The Scottish Independent Review of the Use, Safety and Efficacy of Transvaginal Mesh Implants in the Treatment of Stress Urinary Incontinence and Pelvic Organ Prolapse in Women

Interim Report

2 October 2015

Contents

***These documents have been provided separately due to their size and are available online**

Preface

This Independent Review (IR) into the use of transvaginal mesh in surgery for incontinence and pelvic organ prolapse 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 have 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 NHS Scotland to suspend transvaginal mesh procedures pending the outcome of this review.

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 Independent Review 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 suggest ways the government should consider to ensure this area is improved. We

differentiate between the use of mesh in the treatment of stress urinary incontinence and when it is used in the repair of pelvic organ prolapse. 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

Executive Summary

This report outlines the work 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 an interim report as the publication of further pieces of work are awaited, including: Opinion of the European Commission and its Scientific Committee on Emerging and Newly Identified Health Risks Opinion (SCENIHR) and PROSPECT (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials). However as the main programme of work has been completed the IR has been able to draw conclusions and make recommendations.

The work has taken several months and 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 considering 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.

The IR meetings have also assessed verbal evidence from different experts, including patients, to reach consensus conclusions. It is expected that these will improve the quality of care in a field that crosses primary, secondary and specialist care and can have lifelong effects on women's quality of life.

Some conclusions are specific to improving care in the use of transvaginal mesh. Others are intended to benefit patients in general. All conclusions are described below:

Conclusion 1

Robust clinical governance must surround treatment, the decision to use mesh and the surgical approach used. To support decision making, management of the individual patient should take place in the context of multi-disciplinary team assessment, audit and review. The use of a comprehensive information system will underpin this. **The Expert Group should address this with NHS planners, including an assessment of any administrative support required for the clinical teams.**

Conclusion 2

Evidence of involvement in multi-disciplinary team working, engagement in audit activity and recording and reporting of adverse events should be an important part of consultant appraisal and thus statutory revalidation of medical staff. **The Expert Group should work with Medical Directors as Responsible Officers to include this in the conduct and supervision of appraisal. In addition the Scottish Government should consider the alternative methods for the capture of adverse events set out in chapter 8 to determine further the most effective way to ensure complete notification.**

Conclusion 3

Informed consent is a fundamental principle underlying all healthcare. There has been extensive work done by the Expert Group which preceded the establishment of the Independent Review, with leadership by both patients and clinicians. This has resulted in an SUI information leaflet and consent form. **Following on from this the Independent Review concludes that additional work is required to ensure that this work is extended to include POP procedures and that the 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 Independent Review include the provision of adequate time for discussion and reflection. Patients should be provided with information enabling them to report adverse events if these occur.**

Conclusion 4

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

Conclusion 5

Good information, as stated before, is essential to good patient care. The experience of the Independent Review has been that there are many gaps although there is information both in a professionally led database (the BSUG database) and routine NHS information (SMR01 and SMR00). **It is recommended that the Expert Group works with ISD, BSUG and others to ensure that an information system is developed which is universal, robust, clinically sound and focused on fostering good patient outcomes. Work already underway on consistent coding by ISD will be vital to this endeavour.**

Conclusion 6

The Independent Review expressed serious concern that some women who had adverse events found they were not believed, adding to their distress and increasing the time before any remedial intervention could take place. Improving awareness of 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 Independent Review concluded that the Expert Group should review the training and information available to clinical teams and find ways of incorporating patient views in multi-disciplinary working. It should also continue oversight of the mesh Helpline.**

Conclusion 7

A review of the different sources of evidence available to and considered by the Independent Review (patient experience, clinical expert opinion, research evidence and epidemiological evidence from routine information) has led us to express concern in this Interim Report at the use of the transobturator rather than the retropubic approach for routine surgery for stress urinary incontinence using mesh. The clinical governance arrangements that we have recommended will allow an individual case to be considered in the context of a multi-disciplinary assessment, including patient views**. We await the final publication of key research reports but wish to register these concerns and to recommend that the Expert Group in the following months before the publication of the final report explore further appropriate pathways to ensure the techniques chosen take the differential patient and clinical experience, as well as research evidence into account.**

Conclusion 8

Similar concern is expressed, both for effectiveness and adverse events, at the use of transvaginal mesh in surgery for pelvic organ prolapse. The clinical governance arrangements that we have recommended will allow an individual case to be considered in the context of a multi-disciplinary assessment, including patient views. **We await the final publication of key research reports but wish to register these concerns and to recommend that the Expert Group in the following months before the publication of the final report explore further appropriate pathways to ensure the techniques chosen take the differential patient and clinical experience, as well as research evidence into account.**

Chapter 1: Introduction

1.1 Background

Stress urinary incontinence (SUI) and pelvic organ prolapse (POP) are conditions affecting a significant number of women and can result in a reduced quality of life for many. Synthetic polypropylene mesh is a permanent implantable medical device used in a number of operations to correct SUI and POP. 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.

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 these procedures 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 product Regulatory Agency (MHRA). Many women have experienced a positive outcome and because of this, combined with less successful outcomes associated with alternative surgical procedures, consider that they are the most effective way to treat these distressing conditions.

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 has been taken forward by the Expert Working Group.

The Scottish Mesh Survivors Group (SMSG) brought together women affected by polypropylene mesh 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 occurring, allied with under-reporting of these adverse events, has understandably 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 Scottish Mesh Survivors Group. The petition called on the Scottish Parliament to urge the Scottish Government to:

1. Suspend use of polypropylene Transvaginal Mesh (TVM) 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 TVM devices to heightened alert status to reflect ongoing 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 Independent Review of transvaginal mesh surgery was necessary to establish the facts. The former Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, announced the Independent Review 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 Review has reported its findings.

1.2 Remit of the Independent Review

The published remit of the Independent Review is to evaluate both the efficacy and the extent and causes of adverse incidents and complication rates associated with stress urinary incontinence and for pelvic organ prolapse. The Independent Review recognises that these are different conditions, each managed by several different procedures and will take account of this.

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

1.2.1 Purpose

1. To determine the safety of vaginal mesh implants for both stress urinary incontinence and pelvic organ prolapse 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 stress urinary incontinence and pelvic organ prolapse 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.
- Whether the information provided to patients before undergoing these procedures should be updated.

The full remit and membership of the Independent Review is set out at Appendix A and B.

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 to review current clinical practice and make recommendations for change. The following areas are currently being considered by the Expert Group:

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 stress urinary incontinence[1] which was published June 2014 on the Scottish Government website. This

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

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 Independent Review has a distinct remit and constitution. The Expert Group suspended its activities during the period of the Independent Review's main work programme and re-formed in August 2015.

1.4 What are Medical Devices?

A medical device means: 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,
- 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.

MHRA regulates devices placed on the market by the manufacturer, but the healthcare services or clinical procedures they are used for 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 this function by the member states competent authorities. Once Notified Body certification is obtained and their other obligations under the Medical Devices Regulations are being met the manufacturer can put the CE marking on the device and place it on the EU market.

The MHRA as the Competent Designating Authority in the UK oversees UK Notified Bodies, for example, the British Standards Institute a list of which may 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 conduct regular audits of Notified Bodies quality assurance processes, monitor their certification and sample witness their compliance assessments of manufacturers to ensure that they operate to high standards:

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

MHRA also witness their 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

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 in compliance 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 demonstrate verify that they the devices meet the relevant essential requirements laid down in the regulations for things such as including for example biocompatibility, toxicity, technical specifications, clinical data, sterilisation, right through to packaging and labelling and quality management systems.

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, whether or not they are considered to be active (i.e. have a power source), particularly invasiveness, duration of continuous contact, nature of the tissue contact, and distinction between non-active and active devices. For transvaginal use, Polypropylene mesh, used in urogynaecological surgery is a class IIb device, while meshes containing or which are entirely made of biological material (outside the remit of this Review) are Class III devices.

Classification of medical devices varies across the world and while there is some read across with the United States, there is not equivalence. Therefore a direct comparison between US and EU criteria is not possible. The FDA classifies mesh devices as Class II and this remains the case as of 21 Sep 2015.

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 April 2014 the FDA issued two proposed orders to reclassify mesh devices and a decision on these orders is awaited.

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 devices as non-active implantable devices.

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

The Independent Review'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. In part this is because the reports on some important research work have not yet been published and has led the Review to publish an Interim Report. Once other evidence strands become 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 Independent Review will be 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

2.1 Clinical indications

2.1.2 Stress Urinary Incontinence

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 stress urinary incontinence may occur. The problems can be mild, moderate or severe and can lead to a considerable loss 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;
- Pharmaceutical 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 transvaginal mesh tapes;
- Transobturator transvaginal mesh tapes; and
- Single incision mini-slings.

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

<u>Retropubic mesh tape procedure</u>

This was the first mid-urethral tape procedure introduced and 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.

<u>Transobturator mesh tape procedures</u>

This procedure was developed to minimise the potential for bladder and bowel injuries associated with the retropubic mesh tape procedure. 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 through 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 enterocoele) 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 ant wall prolapse with implant, usually mesh
- Posterior colporrhaphy with implant: repair of post wall prolapse with implant, usually mesh
- Vaginal hysterectomy;
- Vaginal colpopexy/hysteropexy; vaginal vault support without mesh

Vaginal colpopexy/hysteropexy with implant: approach suspension with mesh;
Sacrocolpopexy / Sacrohysteropexy: Abdominal approach suspension with mesh (this procedure is outwith the remit of this Review)

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 to offer. In NHSScotland it is obligatory to use the guidance from the National Institute for Health and Care Excellence's (NICE) interventional procedures programme. This programme includes a range of procedures from 2005 – 2009 for both SUI and POP [2]. In addition NICE published a detailed clinical guideline in 2013 on urinary

[2] http://www.nice.org.uk/guidance/published?type=ipg

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

Transvaginal mesh used can be one of a range of type: absorbable synthetic; 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 are a range of methods to use mesh, including:

- Mesh-inlay: the mesh is cut to the desired shape and size and placed through a single incision inside the vagina.
- Mesh-kit: pre-shaped mesh is placed using introduction needles or trocars that may require external skin incisions at several points.

The International Urogynaecological 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

[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/

Chapter 3: Women's experiences

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 were characterised by the histories of painful and debilitating complications; often experienced several years after the original SUI or POP; of being told by clinicians that their experiences were rare; not being believed when they sought help; of further surgery; of loss of quality of life; and even that it 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, these stories at not the only ones that came to be told. Other stories of good outcomes and everyday lives restored also came to light. 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 they simply want to move on.

Without detailed, qualitative research evidence, it is hard to fully understand these differing experiences from 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, some insight at least 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 UK 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, sent to the Cabinet Secretary for Health, Wellbeing and Sport; the collected experiences of those women who are associated with the Scottish Mesh Survivors Group (SMSG); and 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 it 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 have its own limitations which have a bearing on how it can be interpreted.

Patient stories – all written responses to the Cabinet Secretary were reviewed and a sample of these, representing the balance of experiences were turned into anonymised patients stories. Whilst women were asked to provide such written responses, the specific content of them 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 SMSG data – All women who are in contact with the SMSG 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.

PROSPECT trial qualitative data – Personal experience data from women undergoing the PROSPECT trial has been collected at one year and two years post surgery. These data have only recently become available and only a very preliminary analysis is included in the review. This has simply calculated the number of positive versus negative comments at the two post-surgery time intervals.

3.4 Results

3.4.1 Patient stories

In total nine patent stories were developed from the written submissions to the Cabinet-secretary. Five of these describe adverse outcomes and four positive ones. 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.

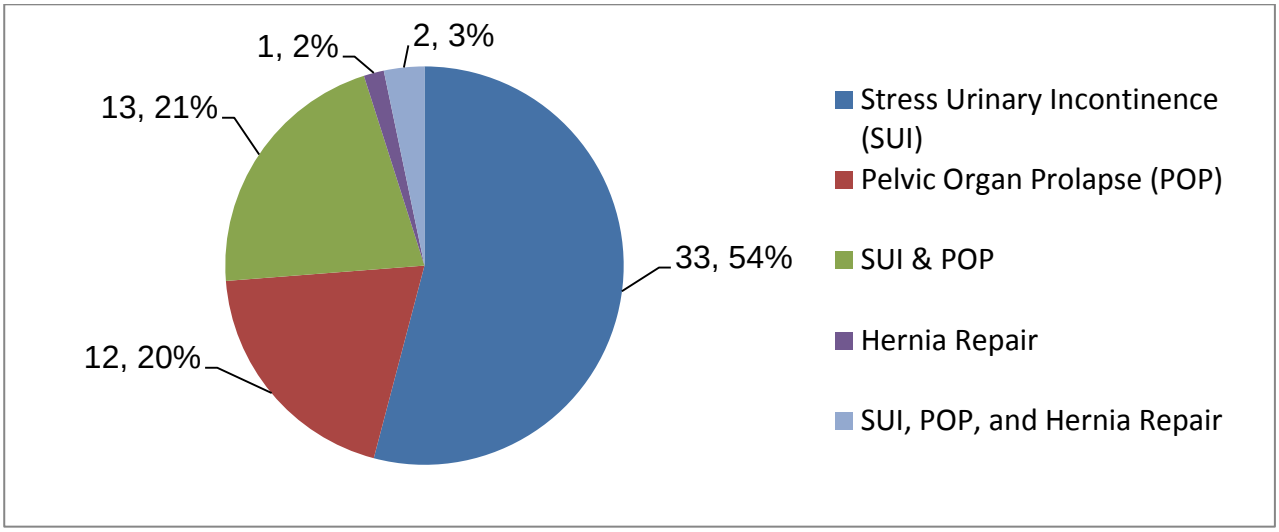
3.4.2 Analysis of Scottish Mesh Survivors Group data

The SMSG questionnaire was circulated to *approximately* 80 women, though no precise record was made of this. This provides an approximate response rate of 77.5% (95% CI: 67% - 85%) completed questionnaires. No demographic data were collected, which focussed on details of the mesh procedure and the women’s subsequent experiences.

