·73);
			
			• Adverse effects in second year – no differences found between procedures:
			  ○ Serious non mesh adverse effects – (Mean = 0·66; 95% CI 0·19 to 2·30);
			  ○ Any mesh complications – (NTR <1% v TM 6%);
			  ○ Surgical removal – (NTR 0% v TM 4%);
			  ○ Conservative treatment – (NTR <1% v TM <1%);
			  ○ No treatment – (NTR 0% v TM <1%);
			  ○ De novo mesh procedure – (NTR 0% v TM 5·3%)
			  ○ Concomitant mesh procedure – (NTR <1% v TM <1%).
			
			Quality of Life Outcomes
			
			• Prolapse-related QoL score – no significant differences noted at:
			  ○ 6 months – (Mean = 0·22, 95% CI –0·16 to 0·60);
			  ○ 1 year – (Mean = 0·13, 95% CI –0·25 to 0·51);
			  ○ 2 years – (Mean = 0·15, 95% CI –0·23 to 0·54);
			• EQ-5D-3L score – no significant differences noted at:
			  ○ 6 months – (Mean = 0·01, 95% CI –0·02 to 0·04);	

Author(s) & Title	Aim Review type, Evidence quality	Level of evidence & Description of study	Findings • Surgical • Adverse • QoL	Conclusions
			○ 1-year – (Mean = 0·01, 95% CI –0·02 to 0·04); ○ 2-years – (Mean = 0·02, 95% CI –0·02 to 0·06).	

Chapter 6: Reviewing the evidence on mesh implantation for the treatment of stress urinary incontinence and pelvic organ prolapse in women: clinical nuances of interpretation

What's new in this Chapter?

In our interim report, chapter 6 provided additional information and clinical interpretation on several pieces of evidence not included in the main literature review in chapter 5. In this final report these, and other more recent publications have been incorporated into chapter 5. This chapter is now used to explore some of the nuances of clinical interpretation of the evidence presented earlier. It is hoped that readers might find this helpful in understanding how we have reached our conclusions and recommendations; clinicians may find it of value during their counselling of patients considering surgical treatment for SUI or POP.

Although many non-surgical and surgical options for the management of SUI and POP are included in chapter 2, and many others have been advocated, we have restricted our consideration here to those used most commonly in Scotland (as in chapter 4) and covered in the literature review in chapter 5.

6.1 Outcome measures

The outcome measures used in the available trials and systematic reviews are described in chapter 5. These were considered under a number of key outcome areas including the effectiveness of the procedure(s), safety issues, patient-focussed outcomes (positive or negative), surgical capacity and competency issues. It has been traditional in urogynaecology/functional urology to consider so-called 'objective' outcome measures, *e.g.* the finding (or absence) of urodynamically-proven SUI to have greater credibility than so-called 'subjective' outcomes, *e.g.* patient reported symptoms. This position is, however, changing, and patient-reported measures are now considered the more meaningful trial outcomes.

In the management of individual patients, it is important that their own goals and expectations from treatment are defined as part of the counselling process; if these are not linked to known surgical outcomes, patient satisfaction from treatment will inevitably be compromised.

6.2 No treatment and non-surgical options

It is not only inherent in the recent Supreme Court ruling,[10] but also fundamental to shared decision making, and patient-centred care as described in 'Realistic Medicine',[11] that all reasonable options should be discussed with a patient requesting treatment for any condition. Although our report focusses on the place of mesh implants as a component of the surgical treatment of SUI and POP, we feel it is important to emphasise to all patients presenting with these conditions, that they do not necessarily need to undergo surgery. The reassurance that they could live with their symptoms without any treatment may in itself be a huge relief for

[10] Montgomery *vs.* Lanarkshire Health Board, 2015
[11] http://www.gov.scot/Resource/0049/00492520.pdf

many women. Non-surgical options may provide satisfactory symptom control for the majority in the short to medium term (*e.g.* pelvic floor muscle exercise (PFME) for SUI or POP), or indeed in the long-term (*e.g.* vaginal pessaries for POP). In either case these options may mean that they could avoid surgery altogether, or at least defer intervention until a more suitable time for them.

6.3 Safety issues

None of the previously published safety reviews has recommended the withdrawal of mesh products in current use in surgery for SUI or POP, and we have found no additional evidence to support such an approach. Nevertheless, we do recognise that there can be adverse outcomes, some serious, albeit that these occur in small numbers of patients.

Adverse events are more prevalent following the use of synthetic mesh in the treatment of POP than SUI. In POP adverse events are more common following vaginal than abdominal insertion of mesh, and in SUI serious adverse events are more common following transobturator than retropubic tape insertion.

There is a higher risk of bladder injury from retropubic mesh tape than open colposuspension (and transobturator mesh tape), although it should be noted that bladder injury with mesh tape is diagnosed intra-operatively in almost all cases, as cystoscopy is routinely employed. It is believed that if the tape is replaced in the correct position, no long-term problems are expected. In contrast, bladder injury with colposuspension may require formal repair and several days' additional postoperative catheterisation.

6.4 Synthetic tape or mesh removal

Whilst it may seem counter-intuitive to consider the removal of a device intended for permanent implantation, explantation of both mesh tapes used in SUI surgery, and synthetic meshes used in POP surgery, may have to be considered on rare occasions. It is the view of the clinicians on the group that retropubic mesh tapes can be removed in their entirety regardless of duration of implantation, although this would usually require an open or laparoscopic abdomino-perineal approach. The same could be said of 'simple' mesh implants for POP, via a vaginal approach. Complete removal of a transobturator mesh tape (or POP mesh kit) can be difficult. These are easier to remove within a few weeks of implantation, but with appropriate skill and experience, a surgeon may be able to remove an implant at any time. The majority of requests for removal come some years after surgery, and the longer the implant is in place, the more difficult it is to remove completely. Since the link between mesh tape (for SUI) or mesh (for POP) insertion and the development of symptoms remains uncertain, and it is never possible to say that removal of a mesh tape or mesh will resolve symptoms, a stage is inevitably reached where the risks of removing the mesh exceed the possible benefit.

6.5 Efficacy issues

6.5.1 Efficacy of surgery for SUI

Although our review includes analysis of data on anterior colporrhaphy, bladder neck needle suspension, and laparoscopic colposuspension, in common with NICE guidance, we do not feel that the first two of these should be offered in the treatment of SUI. Laparoscopic colposuspension should not be offered routinely, and should only be considered where an

experienced laparoscopic surgeon is working in an MDT with expertise in the assessment and treatment of UI.

Mesh tape procedures are as effective as traditional surgical approaches (*i.e.* colposuspension and traditional pubo-vaginal sling procedures) and have the benefit of shorter operative time, less anaesthetic requirement, less requirement for catheterisation, shorter hospital stay, reduced NHS costs and more rapid return to normal activities of daily living and work. There is also a lower risk of subsequent prolapse and need for prolapse surgery.

Although in the short-term, efficacy of mesh tapes inserted by the retropubic and transobturator routes is not significantly different, beyond 12 months there is a substantially greater need for repeat SUI surgery following the transobturator approach; the emerging evidence on single-incision mesh tapes also suggests even greater need for repeat SUI surgery than following the transobturator approach.

