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O'Brien Institute for Public Health
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# Surgical mesh for stress urinary incontinence and pelvic organ prolapse

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**Acknowledgements**

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## Abbreviations

| | |
|---|---|
| **AFNOR** | Association Française de Normalisation |
| **AFS** | Autologous fascial sling |
| **ANSM** | Agence nationale de sécurité du médicament et des produits de santé (France) |
| **ARTG** | Australian Register of Therapeutic Goods (Australia) |
| **CADTH** | Canadian Agency for Drug and Technologies in Health |
| **CCI** | Canadian Classification of Health Interventions |
| **CMO** | Chief Medical Officer |
| **CUA** | Canadian Urological Association (Canada) |
| **EAU** | European Association of Urology (EU) |
| **EUGA** | European Urogynaecological Association (EU) |
| **FDA** | Food and Drug Administration (USA) |
| **GP** | General practitioner |
| **HSE** | Health Service Executive |
| **HTA** | Health technology assessment |
| **ISD** | Intrinsic sphincter deficiency |
| **LUT** | Lower urinary tract |
| **MUS** | Mid-urethral sling |
| **NHS** | National Health Service (UK) |
| **NICE** | National Institute for Health Care Excellence (UK) |
| **NIHR** | National Institute of Health Research (UK) |
| **OAB** | Overactive bladder |
| **OHTAC** | Ontario Health Technology Advisory Committee |
| **PRISMA** | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| **POP** | Pelvic organ prolapse |
| **QoL** | Quality of life |
| **RCT** | Randomized controlled trial |
| **SCENIHR** | Scientific Committee on Emerging and Newly Identified Health Risks (EU) |
| **SIS (SIMS)** | Single-incision sling (single-incision mini-sling) |
| **SPARC** | Suprapubic arch system |

| | |
|---|---|
| **SUFU** | Society of Urodynamics, Female Pelvic medicine and Urogenital Reconstruction |
| **SUI** | Stress urinary incontinence |
| **TOT** | Tension-free obturator tape |
| **TVM** | Transvaginal mesh |
| **TVT** | Tension-free vaginal tape |
| **TVT-O** | Tension-free vaginal tape- obturator |
| **UTI** | Urinary tract infection |

## Executive Summary

### Purpose

This report summarizes the findings and conclusions of reviews of efficacy and safety of polypropylene surgical mesh and its comparators for the treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP).

### Background

"Surgical mesh" refers to a flexible material implant used to support and repair soft tissues in the body. Meshes may be made of biological material such as porcine dermis, autologous tissue from the patient's body, absorbable synthetic material, or non-absorbable synthetic material like polypropylene. Mesh is a popular and long-standing method of hernia repair. Recently synthetic polypropylene mesh has also been used to support pelvic organs as treatment for SUI and POP.[1]

### Methods

The following methodological approaches were used to gather and synthesize the available evidence:

I. Environmental scan of licensure of surgical mesh for SUI and POP across Canada and internationally
II. Review of guidelines and best practice recommendations for surgical mesh
III. Systematic review and grey literature scan of health technology assessments of surgical mesh for SUI and POP
IV. Systematic reviews of safety and clinical effectiveness of surgical mesh for SUI, and for POP

### Key Findings

*Environmental Scan of Licensure of Surgical Mesh for SUI and POP across Canada and Internationally*

Many synthetic surgical meshes are available for use in Canada and the United States. Canada has issued a notice to hospitals to inform healthcare practitioners about the complications associated with surgical mesh for POP and SUI. In late 2018 and early 2019, Health Canada

bolstered its oversight of medical devices in general, and announced plans to establish an advisory group concerning medical technologies and women's health. The US has reclassified urogynecologic surgical mesh in general to class II and surgical mesh for POP specifically to class III. In early 2019, the US issued a notice to ban the use of surgical mesh products for transvaginal repair of prolapse. Recalls and pauses on the use of surgical mesh products have been issued in other countries. Australia and New Zealand have paused the use of mesh for POP and some meshes for SUI. In 2018, the National Health Service (NHS) in the UK halted regular use of mesh for urogynaecological surgery (POP and SUI) where mesh is inserted through the vaginal wall. However in 2019, the National Institute for Health and Care Excellence (NICE) updated their guideline for the management of SUI and POP in women, ending the pause on surgical mesh.[2] The guideline covers assessing and managing patients with SUI and POP with specialized multidisciplinary teams, careful selection of patients and involving patients in the disease management discussion to make informed decisions about their care, establishment of a national registry to report surgery and surgical complications, and how to assess and manage complications associated with mesh surgery.

*Review of Guidelines and Best Practice Recommendations for Surgical Mesh*

Eighteen guidelines published between 2003 and 2019 were initially identified. Eight guidelines provide recommendations for the use of surgical mesh for POP, seven for SUI, and three for both. In guidelines published after 2015, surgical mesh for POP and SUI is generally recommended for research only or if special arrangements for clinical governance are in place. Recent guidelines emphasize the importance of informing patients of the potential complications of surgical mesh and treatment alternatives. Only surgeons with specific up-to-date training on mesh implantation should perform mesh procedures. Lastly, guidelines recommend long-term post-operative follow-up with patients, and diligent reporting of adverse events.

The most current guideline, issued by NICE in 2019, established new guidelines for the treatment of SUI and POP.[3] It continued to emphasize the importance of patients being informed about the risks and benefits of surgery with mesh and keeping long term detailed records of their post-surgery conditions including all complications. NICE also made several key recommendations for research, including long term risks of surgery with and without mesh, how to assess mesh complications and the effectiveness of current pain management. The guideline also includes

details for how to assess and manage complications that arise with mesh surgery. Due to the wide variety of procedures and implanted materials being used, many different complications can arise therefore no generalized recommendations can be made. However, women with suspected mesh-related complications should be referred to a specialist center for further assessment including possible mesh removal surgery.

*Review of Health Technology Assessments of Surgical Mesh for SUI and POP*

Two HTAs addressing the use of surgical mesh for SUI were identified as part of this review; one from Canada and one from the UK. Both HTAs found that tension-free vaginal tape (TVT) had comparable clinical effectiveness to other treatments and that it was likely more cost-effective than colposuspension (native tissue repair). Neither of the HTAs included in this review provided any specific recommendations regarding the use of surgical mesh for SUI, and both suggested that additional research is warranted. No HTAs for POP were identified.

*Systematic Review of Clinical Effectiveness of Surgical Mesh for SUI*

Twenty-nine unique RCTs were identified that evaluated the effectiveness of synthetic surgical mesh for SUI. Nineteen studies compared synthetic mesh to native tissue suspension, seven compared synthetic mesh to AFS, and five compared synthetic mesh to porcine mesh. Studies ranged from 3-24 months in follow-up, and ≥18 months was the most common follow-up time-point that provided the most data for meta-analyses of cure rates across the three comparisons. None of the meta-analysis comparisons of cure rates were significant, suggesting that, ≥18 months, synthetic mesh is not largely different from either native tissue suspension (OR=0.96 [95% CI: 0.66, 1.39]), AFS (OR=0.72 [95% CI: 0.39, 1.34]), or porcine mesh (OR=1.66 [95% CI: 0.87, 3.19]). The most frequently reported complication across the three comparison groups was bladder injury: an intraoperative complication. Mesh erosion in the synthetic mesh group ranged from 0.59%-12% by 12 months, and the rate of mesh exposure was 1.6% at 10 years. Studies generally differed in their definitions of cure, duration of follow-up times, and availability of QoL data. Therefore considerable uncertainty remains regarding the effectiveness and safety of synthetic surgical mesh for SUI.

*Systematic Review of Clinical Effectiveness of Surgical Mesh for POP*

Thirty-two unique RCTs and 11 follow-up studies were identified that evaluated the effectiveness of synthetic surgical mesh for POP. Thirty-eight studies compared synthetic mesh to native tissue suspension, three compared synthetic mesh to porcine mesh, two compared synthetic mesh to autologous/cadaver tissue, and two compared synthetic tissue to semi-dissolvable/dissolvable mesh. The most common follow-up times across comparators were 12 months and 24 months. Sufficient data for meta-analysis were only available for the native tissue and porcine mesh comparators. Results suggest that synthetic surgical mesh results in significantly better cure rates than porcine mesh at 24 months (OR=1.95 [95% CI: 1.02, 3.74]) and native tissue suspension at 12 months (OR=5.38 [95% CI: 3.16, 9.15]); however, the latter finding should be interpreted with caution due to heterogeneity of the effect ($i^2$=67%). Meta-analysis results suggest that synthetic mesh is significantly associated with more bladder injury, intraoperative blood loss, and urinary retention than native tissue suspension. Literature on the efficacy and safety of synthetic mesh vs. other comparators is scarce and limited conclusions can be made. Rates of mesh exposure and mesh erosion at 12 months in the synthetic mesh group range from 1.59%-17.3% and 6.9%-35.7%, respectively. Overall, much uncertainty remains regarding the efficacy and safety of synthetic surgical mesh for POP.

**Conclusions**

The guidelines reviewed demonstrated escalating caution since 2017 regarding urogynaecological uses of surgical mesh. Recent guidelines recommend strong provisions for clinical governance, informed consent, and reporting of complications. The environmental scan revealed numerous actions undertaken by health authorities around the world to curtail or regulate the use of surgical mesh.

Reviews of published scientific studies regarding the use of surgical mesh for SUI and POP were limited by features of the literature. A variety of QoL instruments precluded robust analysis of patient experience. Diverse cure definitions may affect the proportion of treatment success in different studies. A scarcity of long-term data prohibits conclusions about recurrence and complications years after mesh implantation. Where analyses were possible, the data demonstrated that mesh achieved cure rates similar to other treatments at most time points. Surgical mesh treatments for POP were associated with higher complication rates for some

complications, such as bladder injury and mesh erosion. A high degree of uncertainty was revealed by both the systematic review on mesh for SUI and the systematic review on mesh for POP.

# 1 Purpose of this Health Technology Assessment

The purpose of this health technology assessment (HTA) is to synthesize current evidence on the use of synthetic surgical mesh for treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP). This report summarizes the evidence in the literature on the clinical effectiveness and safety of mesh products for these conditions, and the current context in Canada and globally. The evidence is synthesized to emphasize the safety profile of mesh products.

# 2 Research Question and Research Objectives

The primary research questions are:

1. Is the use of polypropylene surgical mesh as clinically effective as alternative products in the treatment of POP and SUI? In particular:
    a. What is the safety profile and complication rate of polypropylene surgical mesh?
    b. What are the time horizons for the included studies and is there sufficient evidence to support the same conclusions over the long-term?

# 3 Overview of Approach

A variety of methodological approaches were used to gather and synthesize the available evidence in order to address the primary research questions. The following methodologies were used:

I. Environmental scan of licensure of surgical mesh for SUI and POP across Canada and internationally
II. Review of guidelines and best practice recommendations for surgical mesh
III. Systematic review and grey literature review of health technology assessments of surgical mesh for SUI and POP
IV. Systematic reviews of safety and clinical effectiveness of surgical mesh for SUI and POP

# 4 Background

## 4.1 Surgical Mesh

### *4.1.1 Description of Mesh*

"Surgical mesh" refers to a flexible material implant used to support and repair soft tissues in the body. Polypropylene meshes were initially used over fifty years ago to repair abdominal hernias by reinforcing the body wall to prevent recurrence. Recently, mesh has also been used to support pelvic organs to treat pelvic organ prolapse (POP) and stress urinary incontinence (SUI).[1]

Meshes may be made of biological materials such porcine dermis, cadaveric fascia, or autologous fascial tissue harvested from the patient themselves. Absorbable synthetic meshes are also available, although they are not as effective at preventing recurrence.[4] Most synthetic meshes are made of polypropylene fibers woven or knitted together into sheets. Synthetic polypropylene meshes are highly variable across numerous parameters: pore size, coatings, fiber diameter, and method of construction.[1]

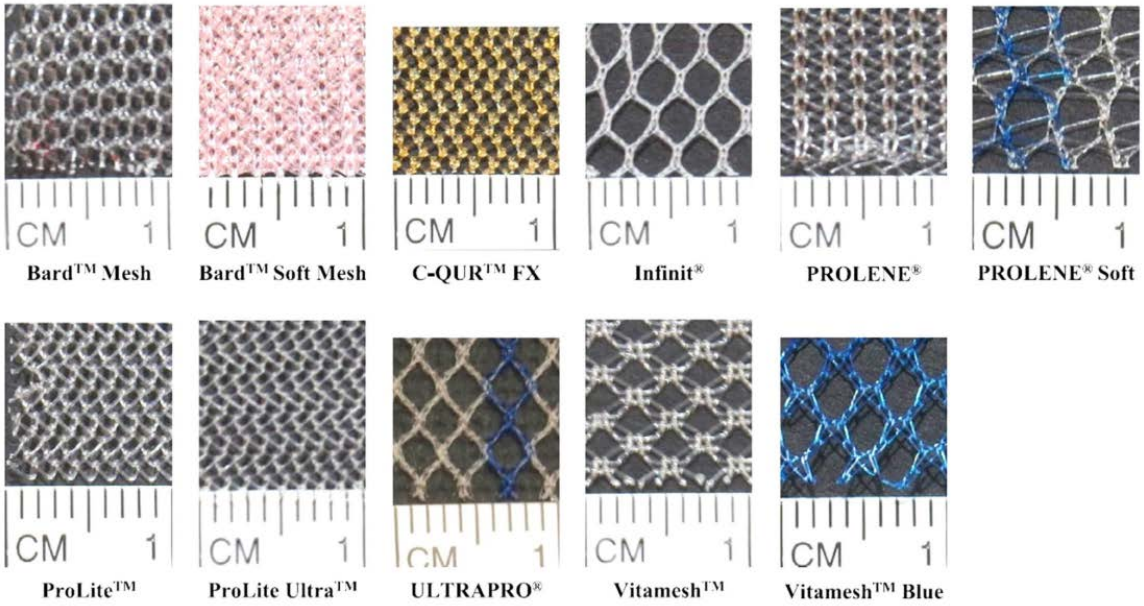
### *4.1.2 Mesh Characteristics*

The material composition of mesh influences its integration into the body. Meshes must be sufficiently strong not to fail and sufficiently elastic to withstand deformation and changes in pressure. Consideration of the mesh pore size is also important; microporous meshes, for example, have smaller pores and are rejected by the host body more frequently, and are associated with chronic inflammation and infection. Scar tissue easily fills the small pores and prevents complete integration of the implant. Macroporous meshes, on the other hand, allow infiltration of immune cells into the mesh, which prevents the formation of bacterial colonies. As such, new connective tissue grows more easily in larger pores and results in more complete mesh integration.

Meshes may be made of monofilament (single strands woven or knitted together) or multifilament (twisted strands woven or knitted together) materials (see Figure 1). Monofilament meshes are stronger, but stiffer. Multifilament meshes are soft, but may host bacterial colonies and erode easily, thereby increasing risk of infection.[4] Mesh erosion may present months or years after mesh implantation, making it difficult to study in short-term trials. Erosion may require

mesh excision, which is a difficult procedure and may not resolve symptoms caused by erosion, such as chronic pelvic pain or pain during sexual intercourse.[5]

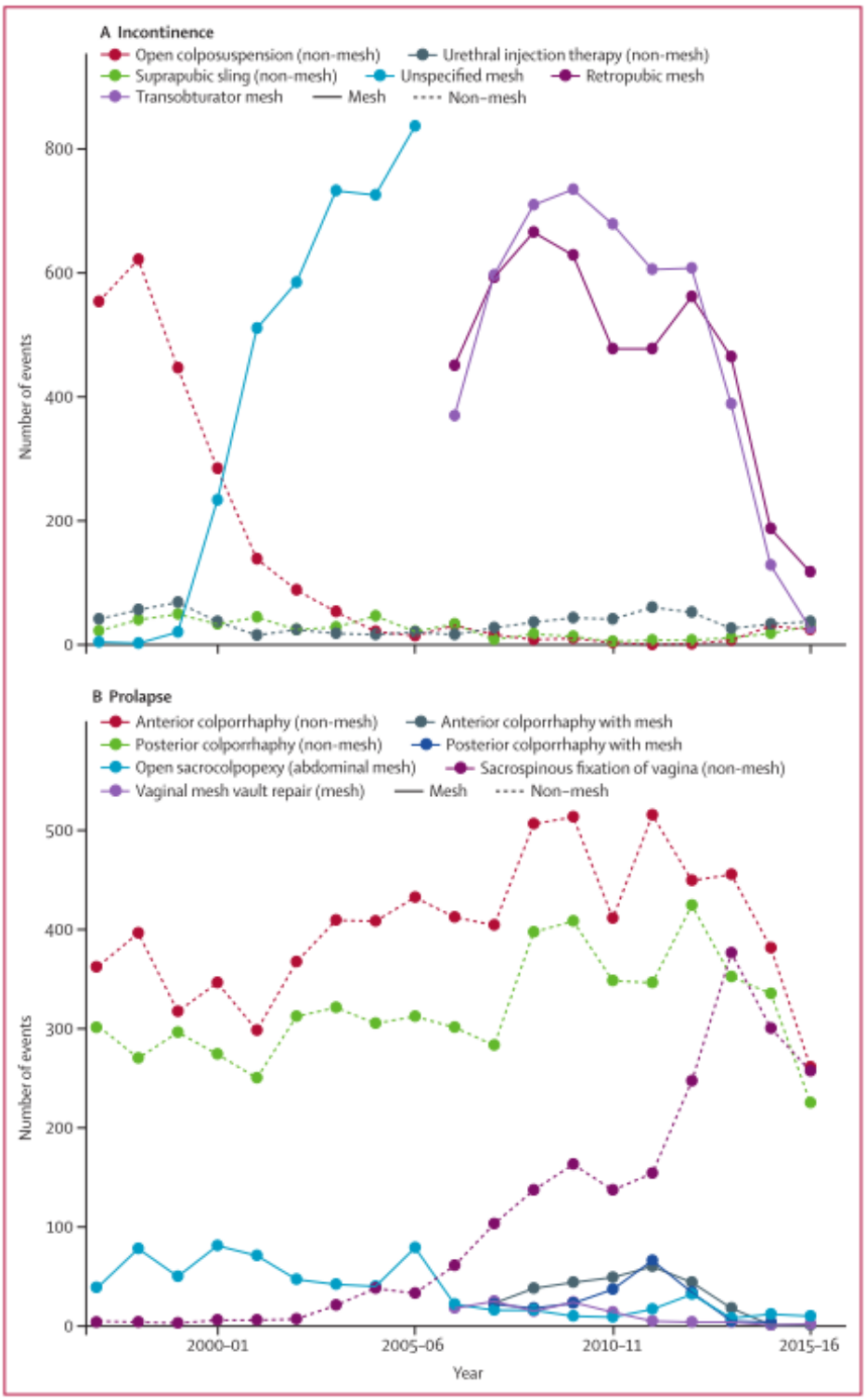
Figure 1: Mesh Materials[6]




### *4.1.3 Utilization of Mesh*

Most corrective procedures for SUI and POP use surgical mesh. One retrospective data analysis from the USA estimated that women have a 20.0% chance of undergoing surgery for either SUI or POP at some point between the ages of 18 and 80.[7] A Scottish cohort study found that between 1997 and 2016, 16,660 women underwent a first-time single incontinence procedure, and 79% of those procedures used mesh (see Figure 2). Only 7% of first-time single POP surgeries used mesh.[8] In the USA in the year 2000, the rate of non-mesh surgery (also known as "native tissue repair," Burch colposuspension) for SUI was similar to the rate of mesh surgery. By 2009, mesh slings represented 89.1% of all SUI surgeries, and Burch represented only 3.8%.[9] The same authors found a similar significant increase in the number of mesh surgeries for prolapse between 2005-2010.[10]

Figure 2: Number of Procedures in Scotland for SUI and POP Between 2001-2016 [8]



### *4.1.4 General Complications of Mesh*

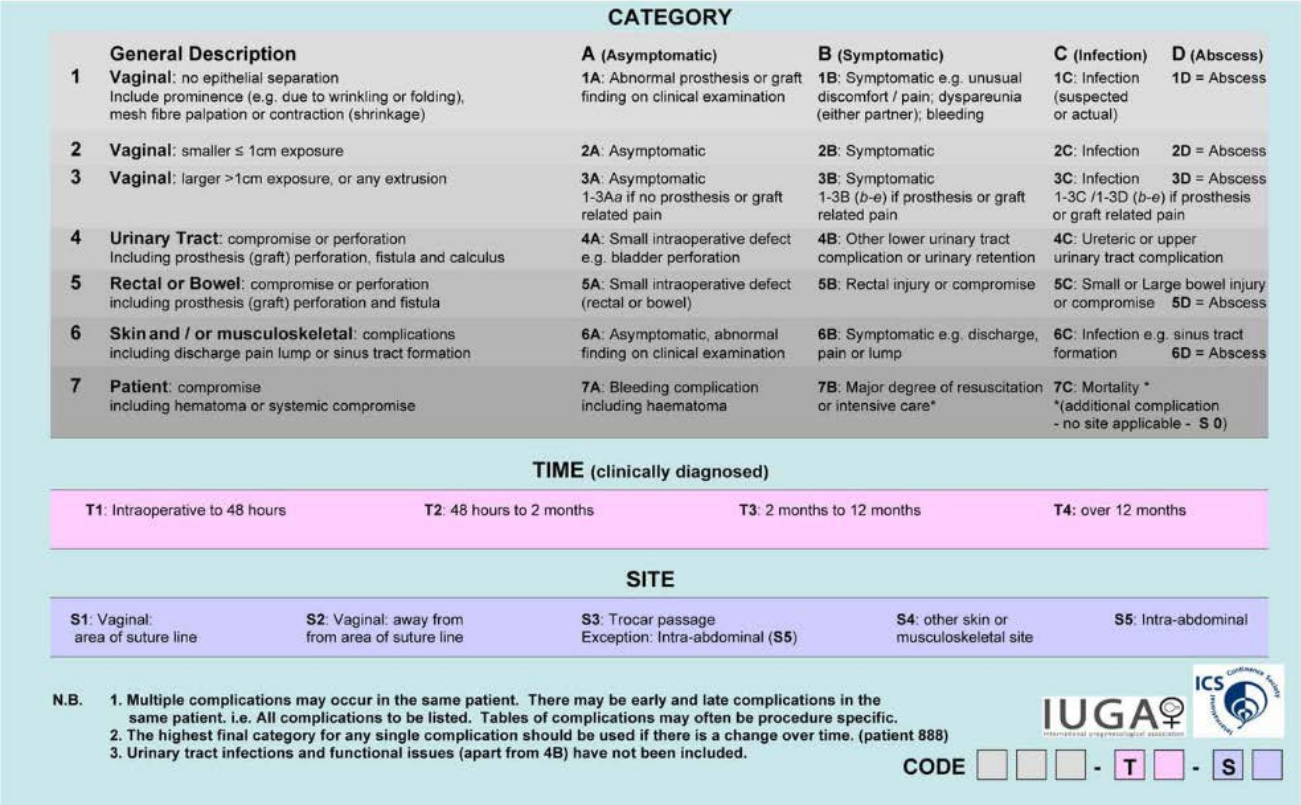
Meshes are foreign implants and may trigger problematic immune responses in the patient's body. When the initial acute stage of inflammation fails to destroy the implant, chronic inflammation may follow.[4] Inflammation triggers a foreign body response, fibrosis, and scar tissue formation, which may result in mesh contraction, severe inflammation, or complete rejection of the implant.[4]

Mesh erosion is a serious, potentially life-altering complication specific to mesh implantation surgeries. Mesh erosion, wherein the mesh fibers penetrate the patient's soft-tissue, can cause severe pain and discomfort.[1] Rates of mesh erosion vary by procedure, mesh placement, and mesh characteristics such as pore size and flexibility. Erosion may occur when the implant fractures and individual pieces of mesh infiltrate the patient's tissues; however, mesh erosion and fracture are not always linked. Excision of eroded mesh may not always be possible, and some patients with eroded mesh may suffer serious adverse effects for their entire lives.[1] Erosion is the primary reason for mesh excision after POP treatment, constituting 60% of cases of mesh removal or revision.[10]

While the use of the term "mesh erosion" is still common in the literature, the ICS/IUGA recommends using more specific terminology. According to the ICS/IUGA, the term mesh exposure specifically refers to the "condition of displaying, revealing, exhibiting, or making accessible" the mesh. More specific terms include mesh extrusion, in which the mesh passes through the tissue, and perforation, in which the mesh opens up a hole into a hollow organ. [11] Despite the ICS/IUGA recommendations, the use of the term "mesh erosion" may still refer generically to the penetration of mesh into soft-tissue depending on the author. Due to this lack of clarity, this review will use the more generic definition of mesh erosion unless a more specific definition is evident.

According to the ICS/IUGA, mesh complications may be classified by their category, timing, and site. These classifications are represented by codes that allow for better communication between health care providers (see Figure 3).[11]

Figure 3: ICS/IUGA Classification of Mesh and Graft Complications



**CATEGORY**

| | General Description | A (Asymptomatic) | B (Symptomatic) | C (Infection) | D (Abscess) |
|---|---|---|---|---|---|
| 1 | **Vaginal**: no epithelial separation<br>Include prominence (e.g. due to wrinkling or folding), mesh fibre palpation or contraction (shrinkage) | **1A**: Abnormal prosthesis or graft finding on clinical examination | **1B**: Symptomatic e.g. unusual discomfort / pain; dyspareunia (either partner); bleeding | **1C**: Infection (suspected or actual) | **1D** = Abscess |
| 2 | **Vaginal**: smaller ≤ 1cm exposure | **2A**: Asymptomatic | **2B**: Symptomatic | **2C**: Infection | **2D** = Abscess |
| 3 | **Vaginal**: larger >1cm exposure, or any extrusion | **3A**: Asymptomatic<br>1-3A*a* if no prosthesis or graft related pain | **3B**: Symptomatic<br>1-3B (*b-e*) if prosthesis or graft related pain | **3C**: Infection<br>1-3C /1-3D (*b-e*) if prosthesis or graft related pain | **3D** = Abscess |
| 4 | **Urinary Tract**: compromise or perforation<br>Including prosthesis (graft) perforation, fistula and calculus | **4A**: Small intraoperative defect e.g. bladder perforation | **4B**: Other lower urinary tract complication or urinary retention | **4C**: Ureteric or upper urinary tract complication | |
| 5 | **Rectal or Bowel**: compromise or perforation<br>including prosthesis (graft) perforation and fistula | **5A**: Small intraoperative defect (rectal or bowel) | **5B**: Rectal injury or compromise | **5C**: Small or Large bowel injury or compromise | **5D** = Abscess |
| 6 | **Skin and / or musculoskeletal**: complications<br>including discharge pain lump or sinus tract formation | **6A**: Asymptomatic, abnormal finding on clinical examination | **6B**: Symptomatic e.g. discharge, pain or lump | **6C**: Infection e.g. sinus tract formation | **6D** = Abscess |
| 7 | **Patient**: compromise<br>including hematoma or systemic compromise | **7A**: Bleeding complication including haematoma | **7B**: Major degree of resuscitation or intensive care* | **7C**: Mortality *<br>*(additional complication - no site applicable - **S 0**) | |

**TIME (clinically diagnosed)**

**T1**: Intraoperative to 48 hours | **T2**: 48 hours to 2 months | **T3**: 2 months to 12 months | **T4:** over 12 months

**SITE**

**S1**: Vaginal: area of suture line | **S2**: Vaginal: away from from area of suture line | **S3**: Trocar passage<br>Exception: Intra-abdominal (**S5**) | **S4**: other skin or musculoskeletal site | **S5**: Intra-abdominal

**N.B.**
1. **Multiple complications may occur in the same patient. There may be early and late complications in the same patient. i.e. All complications to be listed. Tables of complications may often be procedure specific.**
2. **The highest final category for any single complication should be used if there is a change over time. (patient 888)**
3. **Urinary tract infections and functional issues (apart from 4B) have not been included.**

IUGA ICS

**CODE** ☐☐☐ - **T** ☐ - **S** ☐

## 4.2 Stress Urinary Incontinence

### *4.2.1 Description, Population, and Prevalence*

Urinary incontinence is the involuntary loss of urine from the lower urinary tract (LUT). The LUT is comprised of the bladder, urethra, and internal and external sphincters. Its main function is to store the urine produced by the kidneys until a desired time, and then to expel the urine from the body. When the storage function of the LUT is compromised, urine is no longer contained and leaks from the body at inconvenient times. This condition is referred to as 'incontinence.'[12]

To properly store urine, the bladder must be able to accommodate the growing volume of urine from the kidneys without a simultaneous increase in pressure; the nervous system must act to suppress bladder contraction; and the internal urinary sphincter must maintain high pressure. The high pressure of the internal sphincter is important because it prevents urine from flowing out of the bladder into the urethra. As such, the pressure in the urethra must be higher than in the bladder. If the gradient reverses and the pressure in the bladder exceeds the pressure in the urethra, urine will flow out of the bladder. When voiding takes place normally, impulses from

the nervous system cause the bladder to contract and the two sphincters to release; urine is subsequently pushed from the bladder through the urethra and out of the body. In patients with urinary incontinence, some part of the storage mechanism of the LUT is defective, causing urine to leak out of the urethra even when the desire to void is not present.[12]

The three most common types of urinary incontinence are urgency, mixed, and stress urinary incontinence. Most studies report prevalence of urinary incontinence in the range of 25-45% of the female population. SUI is the most common type of urinary incontinence in women and affects 49% of women with incontinence, whereas urgency urinary incontinence (UUI) is the most common type of urinary incontinence in men.[12] Risk factors for SUI include parturition, pregnancy, smoking, obesity, and advanced age.[13] One U.S.-based population analysis found that the lifetime risk of undergoing surgery for SUI was 13.6%.[7]

In patients with SUI, exertion or effort results in bladder leakage[13]. For these patients, any sudden increase in abdominal pressure can cause accidental urine loss as increased abdominal pressure squeezes the bladder. In a normally functioning LUT, a simultaneous increase in urethral pressure prevents urine from leaking out of the bladder into the urethra. However, in cases of SUI, urethral pressure does not rise to sufficiently match the increased abdominal pressure, and urine is squeezed out of the bladder into the urethra, causing accidental leakage.[12]

Women are more likely than men to be affected by SUI because of their weaker bladder necks and shorter urethra; although SUI can also present in men (typically following a radical prostatectomy).[12] Two interrelated mechanisms cause SUI in women. The first is urethral hypermobility, which is caused by a weakness of the pelvic floor. When the pelvic floor is weak, the urethra is not supported, and instead descends when abdominal pressure rises. The pressure is then exerted disproportionately on the bladder instead of the urethra, and the pressure gradient between bladder and urethra reverses: the urethra becomes less pressured than the bladder, so urine leaks out of the bladder into the urethra. The second mechanism of SUI is intrinsic sphincter deficiency (ISD), which occurs when the urethral sphincter lacks sufficient tone to maintain a high pressure. In these cases, even a minute increase in abdominal pressure may cause a reversal in the pressure gradient between the bladder and the urethra, resulting in involuntary urine loss.[12]

In men, SUI most frequently occurs following a radical prostatectomy. A radical prostatectomy involves the removal of the prostate, which plays a role in continence, as well as the bladder neck, which acts as the first barrier to urine loss. Important nerves lie close to the prostate and may be injured during surgery, resulting in defective enervation of the LUT.[12] Due to the rarity of male SUI, the information about SUI reported in this document will henceforth refer to the female anatomy, unless otherwise stated.

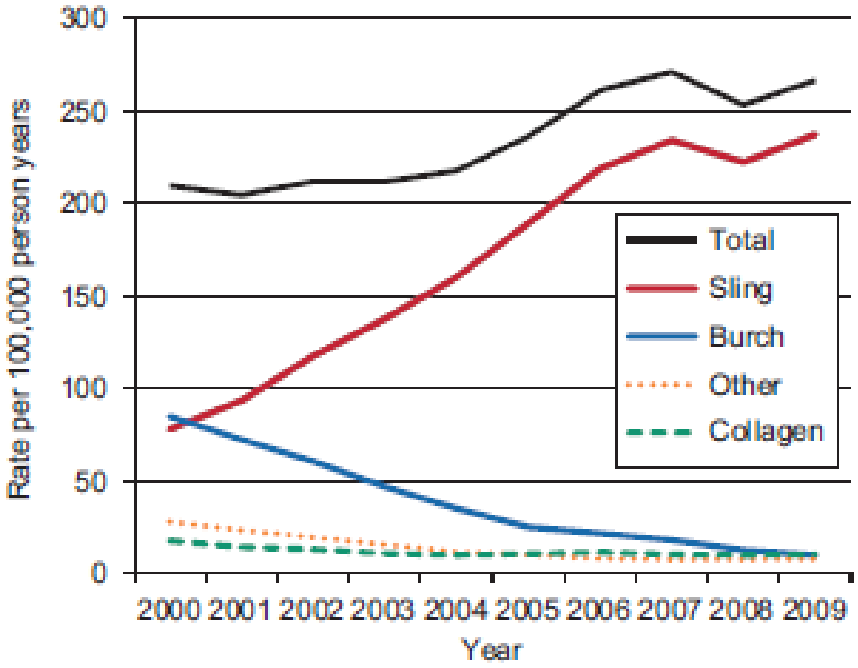
There are various benchmarks for assessing the treatment success for patients with SUI. The Urinary Incontinence Treatment Network defines a "cure" of SUI as "self-reported dryness, no leakage in a three-day voiding diary, negative standardized cough stress test, negative 24-hour pad test, and no retreatment".[14] However, this standard is very stringent and may significantly underestimate the treatment success rate when compared to patient satisfaction. Patient-reported outcome measures (PROMs) are often used to evaluate success, though no single questionnaire has become the definitive standard.[14]

### *4.2.2 Non-mesh Treatments for Stress Urinary Incontinence*

There are several non-surgical options for treatment of SUI. For example, lifestyle changes, such as weight loss and cessation of smoking, may relieve symptoms. Strengthening the pelvic floor with exercise, weighted vaginal cones, or electrical stimulation may also help to resolve SUI. Although some pharmaceutical treatments for SUI exist, they are uncommon; for example, the serotonin-norepinephrine reuptake inhibitor duloxetine improves sphincter tone, but it is poorly tolerated due to its side effects.[15]

Non-mesh surgical treatment of SUI most commonly consists of retropubic colposuspension. In these procedures, the tissues of the bladder neck and urethra are lifted and fixed with sutures. In women, the Burch procedure is a common type of colposuspension in which the anterior vaginal wall and paravesical tissues are attached to the pelvic side wall. The vagina and surrounding structures then act as a sling to support the bladder neck, preventing accidental urine loss.[13] Since the introduction of mesh, native tissue repairs have become less common (see Figure 4).[9]

Figure 4: Rates of Various Techniques in Managing SUI in the USA from 2000-2009 [9]




The most common complications of retropubic colposuspension are infection and hematoma. Other complications include hernia, UTI, injury to internal structures during surgery, urethral obstruction, and fistula. These complications are uncommon, and colposuspension procedures are considered generally safe.[16]

Another non-mesh surgical treatment option for SUI is radiofrequency bladder neck suspension. Radiofrequency causes tissue remodeling, which can harden the tissues that support the bladder neck. In cases of success, the new tissue is stiff and provides the support necessary to keep the bladder neck elevated.[13]

### *4.2.3 Mesh for Stress Urinary Incontinence*

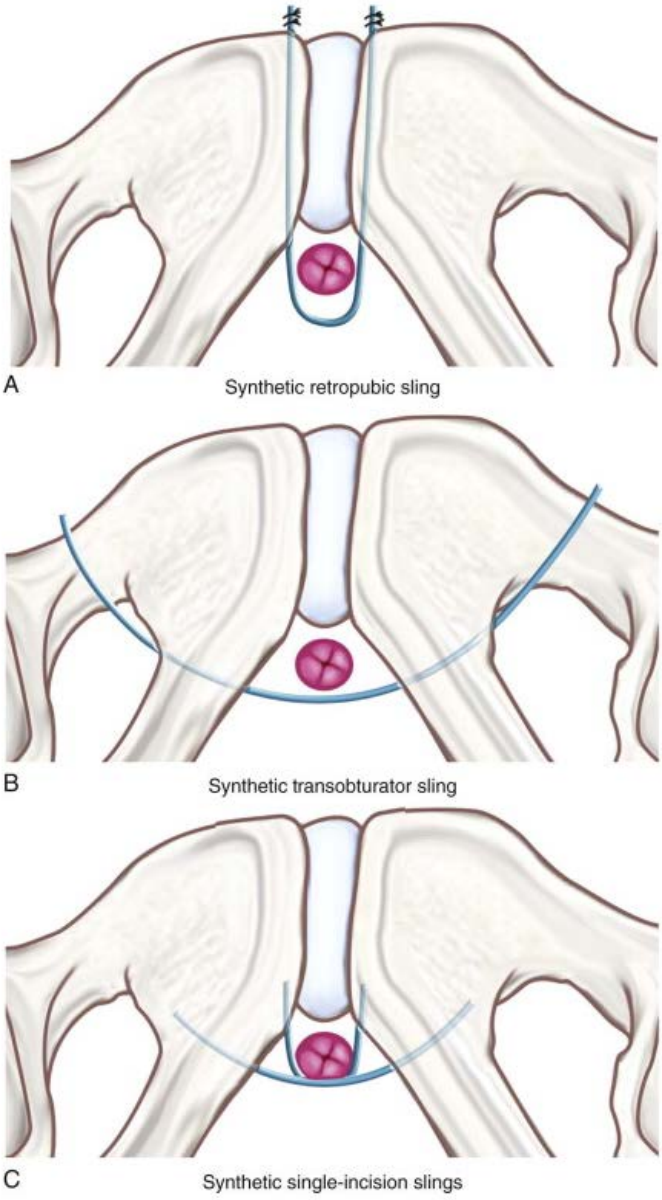
Meshes for SUI create slings to support the urethra. Many types of meshes and the procedures for their insertion have been described, and multiple meshes and surgical approaches are commonly used. Meshes for SUI are commonly referred to as midurethral slings (MUS). Mesh surgery has become the most common treatment for SUI in women, with 3.7 million meshes sold across the world between 2005 and 2013.[17] There are three main types of sling surgeries for SUI: retropubic, transobturator, and single-incision mini-sling (SIS, SIMS) (see Figure 5).

In 1996, Ulf Ulmsten first introduced the tension-free vaginal tape (TVT) procedure, which rapidly became popular.[18] In the TVT procedure, the surgeon makes three incisions: one vaginal incision and two in the lower abdomen. A strip of mesh is attached to a trocar and inserted through a vaginal incision. The trocar is then guided under the midurethra via a retropubic approach to the anterior abdominal wall. The tape is fixed in place, adjusted to decrease tension, and trimmed down to an appropriate length.[18] Numerous successful modifications of the TVT system are in use, including the suprapubic arch (SPARC) system.