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, three procedures),

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

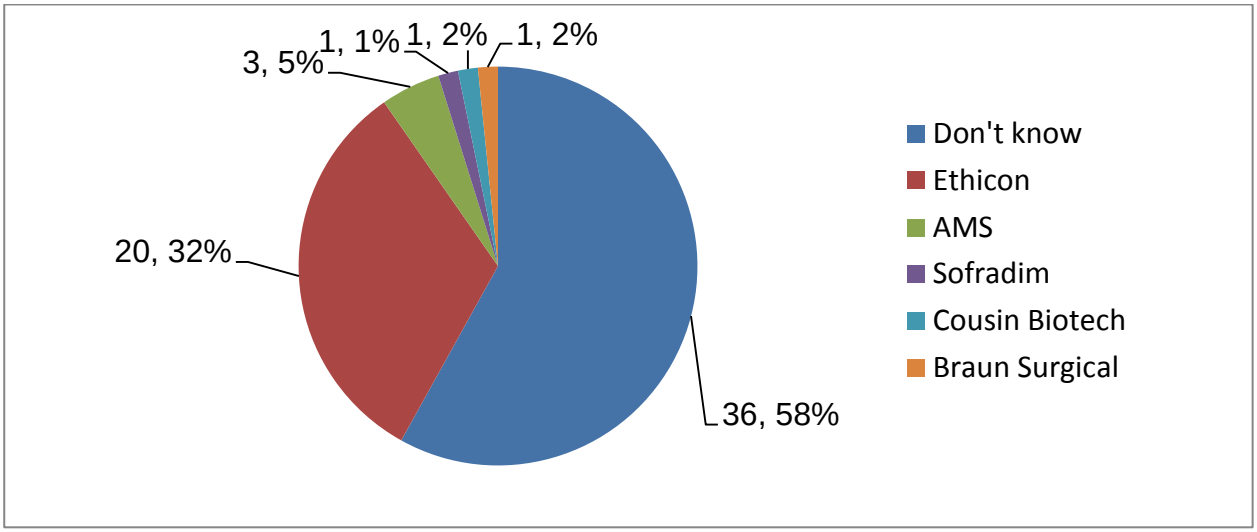
Figure 3.1 Reasons women reported for undergoing mesh procedures



(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 1 in 5 procedures (20%). Of the 62 responders, over half of them do not know what mesh product was fitted (58%) and just under one third 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 survey the women commented on the information they had received and about informed consent. Only 10 of responders answered the question about the information they were given, pre-operation about mesh (35% of the responders). 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 NHS 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 below.

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 ongoing care, some 38% (n=13 /34) were critical of the treatment they were currently receiving; and
- 32% of respondents made a comment indicating they had lost faith in medical professionals or the healthcare system.

More widely smaller numbers of women mentioned issues such as: 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.

3.4.3 PROSPECT Data

As part of the PROSPECT trail, 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 Independent Review 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 analyses 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 medial follow up, even though some are still experiencing unpleasant and debilitating symptoms that reduce their capacity for everyday life.

However, for other women, there are positive outcomes which have occurred. 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 that fact that these women have had positive outcomes. For others, it is a sign that – at best – the surgery has not worked, but these women have chosen not to seek further intervention as this was their “last, best hope”. Finally, there are some for whom this is evidence 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 gynaecologist! 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 Gynaecologist 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. 7

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 family and friends. My family practitioner was able to discuss the proposed surgery in detail and to study closely all the written information.

It 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.

Chapter 4: Assessing the safety and effectiveness of vaginal mesh surgery for stress urinary incontinence and pelvic organ prolapse in Scotland

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

For this study, Information Services Division (ISD) used routine hospital discharge records to identify the different operations provided for stress urinary incontinence and pelvic organ prolapse in Scotland between 1997/98 and 2013/14. Specific types of operation that were provided in reasonably high numbers were included in the analysis.

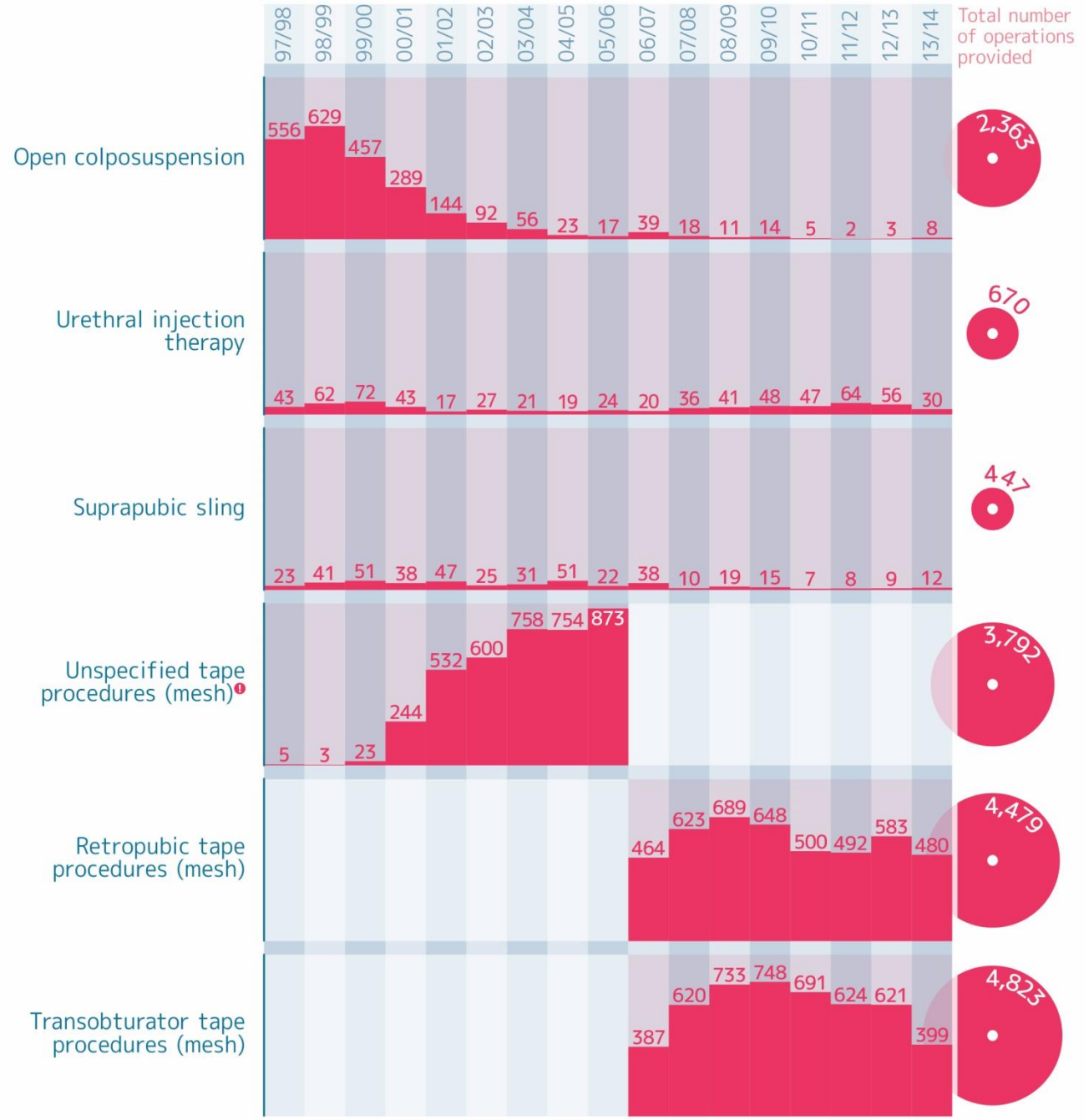
In general, only single operations were included in the analysis. 'Single' means that the woman did not have any additional/second operation for incontinence or prolapse at the same time as the operation being examined. It is quite common for women to have more than one operation at the same time. However 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. Only first operations were included because the risk of complications may be quite different for a woman having a repeat operation, and it was important that the study did not mix operations with different levels of risk.

4.1.1 Operations provided for stress urinary incontinence

Open colposuspension was the main operation provided in Scotland for stress urinary incontinence in the late 1990s. Tape (mesh) procedures were introduced around 2000/01 and quickly became the most common operation type for this condition, however the number of tape procedures done fell substantially in the last year included in the analysis (2013/14). Urethral injection therapy and suprapubic sling operations have been provided in low numbers throughout the time period included in the analysis.

Numbers of first, single operations for stress urinary incontinence by year



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 tape operation had been provided. After April 2006, new codes allowed the particular type of tape operation (retropubic or transobturator) to be recorded.

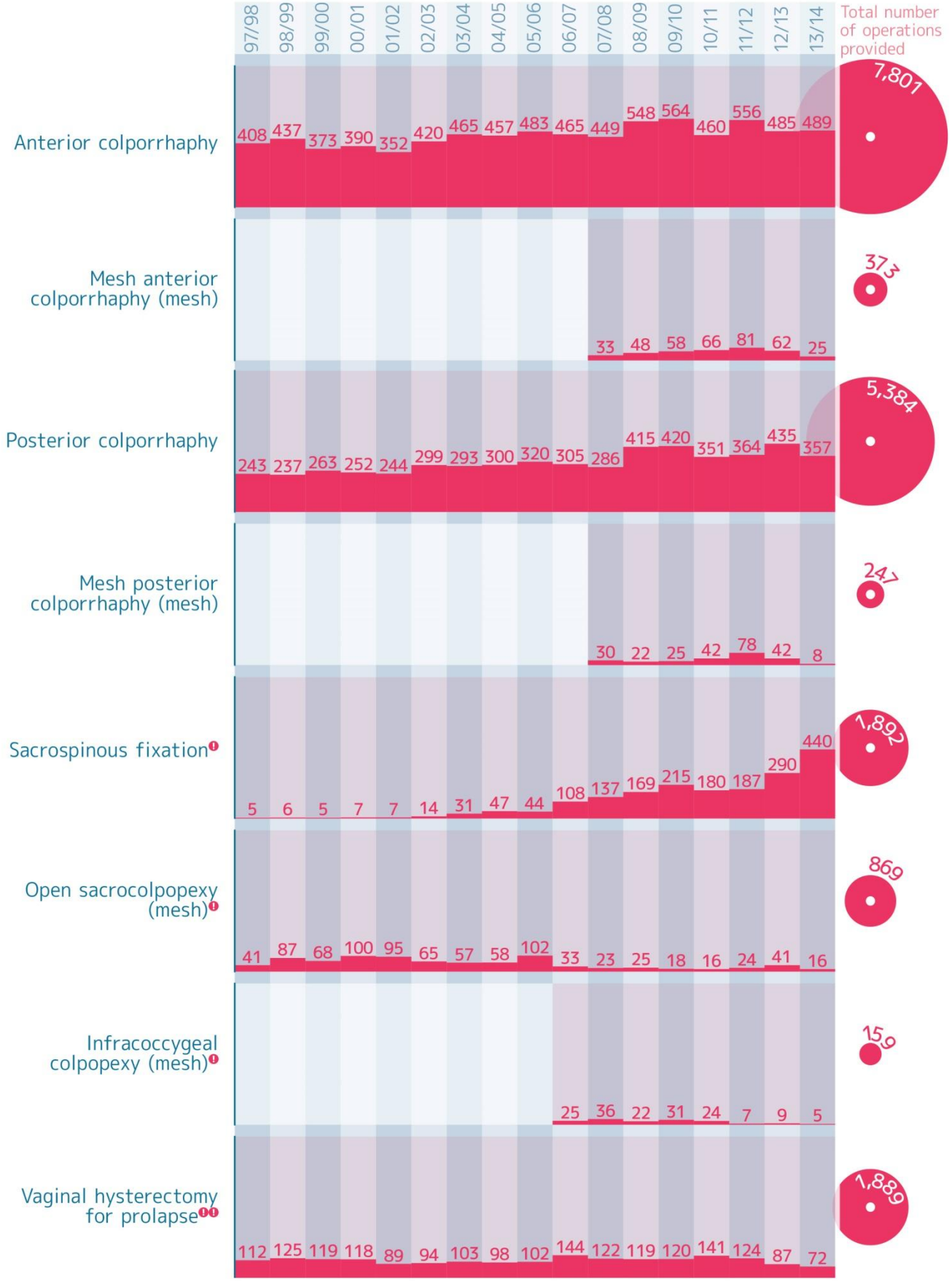
4.1.2 Operations provided for pelvic organ prolapse

Anterior and posterior colporrhaphies (first, single operations) have been provided in increasing numbers over the time period included in the analysis. 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 substantially over recent years. Mesh open sacrocolpopexies have been provided in moderate numbers over the time period included in the analysis. Mesh infracoccygeal colpopexies 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. Moderate numbers of (first, single) vaginal hysterectomies for pelvic organ prolapse have been provided over the time period included in the analysis.