Although urethral injection therapy has been advocated as a minimally invasive option in the treatment of SUI, and systemic review suggests a better short-term safety profile than other interventions, the very much higher rate of re-admission for complications or re-operation for SUI in the longer term is a genuine concern.

In light of the totality of these findings, the members of the IR who perform surgery for SUI are of the view that:

- the retropubic mesh tape is a valid option to be offered routinely to women considering surgical treatment for SUI;

- colposuspension and autologous fascial pubo-vaginal sling are both appropriate alternatives for women who wish to avoid the use of a permanent implant, provided they accept the increased associated short-term morbidities and longer recovery, and increased long-term risk of prolapse following colposuspension;

- women may wish to consider urethral injection therapy; they should be made aware that the efficacy is less than with other interventions, and decreases over time; hence the risk of re-admission for complications or re-operation for SUI is very much higher; and

- small numbers of colposuspension and autologous fascial pubo-vaginal sling procedures have been undertaken in Scotland in recent years (see chapter 4); if a procedure cannot be provided locally, by appropriately skilled and experienced staff, the option of referral to alternative units should be discussed with the patient.

6.5.2 Efficacy of surgery for POP

Whilst many of the data relating to surgery for POP are inadequate to guide practice, we are persuaded by the latest Cochrane review and the recently published outcomes from the PROSPECT study. The former, whilst finding lower rates of prolapse signs or symptoms following mesh implantation at repair surgery, found higher rates of bladder injury and new SUI, and a greater requirement for repeat surgery for recurrence or complications (as a composite outcome), compared to native tissue repair. The authors concluded that transvaginal mesh has limited utility in primary surgery; whilst they speculated as to its place in women at high risk of recurrence, they found no evidence to support its use in this context

either.

The PROSPECT study found that augmentation of a vaginal repair with either synthetic mesh or biological graft material did not improve women's outcomes in terms of effectiveness, quality of life, adverse effects, or any other outcome in the short-term, but more than one in ten women had a mesh complication. Although, as the PROSPECT authors pointed out, addition of the PROSPECT data to the Cochrane review does favour mesh both in terms of awareness of prolapse and anatomical recurrence; nevertheless, we agree that a single large trial that is free from risk of bias is likely to be more powerful and reliable for the specific population included than a meta-analysis of many smaller trials.

Hence, it is the view of the members of the IR who perform surgery for POP that:

- Vaginal wall repair using native tissue (anterior and posterior colporrhaphy) should be the procedure of choice for women seeking surgery for POP.

- The use of polypropylene mesh or biological graft should not be offered routinely but may be considered in complex conditions – only after discussion at an appropriately constituted MDT.

Chapter 7: Legal Judgements

Update Since Interim Report

Legal proceedings in relation to claims for personal injury, the safety of specific mesh and tape devices, and lack of appropriate information regarding possible complications have been raised in a number of countries, including the United States and in the UK. There are a greater number of cases raised in Scotland than in England and Wales.

Since publication of the interim report, the number of claims in relation to the use, by NHSScotland, of vaginal implants in women with SUI and POP has increased to 426 (as at February 2017). The data in this chapter have been updated to reflect this.

7.1 Evidence availability

Legal proceedings in relation to claims for personal injury, the safety of specific mesh and tape devices, and lack of appropriate information regarding possible complications have been launched in both the United States and in the UK as well as other countries worldwide.

In Scotland, the main focus of such litigation is twofold, firstly, in relation to the cases against the Health Boards, the claim is that there was a failure by clinicians to adequately obtain patients' informed consent by fully discussing and disclosing material risks and alternatives. In relation to the case against the manufacturers, the Pursuer is seeking to establish that the manufacturers were negligent under common law by aggressively marketing products which had been inadequately tested and further, misrepresenting failure and complication rates.

The case against the manufacturers can also be brought under the Consumer Protection Act 1987, which requires the Pursuer to establish that a defective product has been manufactured. The statute describes a "defective product" as one in which the safety of the product does not meet the standard which consumers are entitled to expect. This can include the safety of materials and components within the product, any instructions and/or warnings needed in using the product, and what the expected use of the product might be. This is an objective test and all these factors must be taken into account. In order for a manufacturer to be held liable it must be established that:

- they manufactured the product;
- that the product was defective (as defined in statute);
- and the defect caused injury.

Once liability is established, it is not necessary to also establish that the manufacturer was negligent (although separate proceedings to show negligence under the common law may also be pursued).

7.2 Methods

Given that legal proceedings in relation to the use of mesh and mesh tape are still on-going in Scotland, it is not appropriate to discuss the detail of these extant cases at this time. Rather, the NHS Central Legal Office was asked to provide an overview of current legal proceedings in Scotland. In the results section that follows, any counts of cases which are fewer than five cases have been discounted to avoid any possible data protection breach. All manufacturer

and device names have also been removed for confidentiality reasons.

7.3 Results

7.3.1 Litigation in Scotland

As at early February 2017, there were 426 claims in relation to the use of vaginal implants in women with SUI and POP involving NHS treatment. There are additional claims and actions involving only private treatment, but figures in that regard are not available. Of these claims, 390 actions have now been raised in the Court of Session.

Due to the number of actions relating to vaginal implants, the Court of Session fixed a specific procedure for dealing with these actions. When the Court issued its direction about the procedure, defences were required to be lodged in the first 168 cases involving Health Boards by 22 September 2016. Following on from that deadline, the Court indicated that a group of lead cases will be identified from those in which defences have been lodged. All other cases are likely to be frozen pending the outcome of the lead cases.

Of the 168 cases involving Health Boards being considered by the Court of Session, in which defences have been lodged, there were 114 cases associated with mesh tapes for SUI. Of these, 88 involved the use of transobturator mesh tapes, and 31 cases that involve the use of **r**etropubic mesh tapes. There are five cases involving the use of both types of tape. There are 73 cases that involve the use of mesh implants for the treatment of POP. In total, 23 of the 168 cases involve multiple implants.

7.3.2 Litigation in the USA

Data from the US Judicial Panel of Multidistrict Litigation has been used to summarise the situation in the US, as at the end of July 2015. The number of US lawsuits in relation to the use of vaginal implants in women with SUI and POP is estimated at 100,000. The majority are litigated in Federal Courts (Multidistrict Litigation, MDL). These cases are only raised against the manufacturer and do not involve the health care provider or doctor as a party to the action.

So far, 18 trials (relating to 24 patients) have reached verdict or settlement during trial (see below). 11 of the cases related to POP procedures, ten of which related to vaginal mesh implants and one where the POP procedure was combined with an SUI mesh tape. In this combined case and in four of the solely POP procedures, a jury reached a verdict in favour of plaintiffs. No jury verdicts were in favour of the manufacturer and in the remaining six cases, the manufacturer reached a settlement during the trial.

For SUI procedures, one case related to retropubic mesh tape. The case did not reach trial, the Judge directed that the case found in favour of the manufacturer prior to trial commencement. Six cases related to transobturator mesh tapes. Jury verdicts in favour of the plaintiffs were found for five cases and, in a single case, in favour of the manufacturer.