Delorme introduced a new procedure for sling implantation in 2001: the transobturator approach.[18] Complications of the TVT procedure are often associated with the retropubic approach, wherein the surgeon guides the tape blindly. As such, the transobturator techniques were designed to avoid this blind approach. They rely on passing the tape through the obturator foramen, one of the gaps in the pelvis, with three incisions being made: one vaginal and two groin incisions. In the transobturator tape (TOT) procedure, for example, a needle is passed through a groin incision, through the obturator foramen, and guided to the vaginal incision. The tape is then passed through the incision along the route of the needle and exits into the vagina.[13,18] This approach is referred to as the "outside-in" approach, since the tape begins outside the body. In the tension-free vaginal tape obturator (TVT-O) procedure, an introducer is passed through the vaginal incision, followed by tubing containing the tape. The tubing exits through the groin incision. The tubing is retracted back through the vaginal incision, and the tape exits through the groin. This procedure is thus referred to as the "inside-out" procedure, since the tape begins inside the body.

In 2006, the TVT-Secur system was introduced as the first mini-sling. Since then, multiple mini-slings including the Mini-Arc and Ajust systems have been introduced.[19] Mini-slings are shorter than standard TVT, TOT, or TVT-O. These short slings are inserted without the use of a trocar and are thus designed to avoid trocar-related injuries such as bladder or bowel perforation.[18,20] Other than their length, mini-slings are similar to standard slings, and may be inserted via retropubic or transobturator approaches.[20]

Figure 5: Three Styles of Mesh Slings for SUI [21]




### *4.2.4 Complications of Mesh for Stress Urinary Incontinence*

Meshes for SUI have been subject to much controversy and scrutiny due to their complication profile, and lawsuits against mesh manufacturers have been initiated in Australia, Belgium, Canada, England, Israel, Italy, the Netherlands, Scotland, USA, and Venezuela.[17] Complications for standard MUS surgery include "overactive bladder (52%), obstructive micturition (45%), SUI (26%), vaginal mesh exposure (18%), chronic pelvic pain (14%), local infection (12%), dyspareunia (6%), and vesicovaginal fistula (4%)".[22] Though many complications of MUS

surgery are also observed in non-mesh surgical methods, mesh-specific events include mesh erosion, infection of the mesh, mesh contraction, and immune reactions to the mesh by the patient's body.[22,23] While some complications of mesh surgery are caused by the meshes themselves, others are caused by the surgical techniques. Surgical complications include injury to the bowel, bladder, blood vessels, or urethra, and obstructions caused by overtightening of the tape.[24]

Infection of surrounding tissue is generally uncommon after MUS implantation due to the optimization of mesh materials;[24] however, it should be noted that certain types of meshes (i.e., multifilament polypropylene, non-knitted, non-woven polypropylene and composite implants) have been found to be more frequently associated with infection than their monofilament polypropylene counterparts.[24]

Mesh contraction, retraction, or shrinkage can cause pain, recurrence of SUI, dyspareunia, and urinary and defecatory issues. The pain associated with mesh contraction may be severe and adversely affect quality of life.[24] Conservative treatment of mesh contraction includes pain management, local hormone therapy, and local anti-inflammatory injections; in addition, one or more revision surgeries may be required.[24] Chronic pain is another serious issue associated with synthetic mesh surgeries, with 40% of patients who had undergone transobturator MUS placement reporting groin and thigh pain.[24] Lastly, both voiding dysfunction and overactive bladder (OAB) are more frequently observed after retropubic approaches for tape insertion.[25]

Accurate complication rates are difficult to establish due to underreporting and the absence of a registry of complications data.[26] While complications associated with the surgery (e.g. bowel injury) tend to present early, some mesh-related complications present many years after MUS placement.[26] In general, reports suggest that the overall complication rate for MUS placement surgery is at least 4.6%.[26]

One recent review found an increasing number of MUS surgery complication symptoms as time progressed.[26] The period between the surgery and presentation of complications depends on the complication, but one German study of 100 patients undergoing mesh removal for any complication found that the complication causing the patient to seek mesh removal arose at a mean of 13.5 months after mesh insertion. In 48 of their 100 patients, the complication presented

immediately post-surgery (likely to do with defective technique rather than the mesh itself), and 89 of the 100 women in the cohort presented within 2 years of MUS surgery.[25]

In a recent retrospective study of 92,246 patients with a mean follow-up time of 4.2 years, 4.1% of patients with an MUS were admitted to the hospital once for mesh-related complications or revision surgery; 0.8% of TVT patients were admitted twice, and 0.3% were admitted three times. The authors conservatively estimate that 9.8% of SUI patients treated with mesh experience a complication either immediately after surgery, within 30 days, or within 5 years.[17] In particular, a population study in the U.K. found that 3.3% of the women who underwent mesh surgery treatment for SUI ended up undergoing mesh removal surgery within nine years.[27]

## 4.3 Pelvic Organ Prolapse

### *4.3.1 Description of Pelvic Organ Prolapse*

Pelvic organ prolapse (POP) is a type of pelvic floor dysfunction in which the pelvic organs descend into the vaginal canal. Commonly affected pelvic organs include the anterior and posterior walls of the vagina, the apex of the vagina, the uterus, the bladder, or the rectum.[28] Sometimes POP is classified by which structures are involved in the prolapse, e.g. bladder prolapse is called a "cystocele." These classifications require certainty regarding the exact anatomy of the prolapse. More commonly, prolapse is defined by its location only (see Table 1)[16] POP affects only women and is distinct from rectal prolapse which affects both sexes.[29]

POP is associated with defective levator ani muscles. Normally, pelvic support is maintained by the levator ani muscles, which horizontally support the vagina when the body is in a standing position. However, when the levator ani muscles are injured, they re-orient vertically and stop providing support to the pelvic organs. As a result, the burden of supporting the pelvic organs then falls onto the connective tissues that keep the vagina attached to the pelvic walls.[30]

Although there are multiple causes of POP, pregnancy, and vaginal parity in particular, is the single greatest risk factor.[31] Vaginal delivery often damages the levator ani muscles, resulting in high incidence of prolapse.[30] Delivery with forceps additionally increases risk of developing POP.[28,31] Other risk factors include age, menopause (independently of age), family history, and anatomy of a bony pelvis. BMI is one modifiable risk factor for POP; heavier body weight puts

more pressure on the muscles of the pelvic floor, thereby increasing the chance of developing this condition.[31]

Table 1: Prolapse Locations and Associated Structures

| Location of Prolapse | Associated Terms | Structures Commonly Prolapsing |
|---|---|---|
| Anterior | Cystocele, urethrocele | Bladder, urethra |
| Posterior | Rectocele, enterocele | Rectum, small bowel |
| Apical | Uterine prolapse, vaginal vault prolapse | Uterus, vaginal cuff (in cases of hysterectomy) |

Generic symptoms of POP include a sensation of bulging, pressure, or heaviness.[28,32] In some cases, the leading edge of the prolapse may protrude from the vaginal opening, allowing direct visualization of the prolapse. Other symptoms depend on the organs affected; bladder prolapse may manifest with urinary symptoms, and bowel prolapse may present with defecatory symptoms.[32] Uterine prolapse may or may not be accompanied by urinary or defecatory symptoms. All forms of prolapse may result in dyspareunia, i.e. pain or difficulty during sexual intercourse.[28,32] Lastly, POP may cause women to suffer from body image issues and social problems.[33] Overall, POP poses a significant detriment to affected women's quality of life.[30]

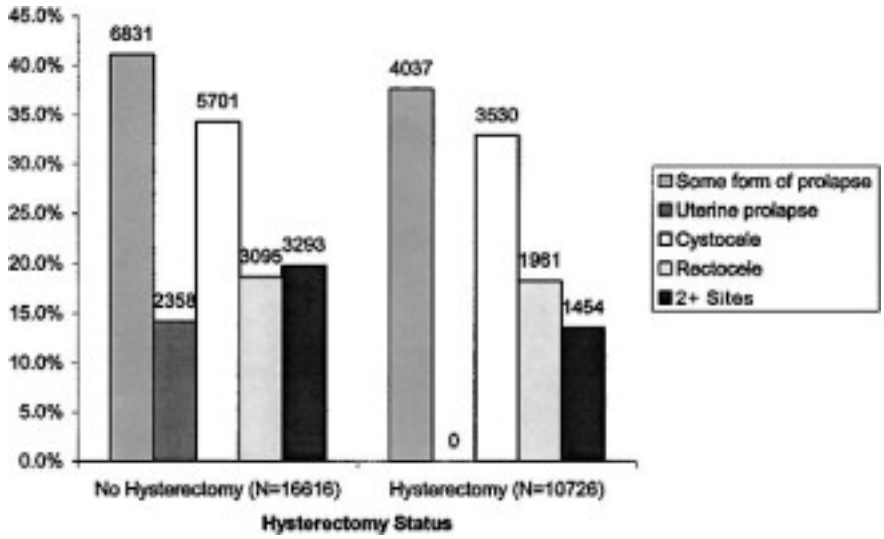
### *4.3.2 Prevalence of Pelvic Organ Prolapse*

The Women's Health Initiative (WHI), a large-scale long-term study commissioned by the USA's National Institute of Health, describes the prevalence of any form of POP as 41% in women with a uterus aged 50-79 years.[33] The same study found that some form of POP presents in 38% of women without a uterus (see Figure 6).[33] Many cases of POP are asymptomatic.[30]

The most common form of POP is anterior wall prolapse, which is twice as common as posterior wall prolapse, or rectocele, and three times more common than apical prolapse.[28,30]Anterior prolapse may involve herniation of the bladder (cystocele), urethra (urethrocele), or the anterior small bowel (anterior enterocele) into the vagina. The most common form of anterior prolapse is cystocele,[29] which occurred in 34% of women in the WHI study.[33] Posterior prolapse describes the intrusion of posterior organs into the vagina, including the rectum (rectocele) and the posterior segments of the small bowel (posterior enterocele). The WHI study detected rectocele in 19% of women.[33] In apical prolapse, the uterus, the cervix, or, in cases of hysterectomy, the

vaginal cuff descends into the vaginal canal.[32] Fourteen percent of women in the WHI study had uterine prolapse.[33]

Figure 6: Incidence of POP in WHI Study Population




### *4.3.3 Stages of Pelvic Organ Prolapse*

POP is commonly staged using the Pelvic Organ Prolapse Quantification (POP-Q) system. In this system, six points in the pelvic viscera are used to describe the elements of the prolapse, and distance from the hymen is used to quantify the degree of prolapse. Points Aa and Ba are located along the anterior vaginal wall, while points Ap and Bp are located along the posterior wall. Point C represents the cervix or vaginal cuff, and point D represents the posterior fornix. Several other measurements are also generated by a POP-Q examination: the genital hiatus (gh), perineal body (pb), and total vaginal length (tvl) (see Figure 7). Using these points and measurements, the degree of prolapse may be staged by referring to the distance between the leading edge of the prolapse and the hymen. At stage 0, no prolapse is present. At stage 4, the leading edge of prolapse is at or beyond 2 cm less than the total vaginal length compared with the hymen; in other words, nearly the total length of the vagina has prolapsed (see Table 2). POP is mostly assessed by a physical exam; imaging is seldom necessary.[32]

Figure 7: POPQ Points and Measurements

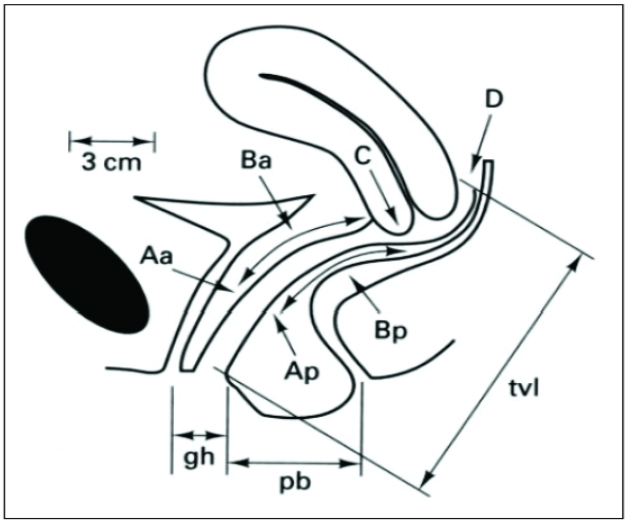


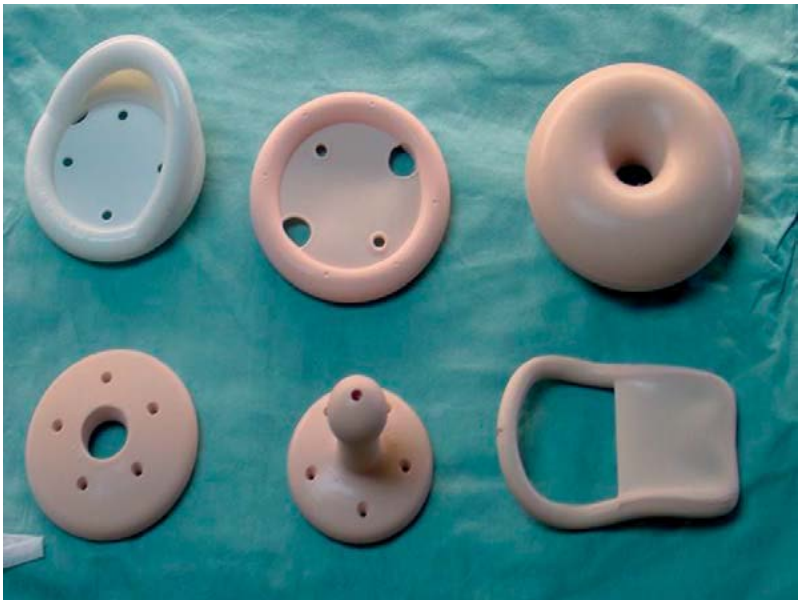

Table 2: POP-Q System Stages

| Stage | Measurement |
|---|---|
| Stage 1 | Leading edge of prolapse at least 1 cm above the plane of the hymen (<-1 cm) |
| Stage 2 | Leading edge of prolapse between 1 cm proximal and 1 cm distal to the plane of the hymen (≥ -1 cm, ≤ 1cm) |
| Stage 3 | Leading edge of prolapse between 1 cm distal to the plan of the hymen and 2 cm less than the total vaginal length (>1 cm, < (tvl-2 cm)) |
| Stage 4 | Leading edge of prolapse equal to or beyond 2 cm less than total vaginal length (≥ (tvl -2 cm)) |

### *4.3.4 Non-mesh Treatments for Pelvic Organ Prolapse*

Non-mesh options for treating POP include conservative treatments and non-mesh surgery. The most effective method of conservative management for POP is the use of pessaries.[34] Pessaries are devices inserted into the vaginal canal to prevent the descent of the pelvic organs (see Figure 8). Some support pessaries, such as ring pessaries, may be compatible with sexual activity. Space occupying pessaries are easier to keep in place because they create suction with the vaginal canal, but they prohibit sexual intercourse.

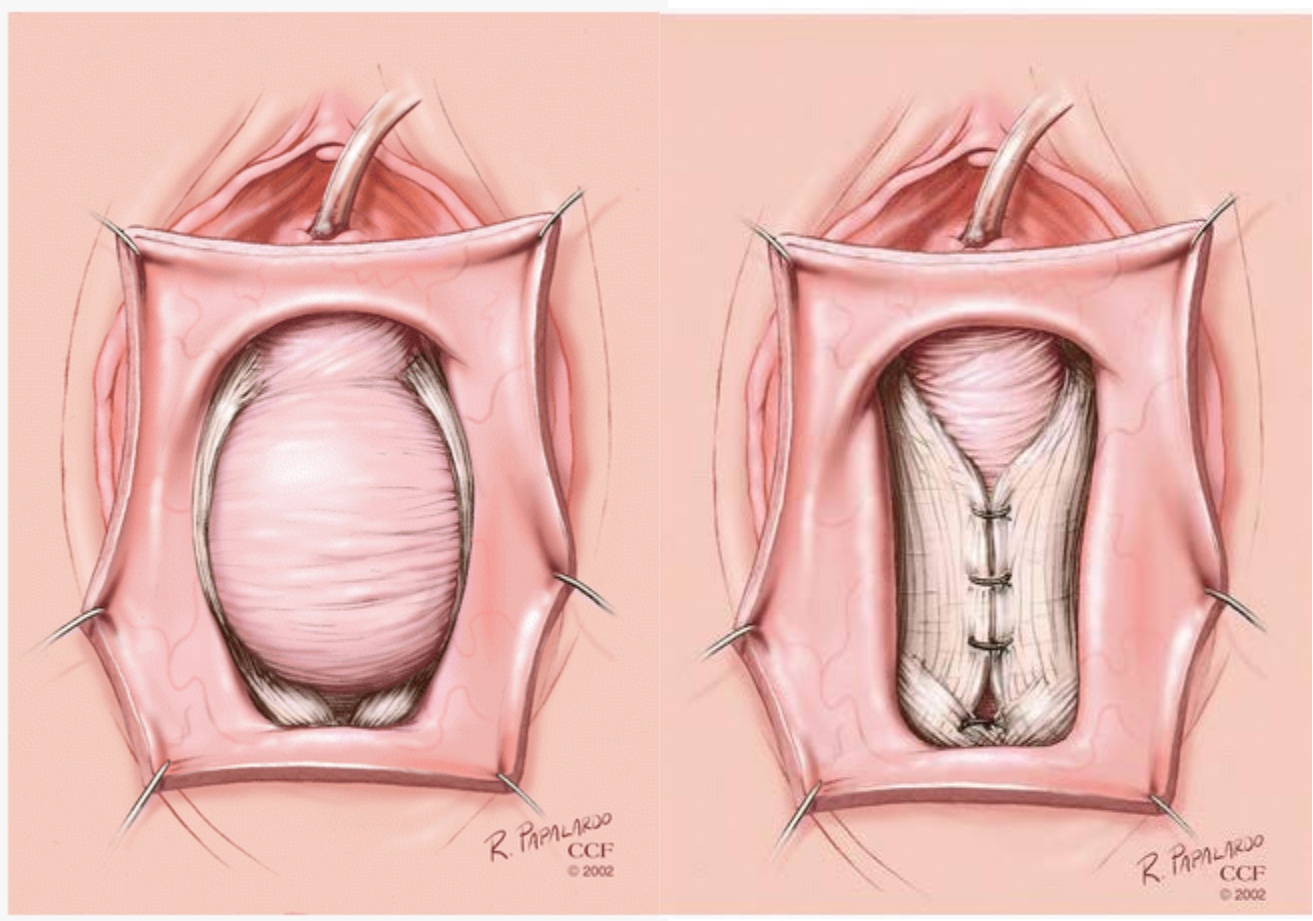
Figure 8: Pessaries



Other conservative treatments are not as well-researched or effective. For instance, while pelvic floor muscle training (PFMT) can help relieve urinary or defecatory symptoms, its use for POP has not been well studied. Although BMI is considered to be a risk factor for POP, reducing body weight has no proven effect in reversing the symptoms or severity of POP.[35] Similarly, recommendations to avoid heavy lifting are based on an understanding of POP anatomy, but have not been studied.[35]

Non-mesh surgery options include anterior and posterior colporrhaphy, as well as restorative and obliterative techniques. Anterior colporrhaphy is a technique used for treatment of anterior prolapse. In this technique, the fibromuscular layer of the anterior vaginal wall is plicated at the midline (the edges of the tissue layer are brought toward the centre) and fixed with sutures to keep the prolapsing organ in place (see Figure 9)

Figure 9: Central Plication of the Fascial Layer in Anterior Native Tissue Repair [32]




Posterior colporrhaphy is used for treating posterior prolapse. The procedure involving the plication of the levator ani muscles results in high rates of anatomic cure of posterior POP; however, it is associated with rates of dyspareunia that are considered to be unacceptably high. Plication of the fascial layer rather than the muscular layer results in less dyspareunia, as does site-specific repair.[29] In site-specific repair, weaknesses or defects in the fascial layer are identified and reinforced with stitches.

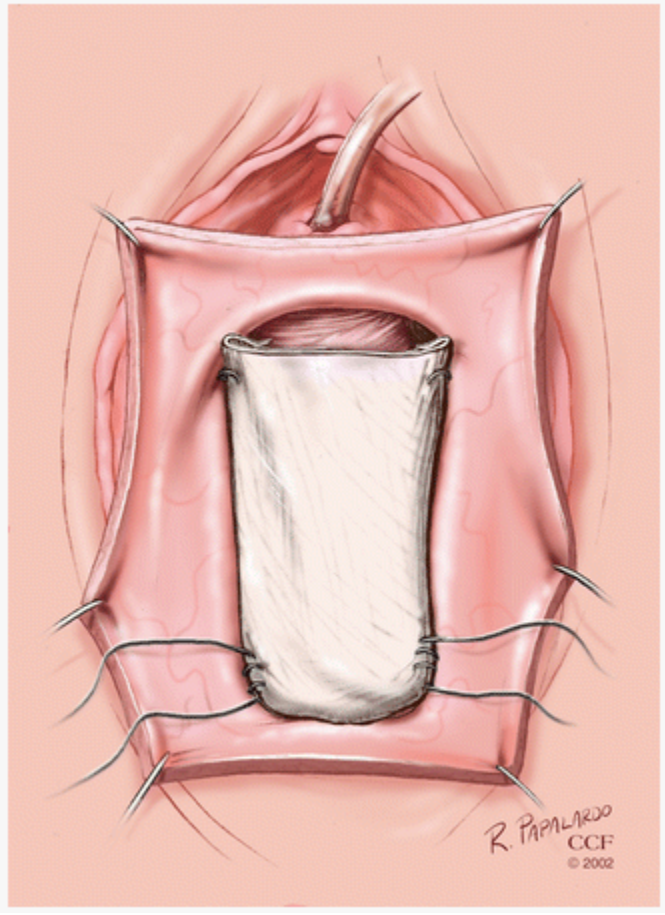
Apical prolapse can be resolved through various surgical techniques, some restorative and some obliterative. Restorative techniques include transvaginal sacrospinous ligament fixation (SSLF).[32] In SSLF, the cervix or upper part of the vaginal vault is suspended from the sacrospinous ligaments.[29] Unfortunately this procedure may exacerbate anterior prolapse. Another alternative restorative procedure is uterosacral ligament suspension (USLS). If a hysterectomy is also indicated, USLS may be more favorable.[32] Obliterative techniques include

colpocleisis, which is simple and effective but results in significant loss of sexual function due to the closure of the vagina.[29]

### *4.3.5 Mesh for Pelvic Organ Prolapse*

Mesh-based repairs for POP use a graft to support the prolapsing organs, thereby keeping them in place. The placement of the mesh differs depending on the site of prolapse. Many commercial mesh kits have been marketed for use in apical prolapse surgery. The exact techniques for mesh placement and fixation differ between mesh kits, but in general the mesh is loosely placed over the site of prolapse to allow for some mesh shrinkage, and is sutured in place to nearby structures (see Figure 10). The mesh then provides the support necessary to prevent the descent of the pelvic organs.[32] Mesh surgeries may be performed transvaginally or abdominally.

Figure 10: POP Repair with Mesh [32]



### *4.3.6 Complications of Mesh for Pelvic Organ Prolapse*

Complications of vaginal mesh for POP are comparable to those that follow mesh surgery for SUI, but occur at different rates. These complications include mesh erosion and exposure, pain, dyspareunia, and infection.[29] Brill found that between 2005-2010, there were 528 medical device reports (MDRs) for mesh erosion in the Manufacturer and User Device Experience (MAUDE) database; 472 MDRs were identified for pain, and 253 were identified for infection. Bleeding, organ perforation, urinary problems, vaginal scarring or shrinkage, neuromuscular problems, and recurrent prolapse were also reported.[36] Pain is a commonly reported complication, and although it may be resolved with time and treatment, patient anecdotes indicate that pain and other adverse events continue to be bothersome years after implantation despite repeated surgical treatments.[1] Lastly, loss of sexual function, discomfort, and dyspareunia are symptoms of POP, but they may also be complications of surgery performed to correct POP.[37,38] These symptoms have a significant impact on patients' quality of life.

The complications associated with mesh surgery present at different times than complications associated with native tissue repair. Initial post-operative complication rates for anterior and posterior prolapse are comparable between the mesh and non-mesh procedures; however, as time progresses, more complications arise from mesh surgery.[8] Late complications have also been found to be associated with a high rate of mesh removal surgery: in one study, 50% of patients admitted for a late complication also underwent subsequent mesh removal.[8] Anterior prolapse surgery with mesh was associated with further surgery for incontinence and for prolapse, and posterior prolapse surgery with mesh was associated with further prolapse surgery.[8] Another population-based study found that patients who underwent mesh surgery had a 66% higher chance of undergoing re-intervention within one year.[39]

The FDA's 2011 safety alert noted that mesh repair for POP may cause complications that do not occur with native tissue repair. While some complications may be uncommon, they may be severe and life-altering despite mesh removal.[40] Mesh contraction, for example, causes severe pain, dyspareunia, and vaginal strictures.[37] Other mesh complications, such as mesh erosion, are both serious and common; one review found that the overall mesh erosion rate for synthetic non-absorbable mesh was approximately 10%,[41] but rates in the literature range between 2-25%.[42] Mesh exposure is another serious condition that often requires re-operation; one trial examining

rates of mesh exposure found that 11 of 27 patients with mesh exposure required re-operation. The same study found that mesh exposure was detected in some participants at their 36 month follow-up, emphasizing that meshes may become exposed years after implantation.[42] It should be noted that mesh exposure may not be completely reversible, and may require several surgeries to excise eroded portions of mesh.[5]

#### *4.3.7 Subjective and Objective Outcomes*

The notion of what is considered a desired outcome for POP surgery is controversial, and variations exist across definitions of objective and subjective success. These differences may result in variability in reported treatment success across studies. Objective success is typically defined by the absence of anatomic POP; however, there may be gradations of what is considered to be objective success. For example, the NIH Workshop on Standardization of Terminology for Researchers in Pelvic Floor Disorders in 2001 defined "satisfactory success" as support present higher than one centimeter above the hymen, and "optimal success" as total absence of POP.[43] Under these definitions, however, 40% of asymptomatic women would not meet the definition of satisfactory success, and 75% of asymptomatic women would not meet the definition of optimal success.[43] This divergence underscores the potential disagreement between definitions of objective success and definitions of subjective success. Many of the women who do not meet the objective criteria for satisfactory success under this definition would likely consider their intervention successful, since they no longer suffer from symptoms of POP.

Subjective success is typically defined as the patient's perception of treatment success, such as the absence of a vaginal bulge sensation. Subjective success rates may differ from objective success rates in the same study. For example, one analysis found that symptomatic vaginal bulging after the operation was reported in less than 10% of study participants, but optimal anatomic success using the NIH workshop definition was reported in only 19% of participants.[43] The authors of that study suggested that composite outcomes that address the presence or absence of the bulge sensation correlate most strongly with the patient's overall assessment of their own treatment success, quality of life, and improvement in symptoms. Thus, composite outcomes that assess bulge sensation symptoms (subjective outcome) in combination with anatomic success (objective outcome) may be the most clinically relevant.[43]

Lastly, special attention should be paid to how recurrence is defined, as there may be differences in recurrence rates per compartment vs. recurrence rates overall. In particular, recurrence rates of prolapse in the treated compartment may be low, but recurrence rates of prolapse in the other (non-treated) compartments may be high. For example, in one study of apical prolapse, 93% of patients did not have apical prolapse recurrence at follow-up; however, 30% of patients developed enterocele.[44] This finding suggests that rates of recurrence in a particular compartment may differ significantly from rates of overall recurrence.

# 5 Environmental Scan of Advisories and Licenses

***Summary:***

- Many meshes are available for implantation in Canada and the United States. In 2019, the United States Food and Drug Administration banned the use of transvaginal mesh kits.[45]
- Canada has issued a notice to hospitals to inform healthcare practitioners about the complications associated with surgical mesh for POP and SUI, and to encourage vigilance and adequate surgical training for mesh implantation teams. The US has reclassified meshes for POP and SUI to higher risk categories.
- The NHS in the UK halted regular use of mesh for urogynaecological surgery in 2018, and the ban was lifted in 2019 when a new NICE guideline was released covering the assessment and management of SUI and POP, and mesh related complications.[2]
- Australia and New Zealand have paused the use of mesh for POP, and some meshes for SUI.
- Much of the regulatory action limiting the use of mesh has been implemented in 2017/2018.

## 5.1 Purpose

An environmental scan was conducted to determine status and licensure of meshes in Canada and internationally.

## 5.2 Methods

The Canadian Medical Devices Active License Listing was searched for mesh products licensed in Canada. The Government of Canada's Recalls and Safety Alerts was searched for mesh-related advisories and recalls. Health Canada was contacted to request a list of mesh products available in Canada. A search of health advisory agencies in the United States, Australia, New Zealand, and the UK was also conducted to characterize these countries' stances on mesh products.

## 5.3 Meshes Available in Canada

Canadian law, specifically the Medical Devices Regulations (SOR/98-282), classifies medical devices according to their risk. Class I devices are associated with the smallest risk, and class IV devices are associated with the highest risk (Table 3).[46] Most surgical meshes licensed in Canada are class III: they are invasive devices that remain in the body for more than 30 days (see Table 4). While some individual meshes have been removed from the market in Canada (Table 6), no broad recalls have been issued. Table 4 shows which permanent, semi-permanent, and dissolvable meshes are currently available in Canada.

Table 3: Canadian Medical Device Classes (Invasive Devices) [46]

| Class | Risk | Description of Devices in Class | Examples |
|---|---|---|---|
| Class I | Lowest | Invasive devices that are placed in oral or nasal cavities | Manual toothbrush, dressing for nosebleed |
| Class II | Low-moderate | Invasive devices that penetrate the body through an orifice or contact the surface of the eye (rule 2; subrule 1) | Contact lenses, urethral catheter |
| Class III | High-moderate | Invasive devices that remain in the body for 30 or more consecutive days, or is intended to be absorbed by the body (rule 2; subrule 3) | Intrauterine contraceptive device, ureteral stent |
| Class IV | Highest | Any device made from or incorporating human or animal tissues or tissue derivatives (rule 14; subrule 1) | Porcine heart valve, bone graft |

Table 4: Selection of Surgical Meshes Available in Canada

| Class | Company Name | Trade Name | Date of License Issue |
|---|---|---|---|
| 2 | Preat Corporation | Fiber kits | 2014-02-27 |
| | | Efiber, Perma Mesh, Everstick, Perma Fiber | 2014-02-27 |
| | Preservation Solutions, Inc | Wittman patch | 2016-02-11 |
| | Rapid Medical, LTD. | Comaneci remodeling mesh | 2018-01-30 |
| 3 | American Medical Systems, Inc. | AMS Advance Male Sling System | 2018-09-13 |
| | Coloplast A/S | Exair posterior prolapse repair system,<br>Exair anterior prolapse repair system | 2016-10-05 |
| | | Restorelle Y | 2018-04-20 |
| | Davol, Inc. | Bard Composix L/P Mesh, oval, ellipse, or rectangle, with introducer tool | 2015-05-08 |
| | | Ventralight ST low profile bioresorbable coated permanent mesh<br>Bioresorbable coating/permanent mesh | 2018-06-22 |
| | | Ventralight ST mesh with echo PS positioning system (circle, oval, ellipse, rectangle) | 2018-06-22 |
| | | Onflex mesh | 2018-06-22 |

| | | | |
|---|---|---|---|
| | | Phasix ST mesh (rectangle, circle, square) | 2016-07-25 |
| | | Ventralight ST mesh with echo 2 positioning system (oval, circle, ellipse) | 2018-08-17 |
| | | Mersiline mesh<br>Vicryl knitted mesh (polyglactin 910)<br>Vicryl woven mesh (polyglactin 910) | 2017-08-04 |
| | Ethicon, Inc. | Prolene 3D patch | 2006-05-25 |
| | | Proceed surgical mesh | 2006-05-25 |
| | Institut Straumann AG | Straumann GBR system- mesh, vario mesh | 2005-02-11 |
| | KLS Martin L.P | IPS Peek | 2017-07-25 |
| | | Resorb-XG- mesh plate | 2017-08-25 |
| | | Resorb-X system- mesh panel | 2016-09-26 |
| | Covidien, Inc. | Surgiopro mesh (monofilament polypropylene clear, multifilament polypropylene clear) | 2015-07-10 |
| | W.L. Gore & Associates, Inc. | Gore-tex soft tissue patch- standard and plus | 2017-09-29 |
| | | Gore-tex dualmesh biomaterial | 2017-10-30 |
| | | Gore-tex bio-a tissue reinforcement | 2018-10-18 |
| | | Timesh titanium fixation and bone graft system- Flexmesh | 2018-08-23 |
| | Stryker Leibinger GMBH & Co | Universal mesh | 2018-09-18 |
| | Medtronic, Inc | Timesh titanium fixation & bone graft system - Flexmesh | 2018-08-23 |
| | Cousin Biotech | Intramesh soft lift | 2011-09-12 |
| | | Plaque Biomesh P1, P8 | 2011-09-12 |
| | | 4D Dome semi-resorbable avec une plaque | 2011-09-12 |
| | | Biomesh soft prolaps- plaque en polypropyene (rectocele, cystocele, rectocele+cystocele) | 2016-09-23 |
| | | Implant de reinforcement parietal | 2011-09-12 |
| | | Plaque P8 adhesive | 2013-08-02 |
| | | Ultrapro advanced macroporous partially absorbable mesh | 2016-09-30 |
| | | Ultrapro plug device | 2013-05-13 |
| | | Proceed ventral patch | 2013-05-13 |
| | | Ethicon physiomesh open flexible composite mesh device | 2016-07-20 |

| | | | |
|---|---|---|---|
| | | Artisyn Y-shaped mesh | 2013-07-10 |
| | PFM Medical, Inc. | Timesh products | 2018-05-28 |
| | | Tiloop products | 2018-05-28 |
| | Desarrollo E Investigacion Medica Aragonesa | Contasure Needless | 2011-04-20 |
| | Biocer Entwicklungs- GMB H | Tio2Mesh | 2016-11-01 |
| | Boston Scientific Corporation | Solyx Sis (single incision sling) system | 2016-08-05 |
| | | Upsylon Y mesh kit | 2015-05-27 |
| | | Polyform synthetic mesh | 2016-06-17 |
| | | Uphold lite vaginal support system with Capio slim | 2018-11-01 |
| | Poriferous | Su-Por surgical implants | 2016-11-22 |
| | Atrium medical corporation | Prolite mesh<br>Prolite ultra mesh<br>Proloop mesh | 2018-04-18 |
| 4 | Atrium medical corporation | C-qur mesh | 2018-10-24 |
| | Lifecell Corporation | Strattice reconstructive tissue matrix,<br>Strattice reconstructive tissue matrix perforated, laparoscopic | 2016-11-02 |
| | | Novomatrix reconstructive tissue matrix | 2018-09-05 |

### 5.4 Advisories and Withdrawals from the Market

In 2016 and 2017, the US FDA ordered the reclassification of some surgical mesh products for POP and SUI to higher risk classes. In 2019, the FDA banned the use of transvaginal mesh kits.[45] In July 2018, the UK's Secretary of State for Health and Social Care and Chief Medical Officer issued a pause on the use of surgical mesh for urogynaecological purposes. This pause initiated a "high vigilance restriction period" for mesh procedures.[47] This pause was ended upon the release of the 2019 NICE guideline on the assessment and management of SUI and POP,[2] including non-surgical and surgical options.[3] The Australian Therapeutic Goods Administration and New Zealand Medicines and Medical Devices Safety Authority have both acted to curtail the use of surgical mesh for POP and limit some products for SUI (see Table 5 below for a summary and Appendix 4: Table 1 for full information). Publicly available information on specific surgical mesh product recalls is reported in Table 6.

Health Canada issued a notice to hospitals in 2010 recommending increased caution in using surgical mesh to treat SUI and POP. This notice was updated in 2014 to emphasize the

uncertainty in the complication profile of surgical mesh. The notice stated that "transvaginal mesh procedures for the treatment of POP are evolving procedures that may carry higher risk of complications," and that "some of these complications may require additional surgery which may not fully correct them." For SUI, the notice indicated that SIMS for SUI are still new and may carry a high complication rate.[48]

On November 29, 2018, the Canadian Minister of Health published a statement in response to "recent reports of serious issues Canadians have been facing with implanted medical devices." The Minister of Health directed Health Canada to implement an Action Plan to intensify the pre-market approval process, increase post-market surveillance, and enhance the transparency of approval and surveillance.[49]

In December 2018, Health Canada published an Action Plan to address these three priorities. To address the Minister's first priority, strengthening the pre-market approval process, starting in early 2019 Health Canada plans to allow medical professionals to apply to conduct investigations into medical devices (where before only manufacturers are able to do so). Health Canada will also review its evidence requirements for approval of high-risk medical devices. Of particular interest to this HTA, in January 2019, Health Canada created a new expert advisory committee focused on women's health in drugs and devices (SAC-HPW).[50]

To address the Minister's second priority of robust post-market surveillance, *Vanessa's Law* will require Canadian hospitals to report medical device complications. Health Canada will also expand the Canadian Medical Devices Sentinel Network. *Vanessa's Law* will also obligate manufacturers to provide more information to Health Canada, such as notifying Health Canada of regulatory actions taken by foreign regulatory agencies, and it will allow Health Canada to require manufacturers to undertake additional studies on devices. The *Regulatory Review of the Drugs and Devices initiative* will propose a framework to increase the use of real-world evidence to evaluate devices throughout their market lifespans. More inspectors, more frequent inspections, onsite inspections of foreign manufacturers, and rigorous investigations will also support post-market surveillance.[50]

To improve transparency, Health Canada will begin to release the evidence upon which it bases its approvals. In March 2019, Health Canada published summaries of its decisions for class III devices[51] (where before only class IV device reports were published). A searchable database will

be launched to allow Canadians to access device incident reports, and Health Canada's inspection results and regulatory actions.[50]

Table 5: Actions against Surgical Mesh in Canada and Internationally

| | SUI | | | POP | | |
|---|---|---|---|---|---|---|
| | **Advisory** | **Pause** | **Ban** | **Advisory** | **Pause** | **Ban** |
| Canada[48] | ✓ | | | ✓ | | |
| US[45,52,53] | ✓ | | | | | ✓† |
| Australia[54] | ✓ | | * | | | ✓ |
| New Zealand[55] | | | ** | | | ✓ |
| UK[3,47,56,57] | ✓ | | | ✓ | | |
| Ireland[58] | | ✓ | | | ✓ | |
| Europe[59] | ✓ | | | ✓ | | |

*single-incision mini-slings no-longer supplied; MUSs not affected, but sponsors now require to included information on adverse events

**One single-incision mini-sling no-longer supplied; MUSs not affected

† Only transvaginal mesh to treat POP is banned, transabdominal mesh to treat POP is still under advisory

Table 6: Publicly Available Information on Specific Product Recalls in Canada, the US, and Australia

| **Country** | **Condition(s)** | **Manufacturer/Product** | **Recall Date** |
|---|---|---|---|
| US | | No recalls issued | |
| Canada | POP | Capio products: Capio Suture Capturing Device; Uphold Vaginal Support System; Pinnacle Pelvic Floor Repair Kit – POSTERIOR; Capio Slim Suture Capturing Device; Uphold Lite with Capio Slim[60] | Feb 2018 |
| | SUI | BC Hammock Mesh Slings[61] | May 2013 |
| Australia[62] | POP | Boston Scientific Pty Ltd: Uphold Range | Dec 15, 2017 |
| | SUI | Boston Scientific Corporation: Solyx | Dec 15, 2017 |
| | POP | Coloplast AS: Restorelle Range | Dec 15, 2017 |
| | SUI | Coloplast AS: Altis | Dec 15, 2017 |

### 5.5 Class-action Lawsuits in Canada and the United States

Several Canadian class action lawsuits have been launched against mesh manufacturers. Affected companies include Johnson & Johnson, American Medical Systems, and Boston Scientific. Class-action lawsuits against mesh companies have been difficult to initiate in Canada.