- Sacrospinous fixation, sacrocolpopexy, and infracoccygeal colpopexy are usually 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.

Numbers of first single operations for pelvic organ prolapse by year



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

4.2.1 Main problems

ISD looked at three main problems that can develop after an operation for stress urinary incontinence or pelvic organ prolapse. These were:

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

4.2.2 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.

4.2.3 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.

4.2.4 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 stress urinary incontinence or pelvic organ prolapse operation at a later date. All readmissions for further surgery were counted if they happened within five years of the operation being examined.

4.2.5 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;
- 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.

4.2.6 Additional problems

ISD also looked at the following additional problems that can develop after incontinence or prolapse surgery:

- readmissions for later complications or further incontinence or prolapse surgery;
- readmissions for any reason;
- referrals to an outpatient pain clinic;
- prescriptions for strong pain relief medication that contained an opiate such as codeine;
- death.

This report shows the results relating to the three main problems only. Full results, including those relating to the additional problems, are available at Annex A.

4.2.7 The risk of developing problems after an operation

The risk of developing problems after an operation for stress urinary incontinence or pelvic organ prolapse depends on the type of operation done and on a number of other factors such as:

- age of the woman;
- how many additional health problems she has;
- 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 was not in itself any more risky than standard colporrhaphy.

Statistical methods can be used to take account of all the 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.

4.3 Problems following operations for stress urinary incontinence

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

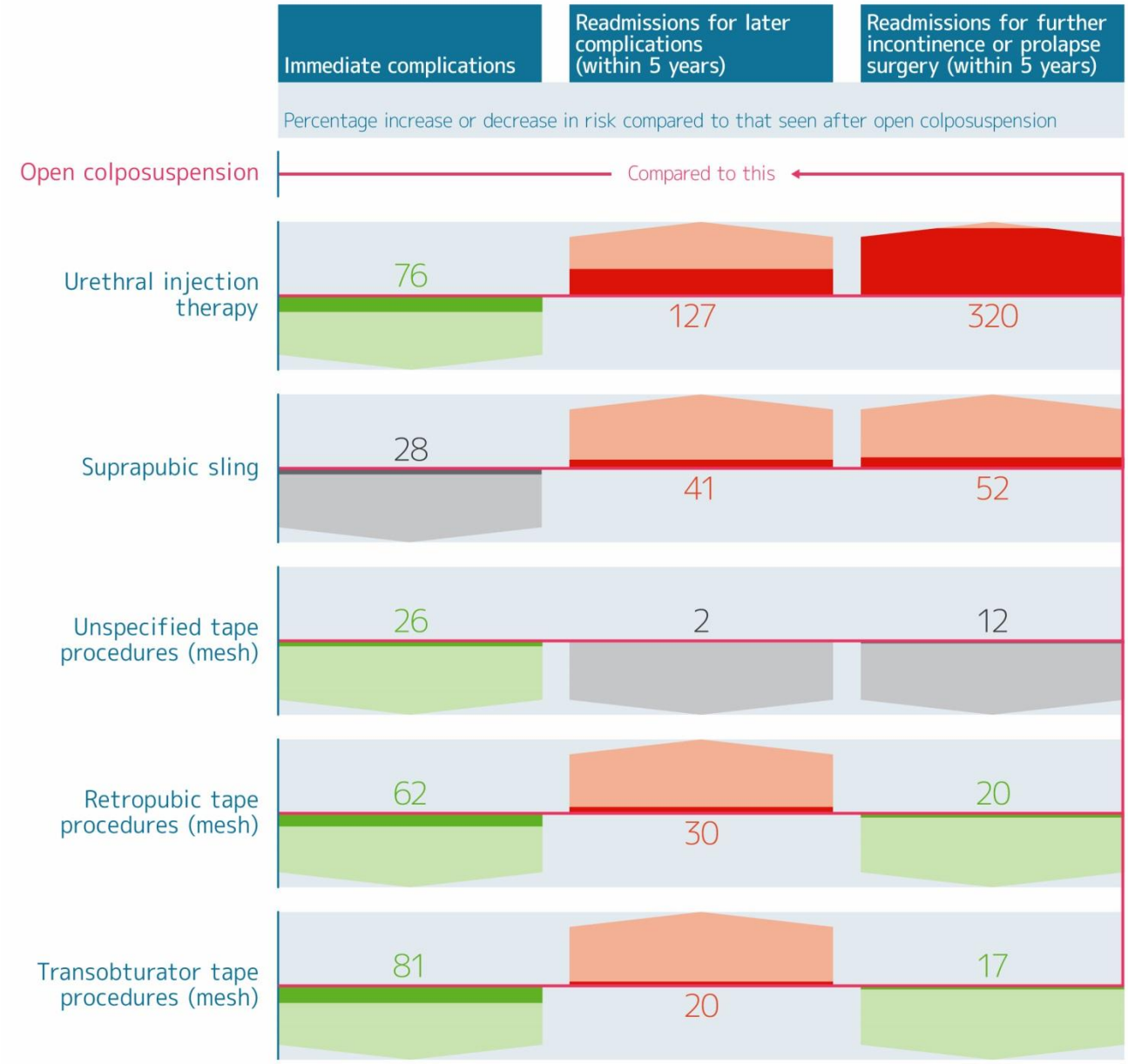
This is the total number of readmissions that would occur on average if 200 women were each monitored for five years after having their stress urinary incontinence operation.

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 a woman'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

4.4 Summary of findings for stress urinary incontinence operations

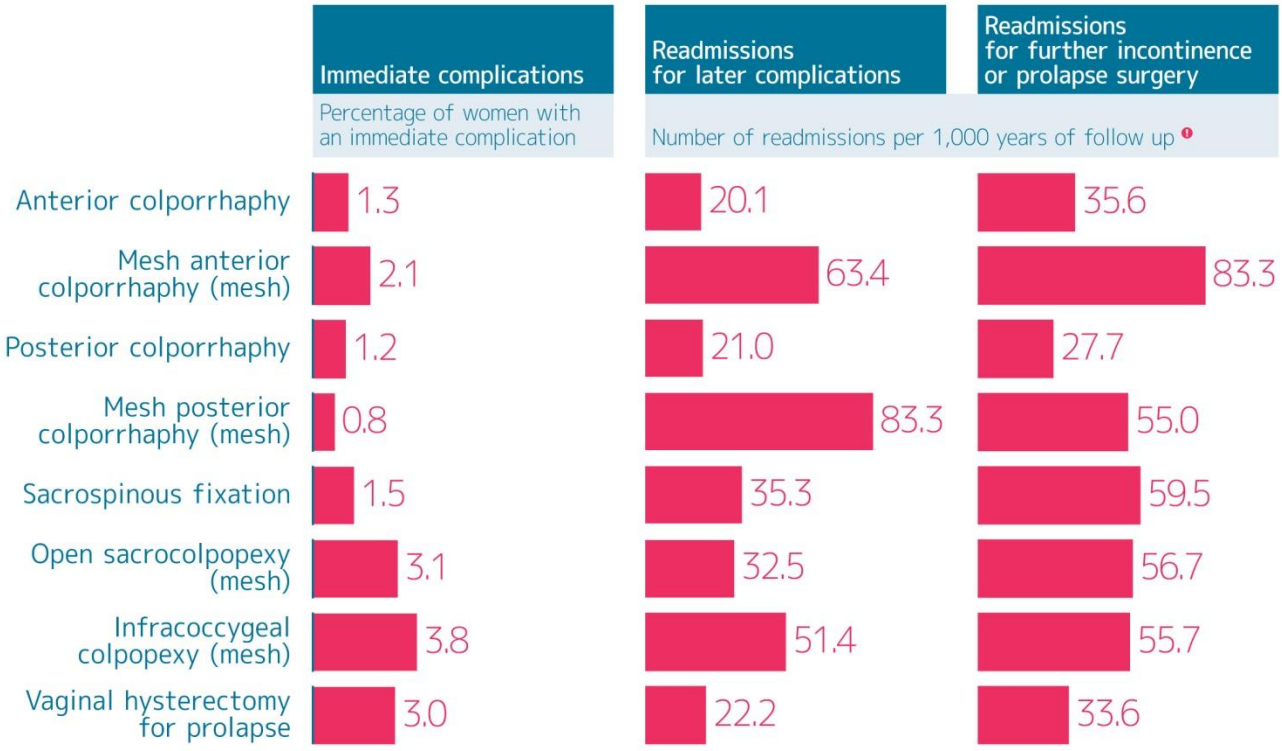
Operations for stress urinary incontinence that involve operating through the abdomen (open colposuspension and suprapubic sling) carried the highest risk of immediate complications. Infections and problems directly related to the operation were the most common immediate complications following all types of stress urinary incontinence operations.

Each of the specific types of operation for stress urinary incontinence included in the analysis carried a somewhat higher risk of being readmitted for a later complication than open colposuspension. The higher risk of later complications seen for urethral injection therapy may be due to the very high risk of needing another incontinence operation after this type of surgery (see below), as every new operation carries new risk of complications. Longer term 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 stress urinary incontinence.

Urethral injection therapy carried a much higher risk of being readmitted for further incontinence or prolapse surgery over the five years following the initial operation than open colposuspension. Suprapubic sling operations carried a somewhat higher risk of needing another operation, and tape operations carried a somewhat lower risk. The type of further surgery needed was different for the different types of stress urinary incontinence operation. Almost all further operations following urethral injection therapy were for stress urinary incontinence, suggesting that the first operation did not completely cure the woman's incontinence. By contrast, around half of further operations following open colposuspension were for stress urinary incontinence and half were for pelvic organ prolapse, suggesting that prolapse problems developed after the colposuspension. After suprapubic slings and tape operations, around 75% of further operations were for incontinence and 25% for prolapse.

4.5 Problems following operations for pelvic organ prolapse

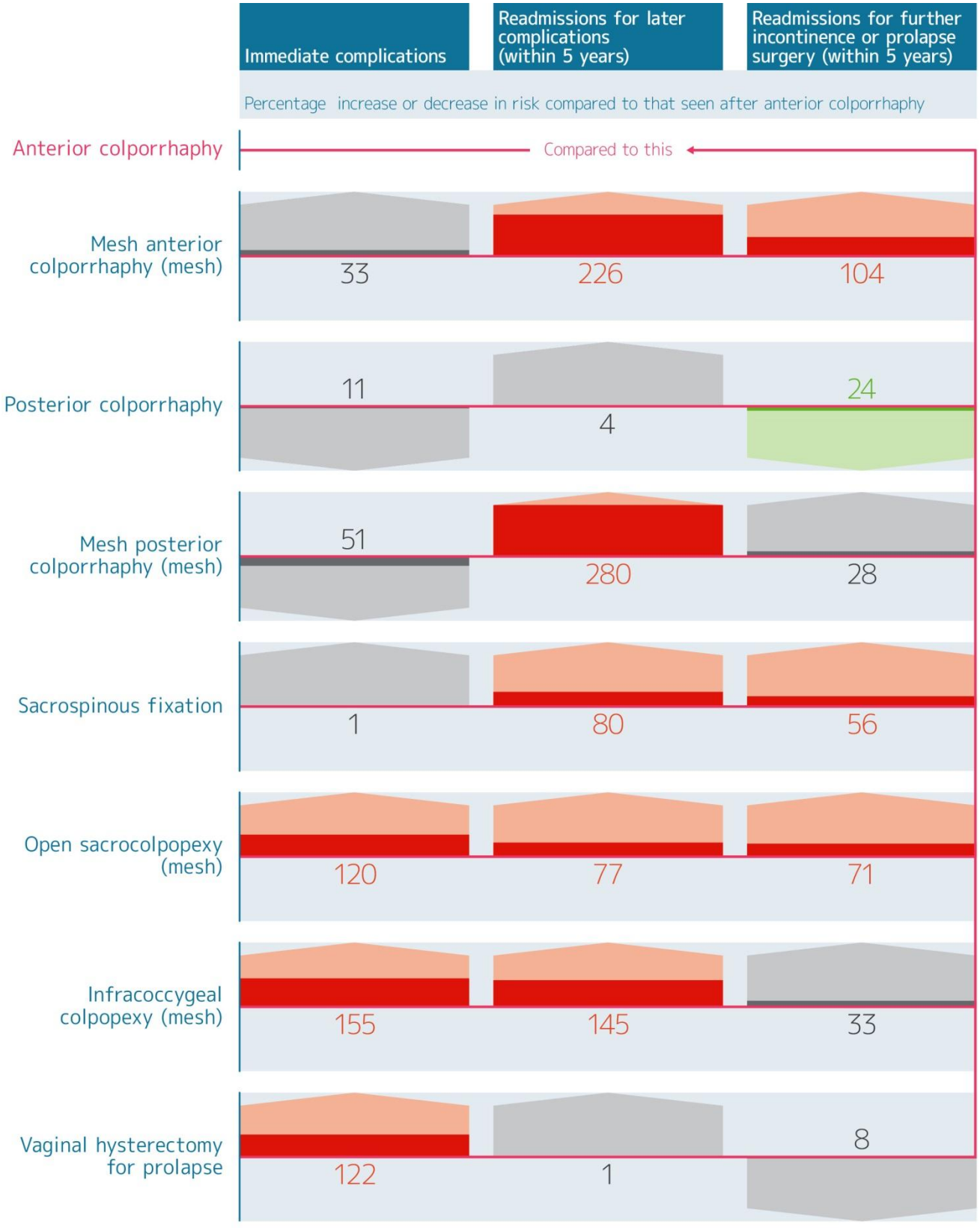
The risk of developing problems after the different types of pelvic organ prolapse operation included in the analysis is shown below.