One manufacturer settled thousands of claims in an out of court settlement without accepting any liability.

In presenting data from the US, it should be noted that the legal tests against which these cases were judged are not those set out in the Consumer Protection Act (1987) that is applicable in Scotland.

7.4 Interpretation

- Legal cases relating to possible clinical negligence and product liability are underway in Scotland and other countries.

- Whilst clinical negligence and product liability may be established for specific cases, generalising from these in the context of this review is difficult given the evolving nature of the evidence and the fact that each case will have its own specific set of circumstances.

Chapter 8: Adverse event reporting

Update Since Interim Report

A National Safety Alerts Oversight Group met for the first time in February 2016, managed by Healthcare Improvement Scotland (HIS) with multiple stakeholders. The aims are to:

- support improvements in implementing safety alerts and
- provide an overview of the improvements that have been implemented as a result of these alerts.

In Scotland there is a statutory duty of candour procedure which was enacted as part of the Health (Tobacco, Nicotine, etc. and Care) (Scotland) Act 2016, receiving Royal Assent on 6 April 2016. This provides the legal basis for the procedures that will be followed by organisations providing health and social care in Scotland when an unintended or unexpected incident that results in death or harm has occurred.

http://www.legislation.gov.uk/asp/2016/14/part/2

The use of the unique device identifier in NHSScotland for patients who receive implants remains an active project. The new consent form included in the SUI leaflet prompts the consultant to provide information on the specific device implanted, so that the patient can refer accurately to their device in future.

8.1 Situation

Reporting adverse events in NHSScotland occurs through a range of statutory and governance procedures. The reports can be initiated by a number of healthcare professionals and patients. The aim of reporting on medical devices is to improve patient safety, to inform local learning systems, and to add to the information necessary for the regulation of medical devices. It is recognised that there is under-reporting, and there are therefore a number of work programmes in development to improve the situation. This chapter describes the background to adverse event reporting, the on-going work programmes, and the specific requirements for reporting incidents that concern transvaginal mesh implants.

8.2 Background

What

Every patient is an individual and, as such, may react to medical treatment in different ways. All interventions in healthcare carry a measureable risk. Reporting adverse events from clinical care is the responsibility of the individual team members involved in that care. The learning is best managed locally but must be shared more widely if there are more generalised lessons. As there was a diversity of systems and definitions in place in 2012, the Scottish Government tasked HIS to develop a framework, examine current practice, and support developments. The framework included a definition[12], which must be clear, be agreed with patients, and consider near misses.

[12] An adverse event can be defined as an event that could have caused, or did result in, harm to people or groups of people.

http://www.healthcareimprovementscotland.org/our_work/governance_and_assurance/management_of_adverse_events1.aspx

For the purposes of this paper an adverse event should be considered as adverse signs and symptoms recorded by the patient or the clinician, and be considered as a consequence of the insertion of transvaginal mesh. To help identify what should be reported, the British Society of Urogynaecology (BSUG) lists adverse events from the use of synthetic meshes for prolapse and incontinence at
http://bsug.org.uk/pages/information/reporting-device-complications-to-the-mhra/104
i.e:

- vaginal exposure;
- erosion into the urinary tract;
- erosion into the bowel or rectum;
- infection;
- pain;
- fistulae;
- mesh shrinkage;
- organ perforation;
- nerve or vascular injury;
- sexual difficulty.

Why

The main function of adverse event reporting is early detection of new, rare or serious problems with a device. Manufacturers have a statutory duty to conduct post market surveillance, i.e. follow-up, via their sales, complaints, research and reports data. Clinicians and patients using the devices provide individual feedback. Reporting is, however, not universal. Research on the reporting of adverse drug reactions to spontaneous (i.e. not routinely collected) reporting systems such as the Yellow Card scheme suggest that only around 20-25% of serious and severe reactions, and around 5% of less serious events[13] are reported. This research found that a number of clinicians did not report if the reaction was known at the time the drug was on the market.

There is a range of reasons adverse events may occur during or after surgery; these include characteristics of the patient, expectations, pre-and post op care, the surgeon, the hospital, and the device itself, where one is used.

Some events are very rare, for example the association of breast cancer with breast implants. This cancer type accounts for less than 1% of all breast malignancies. Such rare events (in this example there were less than 150 cases worldwide and between 5-10 million breast implants used) require the accumulation of data on very large numbers of patients in order to establish an association between a medical device and an adverse event.

In contrast, some adverse events, whilst rare in themselves, may occur commonly with particular procedures. For example, using a connector that is intended for venous access to inject drugs into the spinal cord led to immediate deaths; this was the rationale for the production of new small tube connectors for health services around the world.

[13] 2006 Drug Safety http://www.ncbi.nlm.nih.gov/pubmed/16689555.

From the studies on adverse event reporting on devices and drugs[14] mechanisms to improve reporting are:

- improved feedback – why the report mattered, what else has been reported;
- peer acceptance and training in practice;
- easy electronic methods of reporting greater range of notifiers, including patients; and
- undergraduate and postgraduate training.

In NHSScotland all organisations should have a management system for reporting, reviewing and learning from all types of adverse events. This includes clinical events involving patients, families, staff and carers (including health and safety, accidents or incidents) and non-clinical events (including information governance, health and safety at work and finance).

Adverse event reviews are not about apportioning blame. The aim is to review the care provided to determine whether there are learning points for the organisation or organisations to improve the service. Organisations then need to implement the improvements identified to support a greater level of safety for all people involved in its care systems.

Leaders should make a clear, public commitment to staff that the organisation fully supports an open and fair culture. When things go wrong, staff need to feel able to be open, that they will be treated fairly and they are supported to identify the failures in the system and improve service delivery.

The process must be transparent and include all those involved in the adverse event: patients, service users, families and carers, and staff. To support this, significant adverse event review reports should be shared with everyone involved in the event, and a one-page learning summary completed and published in order to share key learning points more widely. Examples are professional groups working with data in quality assurance schemes, for instance in general surgery; the enhanced appraisal system all doctors must have for their revalidation to discuss their outcomes; Yellow Card promotion for reporting by patients; and simple online reporting to national bodies.

A number of countries in Europe have voluntary 'bottom-up' reporting systems for orthopaedic adverse events which reportedly show useful outcomes, but the examples have not been demonstrated.

How

Notification of adverse events is used for the trend analysis work of the regulator and investigators. There is a simple online process to MHRA (Yellow Card) and the Incident Reporting and Investigation Centre (IRIC) in NHSScotland. The Yellow Card is a reporting mechanism used for over 50 years for gathering adverse events associated with medicines and has been extended to medical device users: https://yellowcard.mhra.gov.uk/.

MHRA has recently embraced media technology to improve functionality and reporting of medicines events: https://www.gov.uk/government/news/digital-evolution-for-ground-breaking-yellow-card-scheme

In Scotland it is currently expected that professional groups will report to IRIC via this link

[14] 2006 Drug Safety http://www.ncbi.nlm.nih.gov/pubmed/16689555.