Certification of a class of plaintiffs requires that the plaintiffs allege similar issues, but mesh patients experience dissimilar complications.[63]

In contrast to the situation in Canada, class action lawsuits against mesh manufacturers have been more common in the US, with more than 90,000 women having entered into class action suits.[63] According to one article, there is evidence that health insurance companies in the US have provided information about patients who have undergone mesh surgery to third-party law companies and contacted women in their networks who have had surgery with mesh to attempt to claim some of the settlement for themselves.[64]

# 6 Review of Guidelines and Best Practice Recommendations

***Summary:***

- Recent guidelines recommend using surgical mesh for POP and SUI only for research, or if special arrangements for clinical governance are in place.
- Guidelines emphasize informing patients of the potential complications of mesh, and treatment alternatives.
- Only surgeons with specific up-to-date training on mesh implantation should perform mesh procedures.
- Guidelines recommend long-term follow-up with patients after the procedure, and diligent reporting of adverse events.

## 6.1 Purpose

To synthesize current guidelines and best practice recommendations on the use of surgical mesh for pelvic organ prolapse (POP) and stress urinary incontinence (SUI).

## 6.1 Methods

A grey literature search was conducted. CADTH's *Grey Matters* guide was used to locate agencies issuing guidelines. Searches were conducted on the websites of these agencies for guidelines related to surgical mesh, mesh slings, and tension-free vaginal tape specifically, and surgical management of SUI and POP generally. A review of the guidelines was conducted to eliminate those guidelines that covered SUI/POP treatment but did not address mesh technologies. Given the evolving nature of this clinical area, the search was update to date as of March 2019.

## 6.2 Results

Eighteen relevant guidelines were identified (see Table 7). Publication dates ranged between 2003 and 2019. All but one guideline were published after 2010,[47,65-79] and eleven guidelines were published between 2017-2019.[3,47,67,72-78] Thirteen guidelines were published in United Kingdom,[47,65,68,71-78,80 3] two in Canada,[66,70] one in France,[79] one in Europe,[69] and one in US.[67] All guidelines provide recommendations for women exclusively, except for one that did not specify a population[78] and two that addressed both male and female populations.[69,70]

Ten guidelines published in 2016-2019 recommended performing procedures using surgical mesh for POP or SUI only if there are special arrangements in place for clinical governance, consent, and audit or research.[3,47,71-78] Thirteen guidelines recommended that patients who want to undergo the procedure of mesh implantation be given clear written information about complications, a detailed list of potentially serious complications, and all alternative treatment options.[47,65,66,68,71-77,80] Several guidelines recommended that patient selection and treatment should only be done by multidisciplinary teams with experience in the assessment and management of women with POP and SUI, and that the procedure should only be performed by specialists/clinicians with specific up-to-date training.[47,65,69,71-75,77,78] Post-operative care should be a high-vigilance process, with suitable arrangements for long-term follow up.[47,65-67,69,71-78,80] Lastly, 12 guidelines recommended publishing outcomes to a registry and reporting all adverse events involving the procedure or surgical mesh to relevant regulatory agencies.[3,47,65,71-78,80]

Two guidelines were published in Canada.[66,70] The 2012 Canadian Urological Association (CUA) guideline focused on the treatment of SUI in general,[63] while the 2013 Ontario Health Technology Advisory Committee (OHTAC) recommendation focused specifically on the use of MUS for SUI.[59] The CUA guideline recommended the use of MUS as one of several treatments for SUI, including artificial sphincters and bladder neck slings. OHTAC recommended that physicians review warnings on devices and inform patients of potential complications, maintain vigilance for intraoperative and post-operative complications, and keep up to date with training.[59]

The French College of Gynecologists and Obstetricians issued a guideline in 2010 concerning the diagnosis and management of SUI.[79] This guideline recommended pre-operative and post-operative testing and endorsed the use of retropubic or transobturator tape as the first line of treatment for female SUI.[79]

In 2015, the European Association of Urology (EAU) issued a guideline on the treatment of SUI advising that medical staff ought to be properly trained in each procedure, and that they should perform sufficient numbers of a procedure to maintain their expertise. The guideline also states that patients should be offered alternative surgical treatments. Post-operatively, the EAU recommends that medical personnel should offer long-term follow-up, and be able to address complications should they arise.[69]

In the US, the American Urological Association (AUA) and Society of Urodynamics, Female Pelvic medicine and Urogenital Reconstruction (SUFU) issued a 2017 surgical guideline addressing surgery for SUI.[67] This guideline states that MUS is one of several potential treatments that may be offered to patients and that it may be offered through either retropubic or transobturator routes. Patients with diabetes, obese patients, patients planning a family, or geriatric patients should receive proper evaluation and counselling. Single incision sling (SIS) should only be offered to patients who are informed about the lack of evidence regarding the safety and efficacy of SIS devices. Furthermore, physicians should be very cautious about implanting a device in patients who may not heal well.[67]

Thirteen guidelines were published in the UK.[3,47,65,68,71-78,80] Of these guidelines, ten were published by the National Institute for Health and Care Excellence (NICE) and issued similar recommendations for careful patient selection, emphasis on informing patients about complications and alternative procedures, long-term follow-up, and reporting of complications.[71-78,80] Six of the NICE guidelines were published in 2017, addressing the use of specific mesh procedures for various conditions: uterine prolapse, vaginal vault prolapse, and posterior wall prolapse.[72-77] The earliest of the NICE guidelines addressed TVT (2003) and recommended its use to treat SUI with the caveat of proper surgical training and long-term surveillance.[80] The guideline addressing the use of the single-incision mini sling (SIMS) (2016), made similar recommendations to the 2017 series of guidelines.[71] The 2018 NICE guideline addressed the use of laparoscopic mesh procedure for apical prolapse and recommended that the procedure only be used in the context of research.[78] A 2018 letter penned by the Mesh Clinical Advisory Group in the UK recommended that the use of mesh be strictly curtailed and that a period of "high vigilance scrutiny" be applied.[47] The last NICE guideline outlined the surgical and non-surgical management of SUI and POP (2019). Recommendations included establishment of multidisciplinary teams on a local and regional level to involve patients in discussions about their treatment options to support them to make informed decisions. Should a patient choose a surgical treatment of SUI and POP, the guideline also made recommendations on how to assess and manage complications associated with mesh surgery. The importance of having a national registry of surgery for SUI and POP to collect short- and long-term outcomes including surgical complications was noted. The guideline also made several research recommendations including

long-term risks of surgery with or without mesh, complications associated with mesh surgery and the effectiveness of pain management post-surgery.

### 6.3 Conclusions

The guidelines focused their recommendations on female patients with POP or SUI wanting to undergo surgical mesh implantation. All other guidelines indicated that the long-term safety of surgical mesh is uncertain and that it is associated with potentially serious complications including risk of mesh erosion or recurrence. It also called for procedures to be performed only by specialists/clinicians with long-term follow-up plans, for surgical results to be published in a registry, and for adverse events to be reported to regulatory agencies. The most recent guideline addresses complications associated with mesh surgery and how to assess and manage them.

Table 7: Guidelines on the Use of Surgical Meshes for SUI/POP

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| **UK Guidelines** | | | | |
| National Institute for Health and Care Excellence (NICE)[81]<br><br>2003<br><br>UK | Final Appraisal Determination | Tension-free vaginal tape (TVT) for stress incontinence | SUI<br><br>Tension free vaginal tape | • TVT recommended as one of a range of surgical options for uncomplicated urodynamic SUI when conservative management has failed<br>• Patients should be fully informed<br>• TVT should only be performed by surgeons who have received appropriate training and who regularly perform surgery for SUI in women<br>• Further research to determine long-term effectiveness and complication rate.<br>• Observational data on effectiveness and safety of the procedure should be collected over a period of 10 years or more in a national coordinated registry of audit data, including the number of procedures carried out, measures of outcome, and adverse events |
| Royal College of Obstetricians and Gynaecologists, British Society of Urogynaecology [65]<br><br>2015<br><br>UK | Green-Top Guideline, Guidelines for good clinical practice | Recommendations on Post-Hysterectomy Vaginal Vault Prolapse | Vaginal Vault Prolapse | • Do not use transvaginal mesh kits/grafts (TVM) as first-line treatment of post-hysterectomy vaginal vault prolapse<br><br>If TVM is considered:<br>• Women should be fully informed of alternative surgical and nonsurgical options<br>• TVM procedure performed by appropriately trained urogynaecologist after multidisciplinary team meeting of each individual case<br>• Result of TVM should be audited and submitted to national surgical database, any complications |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | reported to Medicines and Healthcare Products Regulatory Agency |
| National Institute for Health and Care Excellence (NICE)[71]<br><br>2016<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on single-incision short sling mesh insertion for stress urinary incontinence in women (IPG566) | SUI<br><br>Single-incision short slings | • Procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research<br>• Mesh slings should be used for permanent implants, presence of anchors make removal difficult<br><br>If procedure is used, then:<br>• Patient selection and treatment should be done by multidisciplinary team with experience in the assessment and management of women with SUI<br>• Implantation (or removal) should be done by clinicians with specific training in transobturator surgical techniques<br>• Inform clinical governance leads<br>• Clear written information to ensure patients understand uncertainty (national standard consent form being developed)<br>• Audit and review outcomes of all patients<br>• Continue research, include details of patient selection, measure of long-term outcomes<br>• Continuous reporting to registry, adverse events should be reported to Medicines and Healthcare products Regulatory Agency |
| National Institute for Health and Care | Interventional Procedures Guidance | Evidence-based recommendations on uterine suspension using | Uterine Prolapse | • Procedure can be used provided that standard arrangements are in place for clinical governance, consent and audit |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| Excellence (NICE)[77]<br><br>2017<br><br>UK | | mesh (including sacrohysteropexy) to repair uterine prolapse (IPG584) | Mesh suspensions | If procedure is used, then:<br>• Clear written information about treatment options, the procedure and complications to ensure patients understand uncertainty (national standard consent form being developed)<br>• Patient selection and treatment should only be done by multidisciplinary team with experience in managing organ prolapse and urinary incontinence in women<br>• Procedure should be performed by clinicians with specific up-to-date training and who perform the procedure regularly<br>• Registry for patients and results, adverse events should be reported to Medicines and Healthcare products Regulatory Agency<br>• Although procedure preserves uterus, future pregnancy not recommended |
| National Institute for Health and Care Excellence (NICE)[75]<br><br>2017<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on sacrocolpopexy with hysterectomy using mesh to repair uterine prolapse (IPG577) | Uterine prolapse<br><br>Sacrocolpopexy with hysterectomy | • Procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research<br>• 2-stage procedure (hysterectomy followed by sacrocolpopexy at a future date) is preferred<br><br>If procedure is used, then:<br>• Patient selection and treatment should only be done by specialists with specific up-to-date training, experienced in managing pelvic organ prolapse and urinary incontinence in women<br>• Inform clinical governance leads |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | • Clear written information about treatment options, the procedure and complications to ensure patients understand uncertainty (national standard consent form being developed)<br>• Registry for patients and results, adverse events should be reported to Medicines and Healthcare products Regulatory Agency<br>• Long-term data collection on clinical outcomes and patient-reported QoL outcomes using validated scales |
| National Institute for Health and Care Excellence (NICE)[76]<br><br>2017<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on transvaginal mesh repair of anterior or posterior vaginal wall prolapse (IPG599) | Vaginal wall prolapse<br><br>Transvaginal mesh | • Procedure should only be used in context of research<br>• Further research should include details of patient selection, long-term outcomes including complications, type of mesh used, method of fixation and QoL<br><br>If procedure is used, then:<br>• Adverse events should be reported to Medicines and Healthcare products Regulatory Agency |
| National Institute for Health and Care Excellence (NICE)[74]<br><br>2017<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on sacrocolpopexy using mesh to repair vaginal vault prolapse (IPG583) | Vaginal Vault Prolapse<br><br>Sacrocolpopexy with mesh | • Procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research<br><br>If procedure is used, then:<br>• Patient selection and treatment should only be done by specialists with up-to-date training, experience in managing pelvic organ prolapse and urinary incontinence in women, and do procedure regularly |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | • Inform clinical governance leads<br>• Clear written information about treatment options, the procedure and complications to ensure patients understand uncertainty (national standard consent form being developed)<br>• Registry for patients and results, adverse events should be reported to Medicines and Healthcare products Regulatory Agency<br>• Long-term data collection on clinical outcomes and patient-reported QoL outcomes using validated scales |
| National Institute for Health and Care Excellence (NICE)[73]<br><br>2017<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on infracoccygeal sacropexy using mesh to repair vaginal vault prolapse in women (IPG581) | Vagina Vault Prolapse<br><br>Infracoccygeal Sacropexy (Posterior Sling) | • Procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research<br><br>If procedure is used, then:<br>• Patient selection and treatment should only be done by specialists with specific up-to-date training, experienced in managing pelvic organ prolapse and urinary incontinence in women<br>• Inform clinical governance leads<br>• Clear written information about treatment options, the procedure and complications to ensure patients understand uncertainty (national standard consent form being developed)<br>• Registry for patients and results, adverse events should be reported to Medicines and Healthcare products Regulatory Agency |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | • Long term data collection on clinical outcomes and patient-reported QoL outcomes using validated scales |
| National Institute for Health and Care Excellence (NICE)[72]<br><br>2017<br><br>UK | Interventional Procedures Guidance | Evidence-based recommendations on infracoccygeal sacropexy using mesh to repair uterine prolapse in women (IPG582) | Uterine Prolapse<br><br>Infracoccygeal Sacropexy (Posterior Sling) | • Procedure should not be used unless there are special arrangements in place for clinical governance, consent and audit or research<br><br>If procedure is used, then:<br>• Patient selection and treatment should only be done by specialists with specific up-to-date training, experienced in managing pelvic organ prolapse and urinary incontinence in women<br>• Inform clinical governance leads in their NHS trusts<br>• Clear written information about treatment options, the procedure and complications to ensure patients understand uncertainty (national standard consent form being developed)<br>• Registry for patients and results, adverse events should be reported to Medicines and Healthcare products Regulatory Agency<br>• Long-term data collection on clinical outcomes and patient-reported QoL outcomes using validated scales |
| National Institute for Health and Care Excellence (NICE)[78] | Interventional Procedures Guidance | Recommendations on laparoscopic mesh pectopexy for apical prolapse of the uterus or vagina | Apical prolapse of uterus or vagina<br><br>Laparoscopic mesh pectopexy | • Procedure should only be used in context of research<br>• Procedure should only be done by surgeons experienced and trained in laparoscopic urogynaecological surgery |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| 2018<br><br>UK | | | | • Adverse events should be reported to Medicines and Healthcare products Regulatory Agency |
| NHS Improvement and NHS England[47]<br><br>2018<br><br>UK | Letter | Letter to regional directors, trust medical directors, and clinicians involved in the care of patients with stress urinary incontinence and pelvic organ prolapse | SUI, POP<br><br>Mesh | • "Pause" in use of synthetic mesh/tape to treat SUI and urogynaeological prolapse where mesh is inserted through the vaginal wall, where "pause" is a "restriction of use." "High vigilance restriction period" for any procedure performed and for the wider group of related procedures<br><br>Clinical Advisory Group representing variety of expert groups recommends to CMO the following:<br>• A. Recommend the mesh/tape procedures to be included in the restriction of use<br>• B. Recommend and justify any mesh/tape procedures that should be exempt from the restriction, with or without increased vigilance<br>• C. Recommend alternative non-mesh procedures subject to increased vigilance, given the change in practice caused by the restriction on mesh/tape use<br>• D. Advise high vigilance processes must be followed by NHS and private hospitals for any mesh/tape surgery defined in (A) but deemed clinically essential during the restriction, and for (B) and (C). Require provider trust/hospital medical directors to be accountable for ensuring that procedures to:<br>o Ensure the necessity and appropriateness of any procedure covered by the |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | restriction of use and high vigilance period<br>o Ensure that all appropriate surgical options have been offered, including where secondary referral would be required<br>o Ensure that appropriate information and consenting processes are in place in all cases<br>o Provide assurance of a surgeon's competence for any procedure offered<br>o Ensure there is documenting and registering of included procedures<br>• E. Recommend how trusts and GPs should support patients with advice, including newly referred, diagnosed, waiting list, or previous mesh surgery patients |
| National Institute for Health and Care Excellence (NICE)<br><br>2019<br><br>UK | Interventional Procedures Guidance | Urinary incontinence and pelvic organ prolapse in women: management | SUI, POP<br><br>Mesh | • Patients must be informed of all surgical options and the associated risks and benefits of each<br>• Doctors must keep detailed records about the surgery, including any complications that arise<br>• Description on how to best care for women who have complications due to surgery with mesh is provided |
| **European Guidelines (not including UK)** | | | | |
| French College of Gynaecologists | European Journal of Obstetrics and Gynecology and | Diagnosis and management of adult female stress urinary | Female SUI | • Complete urodynamic investigation prior to surgery |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| and Obstetricians[79]<br><br>2010<br><br>France | Reproductive Biology | incontinence: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians | All diagnosis and management | • For female SUI, sub-urethral tape (retropubic or transobturator) is recommended as first line technique<br>• Modified sub-urethral tape techniques need to be assessed by comparative clinical trials before being put into general practice<br>• Implantable materials used should comply with AFNOR standard S94-801<br>• Assess quality of voiding postoperatively to screen for voiding dysfunction |
| European Association of Urology (EAU)[68]<br><br>2013<br><br>UK | Actas Urol Esp. – Elsevier Doyma | EAU guidelines on surgical treatment of urinary incontinence | Urinary incontinence<br><br>All surgical treatment | Recommendations for uncomplicated SUI in women:<br>• Offer MUS as initial surgical intervention<br>• Offer colposuspension or AFS if not MUS<br>• Warn women about the higher risk of perioperative complications in retropubic approaches compared with transoturator insertion<br>• Warn women who are being offered transobturator insertion about the higher risk of pain and dyspareunia<br>• Warn women undergoing AFS about higher risk of voiding difficulty and the need to perform clean intermittent self-catheterization; ensure they are willing and able to do so<br>• Cystoscopy as part of retropubic insertion of a MUS, or if difficulty is encountered during transobturator sling insertion, or if there is a significant cystocele<br>• Women being offered SIS for which an evidence base exists should be warned that they may be |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | less effective than MUS and that efficacy beyond 1 year remains uncertain<br>• SIS without level 1 evidence of effectiveness should only be implanted as part of structured research<br>• Only offer adjustable MUS as a primary surgical treatment for SUI within structured research<br><br>Recommendations for complicated SUI:<br>• Choice of surgery should be based on careful evaluation of individual patient<br>• Women should be warned that outcome of second-line surgical procedures is likely inferior to first-line<br>• Offer implantation of artificial urinary sphincter or adjustable compression therapy as an option.<br><br>Recommendation for mixed urinary incontinence:<br>• Warn women that they have a higher risk of failing to benefit from SUI surgery |
| European Association of Urology (EAU)[69]<br><br>2015<br><br>Europe | Recommendations | Guidelines on Urinary Incontinence | Urinary incontinence | Surgeons and centers performing surgery should:<br>• be properly trained in each procedure;<br>• not be trained by someone who is not surgically qualified;<br>• perform sufficient numbers of a procedure to maintain expertise;<br>• offer alternative surgical treatments;<br>• be able to deal with complications;<br>• provide suitable arrangements for follow-up long term if necessary |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| **North American Guidelines** | | | | |
| Canadian Urological Association (CUA)[70]<br><br>2012<br><br>Canada | 2012 Update on Guidelines | Guidelines for Adult Urinary Incontinence Collaborative Consensus Document for the Canadian urological Association | Adult urinary incontinence<br><br>Bladder Neck Slings, Artificial sphincter, synthetic mid urethral sling | • Artificial sphincter procedure for female SUI may be considered with non-functioning urethras secondary to trauma to the pelvic nerves, severe ISD with multiple prior failed surgical procedures and significant SUI with poor bladder contractility<br>• For urethral hypermobility, surgical treatment options include retropubic suspension, bladder neck slings, synthetic MUS<br>• For intrinsic urethral deficiency, treatment options include bladder neck slings, synthetic mid urethral sling, and artificial urinary sphincter |
| Ontario Health Technology Advisory Committee (OHTAC)[66]<br><br>2013<br><br>Canada | Recommendation | OHTAC Recommendation on Midurethral Slings for Women with Stress Urinary Incontinence | Female SUI<br><br>Midurethral slings | Original 2006 Recommendation:<br>• Explore the introduction of unique CCI codes so that MUSs can be tracked by retropubic and transobturator routes through administrative databases to assess variation in complication rates<br><br>Update 2013:<br>• Highlights the need for physicians to: 1) review warnings on devices; 2) inform patients of adverse events; 3) watch for signs of intraoperative and post-operative complications; and 4) maintain training for procedure and management of complications |
| American Urological Association, Society of Urodynamics, | Surgical Treatment Guidelines | Surgical treatment of female stress urinary incontinence | Female SUI<br><br>Surgical treatments | • Physicians may offer MUS (synthetic), AFS, Burch colposuspension, bulking agents |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| Female Pelvic medicine and Urogenital Reconstruction (SUFU)[67]<br><br>2017<br><br>USA | | | | • In patients who select MUS surgery, physicians may offer either the retropubic or transobturator MUS<br>• Physician may offer SIS to patients undergoing MUS surgery if the patient is informed about the immaturity of evidence regarding efficacy and safety<br>• Physicians should not place a mesh sling if the urethra is injured<br>• Patients with SUI and a fixed, immobile urethra should be offered pubovaginal sling, retropubic MUS, or urethral bulking agents<br>• Physicians should not implant a synthetic MUS in patients undergoing concomitant urethral diverticulectomy, repair of urethrovaginal fistula, or urethral mesh excision<br>• Physicians should strongly consider avoiding the use of mesh in patients at risk for poor wound healing<br>• Incontinence procedures may be performed in patients undergoing concomitant surgery for pelvic prolapse repair and SUI<br>• After evaluation and counselling, physicians may offer surgical treatment to patients with concomitant neurological disease affecting LUT function<br>• Physicians may offer synthetic MUS (in addition to other sling types) to the following patient populations after evaluation and counselling: |

| Organization, year, country | Type of publication | Title | Condition, Device | Recommendations |
|---|---|---|---|---|
| | | | | patients planning to bear children, patients with diabetes or obesity, and geriatric patients<br>• Physicians should follow up in early postoperative period to assess if patients have experience adverse events, and those patients should be examined<br>• Patients should be seen and examined by physicians within six months post operatively; those with unfavorable outcomes require additional follow-up<br>• Subjective outcome of surgery as perceived by patient should be assessed and documented<br>• Patients should be asked about residual incontinence, ease of voiding/force of stream, recent UTI, pain, sexual function and new onset or worsened OAB symptoms<br>• Physical exam should be performed to evaluate healing, tenderness, mesh extrusion, abnormalities |

Abbreviations: AFS: autologous fascial sling; AFNOR: Association Française de Normalisation; CCI: Canadian Classification of Health Interventions; CMO: Chief Medical Officer; CUA: Canadian Urological Association; EAU: European Association of Urology; GPs: General Practitioners ISD: intrinsic sphincter deficiency; LUT: lower urinary tract; MUS: mid-urethral sling; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; OHTAC: Ontario Health Technology Advisory Committee; QoL: Quality of Life; SIS: single-incision sling; SUFU: Society of Urodynamics, Female Pelvic medicine and Urogenital Reconstruction; SUI: stress urinary incontinence; TVT: tension-free vaginal tape; TVM: transvaginal mesh

# 7 Systematic Review of Health Technology Assessments on Surgical Mesh

***Summary***

- Two SUI HTAs were identified, and both found that TVT had comparable clinical effectiveness to other treatments and that it was likely more cost-effective than colposuspension.
- No HTAs for POP were identified as part of this review.
- Specific recommendations regarding the use of surgical mesh for SUI were not provided; additional research is warranted.

## 7.1 Purpose

To synthesize health technology assessments (HTAs) on synthetic surgical mesh for treatment of SUI and POP.

## 7.2 Methods

### *7.2.1 Search Strategy*

A grey literature search was conducted, guided by the Canadian Agency for Drugs and Technologies in Health's (CADTH) "Grey Matters" document. Grey literature and the websites of known HTA organizations were searched using terms including "surgical mesh," "polypropylene mesh," "surgical mesh pelvic organ prolapse," "transvaginal mesh," "surgical mesh stress urinary incontinence," "tension-free vaginal tape," "tension-free obturator tape," "mid-urethral sling," "stress urinary incontinence surgery," "pelvic organ prolapse surgery," and most broadly, "mesh." A systematic database search for HTAs was completed by searching the University of York Centre for Reviews and Dissemination HTA Database from inception until December 18th, 2018. Terms aimed to capture the technologies of interest, such as "midurethral sling," "tension-free vaginal tape," "mini-sling," or "polypropylene mesh," were combined with the Boolean Operator "or", and searched as text words in titles and abstracts or as subject headings (e.g. MeSH). See Appendix 1: Search Strategies for HTA Review for a complete description of the HTA database search.

### *7.2.2 Study Selection*

The database search did not identify any relevant HTA publications on synthetic surgical mesh for SUI or POP that had not already been identified by the grey literature search. HTAs and evidence reviews retrieved from the grey literature search were screened in duplicate and were included in the review if they met all inclusion criteria and failed to meet any exclusion criteria in Table 8. Only HTA publications with a full systematic review of clinical effectiveness of any of the technologies of interest were included. Any discrepancies between reviewers' inclusions were resolved through discussion between the reviewers.

Table 8: Inclusion and Exclusion criteria for HTA Review

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| • HTA or evidence review on surgical mesh for SUI or POP<br>  o Midurethral slings (e.g., tension-free vaginal tape)<br>• Adult population<br>• English or French Language only | • Not an HTA or evidence review<br>• Not synthetic surgical mesh<br>• Not available in English or French<br>• Full text not available |

Abbreviations: SUI: stress urinary incontinence; POP: pelvic organ prolapse; HTA: health technology assessment

### *7.2.3 Data Extraction*

Data from the included HTAs were extracted in duplicate. Extracted outcomes included: study characteristics (author/date, country, study objectives, data collection methods, amount and type of evidence included), details on clinical effectiveness, cost-effectiveness and any *de novo* models included in each HTA, and recommendations. Discrepancies between reviewers during data extraction were resolved through discussion.

## 7.3 Results

The grey literature search identified two HTAs for SUI; [82,83] no HTAs for POP were identified. No additional records were identified through the HTA database search. Findings from the HTAs included in this review are synthesized below.

### *7.3.1 Study Characteristics*

Two SUI HTAs[82,83] were included in this review. One of the SUI HTAs was published in the UK[83] and one was published in Canada[82]. No POP HTAs were identified as part of this review. A detailed summary of study characteristics is presented in Table 9.

Both of the SUI HTAs conducted clinical and cost-effectiveness reviews;[82,83] one HTA also conducted a cost-effectiveness analysis using a Markov model.[83] The UK National Health Service (NHS) HTA was conducted in 2003 and compared TVT (TVT$^{TM}$, Gynecare, UK) to standard interventions, including colposuspension and traditional slings.[83] The Ontario Medical Advisory Secretariat (MAS) HTA was conducted in 2006 and compared various types of MUS, as well as TVT to colposuspension,[82]

### *7.3.2 Clinical Effectiveness Findings*

The main outcomes assessed across the HTAs were cure rates, quality of life, complications, and hospital outcomes (length of stay and procedure time); see Table 10.[82,83] Both of the HTAs evaluating SUI found that the effectiveness of TVT for SUI was similar to other currently available procedures. Notably, the UK NHS HTA found that TVT had broadly similar cure rates to laparoscopic and open colposuspension and traditional slings.[83] The Ontario MAS HTA found that TVT had similar cure rates to open colposuspension and that various MUS types had similar cure rates.[82] Bladder perforation was reported as the most common complication across the two HTAs. Lastly, both of the HTAs noted that QoL data were limited and that there were variations in how QoL was assessed, as well as variations in definitions of cure rates and follow-up time duration, which made it difficult to compare results across studies.[82,83]

### *7.3.3 Cost-Effectiveness Findings*

Both of the HTAs conducted reviews of cost-effectiveness (see Table 11).[82,83] The Ontario MAS HTA found evidence that MUS economically dominated colposuspension because of the cost-savings achieved.[82] The UK NHS HTA did not find any evidence that fulfilled their search criteria; however, they reported the results of the economic evaluation of an RCT included as part of the industry submission, which found that TVT was probably more cost-effective than colposuspension. The UK NHS HTA also included their own cost-effectiveness model analysis,

which found that TVT dominates open colposuspension: five years after surgery, TVT was associated with a lower mean cost (£267) and the same or more QALYs (+0.00048).[83]

## 7.4 Conclusion

Two SUI HTAs were identified in this review; both of them evaluated clinical effectiveness and found similar evidence for TVT compared to other currently available procedures. Both of the HTAs also conducted cost-effectiveness reviews of the literature. Findings from the literature, as well as the model analysis conducted by the UK NHS HTA suggest that TVT economically dominates colposuspension. No POP HTAs were identified.

Neither of the SUI HTAs provide any specific recommendations for or against the use of surgical mesh. Rather, both outline the need for additional research on these devices using methodologically sound RCTs (see Table 12).

Table 9: Characteristics of Included SUI HTA Publications

| Device | Organization, Country | Year | Research Question | Clinical Effectiveness | Cost Effectiveness | Economic Model |
|---|---|---|---|---|---|---|
| TVT | NHS R&D HTA Programme, UK | 2003 | "to evaluate the effectiveness and cost-effectiveness of tension-free vaginal tape (TVT™, Gynecare, UK) in comparison with the standard surgical interventions currently used" | **Databases**: MEDLINE, EMBASE, DARE, Cochrane Incontinence Review Group<br><br>**Search dates**: covering 1966-2002<br><br>**Primary outcomes**: subjective cure rates and QoL ≥24 months after the procedure | **Databases**: MEDLINE, EMBASE, DARE, Cochrane Incontinence Review Group, Harvard database of CUAs<br><br>**Search dates**: NR,<br><br>**Primary outcomes**: costs | Markov model for TVT vs comparators |
| MUS | Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care, Canada | 2006 | "to evaluate the safety, efficacy, and cost-effectiveness of MUS compared with traditional surgery" | **Databases**: MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, Cochrane Database of Systematic Reviews and CENTRAL, INAHTA<br><br>**Search dates**: January 2000 to February 2006 | **Databases**: MEDLINE, MEDLINE In Process and Other Non-Indexed Citations, EMBASE, Cochrane Database of Systematic Reviews and CENTRAL, INAHTA<br><br>**Search dates**: NR<br><br>**Primary outcomes**: costs | NR |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | **Primary outcomes**: cure rates, hospital outcomes (length of stay, procedure time), QoL. complications | | |

Abbreviations: CUA: cost-utility analysis; HTA: health technology assessment; NHS: National Health Service; POP, pelvic organ prolapse; QoL: quality of life; R&D: research and development; SUI: stress urinary incontinence; TVT: tension-free vaginal tape; UK: United Kingdom

Table 10: Clinical Effectiveness and Safety Findings from Included SUI HTA Publications

| Device | Organization, Country, Year | Evidence Identified | Findings | Conclusions |
|---|---|---|---|---|
| TVT | NHS, UK, 2003 | **82 studies:** 5 RCTs/quasi-RCTs, 9 non-randomized comparative studies, 2 population-based registries, 17 case series (with >2 years of follow-up), and 49 case series (with <2 years follow-up) | • Most assessment has been in the form of description of case series. These showed 2-year subjective 'cure' rates (variously measured) of 74–95%, with between 3 and 16% additional women improved but not cured.<br>• Only limited QoL data were available from case series, but suggest significant improvement following TVT.<br>• The principal operative complication is bladder perforation, occurring in around one in 25 procedures.<br>• In comparison with open colposuspension, at 6 months and based on one trial involving 316 women, the estimated relative cure rate is 9% lower after TVT [relative risk (RR) 0.91; 95% CI 0.78 to 1.07] with an absolute difference of –6% (95% CI –17 to 5%)<br>• Laparoscopic colposuspension and traditional slings have broadly similar cure rates to TVT and open colposuspension based on limited | • The long-term performance of TVT in terms of both continence and unanticipated adverse effects is not known reliably at the moment.<br>• Despite relatively few robust comparative data, it appears that in the short- to medium-term TVT's effectiveness approaches that of alternative procedures currently available, and is of lower cost. |

| | | | | |
|---|---|---|---|---|
| | | | data from direct comparisons with TVT and from systematic reviews. Injectable agents appear to have lower cure rates. | |
| MUS | MAS, Canada, 2006 | **13 RCTs** (TVT vs colposuspension, n=9; suprapubic vs TVT, n=3; TVT vs TVT, n=2; TOT vs TVT or suprapubic, n=2);<br><br>**5 HTAs** (TVT, n=4; TOT, n=1) | **TVT vs colposuspension**:<br>• Pooled analysis indicates there is no significant difference between the cure rates for TVT and colposuspension (odds ratio 1.1; 95% CI, 0.83–2.76);<br>• QoL was reported by two RCTs only, using different measures; QOL improved after surgery for SUI; however, it is unclear if there is a significant difference between patients receiving TVT slings and colposuspension;<br>• The procedure time and the length of hospital stay were significantly shorter for TVT than for colposuspension.<br><br>**Suprapubic vs TVT**:<br>• Overall cure rates in the three RCTs ranged from 69.2% to 95%; no significant differences found between the two slings in cure rate;<br>• Only one RCT examined QoL and found no significant difference between the two groups.<br><br>**TVT vs TVT**: | • At this time, there does not appear to be one procedure that is more effective than another at curing SUI. TVT appears to have similar cure rates to open colposuspension; and the various MUS types seem to have similar cure rates.<br>• Studies differed in their definition of cure rate and duration of follow-up time.<br>• In the studies that reported QOL, there does not appear to be a significant difference in QOL scores between the sling procedures.<br>• The procedure time and length of hospital stay for all MUS appears to be similar.<br>• The most frequently reported complications were bladder perforations, de novo voiding difficulties and device problems. |

| | | | | |
|---|---|---|---|---|
| | | | • Neither of the two RCTs found a significant difference in overall cure rate, which ranged from 69.2% to 88% across studies.<br><br>**TOT vs TVT or suprapubic MUS:**<br>• Neither of the two RCTs found a significant difference in overall cure rate, which was fairly high in both studies;<br>• Only one RCT examined QoL and found that both groups had significant improvements in QoL scores from before surgery to after surgery;<br>• Neither RCT found a significant difference between groups in length of stay;<br>• One RCT found no significant differences in procedure time between TOT and suprapubic groups; another RCT found that TOT had a significantly shorter procedure duration than TVT.<br><br>**Complications:**<br>• The most frequently reported were bladder perforations, de novo voiding difficulties, and device problems. | |

Abbreviations: CI: confidence interval; HTA: health technology assessment; MAS: Medical Advisory Secretariat; MUS: mid-urethral sling; QoL: quality of life; RCT: randomized controlled trial; RR: risk ratio; SUI: stress urinary incontinence; TOT: transobturator; TVT: tension-free vaginal tape; UK: United Kingdom

Table 11: Cost-effectiveness Systematic Review Findings from Included SUI HTA Publications

| Device | Organization, Country, Year | Evidence Identified | Findings | Conclusions |
|---|---|---|---|---|
| TVT | NHS, UK, 2003 | Systematic review: no literature identified that fulfilled the criteria<br><br>1 economic evaluation of an RCT (as part of the industry submission) | Economic evaluation of an RCT:<br>• The probability of TVT being more cost-effective than colposuspension was 95% when the decision-maker is willing to pay at least £30,000 for an additional QALY and was 85% when the decision-maker is willing to pay at least £100,000.<br><br>Model:<br>• On average, TVT dominates open colposuspension: 5 years after surgery, TVT was associated with a lower mean cost (£267) and the same or more QALYs (+0.00048).<br>• In the stochastic analysis, the likelihood of TVT being considered cost-effective was 100% if decision-makers were unwilling to pay for additional QALYs.<br>• If a decision-maker was prepared to pay up to £20,000 for an additional QALY, there was about a 95% chance that TVT is cost-effective; at £30,000 and £40,000 the probabilities were | • TVT was more likely to be considered cost-effective compared with the other surgical procedures based on the assumptions that traditional slings have the same effectiveness as open colposuspension and are also more costly; that laparoscopic colposuspension has the same or lower effectiveness as open colposuspension and similar costs; and that injectable agents are less effective than TVT but of greater cost. |

| Device | Organization, Country, Year | Evidence Identified | Findings | Conclusions |
|---|---|---|---|---|
| | | | approximately 93% and 85%, respectively. | |
| MUS | MAS, Canada, 2006 | Systematic review: 1 CUA, 1 economic evaluation of an RCT | Systematic review:<br>• One study found that TVT added about 0.01 QALYs compared to colposuspension; probability of the TVT being more cost-effective than colposuspension would be 94.6% if the decision maker is willing to pay £30,000/QALY (about CAD $50,000/QALY).<br>• MUS economically "dominates" colposuspension because of the costs savings achieved.<br><br>Author-conducted economic analysis /BIA:<br>• MUS procedures cost approximately $1100 CAD less than the cost of colposuspension (estimated $2650 CAD versus $3715 CAD). | • Given current practice, the TVT sling procedure is 100% certain to be cost-saving and, as long as average length of stay is at least 2 days longer following colposuspension, TVT slings will remain the less costly procedure. |

Abbreviations: BIA: budget impact analysis; CAD: Canadian dollar; HTA: health technology assessment; MAS: Medical Advisory Secretariat; QALY: quality-adjusted life year; RCT: randomized controlled trial; SUI: stress urinary incontinence; TVT: tension-free vaginal tape; UK: United Kingdom

Table 12: Recommendations from Included SUI HTA Publications

| Device | Organization, Country, Year | Conclusions / Recommendations |
|---|---|---|
| TVT | NHS, UK, 2003 | • Despite relatively few robust comparative data, it appears that in the short- to medium-term TVT's effectiveness approaches that of alternative procedures currently available, and is of lower cost.<br>• Further research suggestions include unbiased assessments of longer term performance from follow-up of controlled trials or population-based registries; more data from methodologically sound RCTs using standard outcome measures; a surveillance system to detect longer term complications, if any, associated with the use of tape; and rigorous evaluation before extending the use of TVT to women who are currently managed non-surgically. |
| MUS | MAS, Canada, 2006 | • At this time, there does not appear to be one procedure that is more effective than another at curing SUI. TVT appears to have similar cure rates to open colposuspension; and the various MUS types seem to have similar cure rates. |

Abbreviations: HTA: health technology assessment; MAS: Medical Advisory Secretariat; RCT: randomized controlled trial; SUI: stress urinary incontinence; TVT: tension-free vaginal tape; UK: United Kingdom

# 8 Systematic Review of Safety and Efficacy of Surgical Mesh for Stress Urinary Incontinence

***Summary:***

- Twenty-nine unique RCTs were identified that evaluated the effectiveness of synthetic surgical mesh against a comparator of interest.
- Nineteen studies compared synthetic mesh to native tissue suspension, seven compared synthetic mesh to AFS, and five compared synthetic mesh to porcine mesh.
- None of the meta-analysis comparisons of cure rates were significant, suggesting that synthetic mesh is not largely different from either native tissue suspension, AFS, or porcine mesh; however, studies differed in their definitions of cure and duration of follow-up times, which makes it difficult to draw any definitive conclusions about robustness of these findings.
- The most frequently reported complication across the three comparison groups was bladder injury: an intraoperative complication.
- Mesh erosion in the synthetic mesh group ranged from 0.59%-12% by 12 months, and the rate of mesh exposure was 1.6% at 10 years.