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

As described before, 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 therefore 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

Red indicates significantly higher risk than that seen after anterior colporrhaphy

4.6 Summary of findings for pelvic organ prolapse operations

Among the pelvic organ prolapse operations included in the analysis, open sacrocolpopexy, infracoccygeal colpopexy, 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 quite common after open sacrocolpopexy and vaginal hysterectomy.

Mesh colporrhaphies (anterior and posterior), sacrospinous fixation, open sacrocolpopexy, and infracoccygeal colpopexy all carried considerably higher risk of being readmitted for a complication over the five years following the initial operation than non mesh anterior colporrhaphy. Longer term problems directly related to the operation and (for mesh operations) further surgery to remove the mesh were the most common later complications seen after operations to treat pelvic organ prolapse.

Mesh anterior colporrhaphy, sacrospinous fixation and open sacrocolpopexy carried a higher risk of being readmitted for further incontinence or prolapse surgery over the five years following the initial operation than non mesh anterior colporrhaphy. Non mesh posterior colporrhaphy carried a somewhat lower risk of being readmitted for further surgery compared to non mesh anterior colporrhaphy. Around 80% of the further operations provided after each type of pelvic organ prolapse operation were for prolapse, and around 20% were for stress urinary incontinence.

4.7 What does all this mean for women and doctors?

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

- the number of operations provided in Scotland for stress urinary incontinence and pelvic organ prolapse;
- how often women having the different types of operation develop problems after their surgery.

Some information on the risks associated with different types of operation for stress urinary incontinence and pelvic organ prolapse was available prior to this study.

For example, there have been a number of clinical trials directly comparing different types of incontinence or prolapse operations. Clinical trials are important to improving understanding of how well operations work however they tend to only include patients who are relatively healthy and only look for problems developing quite quickly after the surgery.

In addition, in the UK, if a patient develops a problem after surgery due to a medical device such as a mesh implant, the patient's doctor is required to notify the problem to the appropriate safety regulator such as the Medicines and Healthcare products Regulatory Agency. This is an important system but it is likely that not all problems, particularly less severe problems, are notified in this way.

This study adds to these other types of information by looking at operations provided as part of routine NHS care in Scotland and looking to see how many problems develop over the five years after the operation.

When thinking about the results of this study it is important to remember that in general only first, single operations for stress urinary incontinence or pelvic organ prolapse were included and that only later complications that were severe enough to require a readmission to hospital were included.

4.8 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 any particular woman.

The risk of immediate complications, later complications, and needing further surgery for stress urinary incontinence or pelvic organ prolapse differs between the different types of operation examined. A specific type of 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, tape (mesh) operations for stress urinary incontinence tend to carry a somewhat higher risk of later complications but a somewhat lower risk of needing further incontinence or prolapse surgery. This highlights the difficult choices facing women and doctors as it is difficult to decide if or when the higher risk of complications would outweigh the lower risk of further surgery.

Compared to open colposuspension, urinary injection therapy carries a much higher risk of needing further surgery and an associated higher risk of later complications.

Mesh colporrhaphies for the treatment of pelvic organ prolapse carry a substantially higher risk of later complications than non mesh colporrhaphies. Mesh colporrhaphies also carry a higher risk of needing further surgery for incontinence or prolapse than non mesh colporrhaphies.

Sacrospinous fixation, open sacrocolpopexy, and infracoccygeal colpopexy for prolapse of the top of the vagina all carry a higher risk of later complications than anterior colporrhaphy. Sacrospinous fixation and open sacrocolpopexy also carry a higher risk of needing further incontinence or prolapse surgery than anterior colporrhaphy.

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

5.1 Evidence availability

This section of the Independent Review (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 an international and national 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.

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 do this by producing reviews that summarise the best available evidence generated through research to inform decisions about health and health care. These Cochrane Reviews are systematic reviews of primary research in human health care and health policy. They are internationally accepted as providing evidence-based health care advice of the highest standard. Cochrane Reviews are updated as needed, ensuring that treatment decisions can be based on the most up-to-date and reliable evidence. The full text of every Cochrane systematic review and the Review Protocols for work in progress, 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.

The following databases were searched for relevant reviews: Cochrane Library (2004 to 2015) and Medline (2004 to 2015). The search strategies used a range of key words and subject headings to identify information focussed on mesh implants for the treatment of stress urinary incontinence (SUI) or pelvic organ prolapse (POP), either alone or in comparison with other, alternative approaches to treatment. These two limits were applied to the identification of systematic reviews and safety reviews for inclusion in the review. Selected material was also limited to data reviews published in English, or where an English translation existed.

National and international websites of medical device safety organisations were also searched.

In total ten safety reviews were included[9]. These were:

- Australia – Therapeutic Goods Administration (2014) [AUS];
- Canada – Health Canada (2014) [CA];

[7] http://www.prisma-statement.org/
[8] http://www.cochranelibrary.com/
[9] A full list of refernces in Chapter 5 can be found in the Reference section

- Denmark – Danish Health and Medicines Authority (2012) [DK];
- European Union (consultation draft) - Scientific Committee on Emerging and Newly Identified Health Risks (2015) [EU];
- Netherlands – Health Care Inspectorate (2013) [NL];
- New Zealand – Accident Compensation Corp. (2015) [NZ1];
- New Zealand – MedSafe (2014) [NZ2];
- UK – Medical Devices and Healthcare Regulatory Authority (2014) [UK1];
- UK – York Health Economics Consortium for the Medical Devices and Healthcare Regulatory Authority (2012) [UK2]; and
- USA – Food and Drug Administration (2011) [USA].

Of these, six were full, completed reviews [NL, NZ 1&2, UK 1&2 and USA], one [EU] was reviewed as a provisional draft report published for consultation and three were based on reported summaries on, or news alerts published on, official websites [AUS, CA and DK].

There were 12 pertinent Cochrane systematic reviews completed, of which nine related to mesh use and alternative management approaches for SUI:

- Glazener CMA & Cooper K. (2001). Anterior vaginal repair for urinary incontinence in women. [Glazener 1];
- Dean N et al (2006). Laparoscopic colposuspension for urinary incontinence in women. [Dean];
- Rehman H (2011). Traditional suburethral sling operations for urinary incontinence in women [Rehman];
- Lapitan MCM et al (2012). Open retropubic colposuspension for urinary incontinence in women. [Lapitan];
- Kirchin V (2012).Urethral injection therapy for urinary incontinence in women.[Kirchin];
- Bakali E et al (2013). Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery in women [Bakali];
- Nambiar A (2014). Single-incision sling operations for urinary incontinence in women. [Nambiar];
- Glazener CMA & Cooper K (2014). Bladder neck needle suspension for urinary incontinence in women. [Glazener 2]; and
- Ford et al (2015). Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. [Ford]

In addition there was one health technology assessment completed in relation to SUI:

- Cody J et al. (2003). Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence.[10] [Cody].

Finally, there were three Cochrane systematic reviews were completed in relation to POP;

[10] NICE CG 171 (2013). *"Urinary incontinence in women: the management of urinary incontinence in women"* provides an update to the first edition of the NICE guidance published in 2006. This was informed by the Cody *et al* systematic review undertaken by the UK HTA included here. The 2013 edition of the NICE guideline added material from RCTs not included in the Cody et al review, as well as drawing on the extant Cochrane Reviews available at that time. As four of these Cochrane Reviews were published in 2013 (and therefore drawing on the same additional RCT material as NICE) or post 2013 (and therefore drawing on material not available to NICE, the decision to remain with the original Systematic Review and the updated Cochrane Reviews was taken.

- Maher C et al (2013). Surgical management of pelvic organ prolapse in women. [Maher];
- Bugge C et al (2013). Pessaries (mechanical devices) for pelvic organ prolapse in women [Bugge]; and
- Hagen S & Stark D. (2011). Conservative prevention and management of pelvic organ prolapse in women. [Hagen].

5.2 Methods

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;
  - 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].

5.3 Safety reviews of mesh implants

5.3.1 Nature of the evidence

At its heart, any review of the safety of a medical device is seeking to determine if the device can continue to be used safely and how best to ensure that patient safety is maintained throughout the medical or surgical processes that implant or connect the device to the patient, without reducing the overall effectiveness of the device.

However, it is fair to say that the 10 safety reviews included in this IR differed in their specific focus, the content of the review, and in which actions were considered necessary. Some provided a comprehensive review of the evidence relating to adverse outcomes following mesh implantation; others considered the effectiveness of the original safety review process; whilst others simply provided health care systems with advice on how to proceed in the current set of circumstance.

In the context of the outcomes being considered, such 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 can be classified as being "narrative reviews", reporting on available evidence. For the purposes of this review of safety reviews, the quality of this evidence has been assessed to be in a range from SIGN 1++ to SIGN 4 evidential levels. As such, they represent very good sources of evidence, within the context of the review's stated aim and focus. Four reviews specifically reviewed the safety of synthetic surgical mesh implants for SUI and POP [AUS, EU, NL, and UK 1&2], of which and one specifically considered whether a withdrawal of mesh for POP [NL]. Three reviews were undertaken to provide updated advice to patients, health care providers and clinicians [CA, DK and USA]. Finally, the two reviews from New Zealand [NZ 1&2] only considered data on adverse outcomes following mesh surgery. It is noteed that whilst seven of the reviews considered both SUI and POP procedures as being within scope [AUS, EU, NZ 1&2 & UK 1&2], three reviews only considered POP procedures [DK, NL and USA].

5.3.2 Results

The extracted data in relation to the safety reviews are summarised within two tables. Table 1a provides a detailed analysis of the data contained in each of the International Agency's Safety Reviews, whilst Table 1b gives general observations and findings form the International Agency Safety Reviews. In this section, the main findings are summarised across the reviews.

None of the safety reviews concludes that there is sufficient evidence to withdraw synthetic mesh from clinical use for either SUI or POP [AUS, CA, EU, DK, NL, NZ 1&2, UK 1&2, USA], though one review does recommend that women with mesh implants for POP are recalled to hospital for clinical assessment [DK].

In a similar way, none of the reviews under-estimate the reality that for some women, the use of mesh devices has been associated with long-term, adverse outcomes that have had severe effects which limit their everyday activities and reduce their quality of life. [AUS, CA, EU, DK, NL, NZ1&2, UK1&2, USA]

Mesh safety in treating SUI

The scientific rationale for the use of synthetic mesh is specifically considered in the safety review from the EU's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) [EU].