(also on the MHRA webpage):

http://www.hfs.scot.nhs.uk/services/incident-reporting-and-investigation-centre-iric-1/how-to-report-an-adverse-incident/

Once an event is notified it will be examined electronically for necessary information such as the device type and symptoms. When patients report an adverse event they may not know which type of implant they received, and this information therefore needs to be shared and made easily accessible. The track and trace element of medical devices is currently managed through details entered into the operation note. It is a legal duty to keep these records. Most commonly these are still kept in paper form and full details are not necessarily communicated to a patient or their GP. An improvement to the track and trace is the unique device identifier (UDI) work to store this information in a patient electronic record (either the hospital record, SMR01 or the GP record).

Where

The long-term aim is for one report on an adverse event to be made locally when it happens and fed into local learning systems and at the same time transmitted to all other necessary users (patient safety groups, IRIC and MHRA in terms of the medical device).

Adverse events ideally should be reported through a local Health Board's incident report form which feeds into all necessary databases, but currently this is not the case due to IT and confidentiality issues.

Where reports are made to IRIC by professionals, these are shared on a regular basis with the MHRA as the UK regulator. Equally, if the MHRA is aware of a report from a resident in Scotland, it will inform IRIC so both systems have comparable and timely information.

When

Reports can be made at any time in the life of an implant. Most patients who receive surgery are discharged to the care of their GP and are not routinely followed-up in hospital outpatient departments. Even new symptoms seen in patients in outpatient departments may not be recognised as adverse events. New symptoms will require primary and secondary care knowledge of adverse events that should be reported and the requirement to report. In future, once the UDI system is in use, a change to – or removal of – an implant will also be noted. Once an adverse event report has been fully reviewed, it is a legal duty of the regulator to share this with the manufacturers who will respond with a further range of questions, which can require extensive review of the notes. This additional work is unlikely to be accounted for in the present job plans of consultants.

8.3 Assessment

There is a range of current activities to support and improve adverse event reporting in NHSScotland and across the UK. This includes:

- local system improvements;
- electronic track and trace methods;
- multi-professional guidance;
- mandatory systems of candour; and

- MHRA and NLRS initiatives.

8.4 Professional guidance and feedback to clinicians and patients

Research has shown that if those making a report gain feedback on the value and use to which reports are put, further reporting is encouraged. The Chief Medical Officer endorsed the British Association of Urological Surgeons' (BAUS) letter of March 2016, which required the collection of data including SUI to six national urological databases. The guidance was addressed to all urological surgeons practicing in Scotland, and required data input by surgeons as an extension to the 'op note'. A letter was also issued to the Medical Directors and Chief Executives of the Health Boards.

Providing feedback on the value of a report, as opposed to merely acknowledging a notification, requires additional systems to be in place.The MHRA is presently working with manufacturers to investigate the release of data to external bodies, including those who submit reports.

IRIC provides regular reports on the annual number of incidents it has reported. The detail is high level, and dependent on the quality and completeness of information received. The feedback needs to be used at quality assurance meetings and shared among Health Boards. The community of practice on adverse events developed by HIS http://www.knowledge.scot.nhs.uk/adverse-events/sharing-learning.aspx is gathering interest but it is not yet clear whether individual clinical groups receive feedback on a regular basis from a Health Board's incident reports.

The development of the NHS England patient safety incident management system is currently managing a change scenario with the move to NHS Improvement[15]. The aims were to improve efficiency by introduction of a single process for reporting patient safety incidents, capturing high quality, standardised data about safety and harm with reduced duplication and omission; and to improve the quality of support provided by the national patient safety function, in order to enable more learning and improvement in all organisations at all levels.

8.5 Resources to report mesh adverse events – staff and follow-up

NHSScotland is committed to making reporting easier and to increasing clinicians awareness of what to report. This is intended to encourage clinicians and patients to report more often and to increase their confidence in the system. For clinicians this may need:

- further training on adverse events reporting in addition to the letters already sent describing mesh adverse events;
- inclusion of physiotherapists in reporting information;
- discussion on pathways and administrative support to ensure that longer term events are recorded;
- involvement of the multi -disciplinary teams in knowing what and when to report;
- additional guidance on how enhanced appraisals can use better indicators of work in this area for the revalidation assessments; and
- in the longer term, one reporting system (using all forms of communication including apps) that serves a number of purposes and provides regular feedback.

[15] https://improvement.nhs.uk.

8.6 Legislation

One of the key requirements from the public petition is a mandatory system of reporting adverse events. In considering a legislative route, we need to demonstrate that we have used all the levers at our disposal to try to effect change and assess to what extent these have been effective. We need to have regard to enforcement, and consider inspection, monitoring and evaluation regimes. As noted in discussions in the IR, there are pros and cons to this approach. The policy development process would assess the pros and issues, based on available evidence.

Pros

There would be a statutory duty to report.

Issues

- Legislation requires development of the policy. All polices need to be tested against their impact and equality, ensuring that one area does not disadvantage another. Policy development needs to take account of current legal frameworks and demonstrate additional benefit.

- Agreement on the rules to enforce the policy with penalties for not reporting (penalties are contrary to the Scottish Patient Safety Programme and the policy position on duty of candour).

- Parliamentary time.

- Resources (which then would not be available for other services) to develop and to ensure the impact.

Routine data collection versus standalone system

The IR has discussed whether there should be a new mesh database (registry) to collect all the implant data and/or improve the data capture for NHSScotland's routine data collection and analysis (SMR data). The data would need to be examined locally for actionable learning and change.

Pros of routine data

Routine data on a range of health interventions in Scotland is gathered by trained data collectors (in hospitals), and by electronic systems in primary care, and is then analysed by ISD. This system has been in place for decades (for example the cancer registry has been running since 1958). The systems are regularly updated and funded. ISD is working on data for the IR and this level of information could be provided on a regular basis to multi-disciplinary teams or the Expert Group. In addition, new indicators for performance can be developed for specific topics, and are currently in use for certain cancers.

Cons of routine data

Routine data is not presently set-up to analyse all areas that are of interest to mesh implant patients. In addition, routine data may not be 100% completed. Changing coding can take

time and place demands on resources.

Pros of a new mesh database / standalone data system

A new mesh database could concentrate on mesh implants and potentially collect more detailed information. The BSUG database is an example of a standalone system which collects a range of information, and can be completed in theatre or outpatient departments. It also has the advantage of enabling comparison across Scotland and throughout the United Kingdom.

Cons of a new mesh database / standalone data system

Setting up a new single issue database takes substantial time and resources and therefore requires justification that it is covering an area that has no other support. Having a single issue database does not guarantee all the information of interest can be included, depending on the IT infrastructure used. Setting up a system and then ensuring coverage by clinicians and administrative staff, ensuring confidentiality, transparency and use for patient groups as well as independent analysts is complicated. Standalone data may not be 100% completed. The current BSUG database can only be accessed by members, is not available to general practice, and some Health Boards' IT systems do not currently allow access.

Summary

Adverse event reporting and analysis for clinical care in general remain a key aspect of the Patient Safety Programme and local learning methodologies. The reporting of adverse events is therefore mandatory, in line with The General Medical Council's *Good Medical Practice* which states that, to help keep patients safe, clinicians must:

> "report adverse incidents involving medical devices that put or have the potential to put the safety of a patient, or another person, at risk."
>
> http://www.gmc-uk.org/guidance/good_medical_practice/systems_protect.asp

Further, in paragraph 47 of the Prescribing guidance, the GMC states that the MHRA must be informed.