## 8.1 Purpose

To assess the clinical effectiveness and safety profile of permanent, synthetic surgical mesh for treatment of SUI in adults.

## 8.2 Methods

### *8.2.1 Search Strategy*

A systematic review of the literature was completed. MEDLINE, EMBASE, Cochrane Central, and CINAHL were searched from inception. The search was performed on November 9th, 2018. Terms capturing surgical mesh for SUI (e.g. "midurethral sling," "tension-free vaginal tape") were searched in combination with terms capturing the condition of interest (e.g. "stress incontinence," stress urinary incontinence"). The search was limited to exclude animal studies, conference abstracts, editorials, and letters. The full search strategy is reported in Appendix 1: Search Strategies for HTA Review.

### *8.2.2 Study Selection*

RCTs examining permanent synthetic surgical mesh for SUI compared to biological mesh or native tissue suspension (e.g., colposuspension) were included. Abstracts were screened in duplicate by independent reviewers using *a priori* inclusion and exclusion criteria listed in Table

13. Abstracts that were included by either reviewer proceeded to full-text review. At the full-text review stage, studies were screened in duplicate by two reviewers, with any discrepancies resolved through discussion and consensus. Studies were excluded if they were not RCTs, did not report outcomes specifically for SUI (e.g., if they included mixed or urge urinary incontinence), did not examine permanent synthetic mesh compared to biological mesh or native tissue, were not available in English or French, did not report original data, or were animal studies.

Table 13: Inclusion and Exclusion Criteria for SUI Review

| | **Inclusion** | **Exclusion** |
|---|---|---|
| Population | Adult population (stratified by sex) | Animal studies; pediatric population; mixed sex population not stratified |
| Intervention | Assesses use of surgical mesh for SUI<br>• Transvaginal mesh<br>• MUS<br>• TVT<br>• Mini-sling<br><br>Assesses use of surgical mesh for SUI secondary to POP (stratified in the analysis)<br><br>Assesses use of synthetic mesh<br>• Polypropylene material<br>• Permanent meshes | • Assesses use of surgical mesh not for SUI<br>• Does not assess surgical mesh<br>• Assesses use of biological mesh, grafts, pessaries<br>• Assesses surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open)<br>• Semi-permanent or dissolvable mesh |
| Comparator | Compares surgical mesh for SUI to:<br>• Non-mesh surgical procedures<br>• Conservative management<br>• Other surgical meshes for SUI (semi-permanent or dissolvable mesh)<br>• Another permanent surgical mesh with different characteristics | • Surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open) |
| Outcome | Clinical outcome- any; or QoL outcome | No clinical outcome; no QoL outcome |
| Design | RCT design- any | Not an RCT; secondary RCT data analysis (not planned *a priori*) |
| | English or French | Not English or French |
| | Full-text available | No full-text |

Abbreviations: MUS: midurethral sling; POP: pelvic organ prolapse; QoL: quality of life; RCT: randomized controlled trial; SUI: stress urinary incontinence; TVT: tension-free vaginal tape

### *8.2.3 Data Extraction*

For all studies, year of publication, country, patient selection, patient characteristics, description of technologies, definition of objective and subjective cure, objective and subjective cure rates, recurrence rates, and follow-up time were extracted using standardized data extraction forms. Safety outcomes consisting of complications (e.g., bladder injury) were also extracted. Discrepancies between reviewers during data extraction were resolved through consensus.

### *8.2.4 Quality Assessment*

During data extraction, each included study was assessed for quality using The Cochrane Risk of Bias Tool.[84] Quality assessment was completed in duplicate with discrepancies being resolved through discussion. Using this tool, each study was assessed across five potential domains of bias (randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result). Each domain was assigned a "low, "high," or "some concern" risk of bias, based on the answers to the signaling questions.

### *8.2.5 Meta-Analysis*

A meta-analysis was conducted for comparisons with two or more studies to inform the magnitude of treatment effect for synthetic surgical mesh for SUI with respect to cure rates and complications. The following comparator pairs were assessed: synthetic mesh vs. autologous fascial sling (AFS), synthetic mesh vs. porcine mesh, and synthetic mesh vs. native tissue suspension (e.g., colposuspension). For each study, the number of participants who were cured and who had experienced treatment complications were compared between the synthetic mesh and the comparator group. A pooled analysis including all the cure definitions was conducted, with a sub-analysis based on different cure definitions, where data were available (i.e., for two or more studies using the same cure definition).

A random effects model using the method of DerSimonian and Laird [85] was used, with a continuity correction of 0.5 where appropriate. The same continuity correction was used to allow inclusion of zero-total event trials.[86] Separate analyses were conducted based on the comparator groupings established during data extraction (as outlined above). Meta-analyses were conducted using odds ratio to express the effectiveness of permanent synthetic surgical mesh in relation to other comparators. For studies only reporting a median follow-up time, normal distributions were

assumed and median follow-up time value was used. Statistical analysis was completed in STATA 14.[87]

### 8.3 Results

A total of 8735 citations were identified from the literature search. Of those, 5284 were screened during abstract review, of which 5066 were excluded, and 218 proceeded to full-text review. A total of 190 articles were excluded at full-text review for the following reasons: 77 examined differences in surgical technique only, rather than differences in mesh; 37 did not assess mesh for SUI exclusively; 33 were not available as full-text; 24 were not RCTs; eight did not assess mesh; six did not assess permanent synthetic mesh; three did not report clinical or QoL outcome; and two were not published in English or French. One study was identified during hand-searching of the included full-text publications (a prior study of one of the follow-up papers already included). In total, 29 final papers were included in the review (22 original RCTs and seven follow-up studies). Four of the included studies had three comparator arms, which have been grouped according to each intervention and specific comparator. Nineteen studies (14 original RCTs[88-101] and five follow-up studies[102-106]) compared synthetic mesh to native tissue suspension, seven (six original RCTs,[88,107-111] and one follow-up study[112]) compared synthetic mesh to AFS, and five (three original RCTs[108,113,114] and two follow-up studies[112,115]) compared synthetic mesh to porcine mesh (see Figure 11).

Figure 11: Comparators Examined in Studies in the SUI Review, N=32 (Three 3-arm Studies)

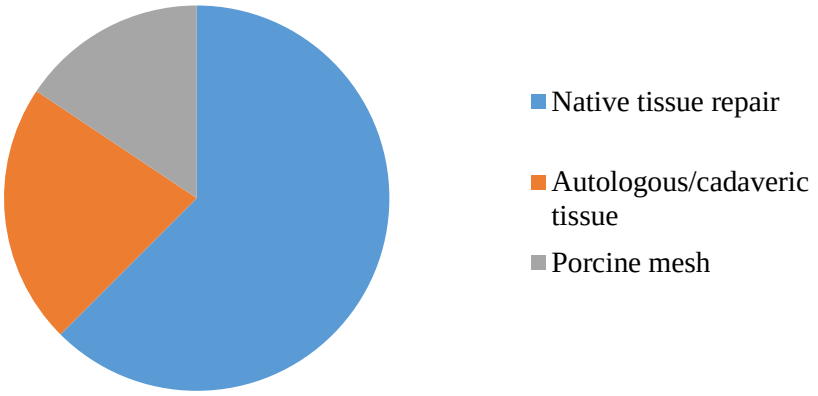
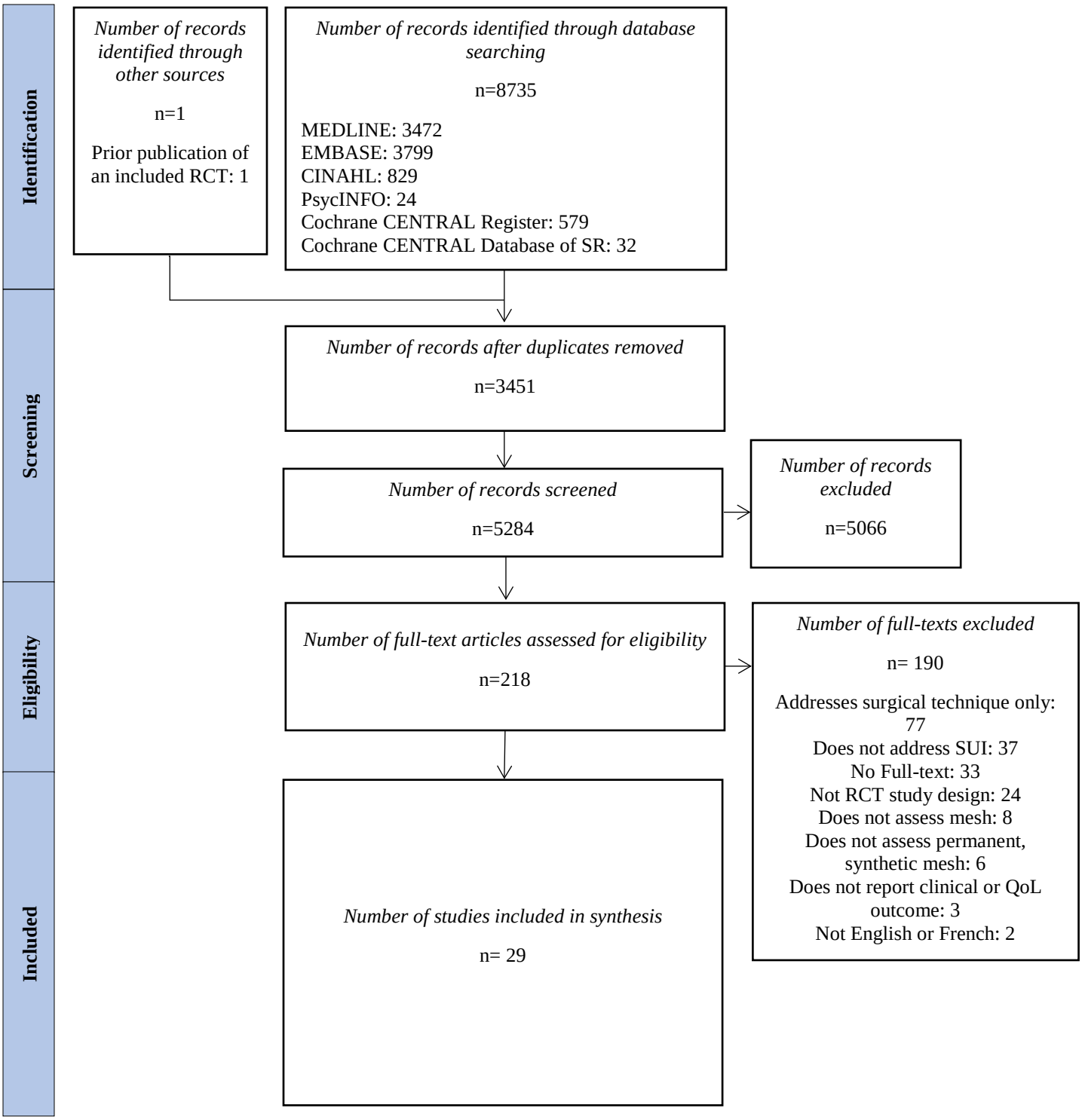
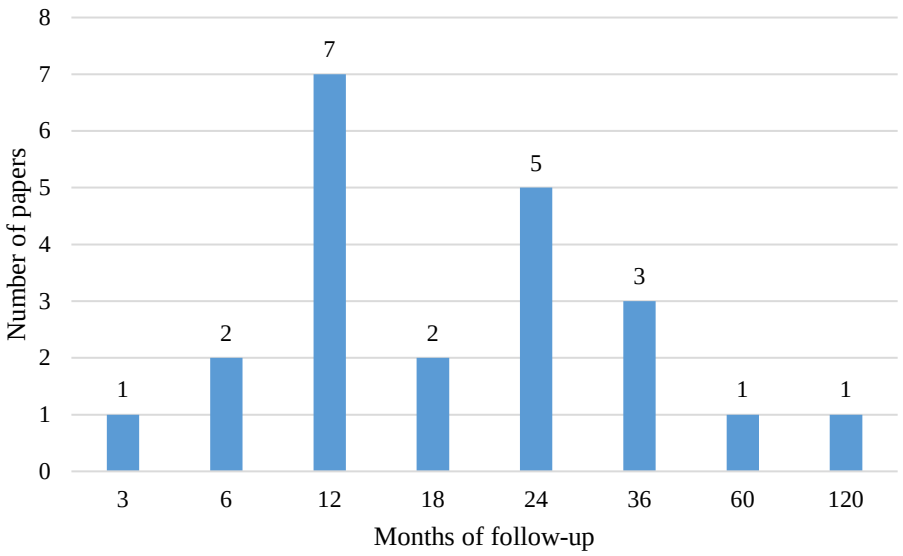


Figure 12: PRISMA Flow-chart for SUI review



Follow-up times across the three comparators included in the SUI review ranged from 3-120 months; 12 and 24 months were the most common follow-up time-points (see Figure 13).

Figure 13: Follow-up Times in SUI Papers n=22




*Only papers reporting exact or mean follow-up time are included in the graph; papers reporting follow-up as median or range are excluded

### *8.3.1 Synthetic Mesh vs Native Tissue Suspension*

#### 8.3.1.1 Characteristics of Included Studies

Nineteen studies (14 original RCTs[88-101] and five follow-up studies[102-106]) examining synthetic mesh vs. native tissue suspension were identified. One was from Korea,[88] two from Iran,[89,97] four from the US,[94,95,102,103] one from Kuwait,[90] one from Australia,[91] one from Greece,[92] three from Italy,[93,101,106] two from Turkey,[96,98] one from Taiwan,[99] and three from the UK.[100,104,105] The studies were published between 2000 and 2015, with the majority of the studies published in the early-to-mid 2000s.

The majority of the studies focused on a short-to-intermediate follow-up time period (3 to 12 months), with a number of studies conducting a follow-up at 24 months and beyond. Study sample sizes ranged from 36-344 patients, with a median of ~60 patients per study (~30 patients per group). Common study inclusion criteria were women ≥18 years of age, urodynamically proven SUI, and completed family. Common exclusion criteria were previous SUI surgery,

detrusor overactivity and POP >stage II. Study characteristics are reported in Table A2 in Appendix 2: Search Strategies for SUI.

#### 8.3.1.2 Quality of Included Studies

Of the 19 studies that compared synthetic mesh to native tissue repair, nine were considered to be of moderate concern for risk of bias due to randomization.[88-90,93,98,99,101,106] Only one study's randomization was deemed to be high risk because patients were randomized in an alternating fashion to the intervention and control groups;[92] the deviation, measurement, and reporting domains were all considered to have low risk of bias, and the missing data in the study were of some concern.

All the 19 studies were determined to be at low risk of bias from deviation.

Two studies were of some concern, with respect to bias stemming from missing outcome data; [92,103] two other studies were high risk.[104,105] Neither of the studies at high risk for bias stemming from missing data had any concerns in any other categories, and both of them reported long-term follow-up times for the same study.[100] They were considered to be at high risk for bias because of steep, asymmetrical drop-out rates for patients at the two later follow-up points (i.e., two and five years).

Two studies were considered to be of some concern for bias due to measurement.[90,98] Both of them were also of some concern in their randomization. Three papers were deemed to be at high risk of bias from measurement;[88,91,102] one of these studies was of concern in another category (randomization). Patients were considered to be the assessors of outcomes if the primary outcome of the paper included significant subjective features, such as patient-reported continence. Most papers did not blind the patients to the allocation, so in these cases the potential of bias from measurement was considered to be high because the outcome assessors (patients) were not blinded to their allocation, and the outcome being assessed was prone to subjectivity.

Only one paper was considered to be at high risk from reporting results,[99] due to its reporting of only select time points despite performing numerous unreported follow-up examinations. It was of moderate concern for its randomization, and at low risk for all other forms of bias. Quality assessment for synthetic mesh vs. native tissue suspension studies is reported in Table 14.

Table 14: Quality Assessment of Synthetic Mesh vs. Native Tissue Suspension SUI Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Bai, Korea, 2005[88] | some concern | low risk | low risk | high risk | low risk |
| Bandarian, Iran, 2011[89] | some concern | low risk | low risk | low risk | low risk |
| Jelovsek (see Paraiso 2004), USA, 2008[102] | low risk | low risk | low risk | high risk | low risk |
| Culligan (see Sand 2000), USA, 2003[103] | low risk | low risk | some concern | low risk | low risk |
| El-Barky, Kuwait, 2005[90] | some concern | low risk | low risk | some concern | low risk |
| Foote, Australia, 2006[91] | low risk | low risk | low risk | high risk | low risk |
| Liapis, Greece, 2002[92] | high risk | low risk | some concern | low risk | low risk |
| Palomba, Italy, 2002[93] | some concern | low risk | low risk | low risk | low risk |
| Paraiso, USA, 2004[94] | low risk | low risk | low risk | low risk | low risk |
| Sand, USA, 2000[95] | low risk | low risk | low risk | low risk | low risk |
| Sivaslioglu, Turkey, 2007[96] | low risk | low risk | low risk | low risk | low risk |
| Sohbati, Iran, 2015[97] | low risk | low risk | low risk | low risk | low risk |
| Ustun, Turkey, 2003[98] | some concern | low risk | low risk | some concern | low risk |
| Wang, Taiwan, 2003[99] | some concern | low risk | low risk | low risk | high risk |
| Ward, UK and Eire, 2002[100] | low risk | low risk | low risk | low risk | low risk |

| | | | | | |
|---|---|---|---|---|---|
| Ward (see Ward 2002, 2004), UK and Eire, 2008[105] | **low risk** | **low risk** | **high risk** | **low risk** | **low risk** |
| Ward (see Ward 2002, 2008), UK and Eire, 2004[104] | **low risk** | **low risk** | **high risk** | **low risk** | **low risk** |
| Zullo (see Zullo 2001), Italy, 2004[106] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Zullo (see Zullo 2004), Italy, 2001[101] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |

#### 8.3.1.3 Meta-analysis of Cure Rates

Five of the synthetic mesh vs. native tissue suspension studies provided adequate data on cure rates to permit pooling at ≤3 months,[88,93,95,97,101] seven provided data for pooling at 6 months,[88,90,91,93,97,100,101] eight provided data for pooling at 12 months,[88,93,94,96-99,101] and nine studies provided data for pooling at ≥18 months.[89,91,92,96,102-106]

Figure 14 shows the pooled overall cure rate results (forest plot) for synthetic mesh vs. AFS; all cure definitions as defined by the study authors were used in this analysis. The most common cure definitions were "absence of urinary incontinence" (two studies); "pad test weight difference <1g" (three studies; two original RCTs and one follow-up paper); and "failure defined as urine loss on cough or Valsalva stress tests" (two studies).

None of the comparisons between synthetic mesh and native tissue suspension are statistically significant with respect to cure. At 3 months or less, the overall pooled odds ratio for synthetic mesh vs. native tissue suspension is 1.43 (95% confidence interval [CI]: 0.56, 3.69), which suggests that the odds of achieving cure using synthetic mesh are slightly higher than if using native tissue suspension (Figure 14). However, because the CI of this pooled estimate crosses the null line (1.00), this effect is not statistically significant.

This finding is similar to 6 and 12 months, at which point the odds ratios for the two treatments are 1.21 (95% CI: 0.85, 1.72) and 1.13 (0.66, 1.92), respectively, suggesting that the odds of

achieving cure using synthetic mesh remain slightly higher than if using native tissue suspension (Figure 14). However, these effects are also not statistically significant.

There is a trend in the opposite direction at the ≥18 months follow-up, at which point the odds ratio for the two treatments is 0.96 (95% CI: 0.66, 1.39), which suggests that the odds of achieving cure using synthetic mesh are slightly lower at this longer follow-up time than if using native tissue suspension (Figure 14). However, this effect is not statistically significant.

The pooled studies were assessed for risk of publication bias (see Figure A5 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots). The funnel plot is largely symmetrical, which suggests that the risk of publication bias is low.

Rates of cure vs. failure at 12 months in individual studies included in the meta-analysis of overall cure rates are reported in Figure 15 for synthetic mesh and Figure 16 for the native tissue group. Overall risk of bias ratings for the individual studies are included to aid with interpretation of the study findings: studies classified as “low risk” had low risk ratings across all potential bias domains; studies classified as “some concern” had that risk rating for at least one of the domains; studies classified as “high risk” had a high risk rating for at least one of the domains. No trends were observed between a study’s risk of bias rating and cure rates in either the synthetic or native tissue suspension groups.

Figure 14: Forest Plot of Cure Rates in Patients with SUI Receiving Synthetic Mesh vs. Native Tissue Suspension

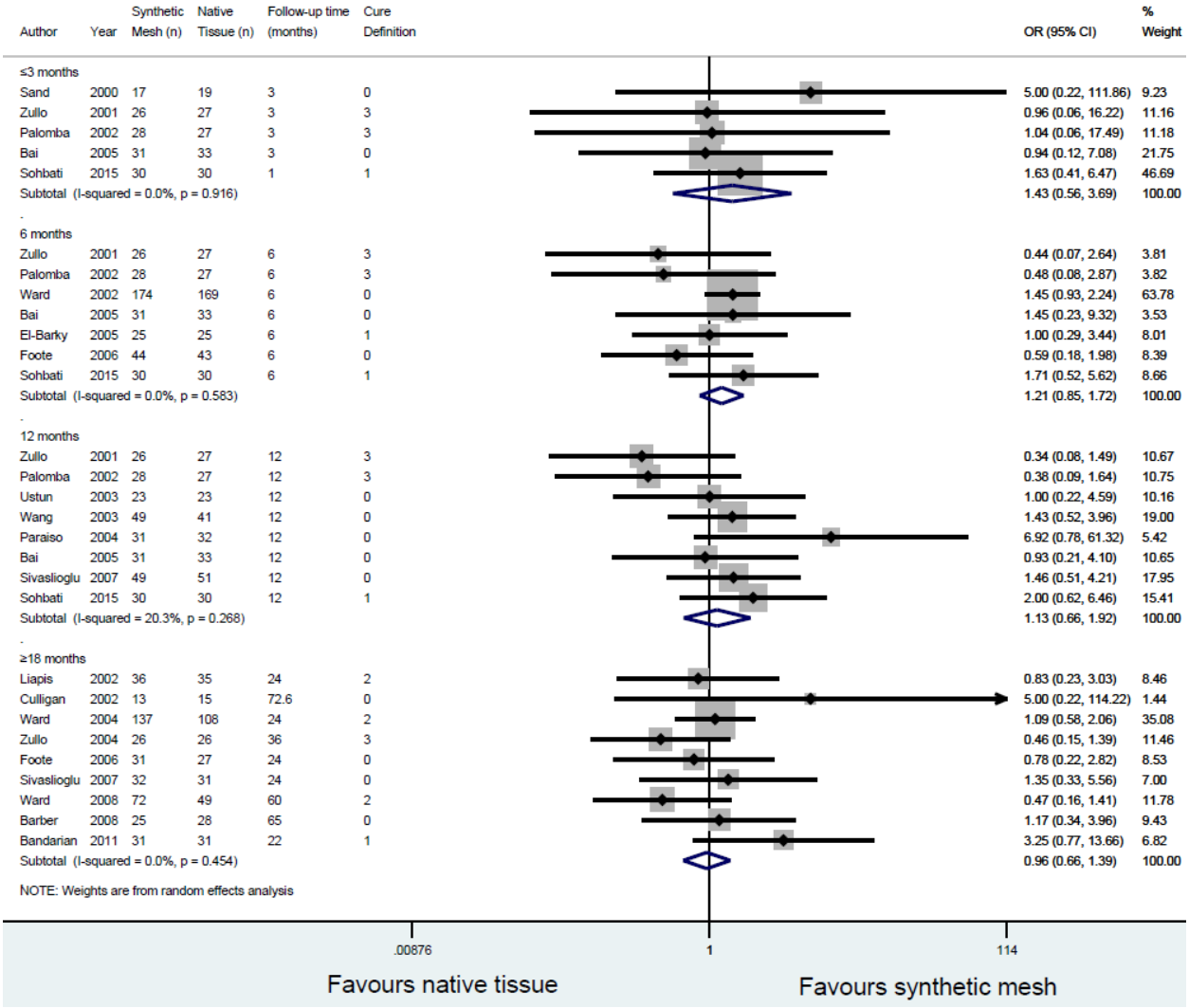


Figure 15: Cure Rates at 12 Months in Patients with SUI Receiving Synthetic Mesh

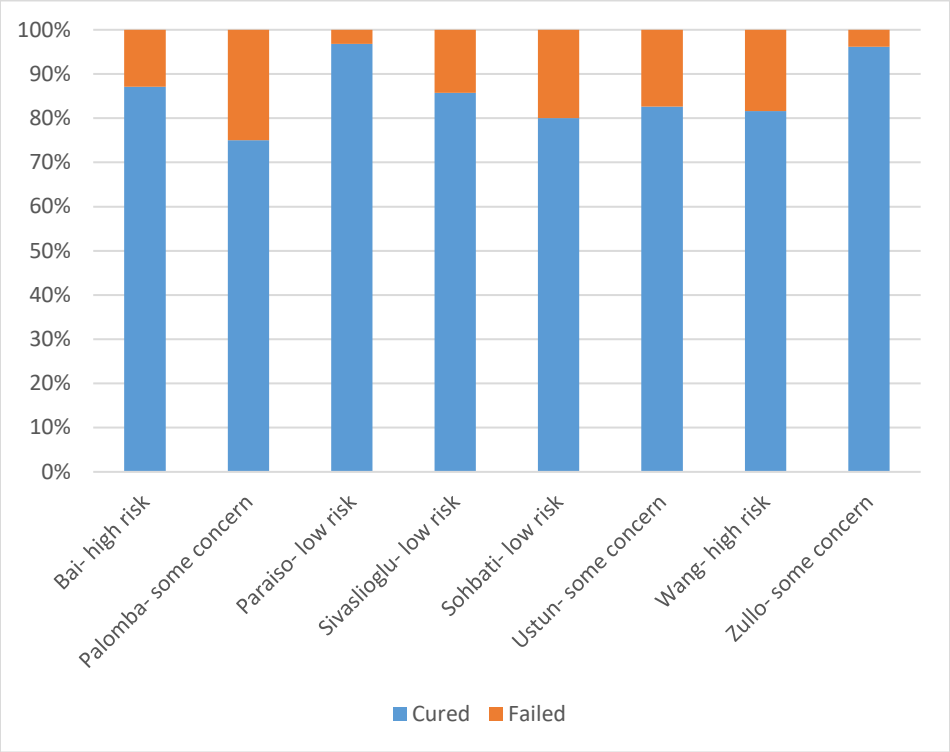
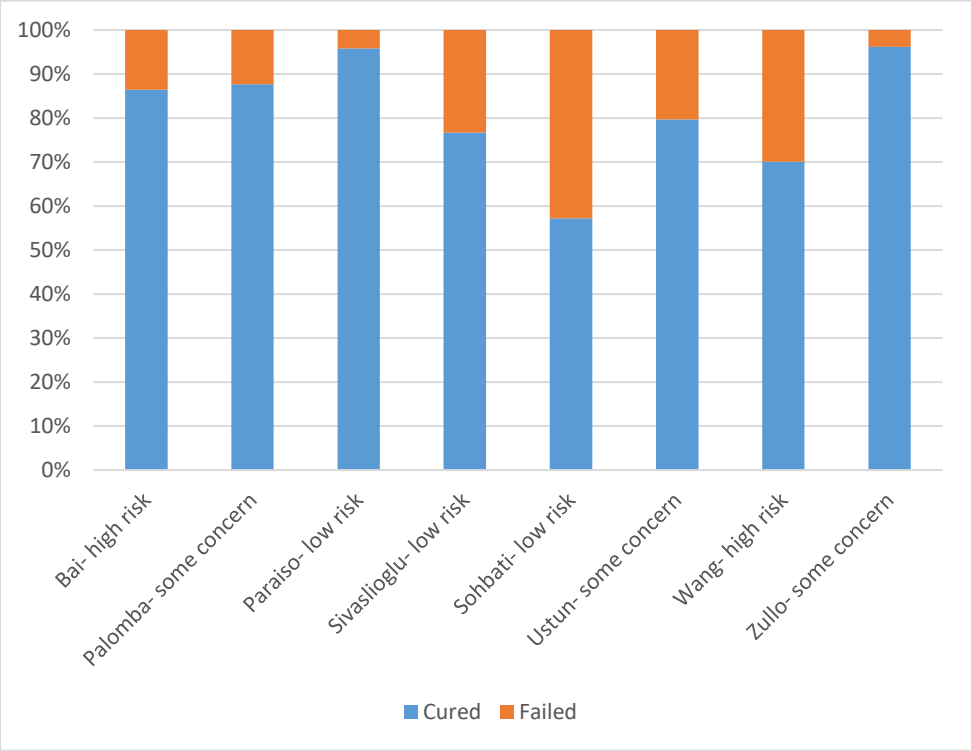


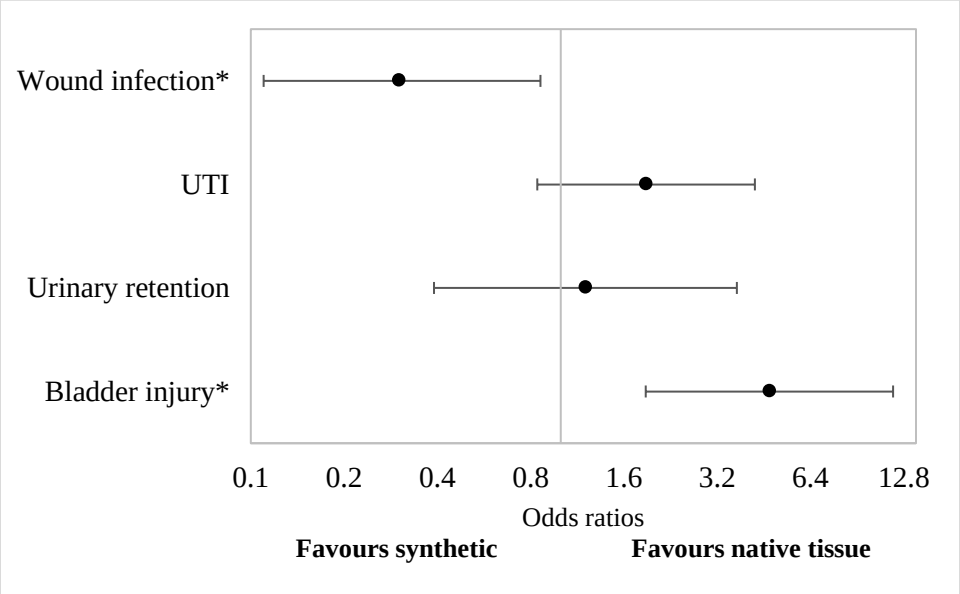

Figure 16: Cure Rates at 12 Months in Patients with SUI Receiving Native Tissue Suspension



#### 8.3.1.4 Meta-analysis of Complications

Sufficient data were available to conduct meta-analyses of four complications reported in the synthetic mesh vs. native tissue suspension studies: bladder injury, urinary retention, urinary tract infection (UTI), and wound infection. Synthetic mesh was associated with significantly lower odds of wound infection, and significantly greater odds of bladder injury than native tissue suspension. Odds of UTI and urinary retention were not statistically different. A summary of the odds ratios is reported in Figure 17, with more granular details reported in the sections below; forest plots for the SUI complications analyses are reported in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots.

Figure 17: Odds Ratios for Complications in SUI Patients Receiving Synthetic Mesh vs. Native Tissue




*Indicates a significant effect

##### 8.3.1.4.1 Bladder Injury

Bladder injury was the most frequently reported intraoperative adverse effect and was reported in seven studies.[89-92,96,100,101] A meta-analysis was conducted using the data from five of those studies (two studies reported null event rates for both groups) to examine the odds of experiencing bladder injury when undergoing a procedure using synthetic mesh vs. native tissue suspension (see Figure A1 in Appendix 6).[90-92,100,101] The pooled odds ratio for bladder injury is

4.71 (95% CI: 1.88, 11.81), suggesting that patients undergoing synthetic mesh surgery are almost five times as likely to experience bladder injury than if undergoing native tissue suspension; this effect was significant due to the CI of this pooled estimate not crossing the null line (1.00).

#### 8.3.1.4.2 Urinary Retention

Urinary retention was the most frequently reported short-term complication and was assessed in five studies.[88,90,92,96,103] A meta-analysis of urinary retention resulted a pooled odds ratio of 1.20 (95% CI: 0.39, 3.70); see Figure A2 in Appendix 6. This suggests that patients undergoing synthetic mesh surgery have slightly higher odds of experiencing urinary retention than if undergoing native tissue suspension surgery; however, this effect is not significant.

#### 8.3.1.4.3 Urinary Tract Infection

UTI was reported in six studies and was the most frequently reported longer-term complication.[89,90,92,96,100,104] A meta-analysis of UTI using data from four out of the six studies was conducted: one study reported null rates for both groups[89] and the other study reported UTI within three weeks,[100] which was not pooled because it was deemed to be too different from the other follow-up durations. The meta-analysis resulted in a pooled odds ratio of 1.88 (95% CI: 0.84, 4.23); see Figure A3 in Appendix 6. This suggests that patients undergoing mesh surgery have higher odds of experiencing UTI than patients undergoing native suspension surgery; however, this effect is not significant. Furthermore, follow-up times for this complication ranged from 6-28 months.

#### 8.3.1.4.4 Wound Infection

Would infection (short-term complication) was reported in three studies.[89,90,100] A meta-analysis of wound infection resulted in a pooled odds ratio of 0.30 (95% CI: 0.11, 0.86), which suggests that patients undergoing synthetic mesh surgery have lower odds of experiencing wound infection than if undergoing native tissue suspension surgery; this effect was significant (see Figure A4 in Appendix 6).

#### 8.3.1.4.5 De Novo Detrusor Instability and Urgency

Both de novo detrusor instability[92,95,101] and de novo urgency[90,92,105] were reported in three studies; however, meta-analyses of these adverse effects could not be conducted due to variability in follow-up times across studies. De novo detrusor instability was more common in the synthetic mesh group (ranging from 11.54%-23.53%) than in the native tissue suspension

group (ranging from 5.26%-14.29%).[92,95,101] De novo urgency rates were more common in the native tissue suspension group (ranging from 2.85%-12%) than the synthetic mesh group (ranging from 2.78%-8%).[90,92,105]

8.3.1.4.6 Mesh Exposure and Erosion

Mesh erosion was reported in three studies comparing synthetic mesh to native tissue suspension; a meta-analysis was not conducted due to differences in follow-up times.[94,100,103] Mesh erosion in the synthetic mesh group ranged from 0.59%-12% by 12 months.

8.3.1.4.7 Other Complications

Other notable adverse effects were intraoperative bleeding rates[89,96] and voiding difficulties,[96,104] both of which were reported in two studies and could not be meta-analyzed due to an insufficient number of studies. Bleeding rates were more common with synthetic mesh than native tissue in one study (2.04% vs. 0%, respectively),[96] and more common with native tissue than synthetic mesh in the other study (9.68% vs. 3.23%, respectively).[89] Similarly, voiding difficulties were more common with synthetic mesh than native tissue in one study (2.04% vs. 1.96%, respectively),[96] and more common with native tissue than synthetic mesh in the other (3.7% vs. 0%, respectively).[104]

8.3.1.5 Subjective Outcomes

Only nine of the studies examining synthetic mesh vs. native tissue suspension reported patient-reported measures assessing urinary symptoms (e.g., Bristol Female Lower Urinary Tract Symptom Questionnaire [BFLUTS]) and QoL (e.g., Short Form Health Survey [SF-36] and Visual Analog Scales [VAS]) (see Table 15). Due to the small number of studies reporting patient-reported measures and variability in the types of questionnaires used, there was an insufficient number of studies that could be pooled to conduct a meta-analysis of these outcomes. In general, there was a positive trend following treatment with both treatment and control arms across all subjective outcome measures.

Table 15: Patient-reported Outcome Measures across the Synthetic Mesh vs. Native Tissue Studies

| | 24-hr voiding diary | UDI-6 | ISI | IIQ | VAS | BFLUTS | SF-36 | KHQ | PISQ-12 | None |
|---|---|---|---|---|---|---|---|---|---|---|
| Bandarian, Iran, 2011[89] | | ✓ | ✓ | | | | | | | |
| Jelovsek, USA, 2008[102] | ✓ | | | | | | | | | |
| El-Barky, Kuwait, 2005[90] | | | | ✓ | ✓ | | | | | |
| Foote, Australia, 2006[91] | | | | | | ✓ | | | | |
| Liapis, Greece, 2002[92] | | | | | | | | ✓ | ✓ | |
| Wang, Taiwan, 2003[99] | | | | | ✓ | | | | | |
| Ward, UK and Eire, 2002[100] | | | | | | ✓ | ✓ | | | |
| Ward, UK and Eire, 2008[105] | | | | | | ✓ | ✓ | | | |
| Ward, UK and Eire, 2004[104] | | | | | | ✓ | ✓ | | | |
| Bai, Korea, 2005[88]<br>Culligan, USA, 2003[103]<br>Palomba, Italy, 2002[93]<br>Paraiso, USA, 2004[94]<br>Sand, USA, 2000[95]<br>Sivaslioglu, Turkey, 2007[96]<br>Sohbati, Iran, 2015[97]<br>Ustun, Turkey, 2003[98]<br>Zullo, Italy, 2004[106]<br>Zullo, Italy, 2001[101] | | | | | | | | | | ✓ |

Abbreviations: BFLUTS: Bristol Female Lower Urinary Tract Symptoms; IIQ: Incontinence Impact Questionnaire; ISI: Incontinence Severity Index; KHQ: King's Health Questionnaire; PISQ-12: Pelvic organ prolapse Incontinence Sexual Questionnaire 12; SF-36: Short- form Health Survey-36; UDI-6: Urogenital Distress Inventory- 6; VAS: visual analogue scale.

### *8.3.2 Synthetic Mesh vs AFS*

#### 8.3.2.1 Characteristics of Included Studies

Seven studies (six original RCTs,[88,107-111] one of which was a three-armed study comparing synthetic mesh to two types of AFS,[110] and one follow-up study[112]) examining synthetic mesh vs. AFS were identified. Two studies were from Brazil,[107,109] two from the UK, [108,112] one from Korea,[88] and two from Egypt.[110,111] The studies were published between 2005 and 2015.