They conclude in relation to SUI procedures that there is a robust evidence-base to support the use of Mid Urethral Slings (MUS) which they described as being *"the most extensively reviewed and evaluated procedure for female SUI now in use"* [EU]. This is the case for both retropubic and transobturator MUS procedures [EU]. It should be noted that the safety review by the Australian Therapeutic Goods Agency, as reported on their website described the evidence base for SUI as "adequate". (AUS) The EU review notes that, as with any surgical procedure, there can be complications associated with MUS. Where these do occur, the surgical complication rates are low [AUS, EU, NZ1, UK 1&2]. Complications found to be associated with MUS procedures include bleeding, damage to the bladder and bowel, voiding difficulty, mesh tape exposure and pelvic pain. All these complications may require repeated surgery, but this is uncommon. [CA, EU, NZ1, UK 1&2] What evidence of longer term effectiveness that does exist suggests that treatment success decreases over five years for both retropubic and transobturator MUS procedures, though patient satisfaction with both types of slings remained high. [EU] New mesh erosions occurred in both types over time at a similar rate. [EU, NZ1, UK1&2]

Mesh safety in treating POP

For POP procedures the EU safety review concluded that there is convincing evidence in favour of the use of a synthetic mesh to repair a prolapsed anterior vaginal wall. The evidence suggests that mesh implants are both subjectively and objectively superior in terms of clinical outcomes to a native tissue repair, though the reported health-related QoL post-surgery is no different (EU). Complications are reported with the rate of new pelvic organ prolapse in the untreated vaginal compartment significantly higher when synthetic mesh is used, though there is no evidence that this leads to a need for subsequent operations for POP. A similar pattern is observed for post-procedure SUI where the use of mesh is associated with higher rates of reported SUI; again this is not reflected in the need for SUI surgery. [EU] Mesh exposure is reported frequently following anterior wall repair with mesh, though there are no differences in reported rates for new dyspareunia or sexual dysfunction. [EU]

For repairs to the posterior vaginal compartment, the review concluded that there is moderate evidence that the use of mesh results in higher rates of objective cure. This, however, is also associated with higher rates of new POP of the anterior vaginal compartment. Subjective cure or cases of new SUI are observed to be no different from native tissue repair. As with anterior vaginal wall repairs, mesh exposures are reported frequently. [EU, NZ1] This pattern is also broadly observed for mesh repairs in more than one vaginal compartment. Repairs using mesh were found to result in higher rates of subjective and objective cure, but also in significantly higher rates of new POP of the untreated vaginal compartments. No differences in other outcomes or surgical complications were found, though mesh exposures were frequently reported. [EU, NZ1]

Surgical approach to POP repair was considered in the Australian review. This concluded that whilst there was evidence of effective use of mesh in abdominal POP, there was insufficient evidence to support its use in transvaginal POP repairs. [AUS] This is consistent with the advice provided by both Health Canada and the Food and Drug Administration (FDA) in the United States which advised clinicians to note that transvaginal procedures may carry a higher risk of complications than abdominal POP or native tissue repairs. [CA, USA]

For all types of POP repair, reported mesh exposure, (symptomatic or asymptomatic), obviously differed from that in native tissue repair (observed complication rates 4-19%); however no differences in complication rates were observed for dyspareunia (post-surgical

or new), post-surgical pain, haemorrhage, bowel and/or rectal injury, urinary infection and postoperative urinary retention between mesh and native tissue surgery. [EU] Overall, complication rates for POP were reported to be low. [AUS, EU] However, it was noted that the follow-ups in papers in these meta-analyses were mainly short-term (up to 12 months); a few were medium-term (1-5 years). Long-term results (5-10 years) of RCT's are not yet published but are needed for the full appreciation of outcomes. [EU, UK 1&2, USA]

Risk factors for adverse outcomes

The EU review undertook a very detailed analysis to identify possible sources of risk associated with adverse outcomes in the use of mesh implants. This review has been used as the basis for this section of the report, augmented by other evidence from safety reviews where appropriate.

An analysis of adverse outcomes associated with the type of synthetic surgical meshes for treating SUI and POP was undertaken. At present, four major types of mesh are produced commercially. The data suggested that two types of mesh are "most appropriate" for mesh implants:

- synthetic mesh type 1 (polypropylene monofilament, macroporous >75µm):
  - synthetic mesh for vaginal use; and
  - synthetic mesh for insertion via the abdominal route; and
- synthetic mesh type 3 (polyester ,multifilament , microporous <10µm):
  - synthetic mesh for insertion via the abdominal route .[EU]

Synthetic mesh type 2 (mono and multifilament, microporous, and synthetic mesh type 4 (monofilament, nanoporous <1µm) were considered to be "not appropriate" for this clinical use. For all other forms of synthetic mesh materials, the EU review concluded that there was insufficient evidence on which to base an opinion. [EU] When considering factors which may be associated with mesh design, the review highlighted a number of factors that may be possible potential sources of risk. These included: overall surface area of mesh used, (which is greater for POP than for SUI); the composition of the mesh weave and its porosity; the physical character of the mesh and its durability within the context of long-term indwelling of the device in human tissue on a long-term basis. [EU]

Whilst the available evidence only allows for a two year follow up, specific surgical techniques were noted to be associated with a higher risk of adverse outcomes. At the most fundamental level, it was noted that mesh exposure is ***only*** seen with a non-absorbable material such as synthetic mesh, this is true of all synthetic materials. Generally, it was concluded that vaginal surgery is associated with a higher risk of mesh-related complications and morbidity than abdominal mesh procedures. [AUS, CA, EU, NZ1, UK 1&2, USA] Overall, the EU review was of the opinion that the risk assessment of the use of mesh needs to differentiate between its use in SUI and POP in that the evidence:

- on efficacy and use of implanted meshes for SUI suggested that the associated risk of complications was low (albeit that follow data were limited and there was an absence of long-term -up (5-10 years) follow up data;
- on vaginal insertion of non-absorbable synthetic mesh with a large surface area for POP suggests it is associated with the highest incidence of complications; and
- that vaginally implanted mesh for POP is associated with increased risks compared to mesh implantation for SUI. [AUS, CA, EU, NZ1, UK 1&2. USA]

In the light of these considerations, the EU review concluded that the use vaginally implanted mesh for POP should be restricted [EU]. This is, however, the only review to reach such a conclusion.

Surgeons' experience of the procedures in question was considered a risk factor for adverse outcomes in a number of the safety reviews. These can be summarised as:

- surgical experience in SUI and POP MUS procedures – the evidence suggests only surgeons with experience should perform these procedures, though there is not clarity on the definition of an "experienced surgeon"; [AUS, EU, UK1&2]
- level of surgical training and maintaining competence – the evidence suggests that successful learning may vary from one trainee to another and may be affected by factors such as: the trainee's prior surgical experience; the difficulty of the procedures; and the level/quality of the clinical supervision; [CA, EU, UK1, USA] and
- adherence with clinical guidelines – the evidence suggests that there is a greater risk of adverse outcomes if surgeons do not follow appropriate clinical guidelines or the manufacturer's instructions. [EU, NZ1, UK 1&2]

The potential to identify patient groups that were at a higher risk of complication was noted in four safety reviews [AUS, EU, UK1&2]. However, there is at present very little robust evidence available to inform patient selection when synthetic mesh is proposed for use in POP or SUI procedures. More research needs to be done on this, at present it is recognised that: smoking is statistically associated with an increased risk of mesh exposure; and factors such as obesity and age may also be important. In this latter regard, the EU review concluded that it was prudent to be "more reluctant" to use mesh devices for POP in younger age groups. [EU]

Patient Consent

The need to ensure that patient decisions to undergo a mesh procedure must be based on appropriately informed patient consent is noted in six safety reviews [AUS, CA, EU, NL, UK1, USA]. They note that gaining effective patient consent should be the result of a wide-ranging discussion regarding the patient's specific situation and all the potential benefits and risks from the use of synthetic mesh for either SUI or POP procedures. Safety reviews providing specific guidance on what should be included in such patient consent discussions include those from Health Canada [CA], SCENIHR [EU], The Dutch Healthcare Inspectorate [NL], the UK Medicines and Healthcare products Regulatory Agency [UK1], and the US Food and Drug Administration. [USA]

Data gaps and long-term follow up

The need for more detailed data, or the relative lack of such data, was mentioned in some way by all the safety reviews. In general data identified as being lacking related to:

- research evidence on long-term follow up (greater than 5 years post-surgery) for patients receiving mesh procedures for SUI or POP; [EU, UK1&2, USA] ,
- the lack of traceability for individual mesh devices used in such procedures; [EU]
- the lack of data on the specific surgical approaches used in mesh procedures; [EU], and
- the lack of comprehensive adverse outcome reporting. [CA, EU, UK1&2, NL, USA]

Whilst there were differences in proposed approaches to deal with the evidential gaps identified, it is notable that these focused on the need for effective data capture and reporting.

Medical device regulatory systems

Finally, six safety reviews commented on aspects of the processes by which medical devices are assessed for their safety and what could be done to improve this. [AUS, CA, EU, NL, UK1, USA] Whilst the Therapeutic Goods Administration in Australia have indicated that they are reviewing the safety compliance of all mesh devices [AUS] and the US Food and Drug Administration has taken action to bring mesh devices for POP into a level of regulatory requirement more in line with that in Europe, [USA] the most comprehensive consideration of the overall system of assessing medical devices and safety was provided by the Dutch Healthcare Inspectorate. [NL]. They concluded that whilst the processes by which mesh devices had been assessed as being safe were in line with the Dutch regulatory framework, there were areas for improvement. The first of these was that the requirements for the evaluation process of devices should be made stricter, with more time taken to assess safety and judgements taken in the light of clear criteria for effectiveness and safety. The second improvement was that the formal Vigilance and Post-Marketing Surveillance stage of the evaluation process be strengthened in European legislation. This improvement, which was recommended in three other safety reviews [CA, UK1, USA], would allow for longer-term assessment of complications and adverse outcomes, especially when novel procedures were being used with devices deemed to already be safe. [CA]. Finally, the agency recommended the creation of a central, independent registry for implants, recording product information and patient information as a minimum. It was noted, however, that this was not specific to mesh devices and that the registry should include all implants, across all specialties. [NL] Clearly these recommendations are specific to the Dutch circumstances, though the revised EU Medical Devices Directive will address several of these requirements [http://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework/index_en.htm]

5.3.3 Interpretation

The key messages from this analysis are:

- No safety review by an international agency has called for mesh devices used in SUI and POP procedures to be withdrawn from use.
- For some women, there are long-term, adverse outcomes associated with the use of mesh devices that have had severe effects on their everyday activities and quality of life.
- The use of mesh for MUS in treating SUI is generally considered effective with low complication rates, accepting that long-term follow up data are not presently available.
- The use of mesh for some forms of POP repair is considered effective, provided that it is used in abdominal rather than vaginal procedures. The risk of complications/adverse outcomes is higher fololowing the use of mesh for POP than for SUI.
- Risk factors for adverse outcomes include: surgical approach, the experience of the surgeon and some patient characteristics. Factors which may influence risk include the physical characteristics of the mesh device used.
- Well-informed patient consent is essential.
- Data associated with long-term follow up of mesh procedures are not currently collected. This needs to be remedied.

- The systems used to assess the safety of medical devices could be improved, notably in the area of vigilance and post-marketing surveillance.

5.4 Systematic reviews of effectiveness of mesh in stress urinary incontinenece and pelvic organ prolapse

5.4.1 Nature of the evidence

The systematic reviews included in this section of the report are either Cochrane systematic reviews (12 reviews) or Health Technology Assessment s (one review). In each case the methods adopted in creating these reviews mean that they fulfil the highest level of SIGN evidence grades in that they are 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).

Using such systematic reviews, allows the professional and patients within the Independent Review (IR), and those who will read this IR more widely, access to the most recent clinical knowledge in a more readily accessible form. In the context of this review, they can facilitate the process to evaluate clinical effectiveness data of treatments and services across a range of settings and circumstances.

However using such systematic reviews does have some drawbacks. For example, they are not good at summarising evidence "gaps" (you cannot summarise what is not there), at the same time the review system will still work with evidence which is of differing "robustness". Though in this latter regard, the methods used do include ways of assessing the underlying strength or weakness of data included in the systematic review. Another limitation that should be noted is that systematic reviews tend to focus on the experiences of patient groups and not on individual patients. As such it is better at summarising research, than personal experiences.

Whilst such systematic reviews still require interpretation of the reviewed evidence, not least in how it relates to clinical effectiveness and public / patient experience, they are the best available evidence on which to base such assessments.

5.4.2 Results

As noted above (section 5.2 above) 12 systematic reviews were included in this analysis. Nine of these related to SUI procedures and three to POP procedures. The systematic reviews cover not only mesh procedures, but also comparisons with conventional treatment. This was to allow consideration of the effectiveness of mesh against other treatment approaches. The results of the analysis in relation to SUI procedures is shown in Table 2a, whilst that for POP procedures is shown in Table 2b.

In this section, the major conclusions from each of the systematic reviews in relation to effectiveness (clinical and patient outcomes and QoL measures) are presented.

Effectiveness of SUI Procedures
Anterior vaginal repair (without mesh) for urinary incontinence in women [Glazener1]

Open abdominal surgery (retropubic suspension) was more effective than anterior vaginal repair for the treatment of primary urodynamic stress incontinence. The effect was longer lasting, whether or not the women had associated prolapse. Marginal differences in QoL recorded.

No differences in effectiveness or QoL were observed between anterior vaginal repair and needle suspension. No comparative trials were found between anterior vaginal repair and mock operation, laparoscopic colposuspension, and suburethral sling procedures.

Overall the evidence was assessed as being of poor overall quality. Long term follow up data in trials included were limited.

Effectiveness of tension-free vaginal tape [Cody]
Laparoscopic colposuspension and traditional slings have broadly similar cure rates to Tension-free Vaginal Tape (TVT) and open colposuspension. The QoL of patients treated with TVT were significantly better in relation to their emotional state, social functioning, and mental health. However generally all QoL was shown to be better post-operatively compared to pre-operation levels.

Overall, the authors considered that there were "limited" data on which to base the review. The lack of long-term follow up data was specifically noted.

Laparoscopic colposuspension for urinary incontinence [Dean]
Laparoscopic colposuspension is reported to provide a lower objective cure rate for SUI over colposuspension by open surgery (in the shorter-term, less than 18 months). However, no significant differences were found in an 18 month to five year period. There were significantly fewer perioperative complications with Laparoscopic colposuspension and some evidence for less pain. The QoL data did not suggest any differences between the two.