Clinical activities must be recorded, in accordance with *Good Medical Practice* paragraph 19.

There is a range of activities being undertaken in NHSScotland and the UK to further improve the current levels of reporting, including:

- additional training on what and how to report;
- exploring quality indicators and additional data requests led by multi-disciplinary teams and shared across Scotland;
- implementation of the UDI/ implant systems including access to this information by patients;
- devising guidance for enhanced appraisal;
- improving the use of the current BSUG database and noting CMO's guidance on the use of the BAUS database;
- pathways guidance which must include time allocated in job planning;
- legislation for reporting; and
- a standalone data system.

Chapter 9: Conclusions and Recommendations

No surgical intervention is without risk. This IR has shown that mesh procedures for both SUI and POP carry a risk of complications which, in some cases, are life changing and cannot be corrected. However, for the majority, such serious complications do not occur. The aim of our conclusions and recommendations is to minimise and manage that potential risk. Input from clinicians and provision of adequate information will allow patients to make informed choices regarding their treatment.

In the process of coming to its conclusions, the IR has considered evidence from a number of sources; this included patient stories, clinical expert opinion, published scientific evidence, legal reports and the rich epidemiological data provided by ISD. It also benefited from presentations from other bodies such as the Chief Scientist Office and IRIC. The following conclusions, and the recommendations contained within, are drawn from this evidence and discussion.

Conclusion 1

Fundamental to the treatment of patients with SUI and POP is patient-centred care which should include patient choice and shared decision making supported by robust clinical governance. To support shared decision making, management of patients must take place in the context of a multidisciplinary team (MDT), supported by a quality assurance framework. In addition, the Scottish Government should consider the alternative methods for the capture of adverse events set out in chapter 8 to determine the most effective way to ensure complete notification.

Conclusion 2

Evidence of involvement in MDT working; engagement in all relevant local and national audit activity; and the mandatory recording and reporting of adverse events, in line with GMC guidance, should be necessary parts of consultant appraisal and thus statutory revalidation of clinical staff. The Expert Group should work with Medical Directors and Responsible Officers to ensure this is included in the appraisal of all relevant staff.

Conclusion 3

Informed consent is a fundamental principle underlying all healthcare interventions. Extensive work was carried out by the Expert Group prior to the establishment of the IR, with leadership by both patients and clinicians. This has resulted in an information leaflet on Synthetic Vaginal Mesh Tape Procedure for the Surgical Treatment of Stress Urinary Incontinence in Women and consent form. Following on from this, the IR concludes that additional work is required to ensure that this work is extended to include all appropriate SUI and POP procedures and that the existing SUI leaflet is reviewed in the light of this work and other recent developments. This should be addressed by the Expert Group as a matter of urgency. Other points highlighted by the IR include the provision of adequate time for discussion and reflection. Patients should be provided with the information they need in order to make informed choices. Patients also require appropriate information, which must include device identification, to allow them to report adverse events if these occur.

Conclusion 4

The IR does not consider that current research studies on safety and effectiveness provide sufficient evidence on long-term impact of mesh surgery. The lack of long-term follow up and related outcome data, including information on quality of life and activities of daily living, should be addressed. The IR recommends the Expert Group highlights this knowledge gap to the research community and those that fund health research. Opportunities for routine audit

should be explored by the Expert Group in conjunction with NHSScotland.

Conclusion 5

Good information is essential to good patient care. The experience of the IR has been that, although data on the provision of SUI and POP surgery is held both in professionally-led databases and routine NHS activity data, the information derived from such sources could be improved. It is recommended that the Expert Group works with key stakeholders to address information gaps and ensure that available information is used as effectively as possible to support safe and effective care. The IR notes that, as an important first step towards this, ISD has already secured the creation of new data codes that will allow more precise recording of mesh surgery and any subsequent mesh removal/revision within routine NHS activity data records.

Conclusion 6

The IR expressed serious concern that some women who had adverse events felt they were not believed, adding to their distress and increasing the time before any remedial intervention could take place. Improving awareness amongst clinical teams of the possible symptoms of mesh complications together with good communication skills, (including good listening and empathy) is an essential part of good clinical care. The IR concluded that the Expert Group should review the training and information available to clinical teams in primary and secondary care and find ways of incorporating patient views in MDT working. The importance of developing pathways for the treatment of complications is emphasised, ensuring involvement of clinicians with the appropriate skills to take forward the personalised and holistic care necessary in these situations.

Conclusion 7

In the case of surgical treatment for SUI, a review of the different sources of evidence has led us to recommend that women must be offered all appropriate treatments (mesh and non-mesh) as well as the information to make informed choices. Management of patients must follow agreed care pathways and the importance of multidisciplinary assessment is emphasised. When surgery involving polypropylene or other synthetic mesh tape is contemplated, a retropubic approach is recommended. The Expert Group must develop appropriate pathways, including one for management of those suffering complications. Work with Medical Directors and Planners will be required to ensure their smooth implementation.

Conclusion 8

In the surgical treatment of POP, current evidence does not indicate any additional benefit from the use of transvaginal implants (polypropylene mesh or biological graft) over native tissue repair. Transvaginal mesh procedures must not be offered routinely. The Expert Group must develop appropriate pathways to meet clinical needs and also for the management of those suffering complications. Work with Medical Directors and Planners will be required to ensure their smooth implementation.

Chapter 10: Chair's concluding remarks

I would firstly wish to acknowledge the strength of views, care and professionalism that have been brought to this topic both during, and previous, to my time as Chair of this review.

SUI and POP are conditions which, while not life threatening, cause considerable distress to many women, with disruption of their normal lives. The hope of a treatment which can reduce that distress and return their lives to normal is understandably sought eagerly. Similarly, the gynaecologists and urologists who see these symptoms and the distress they cause to their patients seek to test and find new and better ways of producing good outcomes for their patients. The use of mesh in this clinical area came about because of that desire, and many women have had a good outcome from these operations. However, no surgery is without complication, and a number of women have had both minor and major complications due to the surgery itself. Indeed, some have found their lives completely transformed, for the worse, unable to pursue a normal family, personal and working life.

Balancing both good outcomes and very bad experiences has been one of the difficult tasks faced by this review. We have taken an approach of both seeking and sifting the best available research information on both safety and effectiveness, as well as the epidemiological information provided by the routine NHS linked information which is so rich in Scotland. While extensive, there are, nonetheless, many gaps, and we have been cognisant of these in forming our conclusions and recommendations. In addition, we decided to listen and to reflect on what both our patient and clinical members told us when applying their expertise and experience to that research and epidemiology. This led us to the specific recommendation we make on the use of mesh tape in particular circumstances and to ask for work on the clinical pathways to take this concern into account.