The majority of the studies focused on a short-to-intermediate follow-up time period (1 to 12 months), with some studies conducting follow-ups at 18 months[110] and 36 months[107] and 10 years[112]. Study sample sizes ranged from 20-151 patients: two studies had ~20 patients,[109-111] three studies had ~50 patients,[88,107] and two studies had 120-160 patients.[108,112] Common study inclusion criteria were women ≥18 years of age and urodynamically proven SUI. Common exclusion criteria were previous SUI surgery, detrusor overactivity and POP >stage II. Study characteristics are reported in Table A2 in Appendix 5: Characteristics of Included Studies.

#### 8.3.2.2 Quality of Included Studies

Most of the RCTs comparing synthetic mesh vs. AFS had a low risk of bias in each of the five domains. All of the studies used some type of randomization to allocate patients, with the exception of three studies that did not report randomization method or allocation concealment.[88,109,110] All of the interventions seemed to have been performed similarly to everyday practice. All studies had complete outcome data, and the follow-ups had similar rates of drop-out, with reasons for drop-out provided. Primary outcomes were generally objective measures (e.g., pad weight) and their assessment was considered to not have been biased, with the exception of one study that used subjective improvement as their primary outcome.[88] Lastly, there was no evidence of selective reporting of the results. Quality assessment for synthetic mesh vs. AFS studies is reported in Table 16.

Table 16: Quality Assessment of Synthetic Mesh vs. AFS SUI Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Amaro, Brazil, 2009[107] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Bai, | **some concern** | **low risk** | **low risk** | **high risk** | **low risk** |

| | | | | | |
|---|---|---|---|---|---|
| Korea, 2005[88] | | | | | |
| Guerrero (see Khan 2015), UK, 2010[108] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Khan (see Guerrero 2010), UK, 2015[112] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Silva-Filho, Brazil, 2006[109] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Teleb, Egypt, 2011[110] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Wadie, Egypt, 2005[111] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

#### 8.3.2.3 Meta-analysis of Cure Rates

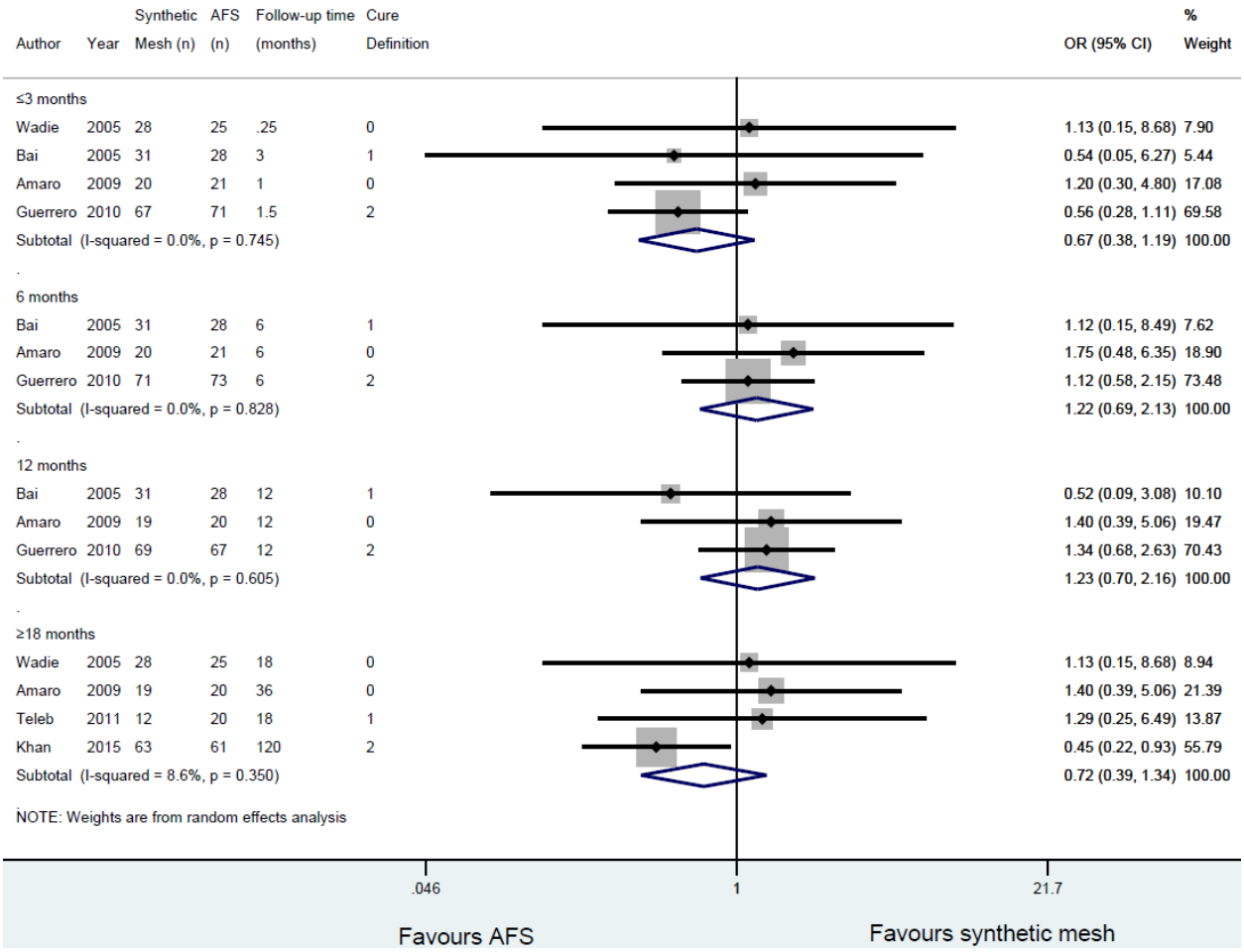
Four of the synthetic mesh vs. AFS studies provided adequate data on cure rates to permit pooling at ≤3 months,[88,107,108,111] three provided data for pooling at 6 and 12 months,[88,107,108] and four studies provided data for pooling at ≥18 months.[107,110-112] Figure 18 shows the pooled overall cure rate results (forest plot) for synthetic mesh vs. AFS; all cure definitions as defined by the study authors were used in this analysis.

None of the comparisons between synthetic mesh and AFS are statistically significant with respect to cure. At 3 months or less, the overall pooled odds ratio for synthetic mesh vs. AFS is 0.67 (95% CI: 0.38, 1.19), which suggests that the odds of achieving cure using synthetic mesh are lower than if using AFS. However, because the CI of this pooled estimate crosses the null line (1.00), this effect is not statistically significant (see Figure 18).

There is a trend in the opposite direction at months 6 and 12, wherein the overall pooled odds ratios of 1.22 (95% CI: 0.69, 2.13) and 1.23 (95% CI: 0.70, 2.16), respectively, suggest that the odds of achieving cure at those follow-up times are higher if using synthetic mesh than if using AFS (see Figure 18). However, neither of those effects are significant. At ≥18 months, this trend reverses back, with the overall pooled odds ratio of 0.72 (95% CI: 0.39, 1.34) suggesting that the odds of achieving cure with synthetic mesh are lower than with AFS, but this effect is not significant.

The pooled studies were assessed for risk of publication bias (see Figure A6 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots). The funnel plot is not symmetrical, which suggests that the risk of publication bias is high.

Figure 18: Forest Plot of Cure Rates in SUI Patients Receiving Synthetic Mesh vs. AFS



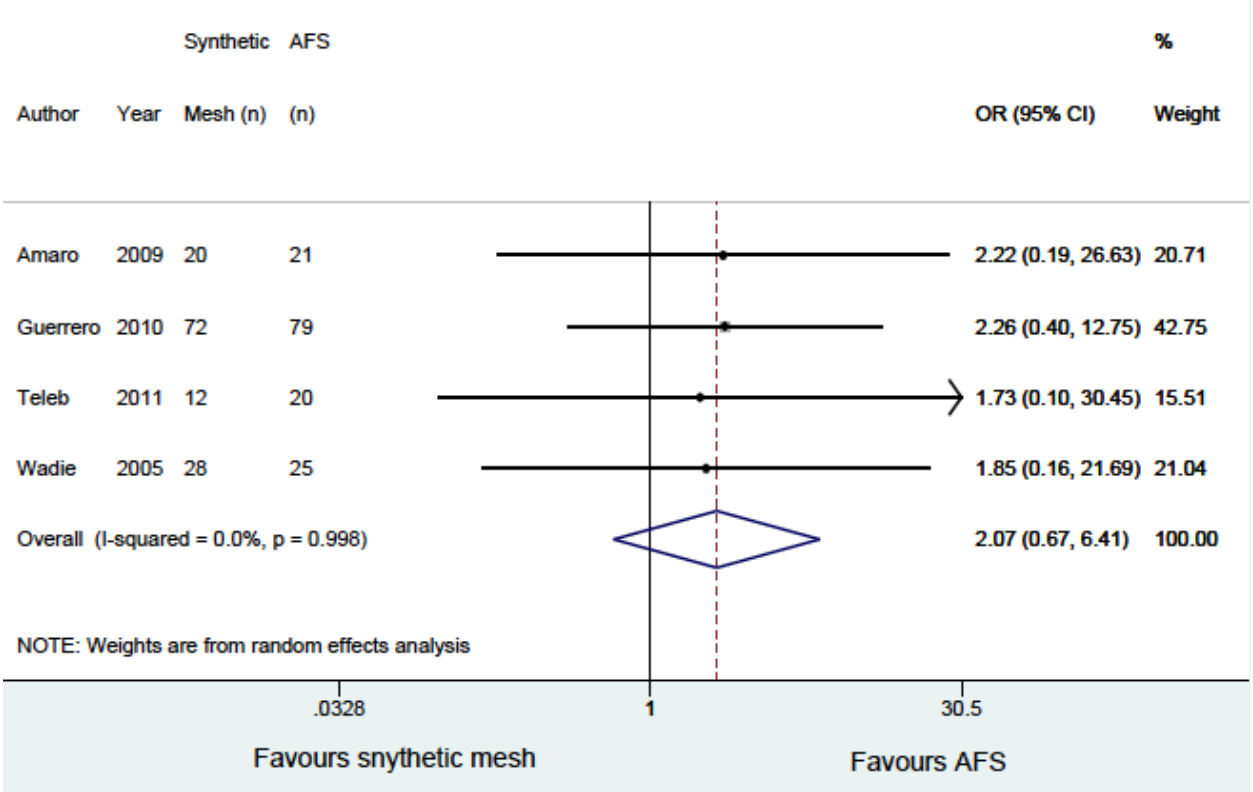

### 8.3.2.4 Meta-analysis of Complications

#### 8.3.2.4.1 Bladder Injury

The most frequently reported intraoperative adverse effect in the seven studies assessing synthetic mesh vs AFS was bladder injury (reported in four studies).[107,108,110,111] A meta-analysis was conducted using the data from those studies to examine the odds of experiencing bladder injury when undergoing a procedure using synthetic mesh vs. AFS (Figure 19). The pooled odds ratio for bladder injury is 2.07 (95% CI: 0.67, 6.41), suggesting that patients undergoing synthetic mesh surgery are twice as likely to experience bladder injury than if undergoing AFS

surgery; however, this effect is not significant due to the CI of this pooled estimate crossing the null line (1.00).

Figure 19: Forest Plot of Bladder Injuries in SUI Patients Receiving Synthetic Mesh vs. AFS




8.3.2.4.2 Other Complications

Other commonly reported adverse effects were de novo urgency (three studies),[107,110,112] urinary retention (two studies),[107,110] and scar pain (two studies).[111,112] A meta-analysis examining those adverse effects could not be conducted due to variability in follow-up time.

De novo urgency rates were higher in the AFS group than the synthetic mesh group at one month (10% vs. 8.33%, respectively)[110] but higher in the synthetic mesh group than the AFS group at three years (42.1% vs. 5%, respectively)[107] and at 10 years (1.59% vs. 0%, respectively).[112]

Urinary retention rates (short-term) were higher in the synthetic mesh group than the AFS group in one study (8.33% vs. 0%, respectively)[110] and similar in the other study (null rates for both).[107]

Lastly, scar pain was more common in the AFS group than the mesh group, with rates of 28% vs. 7.14%, respectively, at six months,[111] and rates of 3.28% vs. 0%, respectively, at 10 years.[112]

#### 8.3.2.4.3 Mesh Exposure and Erosion

Mesh exposure was reported in one study comparing synthetic mesh to AFS; no mesh erosion was reported.[112] As such, a meta-analysis of mesh exposure rates was not conducted. The rate of mesh exposure in the synthetic mesh group was 1.6% at 10 years.

### 8.3.2.5 Subjective Outcomes

Only three of the studies examining synthetic mesh vs. AFS reported patient-reported measures assessing urinary symptoms (e.g., Bristol Female Lower Urinary Tract Symptom Questionnaire [BFLUTS]) and QoL (i.e., King's Health Questionnaire [KHQ]) (see Table 17). Due to the small number of studies reporting patient-reported measures and variability in the types of questionnaires used, there was an insufficient number of studies that could be pooled to conduct a meta-analysis of these outcomes. In general, there was a positive trend following treatment with either intervention across all subjective outcome measures.

Table 17: Patient-reported Outcome Measures across the Synthetic Mesh vs. AFS Studies

| | KHQ | I-QOL | BFLUTS | None |
|---|---|---|---|---|
| Amaro, Brazil, 2009[107] | ✓ | | | |
| Guerrero, UK, 2010[108] | | | ✓ | |
| Khan, UK, 2015[112] | | ✓ | | |
| Bai, Korea, 2005[88]<br>Silva-Filho, Brazil, 2006[109]<br>Teleb, Egypt, 2011[110]<br>Wadie, Egypt, 2005[111] | | | | ✓ |

Abbreviations: BFLUTS: Bristol Female Lower Urinary Tract Symptoms; I-QoL: Incontinence Quality of Life; KHQ: King's Health Questionnaire

## *8.3.3 Synthetic Mesh vs Porcine Mesh*

### 8.3.3.1 Characteristics of Included Studies

Five studies (three original RCTs[108,113,114] and two follow-up studies[112,115]) examining synthetic mesh vs. porcine mesh were identified. Four studies were from the UK[108,112,113,115] and one was from Italy.[114] The studies were published between 2002 and 2015.

Studies ranged from around 3-24 months in follow-up. Study sample sizes ranged from 70-142 patients. Common study inclusion criteria included women ≥18 years of age and urodynamically

proven SUI. Common exclusion criteria were previous SUI surgery, detrusor overactivity and POP >stage II. Study characteristics are reported in Table A2 in Appendix 5.

#### 8.3.3.2 Quality of Included Studies

Most of the RCTs comparing synthetic vs. porcine mesh had a low risk of bias in each of the five domains. All of the studies used some type of randomization to allocate patients. All of the interventions seemed to have been performed similarly to everyday practice. All studies had complete outcome data, and the follow-ups had similar rates of drop-out, with reasons for drop-out provided. Primary outcomes were generally objective measures (e.g., pad weight) and their assessment was considered to not have been biased, with the exception of two studies that used subjective improvement as their primary outcome.[113,115] Lastly, there was no evidence of selective reporting of the results. Quality assessment for synthetic mesh vs. porcine mesh studies is reported in Table 18.

Table 18: Quality Assessment of Synthetic vs. Porcine Mesh SUI Studies

| Study ID | Bias from randomization | Bias from deviation | Bias from missing outcome data | Bias from measurement | Bias in reported results |
|---|---|---|---|---|---|
| Abdel-Fattah (see Arunkalaivanan 2002), UK, 2004[115] | **low risk** | **low risk** | **low risk** | **high risk** | **low risk** |
| Arunkalaivanan (see Abdel-Fattah 2004), UK, 2002[113] | **low risk** | **low risk** | **low risk** | **high risk** | **low risk** |
| Guerrero (see Khan 2015), UK, 2010[108] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Khan (see Guerrero 2010), UK, 2015[112] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Paparella, Italy, 2010[114] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

#### 8.3.3.3 Meta-analysis of Cure Rates

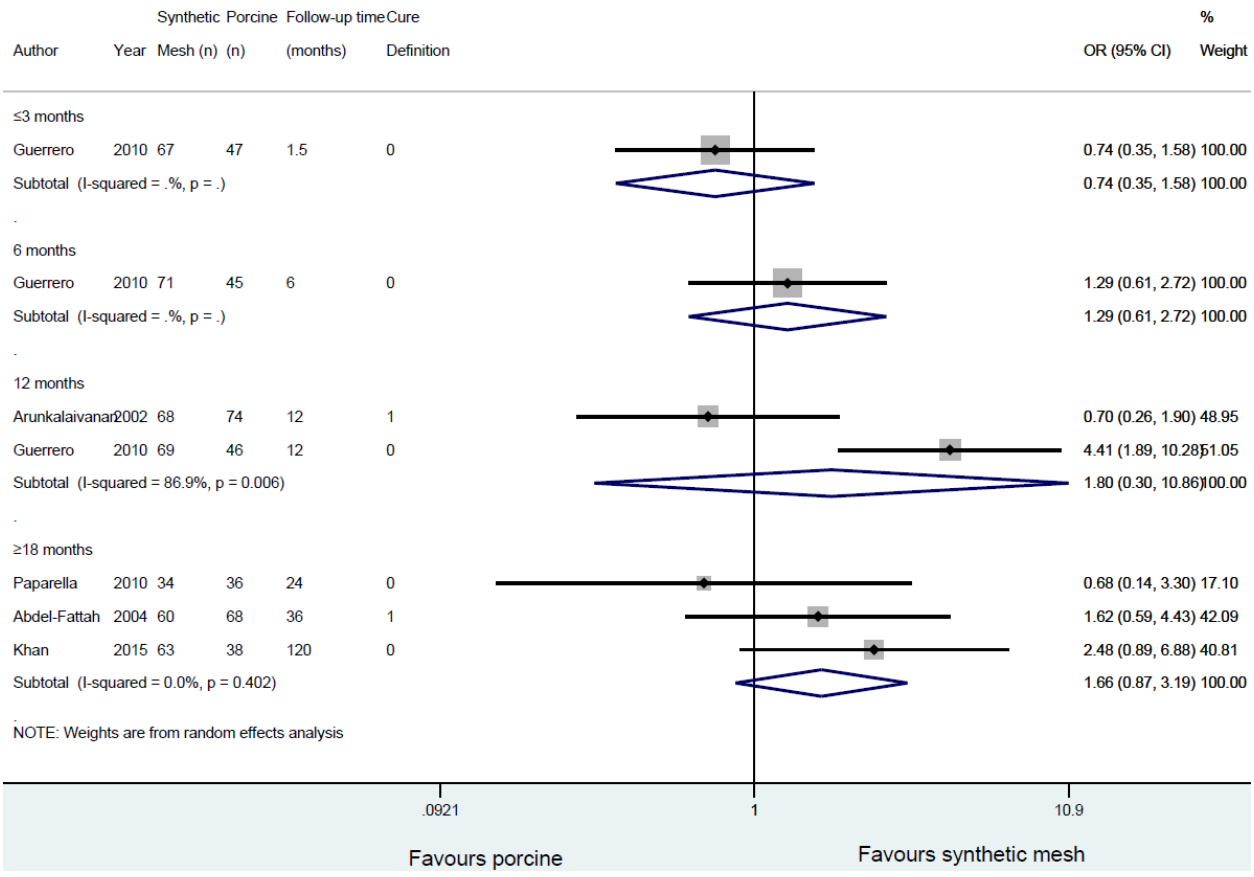
Three of the synthetic mesh vs. porcine mesh studies provided adequate data on cure rates to permit pooling at ≥18 months.[112,114,115] Figure 20 shows the pooled overall cure rate results (forest plot) for synthetic mesh vs. porcine mesh. All cure definitions as defined by the study

authors were used in this analysis. Two studies with a follow-up time of less than 18 months could not be pooled due to differences in follow-up times; data for those studies are presented for descriptive purposes only (see Figure 20).

At ≥18 months, the overall pooled odds ratio was 1.66 (95% CI: 0.87, 3.19), which suggests that the odds of achieving cure are slightly higher if using synthetic mesh than if using porcine mesh (Figure 20). However, because the CI of this pooled estimate crosses the null line (1.00), this effect is not statistically significant.

The pooled studies were assessed for risk of publication bias (see Figure A7 in Appendix 6). The funnel plot is largely symmetrical, which suggests that the risk of publication bias is low.

Figure 20: Forest Plot of Cure Rates in SUI Patients Receiving Synthetic Mesh vs. Porcine Mesh




### 8.3.3.4 Meta-analysis of Complications

A meta-analysis of the complications for synthetic vs porcine mesh could not be conducted because there were not enough studies to provide data for the analysis. The most commonly

reported complications for this comparison were bladder injury (two studies)[108,113] and de novo urge incontinence (two studies).[112,115] One study reported null bladder injury rates for the two groups;[113] the other study reported a not significantly higher rate of bladder injury in the synthetic mesh group (5.6%) than in the porcine mesh group (2%).[108] De novo urgency rates were similar between the synthetic and porcine mesh groups: 15% vs. 17.6%, respectively in the 36-month follow-up study,[115] and 1.6% vs 0%, respectively, in the 120-month follow-up study.[112]

#### 8.3.3.4.1 Mesh Exposure and Mesh Erosion

Mesh exposure was reported in one study comparing synthetic mesh to porcine mesh; no mesh erosion was reported.[112] As such, a meta-analysis of mesh exposure rates was not conducted. The rate of mesh exposure in the synthetic mesh group was 1.6% at 10 years.

#### 8.3.3.5 Subjective Outcomes

Only three of the studies examining synthetic mesh vs. porcine mesh reported patient-reported measures assessing urinary symptoms (e.g., Bristol Female Lower Urinary Tract Symptom Questionnaire [BFLUTS]) and QoL (i.e., King's Health Questionnaire [KHQ]) (see Table 19). Due to the small number of studies reporting patient-reported measures and variability in the types of questionnaires used, there was an insufficient number of studies that could be pooled to conduct a meta-analysis of these outcomes. In general, there was a positive trend following treatment with either intervention across all subjective outcome measures.

Table 19: Patient-reported Outcome Measures across the Synthetic Mesh vs. Porcine Studies

| | KHQ | I-QOL | BFLUTS | None |
|---|---|---|---|---|
| Guerrero, UK, 2010[108] | | | ✓ | |
| Khan, UK, 2015[112] | | ✓ | | |
| Paparella, Italy, 2010[114] | ✓ | | | |
| Abdel-Fattah. UK, 2004[115]<br>Arunkalaivanan, UK, 2002[113] | | | | ✓ |

Abbreviations : BFLUTS: Bristol Female Lower Urinary Tract Symptoms; I-QoL: Incontinence Quality of Life; KHQ: King's Health Questionnaire

## 8.4 Conclusions

Twenty-nine studies (22 original RCTs and seven follow-up studies) were identified that evaluated the effectiveness of synthetic surgical mesh against a comparator of interest. Of these

studies, 19 compared synthetic mesh to native tissue suspension, seven compared synthetic mesh to AFS, and five compared synthetic mesh to porcine mesh. None of the meta-analysis comparisons of cure rates were significant, suggesting that synthetic mesh is not largely different from either native tissue suspension, AFS, or porcine mesh; however, studies differed in their definitions of cure and duration of follow-up times, which makes it difficult to draw any definitive conclusions from these findings. The most frequently reported complication across the three comparison groups was bladder injury (an intraoperative complication). Meta-analysis comparisons suggest that bladder injuries occur more frequently in the synthetic mesh group than in the native tissue suspension or AFS groups; however, those effects are not statistically significant. Mesh erosion in the synthetic mesh group ranged from 0.59%-12% by 12 months, and the rate of mesh exposure was 1.6% at 10 years.

Overall, the included studies were of good quality, as assessed by the Cochrane Risk of Bias tool,[84] with some bias stemming from the randomization domain in select studies; however, study groups appeared to be largely well-balanced across studies with respect to participant demographics and disease characteristics. Some studies were deemed to be of some concern or high risk of bias due to the subjective nature of some of the outcomes that were assessed (e.g., self-report measures); however, the majority of the studies employed objective outcome measures (e.g., pad weight test) that were unlikely to have been biased by self-report.

The outcomes most commonly reported within the included RCTs were objective and subjective cure, which are considered to be clinically relevant outcomes. Few studies reported QoL outcomes, which are important for assessing the impact of the SUI surgery on the patient's everyday life and well-being; studies that did capture QoL outcomes used mostly different measures, which made it difficult to compare the outcomes across comparison groups.

The majority of the studies were conducted in the UK, the US, and Italy, with no studies conducted in Canada. However, there is no reason to suspect that the patient mix and underlying etiology of SUI are substantially different in Canada. As such, the findings from this review should be generalizable to the Canadian context.

Overall, much uncertainty remains regarding the effectiveness and safety of synthetic surgical mesh for SUI. While the existing literature suggests that synthetic surgical mesh may be similar

to AFS, native tissue suspension, and porcine mesh, there is considerable variability across studies with respect to cure definition, follow-up duration, and availability of QoL data.

# 9 Systematic Review of Safety and Efficacy of Surgical Mesh for Pelvic Organ Prolapse

***Summary:***

- Thirty-two unique RCTs and 11 follow-up studies were identified that evaluated the effectiveness of synthetic surgical mesh.
- Thirty-eight studies compared synthetic mesh to native tissue suspension, three compared synthetic mesh to porcine, two compared synthetic mesh to autologous/cadaver tissue, and two compared synthetic tissue to semi-dissolvable/dissolvable mesh.
- A meta-analysis of cure rates for synthetic vs. native tissue found that the odds of cure are five times higher at 12 months and three times higher at 24 months, favoring synthetic mesh. These effects are significant but associated with substantial heterogeneity and should be interpreted with caution.
- A meta-analysis of cure rates for synthetic vs. porcine mesh found that the odds of cure at 24 months are almost two times and significantly higher for synthetic mesh.
- Meta-analysis results suggest that synthetic mesh is significantly associated with more bladder injury, intraoperative blood loss, and urinary retention than native tissue suspension.
- Meta-analyses of cure rates and adverse effects for the other comparators could not be conducted due to insufficient data.
- Rates of mesh exposure and mesh erosion at 12 months in the synthetic mesh group range from 1.59%-17.3% and 2.22%-35.7%, respectively.

## 9.1 Purpose

To assess the clinical effectiveness and safety profile of permanent, synthetic surgical mesh for treatment of POP in adults.

## 9.2 Methods

### *9.2.1 Search Strategy*

A systematic review of the literature was completed. MEDLINE, EMBASE, Cochrane Central, and CINAHL were searched from inception. The search was performed on December 12, 2018. Terms capturing surgical mesh for POP (e.g. “suburethral sling,” “fascial sling”) were searched in combination with terms capturing the condition of interest (e.g. “pelvic organ prolapse, “pelvic floor muscles”). The search was limited to exclude animal studies, conference abstracts, editorials, and letters. The full search strategy is reported in Appendix 3: Search Strategies for POP Systematic Review.

### *9.2.2 Study Selection*

RCTs examining permanent synthetic surgical mesh for POP compared to biological mesh, native tissue suspension, or semi-dissolvable/dissolvable mesh were included. Abstracts were screened in duplicate by independent reviewers using *a priori* inclusion and exclusion criteria listed in Table 20. Abstracts that were included by either reviewer proceeded to full-text review. At the full-text review stage, studies were screened in duplicate by two reviewers, with any discrepancies resolved through discussion and consensus. Studies were excluded if they were not RCTs, were not purely for POP, did not examine permanent synthetic mesh compared to biological mesh, native tissue, or semi-dissolvable/dissolvable mesh, were not available in English or French, did not report original data, or were animal studies.

Table 20: Inclusion and Exclusion Criteria for POP Review

| | **Inclusion** | **Exclusion** |
|---|---|---|
| Population | Female adult population | Animal studies; pediatric population; mixed sex population not stratified |
| Intervention | Assesses use of surgical mesh for POP<br>Assesses use of synthetic mesh<br>• Polypropylene material<br>• Permanent meshes | • Assesses use of surgical mesh not for POP<br>• Does not assess surgical mesh<br>• Assesses use of biological mesh, grafts, pessaries<br>• Assesses surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open)<br>• Semi-permanent or dissolvable mesh |
| Comparator | Compares surgical mesh for POP to:<br>• Non-mesh surgical procedures<br>• Conservative management<br>• Other surgical meshes for POP (semi-permanent or dissolvable mesh) | • Surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open) |
| Outcome | Clinical outcome- any; or QoL outcome | No clinical outcome; no QoL outcome |
| Design | RCT design- any | Not an RCT; secondary RCT data analysis (not planned *a priori*) |
| | English or French | Not English or French |
| | Full-text available | No full-text |

Abbreviations: POP: pelvic organ prolapse; QoL: quality of life; RCT: randomized controlled trial

### *9.2.3 Data Extraction*

For all studies, year of publication, country, patient selection, patient characteristics, description of technologies, definition of objective cure, objective cure and subjective outcomes, and follow-up time were extracted using standardized data extraction forms. Safety outcomes consisting of complications (e.g., bladder injury) were also extracted. Discrepancies between reviewers during data extraction were resolved through consensus.

### *9.2.4 Quality Assessment*

During data extraction, each included study was assessed for quality using The Cochrane Risk of Bias Tool.[84] Quality assessment was completed in duplicate with discrepancies resolved through discussion. Using this tool, each study was assessed across five potential domains of bias (randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result). Each domain was assigned a "low, "high," or "some concern" risk of bias rating, based on the answers to the signaling questions.

### *9.2.5 Meta-Analysis*

A meta-analysis was conducted for comparisons with three or more studies to inform the magnitude of treatment effect for synthetic surgical mesh for POP with respect to cure rates and complications. The following comparator pairs were assessed: synthetic mesh vs. native tissue suspension and synthetic mesh vs. porcine mesh. A pooled analysis including the cure definition of POP stage 0-1 and Ba<-1/Ba<0 was conducted, with a sub-analysis based on different follow-up times. For each study, the number of participants who were cured and who had experienced treatment complications were compared between the synthetic mesh and the comparator group. There was an insufficient number of studies to examine cure rates for the synthetic mesh vs. autologous/cadaver tissue and synthetic mesh vs. semi-dissolvable/dissolvable mesh comparisons. A sufficient number of studies to conduct a meta-analysis was only available for the synthetic vs. native tissue suspension comparison.

A random effects model using the method of DerSimonian and Laird[85] was used, with a continuity correction of 0.5 where appropriate. The same continuity correction was used to allow inclusion of zero-total event trials.[86] Analyses were conducted based on the comparator groupings established during data extraction (as outlined above). Meta-analyses were conducted

using odds ratio to express the effectiveness of permanent synthetic surgical mesh in relation to other comparators. For studies only reporting a median follow-up time, normal distributions were assumed and median follow-up time value was used. Statistical analysis was completed in STATA 14.[87]

### 9.3 Results

A total of 6759 citations were identified from the literature search. After duplicates were removed, 3933 unique citations were screened during abstract review, of which 3807 were excluded at this stage, and 126 proceeded to full-text review. Eighty-three articles were excluded at full-text review for the following reasons: 44 were not RCTs; 17 were not available as full-text; eight did not assess permanent, synthetic mesh; seven examined differences in surgical technique only, rather than differences in mesh; three did not assess mesh; one did not report clinical or QoL outcomes; and one did not assess mesh for POP exclusively. In total, 43 final papers (32 original RCTs and 11 follow-up studies) were included in the review. Two of the included studies had three comparator arms, which have been grouped according to each intervention and specific comparator. There were studies 38 studies (28 original RCTs[34,116-143] and 10 follow-up studies[144-152]) that compared synthetic mesh to native tissue suspension, three (all original RCTs[117,133,153]) that compared synthetic mesh to porcine mesh, two (one original RCT[154] and one follow-up study[155]) that compared synthetic mesh to autologous/cadaver tissue, and two (both original RCTs[42,156]) that compared synthetic tissue to semi-dissolvable/dissolvable mesh.

Figure 21: Comparators Examined in Studies Included in the POP Review, N=43

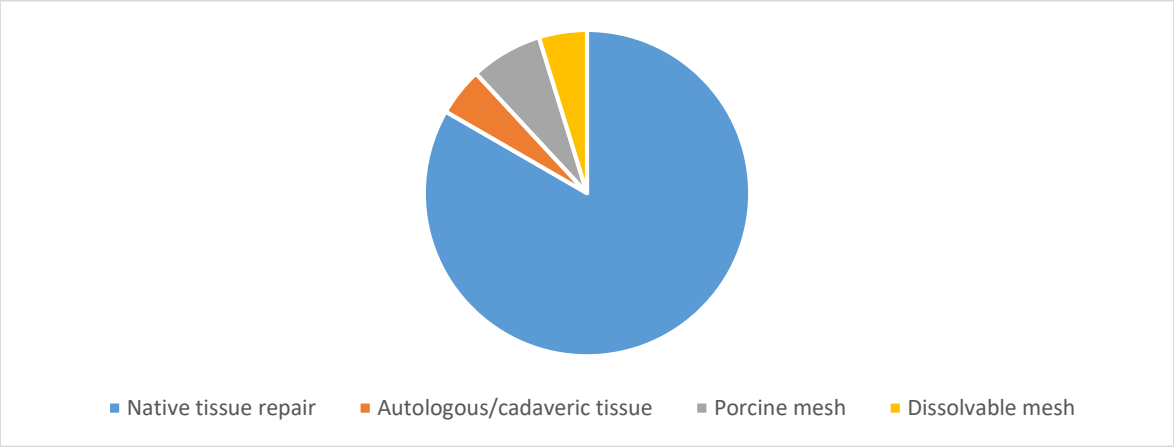
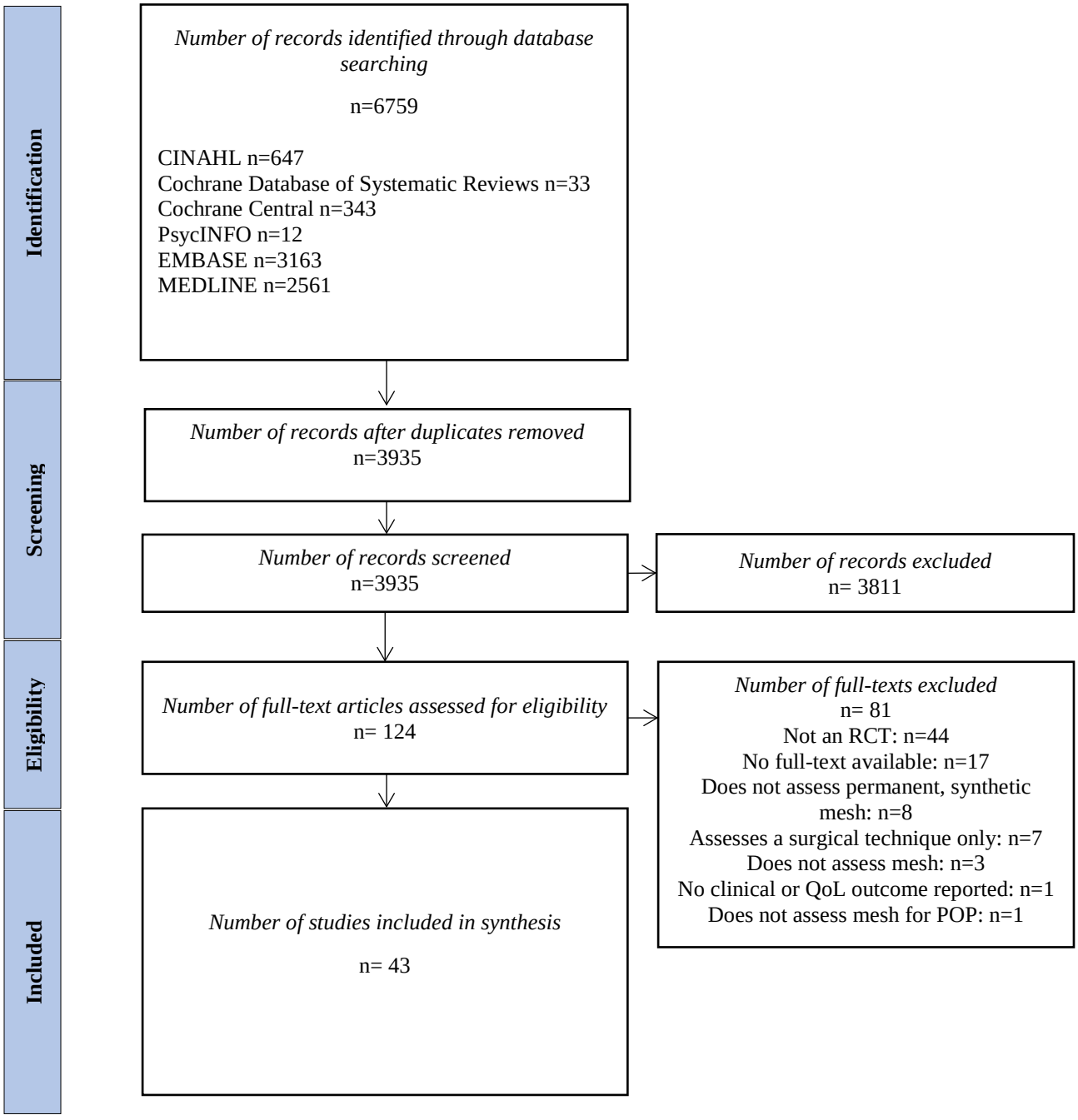
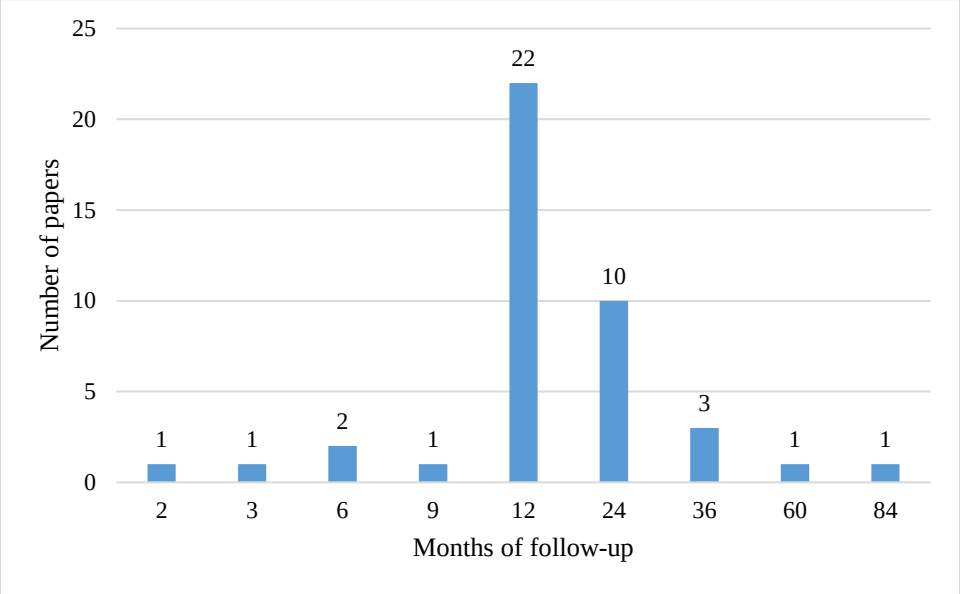


Figure 22: PRISMA Flow-chart for POP review



Follow-up times across the three comparators included in the SUI review ranged from 3-120 months; 12 and 24 months were the most common follow-up time-points (see Figure 23).