In comparison with vaginal mesh slings (self-fixing slings), laparoscopic colposuspension was found to be less effective than mesh in objective cure rate for SUI, though there was no statistically significant difference in subjective cure rate between them. The data on QoL was not pooled, meaning a single analysis was not possible. Of five studies, only one suggested that mesh was associated with improved QoL

When differing approaches to laparoscopic colposuspension were compared it was reported that objective and subjective cure rates were higher when it was performed using sutures for the repair than when it was performed using mesh fixed with surgical staples. In a further comparison, suture repairs that used two sutures were more effective than those using a single suture. QoL was not assessed in these trials.

No research trials which compared laparoscopic colposuspension to mock operation, conservative management, needle suspension, traditional sling procedures, anterior vaginal repairs or peri-urethral injections were found.

The authors considered that the data was adequate in 13 trials and of uncertain quality in a further eight included in the systematic review. One trial was described as inadequate. The lack of long-term follow up data was noted as a specific omission which limited the analysis.

Traditional suburethral sling operations for urinary incontinence [Rehman]
The systematic review concluded that in trials which compared traditional slings with minimally invasive slings using synthetic mesh, there were no differences in the effectiveness of either type of sling on objective or subjective cure rate for SUI. Whilst QoL data were collected in some studies, no differences were found between types of sling procedure.

In comparisons with other surgical techniques – open abdominal retropubic colposuspension, abdominal and vaginal needle suspension and trials of different types of traditional sling materials – suggested that traditional slings may be equally as effective as other surgical approaches. Whilst not suitable for detailed analysis QoL data suggested that patients undergoing open abdominal retropubic colposuspension had better post-operative QoL than those with a traditional sling procedure.

Traditional slings may be more effective than either drugs or injectable agents, synthetic material. However, in comparisons with conservative management, anterior vaginal repair and laparoscopic procedures were not found to be more effective.

The authors considered that caution was needed in interpreting the results of the systematic review. The quality of evidence in the studies was variable; with only short-term follow-up and the lack of focus on primary outcome data (e.g. complication rates).

Open retropubic colposuspension for urinary incontinence [Lapitan]
Open retropubic colposuspension was found to be an effective treatment for stress urinary incontinence compared with other forms of surgery (anterior colporrhaphy (repair), needle suspension, and laparoscopic colposuspension). Long term data were analysed suggesting that it was effective in the long term with approximately 80% patients undergoing open retropubic colposuspension still continent at 5 years. QoL data in these trials were sparse and whilst post-operative improvements were observed, little evidence for differences between procedures was found.

Sling procedures, both traditional and minimally invasive mesh sling procedures, were found to be not significantly different from open retropubic colposuspension in objective or subjective SUI cure. QoL data also showed no significant differences.

More limited evidence in relation to open retropubic colposuspension compared with conservative management, pharmaceutical drug treatment, and injectable synthetic material suggested that surgical intervention may be more successful. No trial data was found for other possible comparisons.

Overall the authors considered the data quality to be classed as “unclear”, though the ability to analyse longer term data was welcomed.

Urethral injection therapy for urinary incontinence [Kirchin]
Injection therapy with synthetic particulate material shows a short-term advantage over home pelvic floor muscle training in reducing SUI and an increased QoL. However, as follow up was limited to three months, it is not clear if this advantage is maintained.

Injection therapy appears inferior to open surgery at 12 months, but has a better safety profile.

Out of 14 trials in the systematic review, risk of bias was assessed as either “low” or “unclear” in all but one trial. This one trial was assessed at “high” risk of bias. Only short-term follow data was considered.

Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery [Bakali]
No trials were found suitable for inclusion.

Non RCT data suggest that repeat suburethral tape surgery is less effective than for primary surgery. There is some evidence that retropubic suburethral tapes are superior to transobturator tapes as secondary procedures.

Single-incision sling operations for urinary incontinence in women [Nambiar]
Single incision (mini) slings were found to be less effective than retropubic, minimally invasive slings in achieving objective or subjective cure. QoL was reported to be statistically significantly better in the retropubic group.

Twenty trials were included which comparison between single incision slings with obturator minimally invasive slings; either the medial-to-lateral ’inside out’ surgical approach (TVT-O) or the lateral-to-medial ’outside-in’ approach (TOT). Objective and subjective cure rates were found to be significantly better for both TVT-O and TVT-O/TOT combined than for single incision slings. No difference was found for TOT alone compared with the single incision sling. No QoL data was reported.

No trials were identified in which single-incision slings were compared with no treatment, conservative treatment, open colposuspension or laparoscopic procedures. Whilst trials comparing them to traditional sub-urethral slings were found, the authors did not consider the data of an appropriate quality on which to confidently identify any differences between any of the different types of single-incision sling.

The overall quality of the data included was assessed by the authors as variable. About half of the trials were considered to have used using adequate methods to reduce the risk of bias, while in the other half, the methods used were considered to be inadequate or were not described. Long term follow up data were noted as lacking.

Bladder neck needle suspension for urinary incontinence in women [Glazener2]
Needle suspension was compared with open abdominal retropubic suspension using different techniques. Subjective outcome at both under and at one year suggested that open abdominal retropubic suspension was the more effective treatment.

When compared with anterior vaginal repair, needle suspension was found to be similar in terms of subjective cure rates after 12 months and long-term problems with voiding dysfunction.

One small trial compared needle suspension with suburethral sling procedures. However it was too small to address differences in cure rates,

No statistically significant differences were found in the one trial that presented comparisons between types of NS. No trials were found which compared needle suspension with mock procedure, conservative management, laparoscopic colposuspension, periurethral injections, or pharmaceutical drug treatment.

Overall the authors considered the quality of the data low. Long term follow data was only available for three of the included trials.

Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women [Ford]
Mid-urethral slings using mesh implants were found to be a highly effective treatment for SUI. Robust short term data suggests no significant differences between the two insertion routes, transobturator; and retropubic, in subjective or objective cure of incontinence. . There is some evidence that the observed equivalence in subjective and objective cure rates in the medium (1 to 5 years) and longer term (over 5 years).

The trials that compared the retropubic, bottom-to-top approach with the retropubic, top-to-bottom one approach showed that inserting the mesh tape through the retropubic route from bottom to- top is the more effective than the top-to-bottom approaches.

Comparisons between the transobturator, medial-to-lateral approach with the transobturator, lateral-to-medial approach showed no evidence of any differences between the two approaches with respect to SUI outcomes. When a retropubic route is employed, a bottom-to-top approach is more effective in terms of subjective cure than a top-to-bottom approach. When traversing the transobturator route, the evidence suggested that medial-to-lateral ('inside-out') and lateral-to-medial ('outside-in') approaches have similar effects.

No significant differences in efficacy or surgical outcomes were observed in those studies which compared one method of mid-urethral tape insertion with another using the same insertion route.

Differences between monofilament tapes and multifilament tapes were assessed. No statistical differences in objective or subjective cure rates were found.

As a general finding, QoL was found to improve significantly post-operatively within treatment groups, whatever the comparison being undertaken. However, no statistically significant differences were found *between* groups in the comparisons.

The majority of the trials included in the systematic review were rated by the authors as being of unclear quality. Longer term data, particularly on the long-term effects of surgery, and how the different insertion routes affect long-term outcomes are lacking.

Effectiveness of POP Procedures

Surgical management of pelvic organ prolapse in women [Maher]
The findings in relation to POP surgery are complex. Overall, the authors conclude that the data they have reviewed does not provide sufficient evidence to guide clinical practice.

Abdominal sacral colpopexy was associated with a lower rate of recurrent vault prolapse and less dyspareunia than vaginal sacrospinous colpopexy.

The use of absorbable polyglactin mesh overlay, absorbable porcine dermis or polypropylene mesh at the time of anterior vaginal wall repair reduces the risk of recurrent cystocele on examination, however improved outcomes including patient satisfaction, quality of life and reduced operations for recurrences have not yet been demonstrated.

Posterior vaginal wall repair may have a better anatomical success rate than transanal repair in the management of posterior vaginal wall prolapse, but the clinical effects are uncertain. There is no evidence to support the use of graft materials in the posterior compartment.

The evidence at this stage does not support the use of transvaginal combined total, anterior or posterior mesh kits for multi-compartment prolapse. Whilst anatomical outcome may be improved (as compared to native tissue repair) no difference was found in symptoms or quality of life outcomes. The mesh exposure rate was nearly 1 in 5, with nearly 1 in 10 requiring surgical intervention.

Performing continence surgery at the time of prolapse surgery in women with stress urinary incontinence is likely to be beneficial. This benefit is also associated with women undergoing prolapse who have been found to have occult stress incontinence pre-operatively.

Generally, the quality of the trials was described as "variable" by the authors in almost all cases, they considered that it was "unclear" what risk of bias the included trials presented. Long-term outcomes were noted as being absent. They should be reported at least at two and five years after surgery, preferably longer.

Pessaries (mechanical devices) for pelvic organ prolapse in women [Bugge]
Formal comparison between the use of a mechanical device and the use of any surgery, with or without any form of mesh, were not considered in this review.

Conservative prevention and management of pelvic organ prolapse in women [Hagen]
In relation to this systematic review, only data relating to the comparison of physical and/or lifestyle interventions supplementing surgery with surgery alone was included. In three areas: physical intervention versus surgery; lifestyle intervention versus surgery; and combined physical and lifestyle intervention against surgery, no trials were identified.

The two trials identified in this systematic review provide contradictory findings. Whilst both compared pelvic floor muscle training (PFMT) following surgery with a control group who underwent surgery alone. In one trial the results indicate that despite the tendency towards improvement in the PFMT group over time, there were no significant differences in manometry scores between the controls and those in the PFMT arm. Change from baseline in the other objective measures (vaginal resting pressure, peak maximum vaginal squeeze pressure, and area maximum vaginal squeeze pressure) did not differ between groups. The second trial, however, reported that improvement in mean maximum pelvic floor muscle squeeze was significantly greater in the PFMT group than the control group.
Both trials reported on urinary function. In one trial it was reported that there were no significant differences between the intervention and control groups in reported incontinence using validated instruments. The second trial reported a significant improvement in urine leakage for both the intervention and control groups, but no significant difference in improvement between the groups.

5.4.3 Interpretation

SUI Procedures

The key messages from these analyses are:

- Abdominal surgery (retropubic colposuspension) was more effective than anterior vaginal repair for the treatment of primary urodynamic stress incontinence.

- Mid-urethral sling procedures were found to be as effective as traditional surgical approaches for SUI. Marginal benefits in QoL were noted.

- Mid-urethral sling procedures were found to be objectively more effective than laparoscopic colposuspension, but not subjectively so. Laparoscopic colposuspension was found to be no more effective than open colposuspension in the medium term. The type of surgical approach to make repairs when undertaking laparoscopic colposuspension may be a factor in achieving successful outcomes. Findings from analysis of QoL data were limited.

- Traditional sling operations are as effective as either mid-urethral sling procedures for SUI or other surgical approaches.

- Whilst open retropubic colposuspension was found to be more effective than other surgical approaches, it was not found to be significantly different from mid-urethral tape procedures.

- What data there is suggests that treating SUI with injectable materials is better than conservative management, but less effective than open surgery.

- There is limited (non-RCT) evidence that retropubic suburethral mesh tapes are superior to transobturator mesh tapes when used in repeat procedures.

- Women were more likely to remain incontinent after surgery with single-incision (mini) slings than after use of inside-out transobturator (TVT-O) tapes.

- Open abdominal retropubic suspension was found to be more effective than needle suspension. Anterior vaginal repair and suburethral (mesh) slings were not significantly different.

- Mid-urethral slings using mesh implants were found to be a highly effective treatment for SUI.

POP Procedures

The key messages from these analyses are:

- The findings in relation to POP surgery are complex. Overall, the authors conclude that the data they have reviewed does not provide sufficient evidence to guide clinical practice.

- Whilst some trial findings to support the use of pelvic floor muscle training as a treatment for women with prolapse, the evidence remains complex and limited. There was insufficient evidence about other interventions or combinations of interventions to inform practice

5.5 Systematic Reviews of Adverse Outcomes in SUI and POP

5.5.1 Nature of the evidence

See section 5.4.1 above.

5.5.2 Results

As noted above (section 5.2 above) 12 systematic reviews were included in this analysis. Nine of these related to SUI procedures and three to POP procedures. The systematic reviews cover not only mesh procedures, but also comparisons with conventional treatment. This was to allow consideration of the effectiveness of mesh against other treatment approaches. The results of the analysis in relation to SUI procedures in shown in Table 2a, whilst that for POP procedures is shown in Table 2b.

In this section, the major conclusions from each of the systematic reviews in relation to adverse outcomes are presented.

Adverse Outcomes in SUI procedures

*Anterior vaginal repair for urinary incontinence in women (*Glazener1]
Clinically relevant post-operative complications were reported for both abdominal retropubic suspension and anterior vaginal repair, but the complication rates were not different. New or recurrent prolapse was found to be less likely after anterior vaginal repair, whilst repeat surgery for recurrent incontinence was higher after anterior vaginal repair. No other differences were found for any other adverse outcomes.

No long-term adverse outcomes were considered.

Adverse outcomes associated with tension-free vaginal tape [Cody]
There were no significant differences in adverse outcomes between TVT and comparative surgery reported.