We can now see a way by which transvaginal mesh implant surgery can be supported on a case by case basis but it will require a number of actions to ensure lessons are learnt and good and safe patient care is ensured. These are outlined in our recommendations but include:

- informed consent is obtained using approved processes and information;
- an approved clinical pathway is followed;
- information, including adverse events, is recorded in a universal and robust way;
- patient treatment and audit is considered as part of a clinical network involving all practitioners;
- the Expert Group develops a pathway and supporting information for the retropubic approach in SUI as the routine mesh procedure with any variation considered as part of the multi-disciplinary team discussions; and
- the Expert Group develops a pathway for the treatment of POP where transvaginal mesh is not used routinely but which supports patients to have access to clinicians with expertise in this area wherever they live. Any variation in the future must be considered through a specific multidisciplinary team discussion after shared decision making with the patient.

Finally, listening is a key part of good and compassionate healthcare. The many women who began the process leading to this review, together with the women who valued this surgery and wanted that benefit to continue, I hope will feel that they have been listened to and that patient care will benefit as a result.

Appendix A – Patient member views on the process of the IR and mesh implants

The paper included here outlines the experiences, and the views on the process, of the member of the Review who considered herself a patient with a positive experience.

i. Personal views of member of the IR with positive experiences

Background

In 2013 the Independent Review (IR) was set up at the request of the former Cabinet Secretary for Health and Wellbeing to assess the evidence relating to surgery using synthetic mesh implants for the treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) in Scotland. This followed a range of investigation prompted by a petition presented by some of the women who have been damaged by mesh procedures, now known as the Scottish Mesh Survivors' Group (SMS). I was invited to join the IR as a patient who had a successful outcome from mesh surgery for Pelvic Organ Prolapse (POP). At the beginning of 2016 I was also invited to join the Expert Group (formerly the Scottish Government's Short Life Working Group) which is addressing the various issues raised by the Survivors' Group petition. I would therefore like to offer my views from the patient perspective and also identify what to me are some of the important issues.

To date, the issue of the severe damage experienced by some women has been given maximum publicity through media coverage, the Survivors' Group campaign and the action of the Scottish Government in requesting the suspension of SUI operations pending investigation. The extremely negative and aggressive media coverage has vilified clinicians involved in this work, and the NHS in general. So far as I am aware there has been no publicity about the success of mesh operations for the many thousands of women who have been helped over the last 10+ years since these were introduced. The female public has, therefore, been subjected to a gross imbalance of information all of which has a completely negative bias. This lack of balance needs to be addressed and a proper perspective attained.

I understand that for more than the past ten years mesh procedures have proved to be beneficial for thousands of women, myself included. My concern is that a minor percentage of women who have been severely damaged by mesh surgery, dreadful though that must be, cannot be allowed to dictate the fate of the majority of women who could potentially benefit from it in the future, nor deny them the opportunity to choose their own pathway. I feel strongly that women should continue to have the choice of which surgical procedure to have, provided they are given all necessary information beforehand, together with guidance from appropriate health professionals to help them arrive at the right decision for them.

The on-going gathering of evidence and future analysis on use of mesh will continue to influence the decision making process for health professionals and prospective patients, and relevant information will be updated to reflect that. However, the immediate future of mesh surgery cannot be decided at an emotional and personal level, but on the basis of the evidence presented by this independent investigation, which has to be recognised by all parties.

Comment

The on-going work of the Expert Group over the past four years has been to address the various issues of concern raised by the SMS Petition to Government, in order to identify what actions need to be taken and how these can best be implemented. This will result in the introduction of new systems and the tightening up of existing systems, procedures and governance which will benefit all women suffering from the extremely unpleasant and humiliating conditions of stress urinary incontinence and will be extended to pelvic organ prolapse. In this regard the input of the Scottish Mesh Survivors' group has been invaluable.

During my membership of the Expert Group I have been impressed by its commitment to the task. It is my understanding that actions as agreed are being implemented by the respective departments within the NHS, and will continue to be so, and that progress will continue to be monitored by the Expert Group. Some of these changes will inevitably take longer to implement than others due to their inherent complexity and universality. In addition, all of this work has to be phased-in with the on-going and ever-escalating needs of patients that still have to be met on a daily basis.

A few of the areas I consider are especially important, from the patient point of view, are touched on below.

Requested Suspension of Mesh Procedures

The actions of the Survivors' Group have resulted in the Scottish Government's interim suspension request of mesh procedures since June 2013. The former have stated that they do not wish other women to suffer what they have suffered, which is very understandable in their position. It is an unalterable fact, however, that all surgery carries risks irrespective of how straightforward the procedure: nothing can be guaranteed. Simplistically, there is also a great diversity of patient characteristics, medical devices, pertinent surgical approaches, as well as the unexpected factors that can adversely affect the outcome of a procedure. We mustn't, however, lose sight of the fact that historically there are many thousands of women who appear not to have suffered major trauma and have had successful outcomes over the last 10+ years.

The reality of the present suspension request therefore, is that there are now many hundreds of women in Scotland who are having to live with distressing, unpleasant and humiliating symptoms, because they are being denied the opportunity to decide whether or not to have mesh surgery. They must be given a choice.

Adverse Effects

<u>Under Reporting</u>

There is some evidence of a degree of under reporting of adverse events to the appropriate medical body (MHRA) in the past, which may or may not have identified many other cases of severe damage sustained by mesh surgery. This has cast some doubt on the statistical evidence available. It seems to me, however, very unlikely that a large percentage of women have been prepared to suffer severe damage following an operation for SUI over a 10+ year period without seeking help and suitable investigations subsequently being carried out. Conversely, nor are they going to publicise to the media, hospitals or even perhaps their surgeons, that they are delighted with their surgery: that just doesn't happen, mainly because they have experienced exactly what they expected to, i.e. a successful outcome.

Reporting and Recording in Data Base /Registry

The Expert Group are currently preparing a system which will establish a clear procedure enabling surgeons to ensure that all adverse events are recorded and reported as they become known. Work is also being undertaken in conjunction, with other professional bodies, to develop a universal information system in which stored data will be accessible to the medical community. A project of this magnitude will inevitably take some time to fully implement.

Serious Adverse Events / Adverse Events

A personal concern of mine is the way in which the terms Serious Adverse Events (SAEs) and Adverse Events (AEs) are sometimes used. My understanding is that SAEs can cause the type of damage that the SMS members have obviously suffered, and AEs are less serious adverse events that often resolve spontaneously, can be successfully treated, or are expected to occur in any surgical procedure. The distinction between the two is obviously medically defined, but I am aware that the term AE at times seems to be used almost as a generic term encompassing the more serious SAE type events. This could cause confusion mainly for the patient community in wrongly applying the term SAE to what is in effect a less serious AE, which could conceivably distort the 'weighting' applied to events until they can be appropriately medically classified.

National Governance

To date no other country in the world has banned the use of mesh procedures for SUI or POP. As a patient I think it is vitally important that the choice of having mesh surgery does not become a geographical issue in any part of the UK. The SMS petition and subsequent Scottish Government Action has allowed the Independent Review to identify areas in which important changes in practice and governance can and should be made. The NHS in Scotland is now running with this particular ball: work will continue, changes will be made, and women will be able to make informed choices about their treatment. On the basis of this commitment and my understanding of the changes already being implemented, I would advocate on behalf of women in the future, that the requested suspension should be lifted now. The needs of women are not going to change and the volume of need is only going to increase. Hundreds of women are awaiting treatment: they must be given the choice of deciding their own pathway.