Figure 23: Follow-up Times in POP Papers




*Only papers reporting exact or mean follow-up time are included in the graph; papers reporting follow-up as median or range are excluded

### *9.3.1 Synthetic Mesh vs Native Tissue Suspension*

#### 9.3.1.1 Characteristics of Included Studies

Thirty-eight studies (28 original RCTs[34,116-143] and 10 follow-up studies[144-152]) examining synthetic mesh vs. native tissue suspension were identified. Studies were from Brazil,[120-122,131,132,140,141,151] USA,[129,133,134,146,150] France,[118,119,130] Finland,[128,148,149] the Netherlands,[34,143,147,152] Egypt,[124] Chili,[136] Australia,[116] India,[126] Italy,[117] the UK,[125] Turkey,[138,142] Czech Republic,[127,139] Jordan,[135], Sweden,[123], and Sweden/Norway/Finland/Denmark.[137,144,145] The studies were published between 2007 and 2018, with the majority of the studies published in the early 2010s.

The majority of the studies focused on the 12-month follow-up period, with a number of studies conducting a follow-up at 24 months and beyond. Study sample sizes ranged from 32-865 patients, with most studies including around 60-100 patients (~30-50 patients per group). Common study inclusion criterion was women with stage 2-4 POP requiring surgical correction;

common exclusion criterion was current or future pregnancy. Some studies included women of all ages (e.g., ≥18 years old), whereas other study included older women only (40+). Study characteristics are reported in Table A3 in Appendix 5.

#### 9.3.1.2 Quality of Included Studies

Of the 38 studies that compared synthetic mesh to native tissue suspension, six[117,127,135,142,143,152] were considered to be at a moderate risk for bias due to randomization largely due to not reporting allocation concealment methods. One study was considered to be high risk due to unclear reporting of randomization methods and baseline imbalance between study groups.[119]

With respect to bias from deviation, three studies[123,137,144] were given a moderate risk of bias rating, and two studies[118,125] were rated as high risk depending on the number of patients that were analyzed in a different study group than the intervention they received.

Bias from missing outcome data was present in three studies, which were given a high risk of bias rating due to imbalances in missing data between groups and substantial drop-out rates that would have underpowered the study based on the study authors' power calculations.[121,135,145]

Bias from measurement was low across most studies, with the exception of two studies that used subjective self-report outcome measures as their primary outcomes, which may have been biased due to lack of blinding.[119,152]

Lastly, all studies with the exception of one[150] were considered to be at low risk for bias in reported results; the one study was rated as high risk was because it reported different patient numbers for related outcomes. Quality assessment for synthetic mesh vs. native tissue suspension is reported in Table 21.

Table 21: Quality Assessment of Synthetic Mesh vs. Native Tissue Suspension POP Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Altman, Sweden, Norway, Finland, Denmark, 2011 (see Ek 2010, 2013)[144] | **low risk** | **some concern** | **low risk** | **low risk** | **low risk** |

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Carey, Australia, 2008[116] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Damiani, Italy, 2016[117] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| de Tayrac, France, 2013[118] | **low risk** | **high risk** | **low risk** | **low risk** | **low risk** |
| de Tayrac, France, 2008[119] | **high risk** | **low risk** | **low risk** | **high risk** | **low risk** |
| Delroy, Brazil, 2013[120] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Dias, Brazil, 2016[121] | **low risk** | **low risk** | **high risk** | **low risk** | **low risk** |
| dos Reis Brandao, Brazil, 2015[122] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Ek, Sweden, Norway, Finland, Denmark, 2013 (see Ek 2010, Altman 2011)[145] | **low risk** | **low risk** | **high risk** | **low risk** | **low risk** |
| Ek, Sweden, 2010 (see Altman 2011, Ek 2013)[123] | **low risk** | **some concern** | **low risk** | **low risk** | **low risk** |
| El-Nazer, Egypt, 2012[124] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Glazner, UK, 2017[125] | **low risk** | **high risk** | **low risk** | **low risk** | **low risk** |
| Gupta, India, 2014[126] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Gutman, USA, 2013 (see Iglasia 2010, Sokol 2012)[146] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Halaska, Czech Republic, 2012[127] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Hiltunen, Finland, 2007[128] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Iglesia, USA, 2010 (see Sokol 2012, Gutman 2013)[129] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Lamblin, France, 2014[130] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Lopes, Brazil, 2010[131] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Lunardelli, Brazil, 2009[132] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Menefee, USA, 2011[133] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Milani, The Netherlands, 2018 (see Withagen 2011) [147] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Nguyen, USA, 2008[134] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Nieminen, Finland, 2008 (see Hiltunen 2007, Nieminen 2010)[148] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Nieminen, Finland, 2010 (see Hiltunen 2007, Nieminen 2008)[149] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Qatawneh, Jordan, 2012[135] | **some concern** | **low risk** | **high risk** | **low risk** | **low risk** |
| Rondini, Chile, 2015[136] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Rudnicki, Denmark, Norway, Sweden and Finland, 2013[137] | **low risk** | **some concern** | **low risk** | **low risk** | **low risk** |
| Sivaslioglu, Turkey, 2008[138] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Sokol, USA, 2012 (see Iglasia | **low risk** | **low risk** | **low risk** | **low risk** | **high risk** |

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| 2010, Gutman 2013)[150] | | | | | |
| Svabik, Czech Republic, 2014[139] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Tamanini, Brazil, 2013(a) (see Tamanini 2013 (b), Tamanini 2015) [141] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Tamanini, Brazil, 2015 (see Tamanini 2013 (a) and (b))[151] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Tamanini, Brazil, 2013 (b) (see Tamanini 2013 (a), Tamanini 2015)[140] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Turgal, Turkey, 2013[142] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Vollebregt, The Netherlands, 2012 (see Vollebregt 2011)[152] | **some concern** | **low risk** | **low risk** | **high risk** | **low risk** |
| Vollebregt, The Netherlands, 2011 (see Vollebregt 2012)[143] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Withagen, The Netherlands, 2011 (see Milani 2018)[34] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

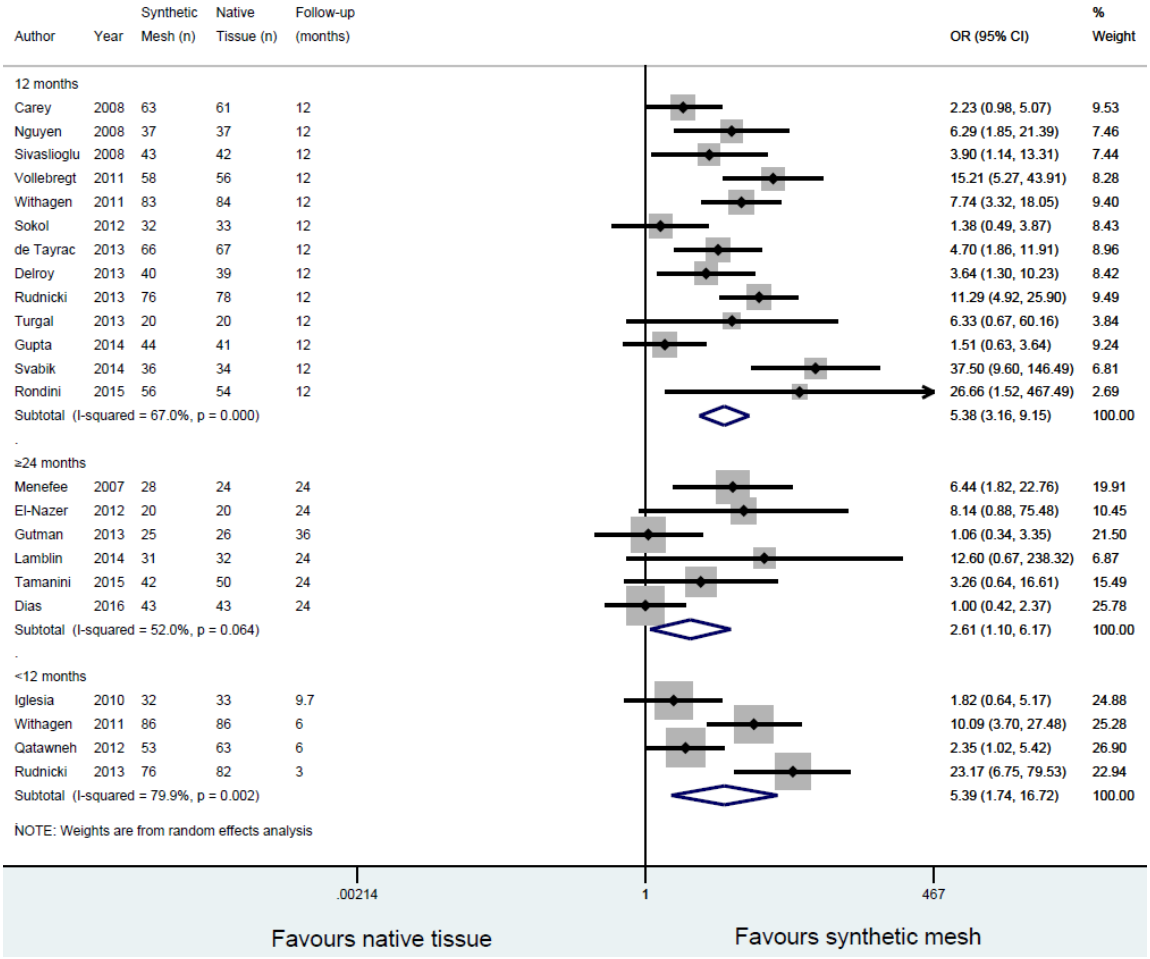
#### 9.3.1.3 Meta-analysis of Cure Rates

Thirteen of the synthetic mesh vs. native tissue suspension studies provided adequate data on cure rates to permit pooling at 12 months,[34,116,118,120,126,134,136,138,139,142,143,150] and five studies provided data for pooling at 24 months.[121,124,130,133,151] Figure 24 shows the pooled overall cure rate results (forest plot) for synthetic mesh vs. native tissue suspension; the cure definitions of POP stage 0-1 and BA<-1/BA<0 were used in this analysis. No additional cure definitions allowed pooling. Four studies with a follow-up time less than 12 months could not be pooled due to differences in follow-up times; data for those studies are presented for descriptive purposes only (see Figure 24).

At 12 months, the overall pooled odds ratio for synthetic mesh vs. native tissue suspension is 5.38 (95% CI: 3.16, 9.15), which suggests that the odds of achieving cure using synthetic mesh are five times higher at 12 months than if using native tissue suspension (Figure 24). This effect is significant; however, the analysis is associated with substantial heterogeneity, $i^2$=67%, suggesting that the results need to be interpreted with caution. At 24 months, the overall pooled odds ratio for synthetic mesh vs. native tissue suspension is 3.57 (95% CI: 3.16, 9.15), which suggests that the odds of achieving cure using synthetic mesh are three times higher at 24 months than if using native tissue suspension Figure 24). This effect is also significant but is also associated with substantial heterogeneity, $i^2$=54.9%.

The pooled studies were assessed for risk of publication bias (see Figure A17 in Appendix 6). The funnel plot is somewhat symmetrical, but some of the studies fall outside of the 95% confidence interval line, suggesting that the risk of publication bias may be uncertain.

Figure 24: Forest Plot of Cure Rates in POP Patients Receiving Synthetic Mesh vs. Native Tissue Suspension




Rates of cure vs. failure at 12 months in individual studies included in the meta-analysis of overall cure rates are reported in Figure 25 for synthetic mesh and Figure 26 for the native tissue group. Overall risk of bias ratings for the individual studies are included to aid with interpretation of the study findings: studies classified as “low risk” had low risk ratings across all potential bias domains; studies classified as “some concern” had that risk rating for at least one of the domains; studies classified as “high risk” had a high risk rating for at least one of the domains. No trends were observed between a study’s risk of bias rating and cure rates in either the synthetic or native tissue suspension groups.

Figure 25: Cure Rates at 12 Months in Patients with POP Receiving Synthetic Mesh

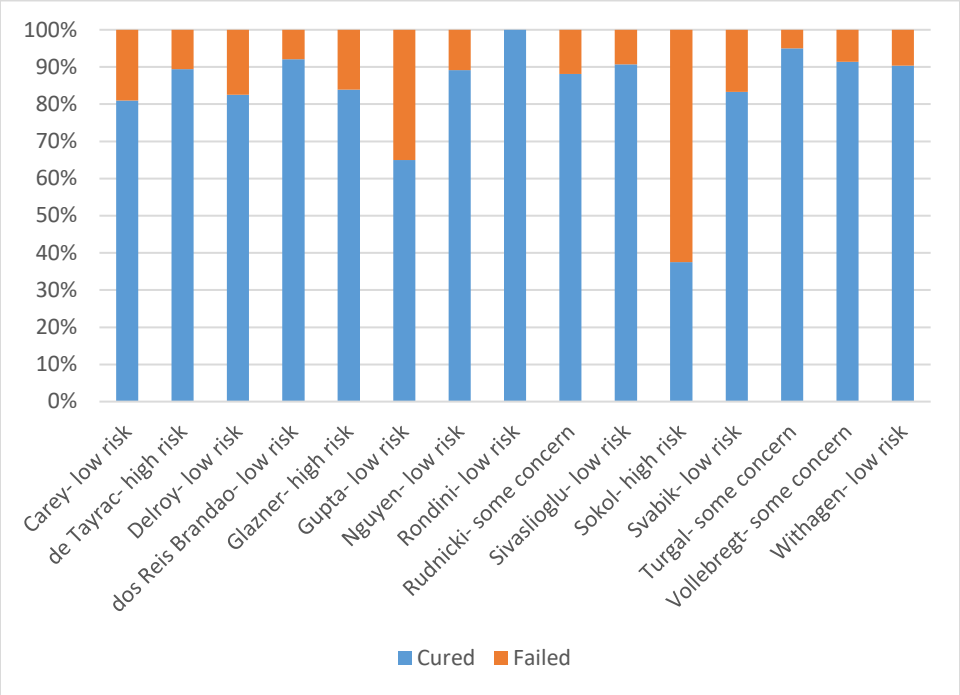
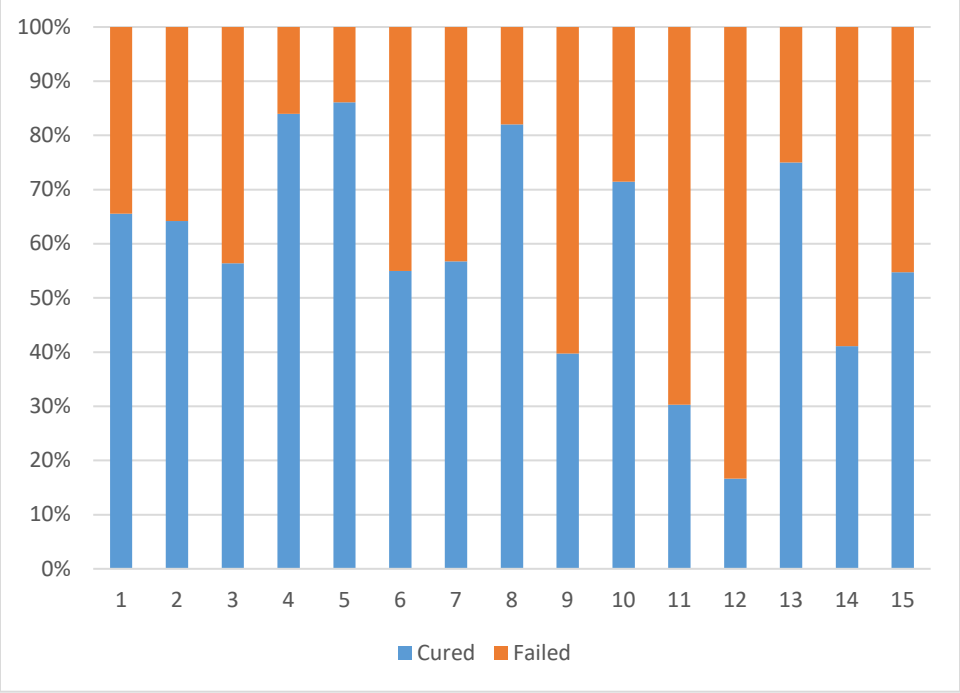


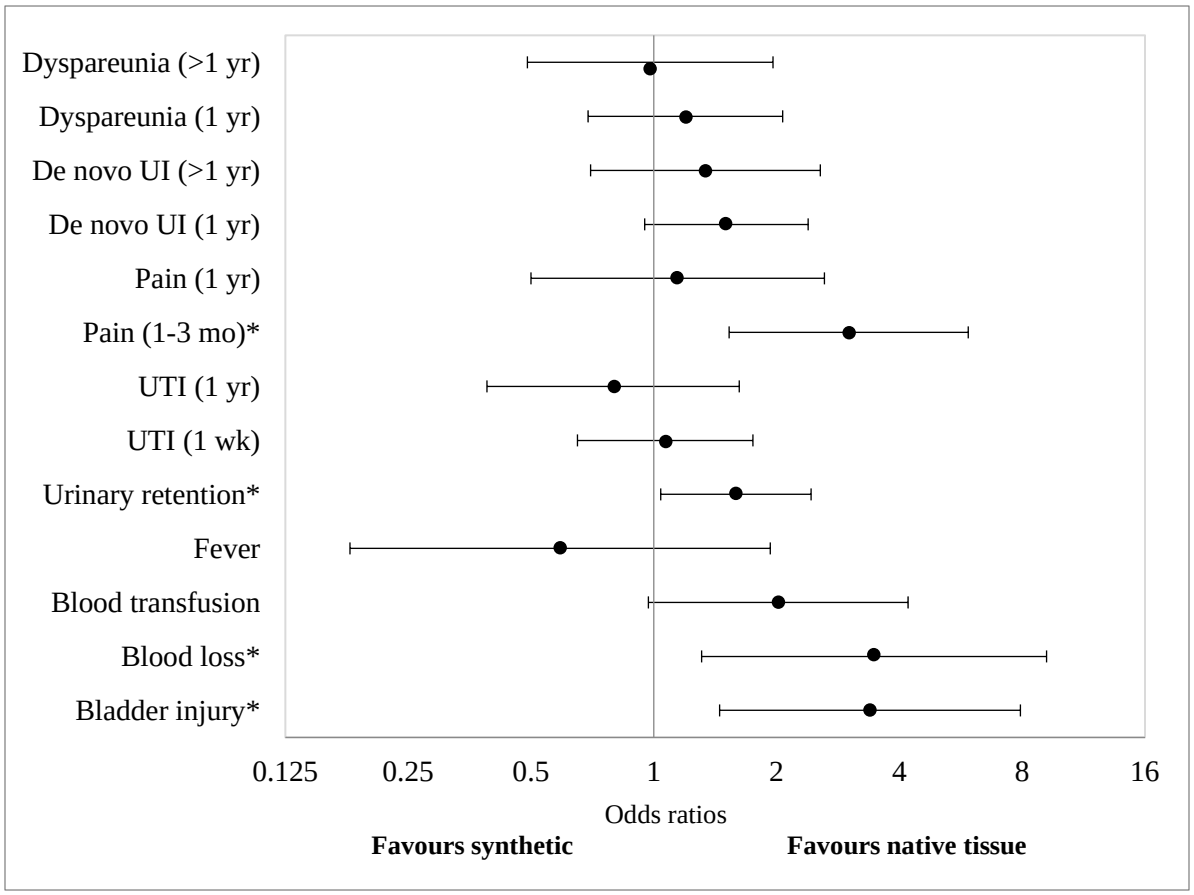

Figure 26: Cure Rates at 12 Months in Patients with POP Receiving Native Tissue Suspension



9.3.1.4 Meta-analysis of Complications

Sufficient data were available to conduct meta-analyses of nine complications reported in the synthetic mesh vs. native tissue suspension studies: bladder injury, blood loss, blood transfusion, fever, urinary retention, UTI (at one week and at one year), pain (at 1-3 months and at one year), de novo urinary incontinence (at one year and after one year), and dyspareunia (at one year and after one year). Synthetic mesh was associated with significant higher odds of intraoperative bladder injury and blood loss, urinary retention, and pain at 1-3 months than native tissue suspension. A summary of the odds ratios is reported in Figure 22, with more granular details reported in the sections below; forest plots for the POP complications analyses are reported in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots.

Figure 27: Odds Ratios for Complications in POP Patients Receiving Synthetic Mesh vs. Native Tissue




*Indicates a significant effect

#### 9.3.1.4.1 Bladder Injury

Bladder injury was the most frequently reported intraoperative adverse effect and was reported in 14 studies.[34,116,119,120,124,127-129,136,137,139,144,150] A meta-analysis was conducted using the data from 11 of those studies (three studies reported null event rates for both groups) to examine the odds of experiencing bladder injury (see Figure A8 in Appendix 6).[34,116,119,127-129,136,137,144,150] The pooled odds ratio for bladder injury is 3.39 (95% CI: 1.45, 7.92), which is significant and suggests that patients undergoing synthetic mesh surgery are three times more likely to experience bladder injury than if undergoing native tissue suspension surgery.

#### 9.3.1.4.2 Blood Loss

Significant blood loss during surgery was an intraoperative adverse effect reported in six studies assessing synthetic mesh vs. native tissue suspension.[116,121,128,137,139,144] A meta-analysis was conducted using the data from five of those studies (one study reported null event rates for both groups) to examine the odds of experiencing significant blood loss.[116,121,128,137,144] The pooled odds ratio for significant blood loss 3.46 (95% CI: 1.31, 9.18), which is significant and suggests that patients undergoing synthetic mesh surgery are three times more likely to experience significant blood loss than if undergoing native tissue suspension surgery (see Figure A9 in Appendix 6).

#### 9.3.1.4.3 Need for Blood Transfusion

Five studies reported the need for blood transfusion during surgery using synthetic mesh vs. native tissue suspension.[120,126,129,134,137] A meta-analysis of these studies found a pooled odds ratio of 2.02 (95% CI: 0.97, 4.20), which suggests that patients undergoing synthetic mesh surgery are two times more likely to require blood transfusion than if undergoing native tissue suspension surgery (see Figure A10 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots). However, this effect is not significant because the CI of this pooled estimate touches the null line (1.00).

#### 9.3.1.4.4 Urinary Retention

Urinary retention is the most frequently reported short-term complication (occurring typically within a week after surgery), which was assessed in thirteen studies.[34,118,120,121,124,128,130,134,137,140,142-144] A meta-analysis of these studies found a pooled odds ratio of 1.59 (95% CI: 1.04, 2.43), which is significant and suggests that patients undergoing synthetic mesh surgery are one-and-a-half times more likely to experience urinary retention than

if undergoing native tissue suspension surgery (see Figure A11 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots).

#### 9.3.1.4.5 Urinary Tract Infection

UTI was the second most frequently reported short-term complication, with eight studies reporting it within a week of surgery,[121,124,126,128,130,135,137,144] two studies reporting it at 1-3 months,[127,144] five studies reporting it at one year,[120,127,134,136,137] and one study reporting it at 24 months.[130] A meta-analysis was conducted using data from eight of these studies that reported UTI within one week (short-term),[121,124,126,128,130,135,137,144] and five studies that reported it at 12 months (long-term), see Figure A12 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots.[120,127,134,136,137] The meta-analysis of short-term urinary retention found a pooled odds ratio of 1.07 (95% CI: 0.65, 1.75), which suggests that patients undergoing synthetic mesh surgery are slightly more likely to experience this adverse effect than if undergoing native tissue suspension surgery. However, this effect is not significant because the CI of this pooled estimate crosses the null line (1.00). The meta-analysis of long-term urinary retention found a pooled odds ratio of 0.80 (95% CI: 0.39, 1.62), which suggests that patients undergoing synthetic mesh surgery are slightly less likely to experience urinary retention at one year than if undergoing native tissue suspension surgery. However, this effect is not significant because the CI of this pooled estimate crosses the null line (1.00).

#### 9.3.1.4.6 Fever

Post-operative fever was reported in four studies.[118,126,130,134] A meta-analysis of these studies found a pooled odds ratio of 0.59 (95% CI: 0.18, 1.93), which suggests that patients undergoing synthetic mesh surgery are slightly less likely to experience fever than if undergoing native tissue suspension surgery (see Figure A13 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots). However, this effect is not significant because the CI of this pooled estimate crosses the null line (1.00).

#### 9.3.1.4.7 De Novo Urinary Incontinence

De novo urinary incontinence (including stress urinary incontinence and urge urinary incontinence) was the most frequently reported long-term adverse effect, with two studies reporting it at 1-3 months,[127,129] one study reporting it at six months,[135] 10 studies reporting it at one year,[34,118,127,128,131,137-139,142,150] and six studies reporting it after 12 months.[119,121,124,146,147,149]

A meta-analysis was conducted using data from the 10 studies reporting de novo urinary

incontinence at one year,[34,118,127,128,131,137-139,142,150] and the six studies reporting it after 12 months (see Figure A14 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots).[119,121,124,146,147,149]

The meta-analysis of de novo urinary incontinence at one year found a pooled odds ratio of 1.50 (95% CI: 0.95, 2.39), which suggests that patients undergoing synthetic mesh surgery are slightly more likely to experience it at one year than if undergoing native tissue suspension surgery. However, this effect is not significant because the CI of this pooled estimate touches the null line (1.00). The meta-analysis of de novo urinary incontinence after 12 months found a pooled odds ratio of 1.34 (95% CI: 0.70, 2.56), which suggests that patients undergoing synthetic mesh surgery are slightly more likely to experience it after 12 months than if undergoing native tissue suspension surgery. However, this effect is not significant.

9.3.1.4.8 Dyspareunia

Dyspareunia was the second most frequently reported long-term adverse effect, with one study reporting it at three months,[127] twelve studies reporting it at one year,[34,116,118,120,122,127,137-140,143,150] and four studies reporting it after one year.[121,124,146,147] A meta-analysis was conducted using data from 12 of these studies that reported dyspareunia at one year,[34,116,118,120,122,127,137-140,143,150] and four studies that reported it after 12 months (see Figure A15 in Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots).[121,124,146,147] The meta-analysis of dyspareunia at one year found a pooled odds ratio of 1.20 (95% CI: 0.69, 2.07), which suggests that patients undergoing synthetic mesh surgery are slightly more likely to experience it at one year than if undergoing native tissue suspension surgery. However, this effect is not significant because the CI of this pooled estimate crosses the null line (1.00). The meta-analysis of dyspareunia reported after 12 months found a pooled odds ratio of 0.98 (95% CI: 0.49, 1.96), which suggests that patients undergoing synthetic mesh surgery are slightly less likely to experience it after 12 months than if undergoing native tissue suspension surgery. However, this effect is not significant.

9.3.1.4.9 Pain

Pain was reported by four studies at 1-3 months,[118,127,140,144] one study at six months,[118], five studies at one year,[34,118,122,127,134], and two studies after 12 months.[121,147] A meta-analysis was conducted using data from four of these studies that reported pain at 1-3 months,[118,127,140,144] and five studies that reported it at one year (see Figure A16 in Appendix 6: Meta-Analysis Funnel

Plots and Additional Forest Plots).[34,118,122,127,134] The meta-analysis of pain at 1-3 months found a pooled odds ratio of 3.01 (95% CI: 1.53, 5.90), which suggests that patients undergoing synthetic mesh surgery are three times significantly more likely to experience pain at short-term than if undergoing native tissue suspension surgery. The meta-analysis of pain reported at one year found a pooled odds ratio of 1.14 (95% CI: 0.50, 2.62), which suggests that patients undergoing synthetic mesh surgery are slightly more likely to experience it at one year than if undergoing native tissue suspension surgery. However, this effect is not significant.

9.3.1.4.10 Voiding Difficulty

Six studies reported voiding difficulty, with one study reporting it at one week,[144] three studies reporting it at one year,[122,128,137], and two studies reporting it after 12 months.[119,124] A meta-analysis could not be conducted due to an insufficient number of studies at each follow-up point. In general, voiding difficulty occurred more frequently in the mesh group (ranging from 0-19%) than the native tissue group (ranging from 0-8.3%).

9.3.1.4.11 Wound Infection

Wound infection was reported in three studies.[120,128,136] A meta-analysis could not be conducted due to insufficient data. One study found a greater rate of infection in the native tissue group than the synthetic mesh group (4.12% vs 1%, respectively),[128] whereas the second study found a greater rate of infection in the synthetic group than the native tissue group (3.57% vs. 0%, respectively);[136] the third study found null event rates for both groups.[120]

9.3.1.4.12 Mesh Exposure and Erosion

Mesh exposure was reported in eight studies[116,118,120,121,127,128,130,146] and mesh erosion was reported in eight studies[124,126,129,131-133,138,142] comparing synthetic mesh to native tissue suspension. A meta-analysis of mesh exposure and erosion rates was not conducted due to fundamental differences between the two treatment types (i.e., no permanent synthetic mesh in the native tissue suspension group). Mesh exposure in the synthetic mesh group ranged from 1.59%-17.3% of patients at the 12-month follow-up (most-common time-point at which mesh exposure was assessed). Mesh erosion in the synthetic mesh group ranged from 5-15.6% within the first three months and 6.9%-35.7% at the 12-month follow-up (see Figure 28).

Figure 28: Rates of Mesh Erosion in Synthetic Mesh Group at 12 Months in POP Studies

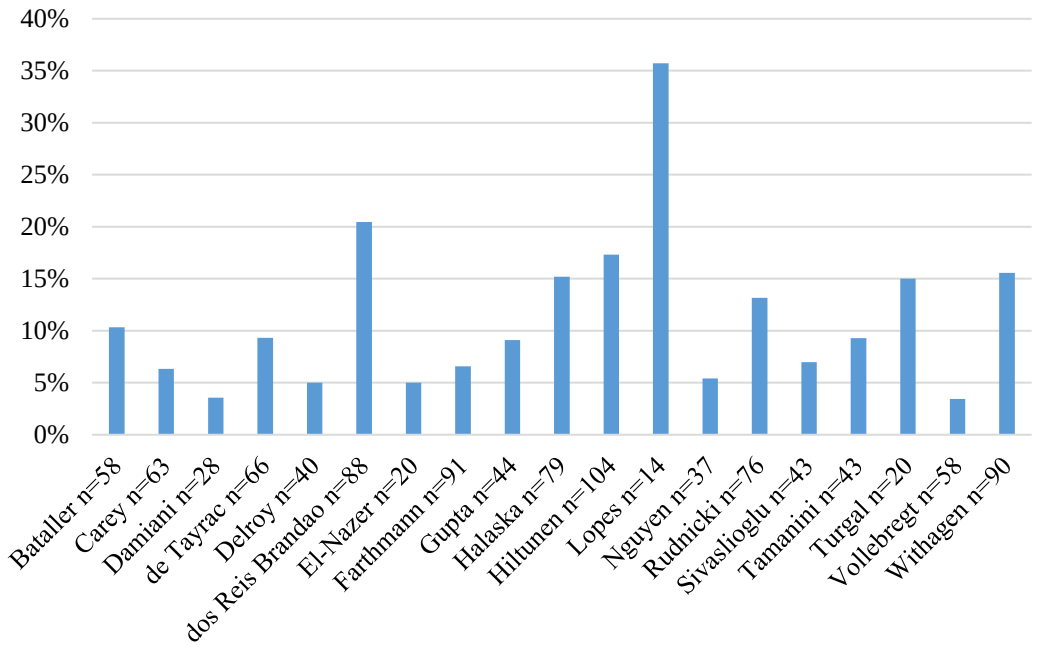



Figure 29: Rates of Mesh Erosion in Synthetic Mesh Group at 24 Months in POP Studies

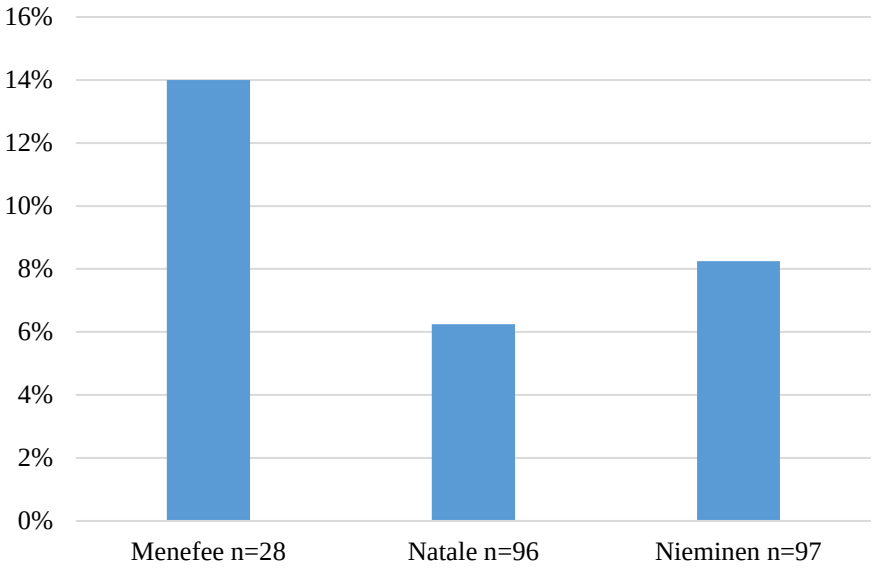
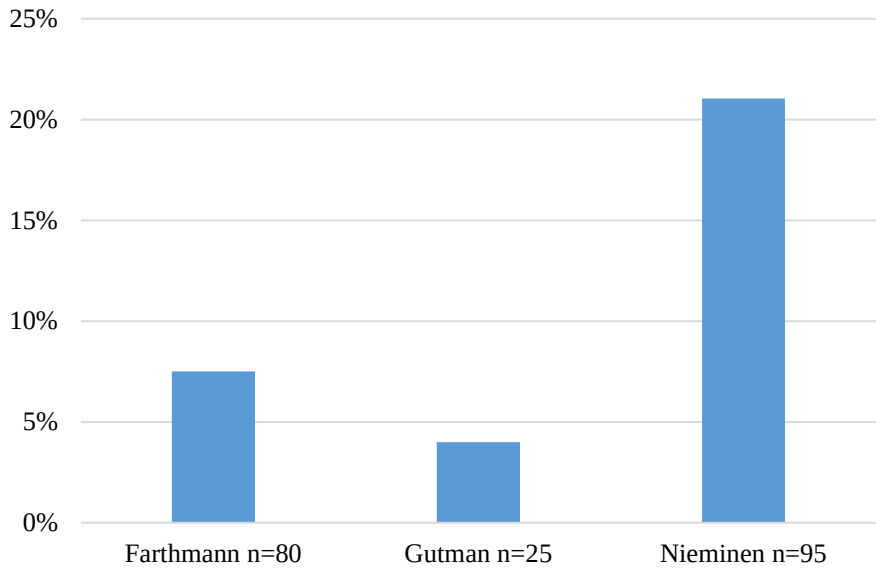


Figure 30: Rates of Mesh Erosion in Synthetic Mesh Group at 36 Months in POP Studies

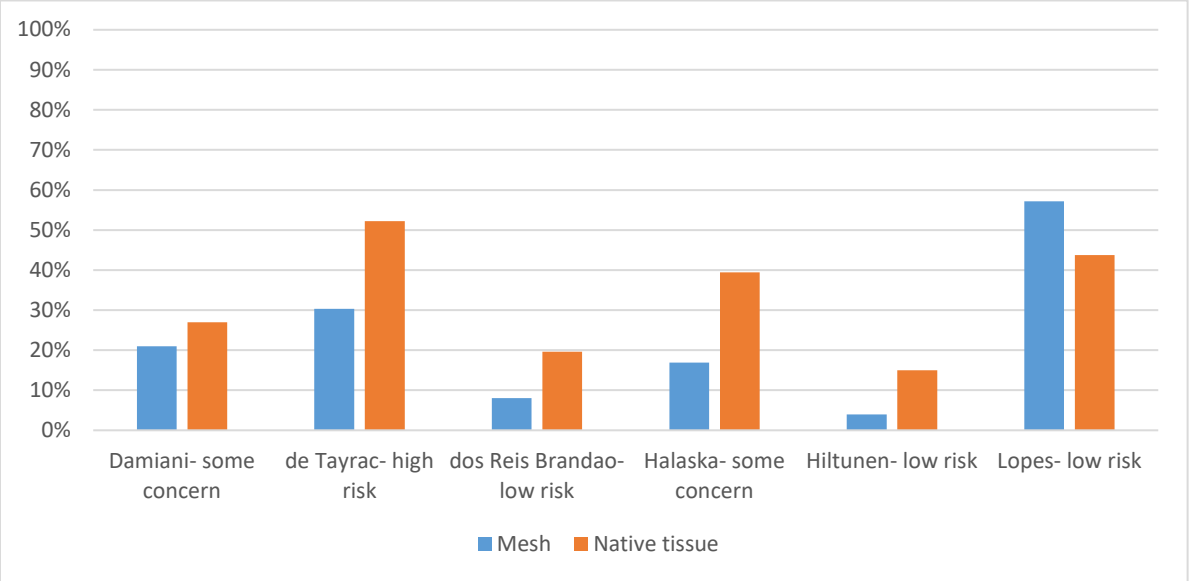



*N= size of mesh group at indicated follow-up time

9.3.1.4.13 Recurrence Rates

Rates of recurrence at 12 months (most common follow-up time) were reported in six studies.[117,118,122,127,128,131] Recurrence rates ranged from 4%-30% at 12 months in the synthetic mesh group and 3.7%-52% in the native tissue group (see Figure 31). One study defined recurrence as both anatomical recurrence and an answer of "no" to the question "Do you usually have a bulge or something falling out that you can see or feel?" In this study, recurrence was significantly higher in the native tissue repair group (52.2%) than in the mesh group (30.3%). Another study reported only anterior wall recurrence: symptomatic recurrence was observed in 15% of patients who received native tissue repair, and 4% of patients treated with mesh (p=0.005).[128] A third study found recurrence (defined as any descent at stage II or greater) was significantly higher in the native tissue repair group (39.4%) compared to the mesh group (16.9%).[127] The other studies did not report a significant difference in recurrence rates between mesh and native tissue repair.[117,131,122]

Figure 31: Rates of Recurrence at 12 Months in POP Studies

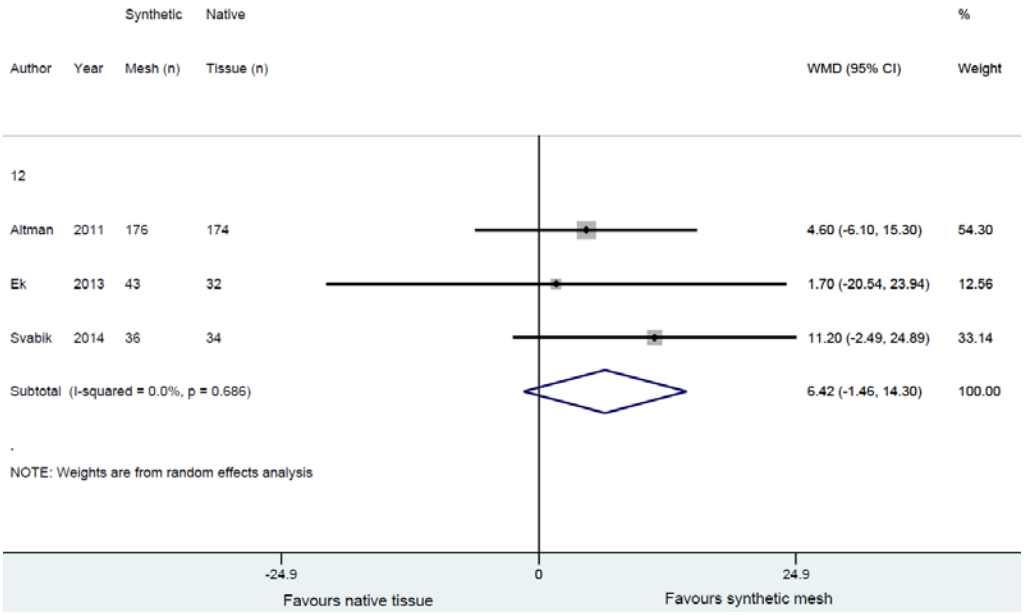



9.3.1.5 Subjective Outcomes

Most of the studies examining synthetic mesh vs. native tissue suspension reported a variety of patient-reported outcome measures assessing urinary symptoms (e.g., Urinary Distress Inventory [UDI]), pelvic organ prolapse symptoms (e.g., Pelvic Organ Prolapse Distress Inventory), and sexual function (e.g., Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire [PISQ-12]). However, due to variability in the types of questionnaires used and differences in reporting (e.g., mean vs. median scores) across studies, there was an insufficient number of studies that could be pooled to conduct a meta-analysis of all the patient-reported outcome measures. In general, there was a positive trend following treatment with either intervention across all studies.