Laparoscopic colposuspension for urinary incontinence [Dean]
Significantly fewer perioperative complications were reported for laparoscopic colposuspension compared with open colposuspension.

No robust, statistically significant differences were found in adverse outcome rates for any other comparisons included in the systematic review. This included the comparison between laparoscopic colposuspension and vaginal mid-urethral mesh tape procedures.

No long-term adverse outcomes were considered.

Traditional suburethral sling operations for urinary incontinence [Rehman]
When comparing traditional slings with mid-urethral mesh tape procedures, perioperative complication rates were found to be higher for the traditional sling. New cases of overactive bladder function were also noted, but no other adverse outcomes were found to be significantly different.

Significantly fewer perioperative complications were found amongst open colposuspension patients than traditional sling patients. Voiding dysfunction was also significantly higher after traditional sling surgery compared with open colposuspension. Significantly more women

who had traditional slings had post-operative complications compared with those who had needle suspension.

No long term adverse outcomes were considered.

Open retropubic colposuspension for urinary incontinence [Lapitan]
Perioperative complication rates for open retropubic colposuspension were lower than those observed for both needle suspension or anterior colporrhaphy. The procedure may also be associated with lower rates of bladder perforation when compared with laparoscopic colposuspension.

The long-term profile of adverse outcomes for sling procedures, in particular with the use of mid-urethral mesh tape procedures, is still unclear.

Urethral injection therapy for urinary incontinence [Kirchin]
Overall, the complication rate for injections was lower than for open surgery. However, the follow up periods were very short and as the approach is not efficacious, the adverse events are not clinically relevant.

Treatment of recurrent stress urinary incontinence after failed minimally invasive synthetic suburethral tape surgery [Bakali]
No trials were included in the systematic review.

Single-incision sling operations for urinary incontinence in women [Nambiar]
Both repeat stress incontinence surgery and new cases of urinary urgency were found to be associated with single incision (mini) slings compared to minimally invasive retropublic slings.

In the comparison between single incision slings and transobturator mid-urtheral mesh tapes, a complex set of adverse outcomes were reported. These may be summarised as:

- Vaginal mesh exposure (erosion): TVT-O had a significantly lower risk of mesh erosion than single-incision slings. No statistically significant difference between the TOT and single incision sling treatment groups.
- Post-operative pain or discomfort: Both TVT-O and TOT patients had more post-operative pain and discomfort than single-incision sling patients.
- Long-term pain or discomfort: TOT was found to be associated with higher rates of long-term pain than single-incision. No differences were observed for TVT-O compared with single-incision slings. TOT and TVT-O are both obturator devices.
- Repeat stress incontinence surgery: women undergoing single-incision slings were nearly six times more likely to need further stress incontinence surgery after single-incision sling surgery than after TVT-O. There was no evidence of a difference between single-incision slings and TOT slings.
- Need for any other additional or new surgical procedure to treat complications: TVT-O was found to be associated with a statistically lower chance of needing surgery whilst no differences in risk was found for TOT compared with single-incision sling surgery.

No long term adverse outcome data were reported.

Bladder neck needle suspension for urinary incontinence in women [Glazener2]

No significant differences were found in complication rates for needle suspension when compared with either open abdominal retropubic suspension or anterior vaginal repair. Sling operations were associated with higher complication rates than needle suspension.

One small trial (n= 9 treatment v 10 controls) found that postoperative pain was significantly less at three months in women whose needle suspension used polytetrafluoroethylene sutures compared with polypropylene ones.

No long term data were considered.

Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women [Ford]
Overall perioperative complication rates for the transobturator route compared to the retropublic route were not statistically significant different.

Where individual adverse outcomes were reported, the transobturator route was associated with significantly fewer: major vascular injuries, bladder / urethral perforations, and post-operative voiding dysfunction. However the clinical importance of these adverse outcomes vary. Vascular and bladder perforation, for example, sound serious, but clinically they should always be detected by cystoscopy and remedied by re-positioning.

Pain rates were found to vary between groups as to which approach was associated with greater pain. Groin pain was higher for the transobturator route whilst suprapubic pain was lower. Most cases of pain resolved within six months. However, in at least one RCT (Teo et al (2011), the trial team decided to finish recruitment early, due to excess leg pain in the tension-free vaginal tape transobturator group[11]. This highlights the clinical importance of adverse outcomes.

The need for repeat incontinence surgery was found to be not significantly different between groups under 12 months, though it was found to be more common for patients undergoing transobturator procedures over one year.

No statistically significant difference was seen in overall perioperative complications when comparing the retropubic bottom-to-top approach with the retropubic top-to-bottom approach. Significantly fewer women undergoing the retropubic bottom-to-top approach experienced bladder perforation, voiding dysfunction or vaginal tape erosion.

In the transobturator, medial-to-lateral approach compared with the transobturator, lateral-to-medial approach analysis, the former was found to be associated with fewer vaginal wall perforations, but higher levels of voiding dysfunction. There were no statistically significant differences between the two groups for: overall perioperative complication rate; major vascular / visceral injury; bladder perforation; de novo urgency symptoms; detrusor overactivity; vaginal tape erosions; and groin/thigh pain. No significant difference in the rates of repeat incontinence surgery in the medium term was found.

Whilst data greater than five years was included in these analyses, it was acknowledged that the long term effects of mesh sling insertion required further detailed research.

[11] Teo R1, Moran P, Mayne C, Tincello D. *Randomized trial of tension-free vaginal tape and tension-free vaginal tape-obturator for urodynamic stress incontinence in women.*
J Urol. 2011 Apr; 185(4):1350-5. doi: 10.1016/j.juro.2010.11.064.

Adverse Outcomes in POP procedures

Surgical management of pelvic organ prolapse in women [Maher]
The data relating to adverse outcomes following POP surgery is of relatively low quality and few conclusions can be drawn from it.
.
Where adverse outcomes are reported, it is difficult to assess the clinical significance of these. In many cases the differences between groups within comparisons are reported as not significant. Of all possible complications, mesh erosion is one of the more commonly identified, adverse outcomes noted following the treatment of POP

Pessaries (mechanical devices) for pelvic organ prolapse in women [Bugge]
No adverse outcomes considered in the report.

Conservative prevention and management of pelvic organ prolapse in women [Hagen]
No data on adverse outcomes was reported in the systematic review.

5.5.3 Interpretation

SUI Procedures

The key messages from these analyses are:

- Anterior vaginal repair was found to increase likelihood of further SUI surgery, but reduce the risk of new or repeat prolapse when compared with abdominal retropublic surgery.

- No significant differences were found in the risk of adverse effects between retropubic and transobturator, mid-urethral mesh tape procedures.

- Mid-urethral mesh tape procedures were not found to be associated with greater risk of adverse outcomes than laparoscopic colposuspension, though long-term, data was not collected.

- Mid-urethral mesh tape procedures were associated with lower complication rates than traditional suburethral sling operations.

- The long-term profile of adverse outcomes associated with the use of TVT mesh, remains unclear due to the absence of adequate research.

- Adverse events are lower for treatment by injection than for open surgery, although efficacy is significantly lower.

- Treatment with single-incision slings is more likely to need further continence surgery and experience mesh exposure more often than those treated with transobturator (TVT-O) tapes.

- Minimally invasive sling procedures appear to have similar in their adverse outcome rates, though long term effects have not been adequately researched.

- The clinical importance of these adverse outcomes do differ: bladder perforation (more common in retropubic procedures) is of little or no clinical importance, whilst groin pain (more common for transobturator procedures) is of greater importance clinically.

POP Procedures

The key messages from these analyses are:

- The data relating to adverse outcomes following POP surgery is of relatively low quality and few conclusions can be drawn.

- Mesh erosion is one of the main adverse outcomes noted following the treatment of POP.

- No data on adverse outcomes were reported in the systematic review on conservative management of POP compared with surgery.

5.6 Conclusions

On the safety of mesh
The evidence from systematic reviews into the safety and effectiveness of SUI and POP mesh procedures and the adverse outcomes associated with them presents a complex picture.

Although the international safety reviews have differing emphasis and explore the issues in a variety of ways, all the international safety reviews recognise that, for some women, there are long-term, adverse outcomes associated with the use of mesh devices that have had severe effects on their everyday activities and quality of life.

At the same time, none of the international safety reviews conclude that this is a need for mesh devices used in SUI and POP procedures to be withdrawn from use.

In those safety reviews which directly addressed the effectiveness of mesh devices, the general conclusion is that mesh use in mid-urethral sling procedures to treat SUI is effective with low, short-term complication rates. The use of mesh for ***some*** forms of POP repair is considered effective, provided that it is used in abdominal rather than vaginal procedures. The risk of complications/adverse outcomes, notably mesh erosion is higher for POP than for SUI.

The reviews which have explored the possible risk factors associated with women who have had serious adverse outcomes have identified the following factors:
- the surgical approach adopted: transobturator versus retropublic in SUI procedures and vaginal versus abdominal in POP procedures;
- the experience of the surgeon undertaking the procedures;
- patient characteristics, including health risk behaviours; and
- the physical characteristics of the mesh device used.

It is accepted in several of the reviews that long-term follow up data are not presently available to capture late complications of mesh surgery. It is also recommended that this

gap in the data needs to be addressed and routinely collected. More widely the systems used to assess the safety of medical devices were identified as areas for further improvement, notably in the area of vigilance and post-marketing surveillance.

All the reviews note the essential need for well-informed patient consent.

On the effectiveness of mesh

The effectiveness of mesh was considered in the systematic reviews. This is also a complicated picture. The key messages sections try and draw out the specific findings, but even they can be complex and difficult to interpret.

The main thrust of the findings in relation to SUI suggest that mid-urethral slings using mesh implants were found to be a highly effective treatment for SUI. There is limited (non-RCT) evidence that retropubic suburethral mesh tapes are superior to transobturator mesh tapes when used in repeat procedures. In comparison with other surgical techniques traditional sling procedures could be as effective as mesh procedures, though this was not the case for other non-mesh surgery.

The findings in relation to POP surgery are complex. Overall, the reviews conclude that the data does not provide sufficient evidence on effectiveness to guide clinical practice regarding the use of mesh implants over other surgical and non-surgical interventions.

For both SUI and POP the absence of appropriate long term data and on patient focussed outcomes was a persistent issue. Long-term data on surgical effectiveness outcomes were simply not being collected in many RCTs. Where patient important outcomes were assessed, these suggested on marginal benefits in terms of improvement in formal Quality of Life measurements, these may not be suitable measure for the types of adverse outcomes experienced by some women.

On adverse outcomes associated with mesh

The data from the reviews on adverse outcomes associated with the use of mesh procedures for SUI procedures suggests that mid-urethral mesh tape procedures were associated with fewer adverse outcomes than traditional suburethral sling or Laparoscopic colposuspension operations, though long-term, data was not collected

There were no statistically significant differences found in the risk of adverse effects between retropubic and transobturator, mid-urethral mesh tape procedures. Though once again, possible long term effects have not been adequately researched.

The clinical importance of these adverse outcomes to mesh procedures for SUI do differ. For example, bladder perforation (more common in retropubic procedures) is of limited or no clinical importance, whilst groin pain (more common for transobturator procedures) is of greater importance clinically.

The reviews were consistent in finding that the data relating to adverse outcomes following POP surgery with mesh is of relatively low quality and few conclusions can be drawn. That aid, even with the limited data that does exist, mesh erosion is one of the main adverse outcomes noted following surgical treatment with mesh

No data on adverse outcomes were reported in the systematic review on conservative management of POP compared with either mesh or traditional POP surgery.

Chapter 6: The choice of surgical approach of mesh device implantation for the treatment of stress urinary incontinence in women: Clinicians' view

6.1 Clinicians' views

For best outcome of surgery, a well-informed patient is as important as a well-informed clinician. In 2014, the Scottish Government's Expert Group first published a comprehensive leaflet for patients considering surgery using synthetic mesh for stress urinary incontinence (SUI). This leaflet is currently being updated with current evidence and adapted for use by all four UK nations later this year[12] .

In 2013, NICE published the document: ***information to assist counselling*** of women considering SUI surgery using mesh implants, mainly aimed at clinicians[13]. The document was largely based on the MHRA York report[14]. The following table represents updated level I evidence from the Cochrane Collaboration, building on the NICE and MHRA document, as interpreted by the Scottish Government's Independent Review. Where research evidence is lacking, expert opinion based on collective experience from the expert group of the clinicians is expressed (level III).

Clinicians counselling patients for such surgery may find the updated information useful during the shared-decision process, alongside the national patient information leaflet available on the Scottish Government website and the relevant full NICE guidance.

[12] http://www.gov.scot/Resource/0045/00453999.pdf

[13] https://www.nice.org.uk/guidance/cg171/chapter/recommendations#information-to-facilitate-discussion-of-risks-and-benefits-of-treatments-for-women-with-stress

[14] http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con205383.pdf

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.

6.2 Conclusion

In light of the above clinical interpretation of evidence, members of the Independent Review who perform surgery for SUI are of the view that

- The retropubic approach (with diagnostic cystoscopy) is preferred when offering routine surgery for women who choose a mesh tape procedure for treatment of stress urinary incontinence.