Patient Information Leaflet (PIL)

A revised PIL is available which has been approved for use in the UK. This contains all the information a woman will need in order to make an informed choice about her treatment. This will be updated every two years, and should be made available to patients at their clinic appointment.

Multi-Disciplinary Team Working and Shared Decision Making

In future the decision on which treatment is considered appropriate for each patient will be made by a Multi-Disciplinary Team (MDT). The MDT will consist of health professionals with the appropriate skills needed to arrive at the best decision for each patient, including the patient's consultant surgeon, and within which the patient's own wishes will also be considered. This practice of shared decision making and clinical interaction together with the

written information given in the PIL will give the patient much more confidence in what is proposed for her.

Manufacturers' Responsibility

The responsibility of manufacturers is being reviewed regarding the introduction and provision of new devices such as mesh tapes and the kits needed to insert them, as required in treatment of SUI and POP This will address quality of product, fitness for use and training and will ensure suitability of product before being introduced into routine surgery.

Negative Repercussions of the Mesh Controversy

While this controversy has undoubtedly had many positive outcomes for which I as a patient am very grateful, in my opinion other issues may arise that could leave women disadvantaged.

- A general 'climate of caution' may prevail in which some surgeons may become unwilling to undertake mesh procedures so as to avoid possible serious adverse outcomes, with the consequent repercussions and possible litigation.

- Manufacturers may decide to stop manufacturing the devices necessary for SUI and POP mesh surgery.

- The longer the suspension of mesh surgery is in place the longer waiting lists will become. Some surgeons may no longer be able to undertake the traditional procedures due to the focus on the newer less invasive procedures over the past 10+ years: and skills in mesh procedures may also be affected, requiring retraining of surgeons.

The reputations of surgeons and the NHS have been severely undermined in the female community, by the very negative and aggressive media publicity. The public depend on the skills of clinicians and none of us know when we might need their help. Young women who have already had procedures carried out will probably need more work done as they grow older. Patient confidence must be restored in the work of surgeons and delivery of good medical care for women, the majority of whom are prone to damage arising from what only women can do, that is – have babies. In turn, surgeons must ensure that they are properly trained and fully competent to carry out mesh procedures.

In Conclusion

The scope of the Independent Review is comprehensive and I have confidence as a participant and as a patient, that the way forward will be clearly identified. I am also confident that the work already being implemented, as addressed in the notes above, will result in better and more patient-centred care for women suffering SUI and that the NHS are committed to delivering this. I would therefore advocate that no further time delays should be put in the way of the many hundreds of women presently awaiting surgery, as alluded to in the Patient Stories in chapter 3 of this document. They must be allowed to choose their own path as soon as possible.

The conclusions below are offered from my perspective as a patient.

1. All parties must recognise the findings of the Independent Review and future action should

be based upon that evidence until further evidence becomes available in the future.

2. The suggested suspension of mesh procedures in Scotland should be lifted now while the actions agreed by the Expert Group continue to be implemented and monitored.

3. While the Independent Review is the Scottish Government's initiative, the future of mesh surgery and the impact on all women should not be a unilateral decision by the latter but based on a consensus of all countries within the U.K.

4. The success and volume of mesh surgery historically must be recognised and acknowledged, unless evidence proves otherwise.

5. The need for SUI and POP procedures is increasing year by year. Governments must consider the future status and consequent effect on women, if mesh surgery is proscribed.

6. The incidence of women reporting adverse events many years after mesh surgery should be considered in perspective, if they have had, say, 10 years of trouble free life which they may not otherwise have had. The opportunity to achieve this, and perhaps an even longer term successful outcome would, in my opinion, be worth considering.

7. The PIL should only be given to patients during their clinic appointment with the consultant to ensure that only the most up to date version is used.

8. The major contribution of the SMS to the improvement of systems and procedures in areas pertaining to mesh operations should be widely acknowledged.

Isobel Montgomery
February 2017

Appendix B - Remit

The remit of the Review is to evaluate both the efficacy and the extent and causes of adverse incidents and complication rates associated with SUI and for POP. The Review Group recognises that these are two very different conditions and will take account of this.

It will involve the clinical and patient community and will have the means both of identifying and determining the causes of issues where this is possible, finding and implementing solutions.

Purpose

1. To determine the safety of vaginal mesh implants for both SUI and POP in Scotland and to compare it to international standards. Information on how many women are experiencing complications and possible reasons for these complications will be examined.

2. To determine the relative efficacy of surgery for SUI and POP with and without the use of mesh or tapes.

The Review will take account the Opinion of the Scientific Committee on Emerging and Newly Identified Health Risks of the European Commission, the MHRA report on Safety/Adverse Effects of Vaginal Tapes/Slings/Meshes for Stress Urinary Incontinence and Prolapse and the output from the UK Working Group on surgery using vaginal mesh.

This will involve:

- Putting the needs of patients first (both need for effective treatment and protection from harm).

- Appraising the current research evidence for the efficacy of these tapes and meshes relative to alternative surgical and non-surgical treatments from unbiased sources, such as Cochrane reviews and randomised controlled trials (RCTs) along with verified alternative sources.

- Reviewing the information on adverse incidents and complications for mesh used for SUI and POP in Scotland and elsewhere.

- Understanding, with the clinical and patient communities, possible reasons for any complications.

- Identifying where possible which complications arise from the device itself, the insertion technique or the procedure as a whole.

- Identify where possible improvements which could improve efficacy, safety or decrease complications.

- Fostering clinical consensus to recommend appropriate clinical pathways for mandatory reporting of any complications or adverse incidents, making recommendations to the Cabinet Secretary of changes that may be required to improve quality, safety or efficacy.

Scope

In determining the appropriate course of action on this issue, the Group is able to consider:

- The available data on procedures using mesh implants for pelvic floor surgery, including data on efficacy and complications compared to alternative surgical and non-surgical treatments.
- Identifying best practice standards in management of SUI and POP.
- Any issues that may lead to clinical practice not conforming to best practice standards.
- Reported safety issues with devices, including improvement in reporting adverse events.
- Barriers to regular prospective auditing of results of surgical procedures.
- Short, medium and long-term patient follow-up.
- Identification of best practice in managing both treatment failure and complications, and resources to do so.
- Whether the information provided to patients before undergoing these procedures should be updated.