Only one subjective outcome measure was commonly reported. Three studies provided adequate data on UDI scores to permit pooling at 12 months.[139,144,145] At 12 months, the pooled weighted mean difference for synthetic mesh vs. native tissue suspension is 6.42 (95% CI: -1.46, 14.30), which suggests that the improvement in urinary distress scores at 12 months is greater for synthetic mesh than native tissue suspension (see Figure 32). However, this effect is also not statistically significant.

Figure 32: Forest Plot of Change in UDI Score at 12 Months in POP Patients Receiving Synthetic Mesh vs. Native Tissue Suspension




### *9.3.2 Synthetic Mesh vs Porcine Tissue*

#### 9.3.2.1 Characteristics of Included Studies

Three studies (all original RCTs) examining synthetic mesh vs. porcine mesh were identified. Studies were from Italy[117,153] and the USA[133] and published in 2007, 2009, and 2016.

Studies ranged from 12-24 months in follow-up. Study sample sizes were ~60 patients for two studies and 190 patients for one study. A common study inclusion criterion was POP >stage II; a common exclusion criterion was pregnancy (current or planned). Study characteristics are reported in Table A3 in Appendix 5: Characteristics of Included Studies.

#### 9.3.2.2 Quality of Included Studies

Two of the three RCTs comparing synthetic mesh vs. porcine mesh had a moderate risk of bias with respect to randomization either due to baseline patient characteristics imbalances[117] or not reporting allocation concealment.[153] All of the interventions seemed to have been performed similar to everyday practice. All studies had complete outcome data, and the follow-ups had similar rates of drop-out, with reasons for drop-out provided. Primary outcomes were generally objective measures (e.g., anatomic success rate) and their assessment was considered to not have

been biased. Lastly, there was no evidence of selective reporting of the results. Quality assessment for synthetic mesh vs. porcine mesh studies is reported in Table 22.

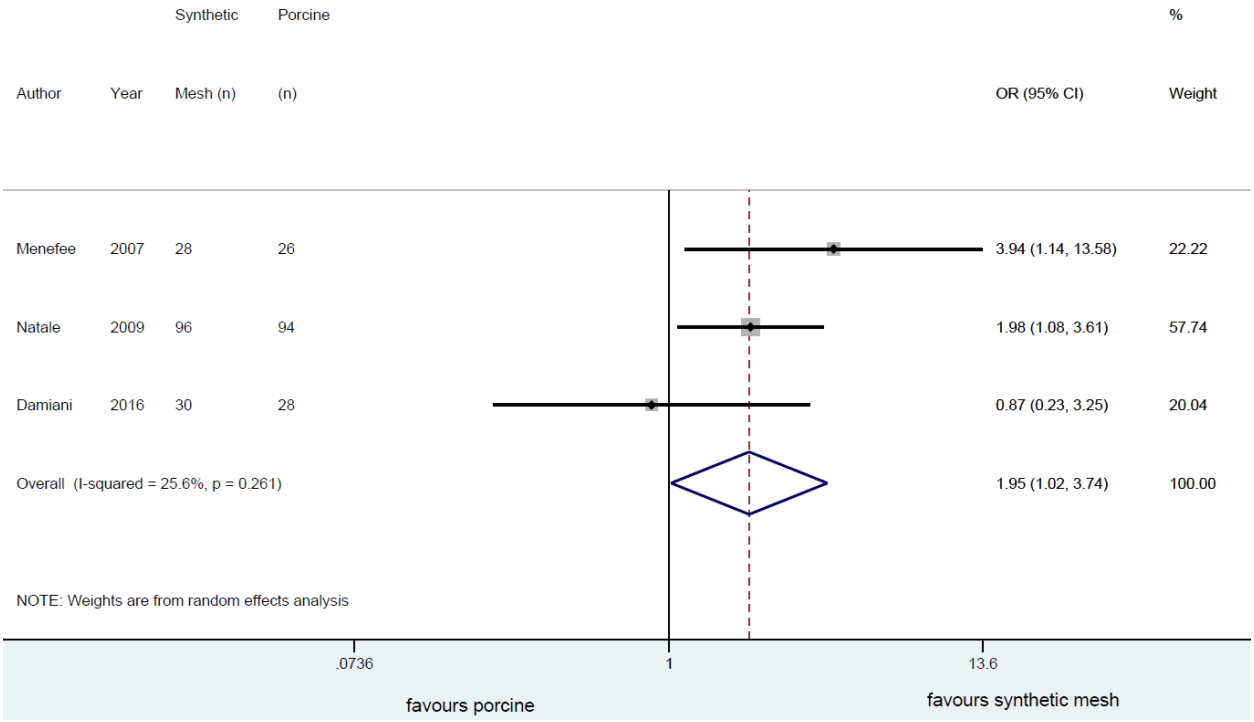
Table 22: Quality Assessment of Synthetic Mesh vs. Porcine Tissue POP Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Damiani, Italy, 2016[117] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |
| Menefee, USA, 2011[133] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Natale, Italy, 2009[153] | **some concern** | **low risk** | **low risk** | **low risk** | **low risk** |

#### 9.3.2.3 Meta-analysis of Cure Rates

All three of the synthetic mesh vs. porcine mesh studies provided adequate data on cure rates to permit pooling at 24 months.[117,133,153] Figure A16 in Appendix 6 shows the pooled overall cure rate results (forest plot) for synthetic mesh vs. porcine mesh comparison; the cure definition of POP stage 0-1 and BA<-1/BA<0 was used in this analysis. A funnel plan to examine publication bias was not generated due to an insufficient number of studies. At 24 months, the overall pooled odds ratio for synthetic mesh vs. porcine mesh is 1.95 (95% CI: 1.02, 3.74), which is significant and suggests that the odds of achieving cure using synthetic mesh are almost two times higher than if using porcine mesh.

Figure 33: Forest Plot of Cure Rates in POP Patients Receiving Synthetic vs. Porcine Mesh




### 9.3.2.4 Meta-analysis of Complications

A meta-analysis of complications could not be conducted due to an insufficient number of synthetic mesh vs. porcine mesh studies reporting similar complications. Only one study reported de novo SUI rates, which occurred in 2.08% of synthetic mesh and 1.06% of porcine mesh patients at 24 months, respectively.[153] One study reported immediate post-operative complications:[117] comparing synthetic vs. porcine mesh, bladder injury (3.33% vs 0%, respectively), urinary retention (10% vs 0%, respectively), severe dynia (6.67% vs 0%, respectively), and granuloma cuff. (13.33% vs 0%, respectively) were more common in the synthetic mesh group than the porcine group. Hematoma and wound infection were more common in the porcine mesh group than the synthetic mesh group (3.57% vs 0%, respectively for both events). No cervical cuff hemorrhages or blood transfusions occurred in either group.

#### 9.3.2.4.1 Mesh Exposure and Erosion

Mesh exposure was reported in one study,[117]and mesh erosion was reported in two studies[133,153] comparing synthetic mesh to porcine mesh. A meta-analysis of mesh exposure and erosion rates was not conducted due to an insufficient number of studies. The rate of mesh exposure was 3.33% in the synthetic mesh group.[117] Mesh erosion rates ranged from 6.3% at six months[153] to

14% at 24 months[133]. The latter study also reported that 4% of porcine mesh patients experienced mesh erosion at 24 months.[133]

#### 9.3.2.5 Subjective Outcomes

Only one study examining synthetic mesh vs. porcine mesh reported a variety of patient-reported outcome measures assessing urinary symptoms (e.g., UDI), pelvic organ prolapse symptoms (e.g., POPDI), and sexual function (e.g., PISQ).[133] As such, a meta-analysis of the patient-reported outcome measures could not be conducted. In general, there was a positive trend following treatment with either intervention across all subjective outcome measures; however, the differences between the two groups were not significant.

### *9.3.3 Synthetic Mesh vs Autologous/Cadaver Tissue*

#### 9.3.3.1 Characteristics of Included Studies

Two studies (one original RCT[154] and one follow-up[155]) examining synthetic mesh vs. autologous/cadaver tissue were identified. Both studies were from the USA and were published in 2005 and 2011.

Both studies examined one population: women with post-hysterectomy vaginal vault prolapse scheduled for sacral colpopexy; no exclusion criteria were reported. The original RCT (N=100)[154] had a 12-month follow-up duration and the follow-up study (N=58)[155] was conducted at 60 months. Study characteristics are reported in Table A3 in Appendix 5: Characteristics of Included Studies.

#### 9.3.3.2 Quality of Included Studies

The two studies (one RCT and one follow-up study) comparing synthetic mesh vs. autologous/cadaver tissue had a low risk of bias across all domains.[154,155] The original RCT reported their randomization method used to allocate patients. All of the interventions seemed to have been performed similar to everyday practice. Both studies had complete outcome data, and the follow-ups had similar rates of drop-out, with reasons for drop-out provided. Primary outcomes were generally objective measures (e.g., anatomic success rate) and their assessment was considered to not have been biased. Lastly, there was no evidence of selective reporting of the results. Quality assessment for synthetic mesh vs. autologous/cadaver tissue is reported in Table 23.

Table 23: Quality Assessment of Synthetic Mesh vs. Autologous/Cadaver Tissue POP Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Culligan, USA, 2005 (see Tate 2011)[154] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |
| Tate, USA, 2011 (see Culligan, 2005)[155] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

#### 9.3.3.3 Meta-analysis of Cure Rates

There was an insufficient number of studies of synthetic mesh vs. autologous/cadaver tissue to conduct a meta-analysis of cure rates. One study examining cure rates at the 1-year follow-up period found that synthetic mesh patients had higher cure rates (91%) than autologous/native tissue patients (68%).[154] This effect was maintained at the five-year follow-up, at which point 93% of synthetic mesh patients and 62% of autologous/native tissue patients remained cured.[155]

#### 9.3.3.4 Meta-analysis of Complications

There was an insufficient number of studies of synthetic mesh vs. autologous/cadaver tissue to conduct a meta-analysis of complications. One study reported immediate post-operative complications:[154] comparing synthetic vs. autologous/cadaver tissue, ileus (3.73% vs. 0%), wound breakdown (14.81% vs. 10.87%), bladder injury (1.85% vs. 0%), need for blood transfusion (1.85% vs. 0%), and post-operative embolism (1.85% vs. 0%) were more common in the synthetic mesh group than the autologous/cadaver tissue group. Rates of post-operative fever was similar across the two groups (3.73% in synthetic mesh and 4.35% in autologous/cadaver tissue).

##### 9.3.3.4.1 Mesh Exposure and Erosion

Mesh erosion rates were reported in both studies comparing synthetic mesh to autologous/cadaver tissue.[154,155] Neither study reported any mesh exposure. A meta-analysis of mesh erosion rates was not conducted due to an insufficient number of studies. The rate of new mesh erosion in the synthetic mesh group was 3.7% within three months,[154] 2.22% at one-year,

and 3.45% at five years.[155] The rate of autologous/cadaver tissue erosion was 2.27% at the one-year follow-up.[155]

#### 9.3.3.5 Subjective Outcomes

Neither study assessing synthetic mesh vs. autologous/cadaver tissue reported any patient-reported outcome measures assessing urinary symptoms (e.g., UDI), pelvic organ prolapse symptoms (e.g., POPDI), or sexual function (e.g., PISQ).

### *9.3.4 Synthetic Mesh vs Dissolvable/Semi-dissolvable Mesh*

#### 9.3.4.1 Characteristics of Included Studies

Two studies (both original RCTs) examining synthetic mesh vs. dissolvable/semi-dissolvable mesh were identified.[42,156] One study was from Germany and published in 2013;[42] the other study was from Spain and published in 2018.[156]

One study (N=60)[156] had a 12-month follow-up duration and the other study (N=198)[42] had follow-up durations of 3, 12, and 36 months. Both studies included adult women with POP >stage II. Study characteristics are reported in Table A3 in Appendix 5.

#### 9.3.4.2 Quality of Included Studies

The two studies comparing synthetic mesh vs. dissolvable/semi-dissolvable mesh had a low risk of bias across all domains.[42,156] Both studies used some type of randomization to allocate patients. All of the interventions seemed to have been performed similarly to everyday practice. Both studies had complete outcome data, and the follow-ups had similar rates of drop-out, with reasons for drop-out provided. Primary outcomes were generally objective measures (e.g., anatomic success rate) and their assessment was considered to not have been biased. Lastly, there was no evidence of selective reporting of the results. Quality assessment for synthetic mesh vs. dissolvable/semi-dissolvable mesh is reported in Table 24.

Table 24: Quality Assessment of Synthetic Mesh vs. Dissolvable/Semi-dissolvable Mesh POP Studies

| Study ID | Bias from Randomization | Bias from Deviation | Bias from Missing Outcome Data | Bias from Measurement | Bias in Reported Results |
|---|---|---|---|---|---|
| Bataller, Spain, 2018[156] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

| | | | | | |
|---|---|---|---|---|---|
| Farthmann, Germany, 2013[42] | **low risk** | **low risk** | **low risk** | **low risk** | **low risk** |

9.3.4.3 Meta-analysis of Cure Rates

There was an insufficient number of studies of synthetic mesh vs. dissolvable/semi-dissolvable mesh to conduct a meta-analysis of cure rates. Only one study examined efficacy outcomes and found anatomical cure rates of 76% in the synthetic group and 79% in the semi-dissolvable mesh groups at 12 months.[156]

9.3.4.4 Meta-analysis of Complications

There was an insufficient number of studies of synthetic mesh vs. dissolvable/semi-dissolvable mesh to conduct a meta-analysis of complications. One study reported rates of bladder injury of 1.67% in both groups;[156] whereas the other study reported rates of bladder/bowel perforation of 3.96% in the synthetic group[156] and 1.03% in the dissolvable mesh group.[42] Significant blood loss occurred more frequently in the synthetic mesh (1%) than the dissolvable mesh group (0%).[42] Lastly, vaginal perforation was more common in the semi-dissolvable mesh group (1.67%) than the synthetic group (0%); and vault hematoma and ovarian tube abscess occurred more frequently in the synthetic mesh group (1.67% for both events) than the semi-dissolvable mesh group (0%).[156] With respect to long-term complications at 12 months, de novo SUI was more common in the synthetic group than the semi-dissolvable group (6.67% vs. 3.33%), whereas de novo detrusor over activity was more common in the semi-dissolvable group than the synthetic group (13.3% vs. 3.33%).[156]

9.3.4.4.1 Mesh Exposure and Erosion

Mesh exposure rates were reported in both studies comparing synthetic mesh to semi-dissolvable/dissolvable mesh.[42,156] Neither study reported any mesh erosion. A meta-analysis of mesh exposure rates was not conducted due to an insufficient number of studies. The rate of mesh exposure in the synthetic mesh group ranged from 10.34%-11.3% at three months to 6.6% at 12 months to 7.5% at 36 months.[42,156] The rate of mesh exposure in the semi-dissolvable mesh group was 5.17% at three months.[156] Lastly, the rate of mesh exposure in the dissolvable mesh group ranged from 3.2% at three months to 6.3% at 12 months to 3.4% at 36 months.[42]

#### 9.3.4.5 Subjective Outcomes

Only one study examining synthetic mesh vs. semi-dissolvable mesh reported a variety of patient-reported outcome measures assessing pelvic organ prolapse symptoms (Pelvic Floor Distress Inventory [PFDI-20]), urinary function (International Consultation on Incontinence Questionnaire-Short Form [ICIQ-UI-SF]), and pain.[156] As such, a meta-analysis of the patient-reported outcome measures could not be conducted. In general, there was a positive trend following treatment with either intervention across all subjective outcome measures. Statistically significant differences were found between the synthetic and semi-dissolvable mesh on the PFDI-20, with the results favoring the synthetic mesh; semi-dissolvable mesh performed worse on the Colorectal-Anal Distress Inventory (CRAD-8) subscale of the PFDI-20.

## 9.4 Conclusions

Forty-three studies (32 original RCTs and 11 follow-up studies) were identified that evaluated the effectiveness of synthetic surgical mesh against a comparator of interest. Of these studies, 38 studies compared synthetic mesh to native tissue suspension, three compared synthetic mesh to porcine mesh, two compared synthetic mesh to autologous/cadaver tissue, and two compared synthetic tissue to semi-dissolvable/dissolvable mesh.

A meta-analysis of cure rates for synthetic vs. native tissue found that the odds of cure were five times higher at 12 months and three times higher at 24 months, favoring synthetic mesh. These effects were significant but associated with substantial heterogeneity and should be interpreted with caution. A meta-analysis of cure rates for synthetic vs. porcine mesh found that the odds of cure at 24 months were almost two times and significantly higher for synthetic mesh. Meta-analyses of cure rates for the autologous/cadaver tissue and semi-dissolvable/dissolvable mesh comparators could not be conducted due to insufficient data. However, results of individual studies suggest that synthetic mesh performs better than autologous/cadaver tissue and similarly to semi-dissolvable mesh.

Meta-analyses of adverse effects could only be conducted for the synthetic vs. native tissue comparisons and found that bladder injury and blood loss were the most frequently reported intraoperative complications, urinary retention was the most frequently reported short-term (1-week) complication, and de novo urinary incontinence was the most frequently reported long-

term (1-year and beyond) complication. Specifically, patients undergoing synthetic mesh surgery are three times more likely to experience bladder injury or intraoperative blood loss and one-and-a-half times more likely to experience urinary retention than if undergoing native tissue suspension surgery; all three of these effects are significant. Patients in the synthetic mesh group are slightly more likely to experience de novo urinary incontinence at 12 and 24 months than patients in the native tissue suspension group; however, this effect is not significant. Lastly, in the native tissue suspension studies, mesh exposure in the synthetic mesh group ranged from 1.59%-17.3% of patients at the 12-month follow-up, and mesh erosion ranged from 5-15.6% within the first three months and 6.9%-35.7% at the 12-month follow-up.

Meta-analyses of adverse effects for porcine, autologous/cadaver tissue, and semi-dissolvable/dissolvable mesh comparators could not be conducted due to insufficient data. Results from individual studies suggest that bladder injury generally occurs at a slightly higher rate in the synthetic mesh group than its comparators, and de novo SUI is a longer-term adverse effect that occurs more frequently in the synthetic mesh group than porcine and semi-dissolvable mesh. In studies of these three comparators, mesh exposure and mesh erosion occurred at slightly higher rates in synthetic mesh group.

Overall, the included studies were of good quality, as assessed by the Cochrane Risk of Bias tool,[84] with some bias stemming from insufficient reporting of the randomization methods in select studies. However, the study groups appeared to be largely well-balanced with respect to participant demographics and disease characteristics. Some studies were deemed to be of some concern or high risk of bias due to deviation depending on the number of patients that were analyzed in a different study group than the intervention they received. Lastly, bias from missing data was observed in a few studies due to imbalances in missing data between groups and substantial drop-out rates that would have underpowered the study based on the study authors' power calculations.

The outcome most commonly reported within the included RCTs was anatomic cure, which is considered to be a clinically relevant outcome. Most synthetic vs. native tissue suspension studies reported patient-reported outcome measures, which are important for assessing the impact of the POP surgery on the patient's everyday life and well-being. However, due to

variability in the types of questionnaires used and differences in reporting (e.g., mean vs. median scores) across studies, there was an insufficient number of studies that could be pooled to conduct a meta-analysis of all the patient-reported outcome measures. In general, there was a positive trend following treatment with either intervention across all studies. This positive trend was also observed in the few studies of the other comparators that included patient-reported outcome measures.

The majority of the studies were conducted in Brazil, the US, and the Netherlands, with no studies conducted in Canada. However, there is no reason to suspect that the patient mix and underlying etiology of POP are substantially different in Canada. As such, the findings from this review should be generalizable to the Canadian context.

Overall, much uncertainty remains regarding the efficacy and safety of synthetic surgical mesh for POP. While meta-analyses of the existing literature suggest that synthetic surgical mesh may result in better cure rates than porcine mesh and native tissue suspension, the latter finding should be interpreted with caution due to heterogeneity of the effect. Meta-analysis results suggest that synthetic mesh is significantly associated with more bladder injury, intraoperative blood loss, and urinary retention than native tissue suspension. However, the literature on the efficacy and safety of synthetic mesh vs. other comparators is scarce and limited conclusions can be made.

# 10 Conclusions

Safety and effectiveness of synthetic surgical mesh for SUI and POP has been an emerging issue. The current HTA aims to distill the existing body of grey literature and peer-reviewed literature to examine the use of synthetic surgical mesh.

The environmental scan found that multiple regulatory authorities (the UK, Northern Ireland, Australia, and New Zealand) have initiated pauses, bans, or recalls of mesh for SUI and POP. The US has increased the risk category of some surgical meshes for SUI and POP, and Health Canada issued notices to hospitals to inform healthcare practitioners about the complications associated with surgical mesh for POP and SUI. In addition, since December 2018, Health Canada has initiated an Action Plan to address the limitations of the regulation of medical devices; one of its plans to be implemented in 2019 is an expert advisory committee on women's health technologies including meshes for SUI and POP.

The guideline review identified 18 guidelines for treatment of SUI and POP, 10 of which were published between 2017 and 2019. The more recent guidelines endorsed more restrictions on the use of mesh, including the need for special arrangements for clinical governance, careful attention to patient consent, long-term research, and assiduous reporting of complications. Similarly, HTAs identified as part of this review (SUI=2, POP=0) called for additional research on surgical mesh using large, methodologically sound RCTs using similar follow-up times, cure definitions, and patient QoL measures. Overall, the grey literature search suggests that governing and regulatory bodies are demanding additional research and special attention to be paid to the use of surgical mesh devices in SUI and POP.

The systematic review of the peer-reviewed literature identified 29 unique RCTs evaluating the effectiveness of synthetic surgical mesh for SUI vs. native tissue suspension (n=19), AFS (n=7), and porcine mesh (n=5). Thirty-two unique RCTs and 11 follow-up studies were identified that evaluated the effectiveness of synthetic surgical mesh for POP vs. native tissue suspension (n=38), porcine mesh (n=3), autologous/cadaver tissue (n=2), and semi-dissolvable/dissolvable mesh (n=2). SUI studies ranged from 3-24 months in follow-up, and ≥18 months was the most common follow-up time-point that provided the most data for meta-analyses of cure rates across

the three comparisons. For POP studies, the most common follow-up times across comparators were 12 months and 24 months.

Analyses of the SUI literature suggest that at ≥18 months, the cure rate among patients treated with synthetic mesh is not significantly different from cure rates of patients treated with native tissue suspension (OR=0.96 [95% CI: 0.66, 1.39]), AFS (OR=0.72 [95% CI: 0.39, 1.34]), or porcine mesh (OR=1.66 [95% CI: 0.87, 3.19]). For POP, analyses suggest that synthetic surgical mesh results in significantly better cure rates than porcine mesh at 24 months (OR=1.95 [95% CI: 1.02, 3.74]) and native tissue suspension at 12 months (OR=5.38 [95% CI: 3.16, 9.15]); however, the latter finding should be interpreted with caution due to heterogeneity of the effect (i2=67%).

Across both SUI and POP, intraoperative bladder injury was the most frequently reported complication. For POP, synthetic mesh was found to be significantly associated with more bladder injury, intraoperative blood loss, urinary retention, and pain at 1-3 months than native tissue suspension. Other commonly reported complications for both mesh groups and comparator groups included de novo dyspareunia, de novo incontinence, UTI, urinary retention, and pain. Rates of mesh erosion by 12 months ranged from 0.59%-12% in SUI patients and 6.9%-35.7% in POP patients with synthetic mesh.

The SUI and POP systematic review findings were consistent with findings of the HTA review with respect to a paucity of patient-reported QoL data, inconsistent cure definitions, and inconsistent follow-up times for select comparators. In particular, some studies reported no QoL data, and QoL instruments used in studies that did assess it were largely incongruent, rendering comparisons between most studies impossible. Definitions of “cure” were also heterogeneous, especially in the SUI review. Composite outcomes including both objective and subjective cure elements were common but not standardized. This is particularly important because cure definitions acutely affect the proportion of patients whose treatment is considered successful. As a result, some studies may have reported lower cure rates on account of a different cure definition rather than because of genuinely different treatment outcomes. Lastly, follow-up times also curtailed the analysis, given the variability in follow-up times across studies and few multi-year RCTs. Thus, the literature may fail to capture long-term complication and recurrence rates.

While relatively robust meta-analysis comparisons could be made for synthetic mesh vs. native tissue groups for both SUI and POP, there were generally insufficient numbers of studies for the remainder of the comparators to provide pooled or meaningful analyses. Overall, analyses of SUI and POP data suggest that, compared to native tissue suspension, synthetic mesh may be associated with comparable or improved cure rates (however, these results are not significant for SUI and are associated with substantial heterogeneity for POP) but an increased risk for complications, particularly intraoperative bladder injury; this risk is more pronounced in POP patients. Mesh treatments for POP and SUI may be complicated by mesh-specific adverse events such as mesh erosion or contraction, which are not complications associated with native tissue repairs. Given the heterogeneity of the data, these effects, particularly for cure rates, are associated with considerable uncertainty and should be interpreted with caution.

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# 12 Appendices

## Appendix 1: Search Strategies for HTA Review

### Stress Urinary Incontinence- 15 results

"midurethral sling" or "TVT" or "tension-free vaginal tape" or "transobturator tape" or "TOT" or "TVT-O" or "mini-sling" or "single-incision sling" or “stress urinary incontinence” or “SUI”

### Pelvic Organ Prolapse- 0 results

"transvaginal mesh" or "surgical mesh" or "polypropylene mesh" or "POP" or "pelvic organ prolapse"

## Appendix 2: Search Strategies for SUI Systematic Review

### MEDLINE- 3472 abstracts

1. Urinary Incontinence, Stress/
2. (stress adj1 incontinence).tw,kf.
3. (stress incontinence or ((urine incontinence or urinary incontinence) adj3 stress)).tw,kf.
4. sui.tw,kf.
5. 1 or 2 or 3 or 4
6. Surgical Mesh/
7. Suburethral Slings/
8. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
9. 6 or 7 or 8
10. 5 and 9
11. limit 10 to (english or french)
12. animals/ not humans/
13. 11 not 12
14. limit 13 to (editorial or letter)
15. 13 not 14

### EMBASE- 3799 abstracts

1. stress incontinence/
2. (stress incontinence or ((urine incontinence or urinary incontinence) adj3 stress)).tw,kw.
3. (stress adj1 incontinence).tw,kw.
4. 1 or 2 or 3
5. exp surgical mesh/
6. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kw.
7. 5 or 6
8. 4 and 7
9. limit 8 to (english or french)
10. limit 9 to animal studies
11. limit 9 to (human and animal studies)
12. 10 not 11

13. 9 not 12
14. limit 13 to (conference abstract or editorial or letter)
15. 13 not 14
16. case report/
17. 15 not 16

**CINAHL- 829 abstracts**

1. ((MH "Surgical Mesh") OR (MH "Suburethral Slings") ) OR TI ( (fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro) ) OR AB ( (fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro) )
2. ((MH "Stress Incontinence") OR (MH "Stress Urinary Incontinence (Saba CCC)") ) OR TI (stress N1 incontinence) OR AB (stress N1 incontinence) OR TI ( (stress incontinence or ((urine incontinence or urinary incontinence) N3 stress)) ) OR AB ( (stress incontinence or ((urine incontinence or urinary incontinence) N3 stress)) )
3. 1 and 2
4. Limit 3 to (English or French) and scholarly peer-reviewed articles

**PsycINFO- 24 abstracts**

1. urinary incontinence/
2. (stress incontinence or ((urine incontinence or urinary incontinence) adj3 stress)).tw,id.
3. (stress adj1 incontinence).tw,id.
4. 1 or 2 or 3
5. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,id.
6. 4 and 5
7. limit 6 to (english or french)
8. limit 7 to ("comment/reply" or editorial)
9. 7 not 8

**Cochrane CENTRAL Register- 579 abstracts**

1. Urinary Incontinence, Stress/
2. (stress adj1 incontinence).tw,kf.
3. (stress incontinence or ((urine incontinence or urinary incontinence) adj3 stress)).tw,kf.
4. sui.tw,kf.
5. 1 or 2 or 3 or 4
6. Surgical Mesh/
7. Suburethral Slings/
8. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
9. 6 or 7 or 8
10. 5 and 9
11. limit 10 to (english or french)
12. animals/ not humans/
13. 11 not 12

**Cochrane database- 32 abstracts**

1. (stress incontinence or ((urine incontinence or urinary incontinence) adj3 stress)).tw,kw.

2. (stress adj1 incontinence).tw,kw.

3. 1 or 2

4. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kw.

5. 3 and 4

**Appendix 3: Search Strategies for POP Systematic Review**

**MEDLINE- 2561 abstracts**

1. exp Pelvic Organ Prolapse/
2. Pelvic Floor/
3. Prolapse/
4. 2 and 3
5. ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)).tw,kf.
6. 1 or 4 or 5
7. Surgical Mesh/
8. Suburethral Slings/
9. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
10. 7 or 8 or 9
11. 6 and 10
12. limit 11 to (english or french)
13. animals/ not humans/
14. 12 not 13
15. limit 14 to (editorial or letter)
16. 14 not 15

**EMBASE- 3163 abstracts**

1. exp pelvic organ prolapse/
2. pelvis floor/
3. ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)).tw,kw.
4. 1 or 2 or 3
5. exp surgical mesh/
6. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kw.

7. 5 or 6
8. 4 and 7
9. limit 8 to (english or french)
10. limit 9 to animal studies
11. limit 9 to (human and animal studies)
12. 10 not 11
13. 9 not 12
14. limit 13 to (conference abstract or editorial or letter)
15. 13 not 14

**CINAHL- 647 abstracts**

1. ( (MH "Pelvic Organ Prolapse+") OR (MH "Pelvic Floor Muscles") OR (MH "Pelvic Floor Disorders") ) OR TI ( ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)) ) OR AB ( ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)) )
2. ((MH "Surgical Mesh") OR (MH "Suburethral Slings") ) OR TI ( (fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro) ) OR AB ( (fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro) )
3. 1 and 2
4. Limit 3 to (English or French) and scholarly peer-reviewed articles

**PsycINFO- 12 abstracts**

1. ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)).tw.
2. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,id.
3. 1 and 2
4. limit 3 to (english or french)

5. limit 4 to (editorial or letter)
6. 4 not 5

**Cochrane CENTRAL- 343 abstracts**

1. exp Pelvic Organ Prolapse/
2. Pelvic Floor/
3. Prolapse/
4. 2 and 3
5. ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)).tw,kf.
6. 1 or 4 or 5
7. Surgical Mesh/
8. Suburethral Slings/
9. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
10. 7 or 8 or 9
11. 6 and 10
12. limit 11 to (english or french)
13. animals/ not humans/
14. 12 not 13

**Cochrane Database- 33 abstracts**

1. ((pelvic or pelvis or uterus or uterine or vagina*) adj3 (prolapse* or reconstructive surger* or repair*)).tw,kf.
2. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
3. 1 and 2

## Appendix 4: Advisories, Pauses, and Bans Issued Against Surgical Mesh for SUI and POP

Table A1: Advisories, Pauses, and Bans against the Use of Surgical Mesh for Treatment of POP and SUI

| Advisories or Action Taken | POP | SUI |
|---|---|---|
| **United States** | **US FDA advisories/orders issued for all mesh use in transvaginal POP repair:**<br>• 2019, banned the use of surgical mesh products for transvaginal repair of prolapse<br>• 2008, 2011: safety notifications issued regarding increased adverse event reports for mesh use in POP repair[52]<br>• Jan 2016: orders issued to manufacturers to strengthen data requirements: 1) reclassification from class II to class III, 2) manufacturers required to submit premarket approval application[157]<br>• Nov 2018: only three surgical mesh products for transvaginal repair of anterior compartment prolapse are currently on the market[158] | **US FDA (Jan 2017):**<br>• Order issued to reclassify mesh used in SUI surgery to class II (higher risk) from class I (lower risk)[53] |
| **Canada** | **Health Canada Advisories**:<br>• 2010 – Notice to Hospitals issued concerning complications associated with use of surgical mesh for POP and SUI (updated May 2014). Canada continued to monitor the safety of surgical mesh devices for treatment of SUI and POP[48] | |
| | **Canadian Urological Association (CUA)** position for transvaginal mesh for SUI and POP:<br>• The currently available literature does not support the routine use of transvaginal mesh for POP repair.<br>• An extensive body of literature supports the routine use of full length transvaginal retropubic or transobturator (midurethral) mesh slings for SUI. | |

| Advisories or Action Taken | POP | SUI |
|---|---|---|
| | • Further evidence is required before a statement applicable to non-full-length transvaginal mesh slings ("e.g. mini-slings") can be made[159] | |
| **United Kingdom** | **NHS Improvement and NHS England (Jul 2018):**<br>• Secretary of State for Health and Social Care and the Chief Medical Officer (CMO) announced a 'pause' in the use of synthetic mesh/tape to treat SUI and urogynaecological prolapse where the mesh is inserted through the vaginal wall.<br>  • Restrictions also apply in Wales and Northern Ireland.[47,56]<br><br>**NHS Scotland (Sep 2018):**<br>• All transvaginal mesh procedures to be completely stopped until new protocols are developed and implemented.<br>  • Other mesh procedures, such as transabdominal mesh, will be kept under active review and will also be subject to high vigilance procedures[57]<br><br>**National Institute for Health and Care Excellence (NICE) guidance (Dec 2017):**<br>• NICE recommends that transvaginal mesh for repair of POP only be used in a research context and that all adverse events be reported to the Medicines and Healthcare products Regulatory Agency.[76] | |
| **Republic of Ireland** | **Department of Health:**<br>• Nov 2018 – A report published by Dr. Tony Holohan, Chief Medical Officer, concludes that there is evidence to support the use of mid-urethral sling to treat SUI and the use of abdominal mesh for management of POP. The report also notes that the use of transvaginal mesh implants (TVMIs) for the treatment of POP should only be restricted to management of complex cases, following failure or contraindication to other treatment options, with patients being fully informed. The pause of the use of mesh procedures implemented in July 2018, remains until the Health Service Executive (HSE) confirms that the key recommendations outlined in the report have been implemented[160]<br><br>• Jul 2018 – "Pause" the use of all procedures involving transvaginal mesh devices for the management of SUI or POP in HSE-funded hospitals, in cases where it is clinically appropriate and safe to do so[58] | |
| **Australia** | **Therapeutic Goods Administration (TGA), Australia (Nov 2017):**<br>• All transvaginal mesh products for which the sole use is treatment of POP via | **TGA, Australia (Nov 2017):**<br>• All mesh products used for single incision mini-slings to be removed from ARTG<br>• Mid-urethral slings (which are different devices) will not be |

| Advisories or Action Taken | POP | SUI |
|---|---|---|
| | transvaginal implantation to be removed from the Australian Register of Therapeutic Goods (ARTG)[54] | removed, however the TGA required sponsors to include information on adverse events |
| **New Zealand** | **Medsafe (Dec 2017):**<br>• All surgical mesh for POP via transvaginal implantation no longer supplied (effective Jan 2018)[55] | **Medsafe (Dec 2017):**<br>• One single incision mini-sling is no longer supplied (effective Jan 2018)<br>• Midurethral slings not affected |
| **France** | No broad actions. As of Nov 2018, French health authority **Agence nationale de sécurité du medicament et des produits de santé (ANSM)** stated that it encourages patients and health professionals to submit information regarding adverse events as a results of the surgical mesh devices used for management of POP and SUI. The ANSM plans to meet with patients and health professionals to discuss risks related to the use of these devices.[161] | |
| **Europe** | **Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) Opinion (2015):**<br>• Implantation of any mesh for the treatment of POP via the vaginal route should only be considered in complex cases (e.g. after the primary repair surgery has failed)<br>• Given the proven efficacy and safety in most patients with moderate-to-severe SUI, when used appropriately and by an experienced surgeon, SCENIHR supports the use of synthetic slings for SUI[162]<br>**European Association of Urology (EAU)** and **European Urogynaecological Association (EUGA)** published a consensus review statement on use of implanted mesh for POP and SUI **(Jul 2017)**:<br>• Synthetic midurethral slings for treatment of SUI in both males and female patients both have good efficacy and acceptable morbidity<br>• Synthetic mesh for POP should only be used in complex cases with recurrent prolapse in the same compartment; its use should be restricted to surgeons who have appropriate training and are working in multidisciplinary referral centres[59] | |

Abbreviations: ANSM: Agence nationale de sécurité du medicament et des produits de santé; ARTG: Australian Register of Therapeutic Goods; EAU: European Association of Urology; HSE: Health Service Executive; NICE: National Institute for Health and Care Excellence; POP: pelvic organ prolapse; SCENIHR: Scientific Committee on Emerging and Newly Identified Health Risks; EUGA: European Urogynaecological Association; SUI: stress urinary incontinence; TGA: Therapeutic Goods Administration; US FDA: US Food and Drug Administration