- The transobturator approach may be offered if a retropubic approach carries additional risks e.g. organ damage in women who had prior extensive abdominal surgery.

- Regardless of the approach employed, patients with persistent groin or pelvic pain for 4-8 weeks following mesh tape insertion should be considered for timely removal surgery. Patients should be aware that even complete removal of tape does not guarantee relief of pain. All patients should be discussed by the multi-disciplinary team and referral to a regional centre may be required.

Chapter 7: Legal Judgements

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.

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 to adequately consent the patient by discussing 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 tape are still ongoing 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

At the end of July 2015, there were 368 claims in relation to the use of vaginal implants in women with SUI and POP. Of these, the largest number (258 cases) was being heard in the Court of Session.

Of the cases being considered by the Court of Session, there were 120 cases associated with mesh implants for SUI. Of these, 45 were related to transobturator mesh implants, with 33 of the cases considering medial-to-lateral procedures and the remaining 12 cases

lateral-to-medial procedures. There were six cases that arose from **r**etropubic mesh implants, with both down-up procedures and up-down procedures represented (NB the specific number of these cases by type of procedure has not been published to protect patient confidentiality). The remaining 69 cases are awaiting categorisation as the mesh devices can be used for either surgical approaches. Of these, 55 cases are for a mesh device from a single manufacturer.

Vaginal mesh implants represents the largest proportion of POP procedures with 75 cases. Of these, 48 of the cases relate to a device which has now been withdrawn from the market. The remaining 27 cases relate to six devices, produced by four manufacturers. Of the other POP procedures, fewer than five cases relate to abdominal implants and 13 cases relate to devices which can be used either vaginally or abdominally. Overall, there were 96 POP mesh claims, though less than five relate to devices used for treatment of rectal prolapse or where the devices was not made of polypropylene.

Finally, there were a further 42 cases where the categorisation of procedures was not complete.

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 stress urinary incontinence (SUI) and pelvic organ prolapse (POP) is estimated at 100,000. The majority are litigated in Federal Courts (Multidistrict Litigation, MDL).

So far, 18 trials (relating to 24 patients) have reached verdict or settlement during trial (see below). POP procedures related to 11 of the cases; ten of which related to vaginal mesh implants and one where the POP procedure was combined with an SUI mesh implant. 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 implants. 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 implants. 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.

In presenting data from the US, it should be noted that the legal tests against which these cases were judged are not those described above. The legal tests assessed within Federal Courts in the US differ from those in Scotland.

7.4 Interpretation

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

- Whilst negligence or product liabilities may be established for specific cases, generalising from these in the context of this review is difficult given the evolving nature of the evidence.

Chapter 8: Adverse event reporting

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 and for two different functions: to aid local learning and to add to the information necessary for the regulation of medical devices. It is recognised that there is under reporting so there are a number of work programmes in development to improve the two functions. This chapter describes the background to adverse event reporting; the on-going work programmes and specific requirements for reporting incidents with respect to 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 involved in the care. The learning must be managed locally but shared if there are generalisable lessons. As there is a diversity of systems and definitions in place in 2012, the Scottish Government tasked Healthcare Improvement Scotland (HIS) to develop a framework, examine current practice and support developments. The framework included a definition[15], which must be clear and agreed with patients, and consider near misses.
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 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/MHRA.php 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 ie 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 (ie not routinely collected) reporting systems such as the Yellow Card scheme suggest that around

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

20-25% of serious and severe reactions are commonly reported, with around 5% of less serious events[16] officially 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.

When a problem occurs after surgery there are a range of reasons why including characteristics of the patient, expectations, pre-and post op care, the surgeon, the hospital, as well as the device.

Some events are very rare, for example the association of a type of breast cancer, and breast implants. The cancer accounts for less than 1% of all breast malignancies and is found in association with breast implants. This rare event (there were less than 150 cases worldwide and between 5-10 million breast implants used) needs the accumulation of lots of data on adverse events in association with a medical device.

In contrast, single cases of using a wrong connector to inject drugs into the spinal cord area as opposed to the vein led to immediate deaths and now is the rationale for a whole new production of small tube connectors for health services around the world, including in the NHS.

From the studies on adverse event reporting on devices and drugs[16] 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
- Undergraduate and postgraduate training

These mechanisms are in variable practice in NHSScotland. 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; simple on line reporting to national bodies.

In addition a number of countries in Europe have voluntary 'bottom-up' reporting systems for orthopaedic adverse events, demonstrating good outcomes.

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 (also on the MHRA webpage)

[16] 2006 Drug Safety http://www.ncbi.nlm.nih.gov/pubmed/16689555

http://www.hfs.scot.nhs.uk/online-services/incident-reporting-and-investigation-centre-iric/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. If patients report they may not know which implant they received. This information needs to be shared and 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 NHS 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 MHRA is aware of a report from a resident in Scotland, they 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 unique device identifier **(**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 current consultant job plans.

8.3 Assessment

There are a range of current activities to support and improve adverse event reporting in NHSScotland and across the UK. They include:

- local system improvements
- electronic track and trace methods
- professional guidance
- mandatory systems of candour
- UK initiatives

8.4 Feedback to clinicians and patients

Research has shown that if those making a report gain feedback on the value and use of it, more reporting is encouraged. To get a response on the value of a report, as opposed to just an acknowledgement of the notification, requires additional systems to be in place to

give summary information. MHRA are taking forward work with manufacturers to release data to external bodies including those who send in reports.

Currently it is possible to get annual figures of events reported to IRIC but the detail is high level, dependent on the information received which may be incomplete and not useful for specific implant analysis. The feedback needs to be used at quality assurance meetings and shared among NHS 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 Board's incident reports.

The development of the NHS England patient safety incident management system has two relevant objectives:

- 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
- Improve the quality of support provided by the national patient safety function to enable more learning and improvement in all organisations at all levels.

http://www.england.nhs.uk/wp-content/uploads/2014/12/nrls-dev-stakeholder-update-dec14.pptx
The Scottish Government remains in dialogue with NHS England as to whether the development would fit our system.

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

The NHSScotland is committed to improving the ease and knowledge on reporting so clinicians and patients report more often and have confidence in the system. For clinicians this may need:

- further training in addition to the letters already sent describing mesh adverse events,
- discussion on pathways and administrative support so 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.

8.6 Legalisation

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 affect 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 Independent Review there are pros and cons to this approach. The policy development process would assess the pros and issues, based on available evidence.

Pros

- The pros are 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.
- 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 Independent Review 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).

Pros of routine data

Routine data collection on a range of health interventions for the population of Scotland is gathered by trained data collectors (in hospitals) and by electronic systems from primary care and analysed by the Information Services Division (ISD). This system has been in place for decades. The systems are regularly updated and funded. ISD is working on data for the Independent Review and this level of information could be provided on a regular basis to multi-disciplinary teams or the Expert Group. In additional 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 set-up to analysis all areas of interest to mesh implant patients. Routine data may not be 100% completed. Changing coding can take time and other 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 NHS Boards IT system do not currently allow access.

8.7 Summary

Adverse event reporting and analysis is important for mesh implants and together with adverse event reporting for clinical care in general, requires on-going improvement. There are a range of activities in NHSScotland and the UK to keep improving the current levels of reporting, including:

- Additional training led by the Expert Group
- Exploring quality indicators and additional data requests led by multi-disciplinary teams overseen by the Expert Group
- Implementation of the unique device identifier (UDI)/ implant systems including access to this information by patients
- Devising guidance for enhanced appraisal
- Improve the use of the current BSUG database
- Pathways guidance which must include job plan requirements
- Legislation for reporting
- Standalone data systems

Chapter 9: The Conclusions and recommendations of the Independent Review

No surgical intervention is without risk. This Independent Review 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 minimize 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 Independent Review 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 the NHS Incident Reporting and Investigation Centre (IRIC). The following conclusions with recommendations (**in bold text**) are drawn from this evidence and discussion.

Conclusion 1

Robust clinical governance must surround treatment, the decision to use mesh and the surgical approach used. To support decision making, management of the individual patient should take place in the context of multi-disciplinary team assessment, audit and review. The use of a comprehensive information system will underpin this. **The Expert Group should address this with NHS planners, including an assessment of any administrative support required for the clinical teams.**

Conclusion 2

Evidence of involvement in multi-disciplinary team working, engagement in audit activity and recording and reporting of adverse events should be an important part of consultant appraisal and thus statutory revalidation of medical staff. **The Expert Group should work with Medical Directors as Responsible Officers to include this in the conduct and supervision of appraisal. In addition the Scottish Government should consider the alternative methods for the capture of adverse events set out in chapter 8 to determine further the most effective way to ensure complete notification.**

Conclusion 3

Informed consent is a fundamental principle underlying all healthcare. There has been extensive work done by the Expert Group which preceded the establishment of the Independent Review, with leadership by both patients and clinicians. This has resulted in an SUI information leaflet and consent form. **Following on from this the Independent Review concludes that additional work is required to ensure that this work is extended to include POP procedures and that the 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 Independent Review include the provision of adequate time for discussion and reflection. Patients should be provided with information enabling them to report adverse events if these occur.**

Conclusion 4

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

Conclusion 5

Good information, as stated before, is essential to good patient care. The experience of the Independent Review has been that there are many gaps although there is information both in a professionally led database (the BSUG database) and routine NHS information (SMR01 and SMR00). **It is recommended that the Expert Group works with ISD, BSUG and others to ensure that an information system is developed which is universal, robust, clinically sound and focused on fostering good patient outcomes. Work already underway on consistent coding by ISD will be vital to this endeavour.**

Conclusion 6

The Independent Review expressed serious concern that some women who had adverse events found they were not believed, adding to their distress and increasing the time before any remedial intervention could take place. Improving awareness of 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 Independent Review concluded that the Expert Group should review the training and information available to clinical teams and find ways of incorporating patient views in multi-disciplinary working. It should also continue oversight of the mesh Helpline.**

Conclusion 7

A review of the different sources of evidence available to and considered by the Independent Review (patient experience, clinical expert opinion, research evidence and epidemiological evidence from routine information) has led us to express concern in this Interim Report at the use of the transobturator rather than the retropubic approach for routine surgery for stress urinary incontinence using mesh. The clinical governance arrangements that we have recommended will allow an individual case to be considered in the context of a multi-disciplinary assessment, including patient views**. We await the final publication of key research reports but wish to register these concerns and to recommend that the Expert Group in the following months before the publication of the final report explore further appropriate pathways to ensure the techniques chosen take the differential patient and clinical experience, as well as research evidence into account.**

Conclusion 8

Similar concern is expressed, both for effectiveness and adverse events, at the use of transvaginal mesh in surgery for pelvic organ prolapse. The clinical governance arrangements that we have recommended will allow an individual case to be considered in the context of a multi-disciplinary assessment, including patient views. **We await the final publication of key research reports but wish to register these concerns and to recommend that the Expert Group in the following months before the publication of the final report explore further appropriate pathways to ensure the techniques chosen take the differential patient and clinical experience, as well as research evidence into account.**

Chapter 10: Chairman's concluding remarks

Stress urinary incontinence and pelvic organ prolapse 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 complications and a number of women have had both minor and major complications due to the surgery itself and some have found their lives transformed completely for the worse, unable to pursue a normal family, personal and working life.

Balancing this knowledge of 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, that left us with many gaps which has formed the basis of our conclusions and recommendations. In addition we decided to listen and reflect on what our patient members and our clinical members tell us as they add 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 surgery can again take place 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 for the retropubic approach in SUI as the routine mesh procedure with any variation considered as part of the multi-disciplinary team; and
- the Expert Group develops a pathway for the treatment of POP where transvaginal mesh is not used routinely. Any variation in the future is considered in light of the awaited results of the PROSPECT study and follows discussion within the multi-disciplinary team.

I also want to acknowledge the opinion of the Scottish Mesh Survivors Group, who consider that the report recommendations should be actioned and able to be monitored before any transvaginal mesh inplant procedures take place.

Further research which is currently awaited, information and opinion will be considered as part of the preparation of the Final Report which will also be informed by the discussions and actions following the publication of the Interim Report.

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 - Remit of the Independent Review of transvaginal mesh implants

The remit of the Review is to evaluate both the efficacy and the extent and causes of adverse incidents and complication rates associated with stress urinary incontinence and for pelvic organ prolapse. The Review Group recognises that these are two very different procedures 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

3. To determine the safety of vaginal mesh implants for both stress urinary incontinence and pelvic organ prolapse 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.
4. To determine the relative efficacy of surgery for stress urinary incontinence and pelvic organ prolapse 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 stress urinary incontinence and pelvic organ prolapse 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 B – Independent Review group members

Lesley Wilkie, Chair of Independent Review, retired Director of Public Health, NHS Grampian
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
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Olive McIlroy - Scottish Mesh Survivors Group
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Medicines and Healthcare products Regulatory Agency
Neil McGuire - Medical Director

Professional Bodies
David Richmond - President of Royal College of Obstetricians and Gynaecologists
Ash Monga - 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

Gillian McCallum, Scottish Government, Secretary to the Independent Review

Acronyms

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 Urogynaecological Association
MDL	Multidistrict Litigation
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
SMSG	Scottish Mesh Survivors Group
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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