Appendix C – Members

Lesley Wilkie, Chair of Independent Review, retired Director of Public Health, NHS Grampian to October 2016
Tracey Gillies, Chair of Independent Review, Medical Director NHS Forth Valley October 2016 – 2017
Gillian McCallum, Scottish Government, Secretary to the Independent Review from inception to June 2016
David Bishop, Scottish Government, Secretary to the Independent Review June 2016 – 2017
Terry O'Kelly, Colorectal Surgeon, NHS Grampian, Scottish Government Senior Medical Officer
Sara Davies, Scottish Government Consultant in Public Health Medicine
Catherine Calderwood, former Scottish Government Senior Medical Officer
Frances Elliot, former Deputy Chief Medical Officer

Patient Representatives

Elaine Holmes – Scottish Mesh Survivors Group Resigned 4th March 2017
Olive McIlroy – Scottish Mesh Survivors Group Resigned 4th March 2017
Isobel Montgomery – Patient representative

Researcher

Cathryn Glazener – Professor of Health Services Research. Chief Investigator, PROSPECT, VUE, MAPS, ProLong. Co-ordinating Editor, Cochrane Incontinence Review Group, University of Aberdeen

Clinicians

Wael Agur–Sub-specialist Urogynaecologist, NHS Ayrshire and Arran Resigned 1st March 17
Paul Hilton – Retired Consultant Gynaecologist and Urogynaecologist
Karen Guerrero – Sub-specialist Urogynaecologist, NHS Greater Glasgow and Clyde
Voula Granitsiotis – Consultant Urologist, NHS Greater Glasgow and Clyde
Elizabeth Crothers – Physiotherapist, Chartered Society of Physiotherapists

Medicines and Healthcare products Regulatory Agency

Neil McGuire – Medical Director

Professional Bodies

David Richmond – President of Royal College of Obstetricians and Gynaecologists 2013-2016 and Past President 2016-2017
Ash Monga – Past Chairman of British Society of Urogynaecology
Alfred Cutner – Chairman of British Society of Urogynaecology
Roland Morley – Chairman of The British Association of Urological Surgeons Section of Female, Neurological and Urodynamic Urology

Scottish Public Health Network

Phil Mackie – Lead Consultant in Public Health, Scottish Public Health Network

Information Services Division

Rachael Wood – Consultant in Public Health Medicine
Jo Morling – Speciality Registrar in Public Health

NHS Lothian and CMO Directorate

Josie Murray Speciality Registrar in Public Health

Appendix D – Interim Report Chapter 6 table

Table 6.1

Outcomes from the recent systematic review from the Cochrane Collaboration (Ford et al)	Retropubic mesh tape device (%)	Transobturator mesh tape device (%)	RR, 95%CI, number of studies and participants	Favours...	Notes on research evidence from the Cochrane Collaboration
Short term efficacy	Similar Subjective: 84.4% Objective: 87.2%	Similar 82.3% 85.7%	 RR 0.98, 95% CI 0.96 to 1.00 36 trials, 5514 women. RR 0.98, 95% CI 0.96 to 1.00 40 trials, 6145 women	None	Research evidence favouring retropubic approach for both patient-reported and clinician-reported outcomes did not reach statistical significance.

Long term efficacy	Similar Subjective: 70.7% Objective: 85.5%	Similar 65.1% 83%	 RR 0.95, 95%CI 0.80 to 1.12. 4 trials, 714 women. RR 0.97, 95% CI 0.90 to 1.06; 3 trials, 400 women	None	Research evidence favouring retropubic approach for both patient-reported and clinician-reported outcomes did not reach statistical significance.
Need for repeat continence surgery after 1 year	Lower 1.1%	Higher 11.3%	RR 8.79, 95% CI 3.36 to 23.00; 4 trials, 695 women	Retropubic	Research evidence favours retropubic approach. Despite reaching statistical significance, the number of studies and participants are relatively smaller than those contributing to short-term efficacy.

Bladder injury	higher risk 4.5%	lower risk 0.6%	RR 0.13, 95% CI 0.08 to 0.20; 40 trials, 6372 women	Obturator	While risk of bladder injury is higher with retropubic approach, it is diagnosed intra-operatively in almost all cases, as cystoscopy is routinely employed. The tape is replaced in the correct position and no long-term problems are expected.
Voiding problems	higher risk 7.2%	lower risk 3.8%	RR 0.53, 95% CI 0.43 to 0.65; 37 trials, 6200 women	Obturator	Retropubic tapes appear to be more 'obstructive'. Patients at increased risk of voiding dysfunction following surgery (using an obturator or retropubic approach) may need to learn self-catheterisation beforehand.

groin, pelvic and thigh pain	lower risk 1.3%;	higher risk 6.4% v	RR 4.12, 95% CI 2.71 to 6.27; 18 trials, 3221 women	Retropubic	Chronic pain and dyspareunia appear to be the most common symptoms reported by mesh-injured women.

mesh exposure	Similar risk 2.1%	Similar risk 2.4%	RR 1.13, 95% CI 0.78 to 1.65; 31 trials, 4743 women	None	None
mesh erosion into bladder or urethra	Similar risk	Similar risk		None	None
Operative blood loss	Higher	Lower	MD 6.49 95%CI 12.33 to 0.65	Obturator	The 6.5-ml statistically-significant difference in favour of the obturator approach is clinically-insignificant.
Operation time	Longer	Shorter	MD 7.54 95%CI 9.31 to 5.77	Obturator	The 7.5-minute statistically significant difference in favour of the obturator approach is thought to be due to usage of cystoscopy to rule out bladder injury during the retropubic approach. The time is thought to be well-invested.

Feasibility and characteristics of complete surgical removal	Possible, regardless of duration of implantation. Removal usually requires an abdomino-perineal approach. The surgical technique and anatomy of the retropubic space are well understood by most surgeons. Removal is usually complete.	Possible, only during the first few weeks of implantation. Removal is difficult afterwards. Removal usually requires only a perineal approach. The surgical technique and anatomy of the upper thigh are poorly understood. Removal is usually incomplete.	Clinical Opinion (Level III)	Retropubic	In either condition, complete removal of the mesh device does not guarantee cure from pain.

Abbreviations

AUS	Australia (research reference)
BAUS	British Association of Urological Surgeons
BSUG	British Society of Urogynaecology
CA	Canada (research reference)
CE	Conformité Européenne
CLO	Central Legal Office
CMO	Chief Medical Officer
DK	Denmark (research reference)
EU	European Union (research reference)
FDA	Food and Drugs Administration
IRIC	Incident Reporting and Investigation Centre
ISD	Information and Services Division
IUGA	International Urogynecological Association
MDL	Multidistrict Litigation
MDT	Multi-disciplinary Team
MHRA	Medicines and Healthcare products Regulatory Agency
MUS	Mid-Urethral Slings
NICE	National Institute for Health and Care Excellence
NL	The Netherlands (research reference)
NZ1	New Zealand 1 (research reference)
NZ2	New Zealand 2 (research reference)
PFMT	Pelvic Floor Muscle Training
POP	Pelvic Organ Prolapse
PROSPECT	PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trial
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoL	Quality of Life
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised Controlled Trial
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
ScotPHN	Scottish Public Health Network
SIGN	Scottish Intercollegiate Guidelines Network
SMR00	Scottish Morbidity Record – outpatients
SMR01	Scottish Morbidity Record – hospital inpatient
SMS	Scottish Mesh Survivors
SUI	Stress Urinary Incontinence
TMWG	Transvaginal Mesh Working Group
TVT-O™	Transobturator Tape
TVT™	Tension-free Vaginal Tape
UDI	Unique Device Identifier
UK1	United Kingdom 1 (research reference)
UK2	United Kingdom 2 (research reference)
USA	United States of America (research reference)

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