## Appendix 5: Characteristics of Included Studies

Table A2: Characteristics of Studies Included in the SUI Review

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| **Synthetic vs. Native Tissue Suspension** | | | | |
| Bai, Korea, 2005[88] | SUI, Stamey grades 1 and 2 | detrusor overactivity, UTIs, ISD, and POP more severe than stage II | Burch<br><br>N= 33<br><br>Age: 56.5 ± 3.1<br>BMI: 28.1 ± 4.7<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 31<br><br>Age: 58.2 ± 3.3<br>BMI: 29.3 ± 3.3<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Bandarian, Iran, 2011[89] | proven SUI, first time surgery, did not respond to medical treatment | collagen vascular disease, neuropathy, coagulopathy, history of urogenital cancer, pregnancy, history of pelvic radiation, previous incontinence surgery, urge incontinence, urodynamic detrusor overactivity, POP-Q stage II or more | Burch<br><br>N= 31<br><br>Age: 46.94 ± 8.98<br>BMI: NR<br>Duration of symptoms: 3.62 ± 3.53 (yrs)<br>SUI severity grade: NR | TOT<br><br>N= 31<br><br>Age: 49.39 ± 12.59<br>BMI: NR<br>Duration of symptoms: 5.40 ± 3.43 (yrs)<br>SUI severity grade: NR |
| Jelovsek (see Paraiso 2004[94]), USA, 2008[102] | urodynamic SUI with abdominal leak point pressures ≥60 cm H2O, or positive cough test; urethral hypermobility, ability to undergo general anaesthesia and laparoscopy, willingness to complete follow-up | previous anti-incontinence surgery, detrusor overactivity, anterior vaginal wall prolapse to or beyond the hymen | Burch<br><br>N= 28<br><br>Age: 54.8 ± 9.3<br>BMI: 28.5 ± 6.1<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 25<br><br>Age: 53.3 ± 9.5<br>BMI: 30.1 ± 6.2<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Culligan (see Sand 2000[95]), USA, 2003[103] | urodynamic SUI with UHM and max closure pressure of ≤20 cm H2O | significant anterior pelvic support defects | modified Burch retropubic urethropexy<br><br>N= 19<br><br>Age: 61.3 ± 10.3<br>BMI: 21.8±3.7<br>Duration of symptoms: NR<br>SUI severity grade: NR | MUS (Gore-tex soft tissue patch), retropubic insertion<br><br>N= 17<br><br>Age: 60.4 ± 8.5<br>BMI: 23.7±5.6<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| El-Barky, Kuwait, 2005[90] | urodynamic SUI | uninhibited detrusor contraction during bladder filling more than 15 cm H2O, incompetent internal urethral sphincter, ≥ grade I cystocele, previous failed surgical repair of SUI | Burch<br><br>N= 25<br><br>Age: 50 ± 12<br>BMI: NR<br>Duration of symptoms: 9 ± 2.5<br>SUI severity grade: NR | TVT<br><br>N= 25<br><br>Age: 50 ± 14<br>BMI: NR<br>Duration of symptoms: 10.2 ± 1.5<br>SUI severity grade: NR |
| Foote, Australia, 2006[91] | urodynamic SUI | other bladder diagnoses (e.g. detrusor instability or voiding difficulty), previous incontinence surgery, weight of >100kg, significant prolapse. Requiring other gynaecological surgery, unsuitable for laparoscopy | laparoscopic colposuspension<br><br>N= 48<br><br>Age: 51.2 ± 8.5<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR | SPARC<br><br>N= 49<br><br>Age: 52.4 ± 10.9<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Khan (see Guerrero 2010[108]), UK, 2015[112] | failed conservative therapy, ≥18 years old, clinically and urodynamically proven SUI | previous SUI surgery, demonstrated evidence of neurological disease, POP >stage II, detrusor overactivity, bladder hypercompliance | Pelvicol- porcine dermis<br><br>N= 38<br><br>Age: 62 (37-85)<br>BMI: 28.8 (20-42)<br>Duration of symptoms: 9.6 (2-30) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 63<br><br>Age: 61.2 (42-77)<br>BMI: 30.3 (21-52)<br>Duration of symptoms: 11.5 (2-38) (yrs)<br>SUI severity grade: NR |
| | | | AFS<br><br>N= 61<br><br>Age: 59.4 (33-81)<br>BMI: 30.0 (24-43)<br>Duration of symptoms: 8.3 (1-31) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 63<br><br>Age: 61.2 (42-77)<br>BMI: 30.3 (21-52)<br>Duration of symptoms: 11.5 (2-38) (yrs)<br>SUI severity grade: NR |
| Liapis, Greece, 2002[92] | anterior prolapse ≤ stage I, no previous operation for UI, absence of urge incontinence, competent intrinsic urethral sphincter | | Burch<br><br>N= 35<br><br>Age: 48.4 (35-64)<br>BMI: 26.6 ± 2.1<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 36<br><br>Age: 46.5 (32-62)<br>BMI: 27.2 ± 2.2<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Nazari, Iran, 2017[163] | women with SUI | diseases such as diabetes, dementia, UUI, POP ≥ grade II, previous UI operation, untreated UTI, chronic pulmonary disease, neurological disorders, vascular insufficiency, MUI | anterior colporrhaphy<br><br>N= 32<br><br>Age: 44.37 ± 5.32<br>BMI: 27.92 ± 2.60<br>Duration of symptoms: 61.87 ± 30.87<br>SUI severity grade: moderate: 7 (21.9%); severe: 25 (78.1%) | TOT<br><br>N= 33<br><br>Age: 45.24 ± 6.78<br>BMI: 25.57 ± 2.19<br>Duration of symptoms: 62.18 ± 28.88<br>SUI severity grade: moderate: 8 (24.4%); severe: 25 (75.8%) |
| Palomba, Italy, 2002[93] | mild and moderate GSI | Severe GSI, associated prolapse ≥stage II, BMI >30, previous pelvic or anti-incontinence surgery, history of severe abdonimopelvic infections, known extensive abdominopelvic adhesions, detrusor instability, intrinsic sphincter dysfunction, other gynecologic pathologies | transperitoneal laparoscopic urethro-colpopexy with non-absorbable sutures<br><br>N= 28<br><br>Age: 52.3 ± 5.8<br>BMI: 24.9 ± 2.1<br>Duration of symptoms: NR<br>SUI severity grade: NR | transperitoneal laparoscopic urethro-colpopexy with polypropylene mesh, 0.5X3cm, fixed with tackers or staples<br><br>N= 28<br><br>Age: 53.7 ± 6.1<br>BMI: 25.1 ± 2.9<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Paraiso (see Jelovsek 2008), USA, 2004[94] | urodynamic SUI with abdominal leak point pressures ≥60 cm H2O, or positive cough test; urethral hypermobility, ability to undergo general anaesthesia and laparoscopy, willingness to complete follow-up | previous anti-incontinence surgery, detrusor overactivity, anterior vaginal wall prolapse to or beyond the hymen | Burch<br><br>N= 36<br><br>Age: 54.8 ± 9.3<br>BMI: 28.5 ± 6.1<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 36<br><br>Age: 53.3 ± 9.5<br>BMI: 30.1 ± 6.2<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Sand (see Culligan 2003[103]), USA, 2000[95] | GSI with UHM, max urethral closure pressure ≤20 cm H2O in sitting position | significant anterior pelvic support defects | modified Burch retropubic urethropexy<br><br>N= 19<br><br>Age: 61.3 ± 10.3<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR | MUS (Gore-tex soft tissue patch), retropubic insertion<br><br>N= 17<br><br>Age: 60.4 ± 8.5<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Sivaslioglu, Turkey, 2007[96] | Urodynamically proven SUI | Previous anti-incontinence surgery, UUI, urodynamic detrusor overactivity, POP-Q ≥ stage II | Burch<br><br>N= 51<br><br>Age: 46.1 ± 7.9<br>BMI: 29.3 ± 7.2<br>Duration of symptoms: 3.6 ± 21 (yrs)<br>SUI severity grade: NR | TOT<br><br>N= 49<br><br>Age: 45.4 ± 6.8<br>BMI: 29.8 ± 5.3<br>Duration of symptoms: 3.2 ± 1.8 (yrs)<br>SUI severity grade: NR |
| Sohbati, Iran, 2015[97] | History of involuntary urine escape in rising intra-abdominal pressure, no POP, no pathological vaginal discharge, no organomegaly, positive cough-stress test, post-voiding residual volume <50 ml, did not respond to medical treatment | other urinary disease or other UI, history of anti-incontinence surgery, disease affecting the urinary system (e.g. neurological), psychological disease, chronic lung disease, drug use including benzodiazapines, anti-cholinergics, calcium channel blockers, alcohol or opium addiction, BMI ≥30. | anterior colporrhaphy with Kelly's plication<br><br>N= 30<br><br>Age: 37.8 ± 8.19<br>BMI: NR<br>Duration of symptoms: 3.43±3.7 (yrs)<br>SUI severity grade: NR | TOT<br><br>N= 30<br><br>Age: 44.13 ± 5.55<br>BMI: NR<br>Duration of symptoms: 2.90±2.1 (yrs)<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Ustun, Turkey, 2003[98] | proven SUI | NR | laparoscopic Burch<br><br>N= 23<br><br>Age: 45.78 ± 11.44<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 23<br><br>Age: 45.57 ± 10.04<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Wang, Taiwan, 2003[99] | urodynamically proven GSI without pelvic prolapse | pre-operative BOO (bladder outlet obstruction), previous anti-incontinence surgery | modified Burch colposuspension<br><br>N= 41<br><br>Age: 50.65 ± 10.25<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 49<br>Age: 52.80 ± 8.89<br>BMI: NR<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Ward (see Ward 2008[105], 2004[104]), UK and Eire, 2002[100] | women with stress incontinence, completed family | detrusor overactivity, vaginal prolapse requiring treatment, previous surgery for prolapse or incontinence, major voiding dysfunction, neurological disease, allergy to local anaesthetic | colposuspension<br><br>N= 169<br><br>Age: 50 (45-59)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 175<br><br>Age: 50 (42-56)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Ward (see Ward 2002[100], 2004[104]), UK and Eire, 2008[105] | women with stress incontinence, completed family | detrusor overactivity, vaginal prolapse requiring treatment, previous surgery for prolapse or incontinence, major voiding dysfunction, neurological disease, allergy to local anaesthetic | colposuspension<br><br>N= 49<br><br>Age: 50 (45-59)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 72<br><br>Age: 50 (42-56)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Ward (see Ward 2002[100], 2008[105]), UK and Eire, 2004[104] | women with stress incontinence, unresponsive to pelvic floor muscle exercise, completed family | detrusor overactivity, vaginal prolapse requiring treatment, previous surgery for prolapse or incontinence, major voiding dysfunction, neurological disease, allergy to local anaesthetic, known bleeding diathesis or current anticoagulant therapy | colposuspension<br><br>N=108<br><br>Age: 50 (45-59)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 137<br><br>Age: 50 (42-56)<br>BMI: 27 (24-30)<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Zullo (see Zullo 2001[101]), Italy, 2004[106] | ambulatory women with mild or moderate GSI | severe GSI, associated prolapse >stage II, BMI >30, previous pelvic or anti-incontinence surgery, history of severe abdonimopelvic infections, known extensive abdominopelvic adhesions, detrusor instability, intrinsic sphincter dysfunction | colposuspension w/ nonabsorbable sutures<br><br>N= 27<br><br>Age: 52.3 ± 5.8<br>BMI: 24.9 ± 2.1<br>Duration of symptoms: 5.8 ± 3.7<br>SUI severity grade: mild: 15 (55.6%); moderate: 12 (44.4%) | colposuspension with prolene mesh fixed w/ tackers or staplers<br><br>N= 26<br><br>Age: 53.7 ± 6.1<br>BMI: 25.1 ± 2.9<br>Duration of symptoms: 6.3 ± 4.3<br>SUI severity grade: mild: 15 (55.6%); moderate: 12 (44.4%) |

| | | | | |
|---|---|---|---|---|
| Zullo (see Zullo 2004[106]), Italy, 2001[101] | ambulatory women with mild or moderate GSI | severe GSI, associated prolapse >stage II, BMI >30, previous pelvic or anti-incontinence surgery, history of severe abdonimopelvic infections, known extensive abdominopelvic adhesions, detrusor instability, intrinsic sphincter dysfunction | colposuspension w/ nonabsorbable sutures<br><br>N= 27<br><br>Age: 52.3 ± 5.8<br>BMI: 24.9 ± 2.1<br>Duration of symptoms: 5.8 ± 3.7<br>SUI severity grade: mild: 15 (55.6%); moderate: 12 (44.4%) | colposuspension with prolene mesh fixed w/ tackers or staplers<br><br>N= 26<br><br>Age: 53.7 ± 6.1<br>BMI: 25.1 ± 2.9<br>Duration of symptoms: 6.3 ± 4.3<br>SUI severity grade: mild: 14 (53.9%); moderate: 12 (46.1%) |
| **Synthetic vs. AFS** | | | | |
| Amaro, Brazil, 2009[107] | principal complaint of stress urinary incontinence | involuntary detrusor contractions; pre-existing bladder outlet obstruction | AFS<br><br>N= 21<br><br>Age: 49 (26-69)<br>BMI: 30.2 (22-34)<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 20<br><br>Age: 52 (26-79)<br>BMI: 28.2 (24-42)<br>Duration of symptoms: NR<br>SUI severity grade: NR |
| Bai, Korea, 2005[88] | SUI, Stamey grades 1 and 2 | detrusor overactivity, UTIs, ISD, and POP more severe than stage II | AFS<br><br>N= 28<br><br>Age: 56.3 ± 2.9<br>BMI: 28.5 ± 6.1<br>Duration of symptoms: NR<br>SUI severity grade: NR | TVT<br><br>N= 31<br><br>Age: 58.2 ± 3.3<br>BMI: 29.3 ± 3.3<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Guerrero (see Khan 2015[112]), UK, 2010[108] | failed conservative therapy, ≥18 years old, clinically and urodynamically proven SUI | previous SUI surgery, demonstrated evidence of neurological disease, POP >stage II, detrusor overactivity, bladder hypercompliance | AFS<br><br>N= 79<br><br>Age: 52.1 (33-72)<br>BMI: 28.7 (20.3-43.4)<br>Duration of symptoms: 8.2 (2-31) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 72<br><br>Age: 54.3 (34-80)<br>BMI: 28.7 (20.2-41)<br>Duration of symptoms: 11.1 (2-35) (yrs)<br>SUI severity grade: NR |
| Khan (see Guerrero 2010[108]), UK, 2015[112] | failed conservative therapy, ≥18 years old, clinically and urodynamically proven SUI | previous SUI surgery, demonstrated evidence of neurological disease, POP >stage II, detrusor overactivity, bladder hypercompliance | AFS<br><br>N= 61<br><br>Age: 59.4 (33-81)<br>BMI: 30.0 (24-43)<br>Duration of symptoms: 8.3 (1-31) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 63<br><br>Age: 61.2 (42-77)<br>BMI: 30.3 (21-52)<br>Duration of symptoms: 11.5 (2-38) (yrs)<br>SUI severity grade: NR |
| Silva-Filho, Brazil, 2006[109] | primary treatment of SUI and urodynamic study showing SUI without detrusor overactivity | NR | AFS<br><br>N= 10<br><br>Age: 49.8 ± 9.1<br>BMI: 27.1 ± 2.5<br>Duration of symptoms: NR<br>SUI severity grade: NR | TOT (SAFYRE)<br><br>N= 10<br><br>Age: 55.2 ± 13.4<br>BMI: 25.1 ± 3.3<br>Duration of symptoms: NR<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Teleb, Egypt, 2011[110] | clinical and urodynamic SUI | neurological disease, OAB, other causes and forms of incontinence, recurrent SUI, any form of prolapse requiring surgery | AFS<br><br>N= 12<br><br>Age: 41.8 ± 8.2<br>BMI: 30.2 ± 3.5<br>Duration of symptoms: NR<br>SUI severity grade: SEAPI: 5.8 ± 1.7 | tailored prolene mesh<br><br>N= 12<br><br>Age: 41.4 ± 7.8<br>BMI: 29.5 ± 3.4<br>Duration of symptoms: NR<br>SUI severity grade: SEAPI: 6.1 ± 1.5 |
| Teleb, Egypt, 2011[110] | clinical and urodynamic SUI | neurological disease, OAB, other causes and forms of incontinence, recurrent SUI, any form of prolapse requiring surgery | anterior vaginal wall sling<br><br>N= 8<br><br>Age: 44.4 ± 9.4<br>BMI: 30.7 ± 3.1<br>Duration of symptoms: NR<br>SUI severity grade: SEAPI: 6.3 ±1.8 | tailored prolene mesh<br><br>N= 12<br><br>Age: 41.4 ± 7.8<br>BMI: 29.5 ± 3.5<br>Duration of symptoms: NR<br>SUI severity grade: SEAPI: 6.1 ± 1.6 |
| Wadie, Egypt, 2005[111] | >21 years old, SUI leading symptom, informed consent, life expectancy >1 year, normal upper tract, normal manual dexterity | pelvic or vaginal surgery within 6 months, predominant urge incontinence, cystocele >grade 2, associated urethral pathology (e.g., urethral diverticulum), associated bladder pathology (e.g., fistula), active UTI as evidenced by positive urine culture | AFS<br><br>N= 25<br><br>Age: 45.32 ± 6.3<br>BMI: 31.6 ± 4.2<br>Duration of symptoms: NR<br>SUI severity grade: grade 1: 9 (36)<br>grade 2: 10 (40)<br>grade 3: 6 (24) | TVT<br><br>N= 28<br><br>Age: 44.9 ± 9<br>BMI: 29.7 ± .2<br>Duration of symptoms: NR<br>SUI severity grade: grade 1: 10 (35.7)<br>grade 2: 14 (50)<br>grade 3: 4 (14.3) |
| **Synthetic vs. Porcine** | | | | |

| | | | | |
|---|---|---|---|---|
| Abdel-Fattah (see Arunkalaivanan 2002[113]), UK, 2004[115] | cystometrically proven genuine stress incontinence, failed conservative therapy | detrusor instability, unwilling to be randomized | Pelvicol<br><br>N= 74<br><br>Age: 53 (34-75)<br>BMI: NR<br>Duration of symptoms: (6–72)<br>SUI severity grade: NR | TVT<br><br>N= 68<br><br>Age: 54 (32-83)<br>BMI: NR<br>Duration of symptoms: (6–120)<br>SUI severity grade: NR |
| Arunkalaivanan (see Abdel-Fattah 2004[115]), UK, 2002[113] | cystometrically proven genuine stress incontinence, failed conservative therapy | detrusor instability, unwilling to be randomized | Pelvicol<br><br>N= 74<br><br>Age: 53 (34-79)<br>BMI: NR<br>Duration of symptoms: 24 (6–72)<br>SUI severity grade: NR | TVT<br><br>N= 68<br><br>Age: 54 (32-91)<br>BMI: NR<br>Duration of symptoms: 24 (6–120)<br>SUI severity grade: NR |
| Guerrero (see Khan 2015[112]), UK, 2010[108] | failed conservative therapy, ≥18 years old, clinically and urodynamically proven SUI | previous SUI surgery, demonstrated evidence of neurological disease, POP >stage II, detrusor overactivity, bladder hypercompliance | Pelvicol- porcine dermis<br><br>N= 50<br><br>Age: 52.4 (31-78)<br>BMI: 28.8 (19.6-40)<br>Duration of symptoms: 9.5 (2-30) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 72<br><br>Age: 54.3 (34-80)<br>BMI: 28.7 (20.2-41)<br>Duration of symptoms: 11.1 (2-35) (yrs)<br>SUI severity grade: NR |

| | | | | |
|---|---|---|---|---|
| Khan (see Guerrero 2010[108]), UK, 2015[112] | failed conservative therapy, ≥18 years old, clinically and urodynamically proven SUI | previous SUI surgery, demonstrated evidence of neurological disease, POP >stage II, detrusor overactivity, bladder hypercompliance | Pelvicol- porcine dermis<br><br>N= 38<br><br>Age: 62 (37-85)<br>BMI: 28.8 (20-42)<br>Duration of symptoms: 9.6 (2-30) (yrs)<br>SUI severity grade: NR | TVT<br><br>N= 63<br><br>Age: 61.2 (42-77)<br>BMI: 30.3 (21-52)<br>Duration of symptoms: 11.5 (2-38) (yrs)<br>SUI severity grade: NR |
| Paparella, Italy, 2010 [114] | Clinical and urodynamic SUI with urethrovesical junction hypermobility without ISD | POP >stage I, previous urogynecologic or anti-incontinence surgery, concurrent disease (including psychiatric), diabetes, peripheral vascular disease, history of pelvic radiation, UUI or MUI, detrusor overactivity, urgency, neurologic bladder, maximum urethral closure pressure <20 cm H2O, Valsalva leak point pressure <60 cm H2O, max flow ≤12ml/s, PVR volume ≥100 ml | PelviLaceTO- porcine dermis<br><br>N= 36<br><br>Age: 59.4 ± 8.4<br>BMI: 25.4 ± 1.8<br>Duration of symptoms: NR<br>SUI severity grade:NR | UretexTO<br><br>N= 34<br><br>Age: 60.7 ± 7.1<br>BMI: 24.9 ± 1.8<br>Duration of symptoms: NR<br>SUI severity grade: NR |

Table A3: Characteristics of Studies Included in the POP Review

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| **Synthetic vs. Native Tissue Suspension** | | | | |
| Altman, Sweden, Norway, Finland, Denmark, 2011 (see Ek 2010[123], 2013[145])[144] | ≥18 years old, primary or recurrent anterior vaginal prolapse POP-Q ≥ 2, with symptoms of vaginal bulging or pelvic heaviness | previous cancer of any pelvic organ, systemic glucocorticoid treatment, insulin-treated diabetes, an inability to participate in study follow-up or to provide informed consent, or the need for concomitant surgery. | traditional colporrhaphy<br><br>N=189<br><br>Age: 65.1 ± 9.8<br>Parity: 2 (0-7)<br>BMI: 25.0 ± 3.0<br>POP-Q: 2-3 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=200<br><br>Age: 64.3 ± 9.8<br>Parity: 2 (0-6)<br>BMI: 26.2 ± 3.4 |
| Carey, Australia, 2009[116] | women recommended vaginal surgery for anterior and posterior vaginal wall prolapse with POP-Q stage 2 or more | Women requiring only anterior or posterior compartment repair or with prolapse of the vaginal vault or cervix beyond the hymen or, in the opinion of the assessing surgeon, required abdominal prolapse surgery with mesh, prior pelvic radiotherapy, pelvic sepsis, planned future pregnancy or immunocompromised | standard anterior and posterior colporrhaphy<br><br>N=70<br><br>Age: 57.6± 11.0<br>Parity: 3.42 ± 1.62<br>BMI:28.66 ± 5.04 | Gynemesh PS; Ethicon<br><br>N=69<br><br>Age:59.1 ± 11.4<br>Parity: 3.24 ± 1.59<br>BMI: 28.89 ± 5.56 |
| Damiani, Italy, 2016[117] | POP-Q >2, symptoms specifically attributed to POP including vaginal bulging, protrusion or pelvic heaviness, and physical | contemplating future pregnancy or had active/latent systemic infections, a compromised immune system, connective tissue | conventional repair<br><br>N=59 | Avaulta Solo; CR Bard<br><br>N=30 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | and mental ability to accomplish the 24-month follow-up | disorders, uncontrolled diabetes mellitus or previous cancer | Age: 55.6 ± 8.6<br>Parity: 2.0 ± 1.1<br>BMI: 27.9 ± 4.1 | Age: 58.3 ± 6.5<br>Parity (vaginal): 2.0 ± 1.2<br>BMI: 27 ± 3.5 |
| de Tayrac, France, 2013[118] | symptomatic POP-Q ≥2 anterior vaginal wall prolapse | stage 0 or 1 anterior vaginal wall support, systemic corticosteroid treatment, uncontrolled diabetes mellitus, previous pelvic irradiation, inability to read French text, untreated vaginal or urinary tract infection, cirrhotic ascites; during the procedure included stage 1 anterior vaginal wall support and bladder injury, to be sure that the surgeon will not use mesh in such cases (patients not followed up); <60 years old | traditional anterior colporrhaphy<br><br>N=72<br><br>Age: 69.6 ± 6.5<br>Parity: 2 (0–6)<br>BMI: 25.4 (±3.6) | trans-obturator Ugytex mesh<br><br>N=75<br><br>Age: 70.1 ± 6<br>Parity :2 (1–10)<br>BMI: 25.5 ± 3.5 |
| de Tayrac, France, 2008[119] | symptomatic uterine or vaginal vault prolapse (stage 2 or higher) | isolated cystocele, stage 1 prolapse, rectal prolapse, and intestinal inflammatory disease | sacrospinous suspension<br><br>N=25<br><br>Age: 59.9 ± 12.2<br>Parity: 2.2 ± 0.9<br>BMI: 25.0 ± 3.5 | IVS Tunneller (Tyco Healthcare) polypropylene mesh<br><br>N=24<br><br>Age: 61.8 ± 9.6<br>Parity: 2.2 ± 0.9<br>BMI: 27.9 ± 4.0 |
| Delroy, Brazil, 2013[120] | anterior POP at least stage II beyond the hymen with point Ba equal to or greater than +1 | malignant urogenital disease or previous pelvic radiotherapy, acute | anterior colporrhaphy<br><br>N=39 | Nazca TC (Promedon) trocar-guided mesh kit |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | according to the POP-Q, primary or recurrent POP primarily in anterior compartment | genitourinary infection, connective tissue disorders, systemic glucocorticoid treatment, insulin-treated diabetes, or clinical contraindications to a surgical procedure | Age: 59.6 ± 10<br>Parity (vaginal): 4 (2–6)<br>BMI: 27.3 ± 3.7 | N=40<br>Age: 62.1 ± 8.3<br>Parity (vaginal): 5.3 (0.7–9.9)<br>BMI: 27.6 ± 4.7 |
| Dias, Brazil, 2016[121] | 45-80 years old, symptomatic POP with predominant advanced anterior vaginal wall prolapse (Ba point ≥+1), either primary or recurrent POP cases, with or without SUI | vaginal vault prolapse post hysterectomy, malignant urogenital disease or previous pelvic radiotherapy, clinical contraindications to a surgical procedure, connective tissue disorders, systemic glucocorticoid treatment and acute genitourinary infection | anterior colporrhaphy<br>N=45<br>Age: 59.4 ± 10.2<br>Parity (vaginal): 3.5 ± 2.0<br>BMI: 27.1 ± 3.6 | Nazca TC (Promedon) trocar-guided mesh kit<br>N=43<br>Age: 61.7 ± 8.3<br>Parity (vaginal): 4.2 ± 3.2<br>BMI: 27.4 ± 4.8 |
| dos Reis Brandao, Brazil, 2015[122] | stage 3 or 4 genital prolapse | NR | Site-specific prolapse repair<br>N=90<br>Age: 64.91 ± 7.48<br>Parity: 4.6 ± 3.0<br>BMI: 27.84 ± 4.03 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br>N=94<br>Age: 66.31 ± 7.01<br>Parity: 4.0±3.3<br>BMI: 27.32±4.62 |
| Ek, Sweden, Norway, Finland, Denmark, 2013 (see Ek 2010[123], Altman 2011[144])[145] | symptomatic anterior vaginal wall prolapse POP-Q ≥ 2 with symptoms of bulging | systemic corticosteroid treatment, insulin-treated diabetes, any previous pelvic organ cancer, or if concomitant prolapse surgery | traditional colporrhaphy<br>N=39 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | in other compartments was required. Furthermore, patients were excluded if unable to participate in follow-up or provide informed consent | Age: 64 ± 9.4<br>Parity: 2 (1–4)<br>BMI: 25.0 ± 3.0 | N=60<br><br>Age: 63.6 ± 9.6<br>Parity: 2 (0–5)<br>BMI: 26.4 ± 2.9 |
| Ek, Sweden, 2010 (see Altman 2011[144], Ek 2013) [123] | symptomatic anterior vaginal wall prolapse POP-Q ≥ 2, able to reach an informed consent to participate and that no surgery other than the allocated treatment was performed | previous pelvic organ cancer; severe rheumatic disease; systemic steroid treatment, connective tissue disorders, insulin-dependent diabetes mellitus, neurological diagnoses that may affect voiding function such as multiple sclerosis or spinal cord injury | traditional colporrhaphy<br><br>N=27<br><br>Age: 66.3 ± 10.8<br>Parity: 2 (1–5)<br>BMI: 24.7 ± 3.2 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=23<br><br>Age: 67.9 ± 11.3<br>Parity: 2 (0–4)<br>BMI: 25.7 ± 3.5 |
| El-Nazer, Egypt, 2012[124] | cystocele grade II or more according to POP-Q system with no plans for pregnancy within 12 months | contemplating/ pregnant women, patients with paravaginal defects or needing anti-incontinence procedure other than suburethral plication, patients with previous Burch colposuspension or vaginal surgery, immunocompromised or diabetic patients, patients with symptoms mainly due to chronic urinary tract infection, patients who did not consent to the study | anterior colporrhaphy<br><br>N=20<br><br>Age: 39.5 ± 5.9<br>Parity: 5 ± 2.2<br>BMI: 31.7 ± 6.6 | Gynemesh PS; Ethicon<br><br>N=20<br><br>Age: 42.3 ± 6.9<br>Parity: 5 ± 2<br>BMI: 33.4 ± 7.01 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| Glazener, UK, 2017[125] | decided to undergo primary POP surgery for anterior or posterior vaginal wall prolapse | unable or unwilling to give informed consent, unable to complete study questionnaires | standard native tissue repair<br><br>N=430<br><br>Age: 59.8 ± 10.1<br>Parity: 2 (0-8) | permanent polypropylene mesh<br><br>N=435<br><br>Age: 59.5 ± 10.4<br>Parity: 2 (0-9) |
| Gupta, India, 2014 [126] | symptomatic anterior vaginal prolapse to the hymen or beyond | concomitant stress urinary incontinence, dominant symptomatic posterior vaginal prolapse, active vaginal infections and presence of any gynaecological malignancy. | traditional anterior colporrhaphy<br><br>N=54<br><br>Age: 51.5 ± 12<br>Parity: 4 (2-6) | vicryl-polypropylene mesh (VYPRO Johnson & Johnson Inc.)<br><br>N=52<br><br>Age: 49.6 ± 10<br>Parity: 4(2-7) |
| Gutman, USA, 2013 (see Iglasia 2010[129], Sokol 2012[150])[146] | ≥ 21 years old, diagnosed with POP-Q stage 2-4 uterovaginal or vaginal prolapse who desired vaginal reconstructive surgery, available for 12 months follow-up, able to complete questionnaire | medical contraindications, current intermittent catheterization, pregnancy less than 12 months postpartum or desire for future fertility, uterus more than 12 weeks' size, adnexal mass, shortened vagina or other known Mullerian anomaly, other laparoscopic or abdominal/pelvic surgery in the previous 3 months, known neurologic or medical condition affecting bladder function, need for concurrent | traditional vaginal reconstructive surgery<br><br>N=33<br><br>Age: 63.1 ± 9.0<br>Parity: 2 (2-3)<br>BMI: 28.2 ± 6.4 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=32<br><br>Age: 62.6 ± 10.6<br>Parity: 2 (2-3)<br>BMI: 27.6 ± 5.5 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | surgery requiring an abdominal incision | | |
| Halaska, Czech Republic, 2012[127] | scheduled for vaginal prolapse surgery with verified POP-Q ≥ 2 | pelvic malignancy, ≤18 years old, history of radiotherapy of the pelvis, or requiring hysterectomy | sacrospinous fixation<br><br>N=83<br><br>Age: 66.41 (9.62)<br>Parity: 2.32 (0.68)<br>BMI: 27.62 (3.80) | Prolift (Gynecare)<br><br>N=85<br><br>Age: 63.37 (10.12)<br>Parity: 2.08 (0.71)<br>BMI: 26.81 (3.73) |
| Hiltunen, Finland, 2007[128] | postmenopausal women with symptomatic anterior vaginal wall prolapse to the hymen or beyond when under strain and referred for reconstructive pelvic surgery | apical defect indicating concomitant vaginal fixation or stress urinary incontinence necessitating surgery or her main symptomatic prolapse component was in the posterior vaginal wall, gynecologic tumor or malignancy calling for laparotomy or laparoscopy and those with untreated vaginal infection | traditional anterior colporrhaphy<br><br>N=97<br><br>Age: 65 ± 9<br>Parity: 2 (1–10)<br>BMI: 27.2 ± 4.1 | Parietene light, Sofradim Co. self-tailored low-weight polypropylene mesh<br><br>N=105<br><br>Age: 66 ± 9<br>Parity: 3 (1–11)<br>BMI: 26.5 ± 3.5 |
| Iglesia, USA, 2010 (see Sokol 2012[150], Gutman 2013[146])[129] | ≥ 21 years old, diagnosed with POP-Q stage 2-4 uterovaginal or vaginal prolapse who desired vaginal reconstructive surgery, available for 12 months follow-up, able to complete questionnaire | medical contraindications, current intermittent catheterization, pregnancy less than 12 months postpartum or desire for future fertility, uterus more than 12 weeks' size, adnexal mass, shortened vagina or other known Mullerian anomaly, other laparoscopic | traditional vaginal reconstructive surgery<br><br>N=33<br><br>Age: 63.5 ± 8.9<br>Parity: 2.6 ± 0.9<br>BMI: 27.8 ± 6.4 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=32<br><br>Age: 64.4 ± 10.8<br>Parity: 2.4 ± 1.1<br>BMI: 27.4 ± 5.1 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | or abdominal/pelvic surgery in the previous 3 months, known neurologic or medical condition affecting bladder function, need for concurrent surgery requiring an abdominal incision | | |
| Lamblin, France, 2014[130] | symptomatic POP-Q stage 3 or 4 anterior vaginal wall prolapse | POP-Q stage <3, asymptomatic; pregnancy or pregnancy project, previous pelvic cancer or pelvic radiation treatment, pelvic surgery within 6 months, impaired lower-limb motion (preventing surgical installation), uncontrolled type-2 diabetes, polypropylene hypersensitivity, treatment affecting immune response, ongoing or terminated within the previous month, and pathology with unacceptable complication risk (coagulation disorder, progressive disease such as malignancy, immunologic disease) | vaginal colposuspension<br><br>N=35<br><br>Age: 64.7 ± 1.3<br>Parity: 2.7 ± 0.2<br>BMI: 26.4 ± 0.7<br>POP-Q: 3.2 ± 0.1 | The Perigee transobturator anterior compartment repair system<br><br>N=33<br><br>Age: 65.3 ± 1.3<br>Parity: 3 ± 0.3<br>BMI: 26.3 ± 0.5<br>POP-Q: 3.3 ± 0.2 |
| Lopes, Brazil, 2010[131] | 50-75 years old, POP-Q stage 3-4 uterine prolapse | history of implants for pelvic reconstructive procedures, diagnosis of coagulation | sacrospinous ligament fixation | NAZCA TC KIT (Promedon) polypropylene mesh |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | disorders, renal failure, history of pelvic irradiation, and cognitive limitation that could possibly hinder the comprehension of the quality of life questionnaire or the informed consent | N=16<br><br>Age: 63.1<br>Parity: 3.3<br>BMI: 25.8 | N=16<br><br>Age: 65.5<br>Parity: 4<br>BMI: 25.7 |
| Lunardelli, Brazil, 2009[132] | 50-75 years old, AVP stage 3 or 4, or recurrent anterior vaginal prolapse | pregnant women, mothers in the puerperal period and up to six months post-partum, patients with a history of use of implants in reconstructive or anti-incontinence pelvic procedures, patients with blood coagulation disorders, kidney failure and/or upper urinary tract obstruction, urethral diverticulum or a history of pelvic irradiation | sacrospinous ligament fixation<br><br>N=16<br><br>Age: 62.3<br>Parity: 4.4<br>BMI: 26.5 | NAZCA TC KIT (Promedon) polypropylene mesh<br><br>N=16<br><br>Age: 64.4<br>Parity: 4.1<br>BMI: 26.2 |
| Menefee, USA, 2011[133] | ≥18 years old, POP-Q ≥ 2 anterior vaginal wall prolapse, symptomatic, desired surgical correction, willing to be randomized | current pregnancy, plans for future pregnancy, a foreshortened vagina (as defined by a total vaginal length of 5 cm or less), a history of vaginal cancer, pelvic irradiation, an adverse reaction to porcine or synthetic materials, a history of graft-reinforced or mesh-reinforced anterior repair, or plans to move outside of the | standard anterior colporrhaphy<br><br>N=32<br><br>Age: 61 ± 11<br>Parity (vaginal): 3 (1–8)<br>BMI: 31 ± 10 | paravaginal repair with polypropylene mesh<br><br>N=36<br><br>Age: 65 ± 7.0<br>Parity (vaginal): 3 (1–7)<br>BMI: 28 ± 4 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | study area within the next 24 months | | |
| Milani, The Netherlands, 2018 (see Withagen 2011[34])[147] | women with recurrent POP ≥ stage 2 of anterior wall, posterior wall, or both, requiring surgical correction | pregnancy or contemplating future pregnancy, prior vaginal prolapse repair with mesh, a compromised immune system or any other condition that would compromise healing, previous pelvic irradiation or cancer, blood coagulation disorders, renal failure, upper urinary tract obstruction, renal failure and upper urinary tract obstruction, or presence of large ovarian cysts or myomas | anterior colporrhaphy<br><br>N=69<br><br>Age: 62.4 ± 10.2<br>Parity: 2 (1–5)<br>BMI: 26.8 ± 4.3 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=58<br><br>Age: 60.9 ± 9.0<br>Parity: 2(1–6)<br>BMI: 26.4 ± 4.1 |
| Nguyen, USA, 2008[134] | ≥ 21 years old, stage ≥2 anterior vaginal prolapse requiring surgical correction | stage 0 or I anterior vaginal support, declined participation, were pregnant or contemplating future pregnancy, had prior anterior vaginal prolapse repair with biologic or synthetic graft, active or latent systemic infection, compromised immune system, uncontrolled diabetes mellitus, previous pelvic irradiation or cancer, known hypersensitivity to polypropylene, were unable | anterior colporrhaphy<br><br>N=38<br><br>Age: 59 ± 9.5<br>Parity: 3 (0–6)<br>BMI: 27 ± 4 | Perigree polypropylene mesh<br><br>N=38<br><br>Age: 61 ± 10.5<br>Parity: 3 (0–5)<br>BMI: 28 ± 3 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | or unwilling to give valid informed consent or comply with the requirements of the protocol, or if scheduled to undergo concomitant Burch colposuspension or pubovaginal sling | | |
| Nieminen, Finland, 2008 (see Hiltunen 2007[128], Nieminen 2010[149])[148] | symptomatic anterior vaginal wall prolapse to the hymen or beyond and referred for reconstructive pelvic surgery | requiring concomitant vaginal vault suspension such as sacrospinous ligament fixation or sacrocolpopexy for vaginal prolapse or uterine procidentia or surgery for stress urinary incontinence or laparotomy or laparoscopy for any reason were excluded | traditional anterior colporrhaphy<br><br>N=97<br><br>Age: 66 ± 9<br>Parity: 2 (1–10)<br>BMI: 27 ± 4 | Parietene light, Sofradim Co. self-tailored low-weight polypropylene mesh<br><br>N=105<br><br>Age: 65 ± 9<br>Parity: 3 (0–11)<br>BMI: 27 ± 4 |
| Nieminen, Finland, 2010 (see Hiltunen 2007[128], Nieminen 2008[148])[149] | symptomatic anterior vaginal wall prolapse to the hymen or beyond and referred for reconstructive pelvic surgery | requiring concomitant vaginal vault suspension such as sacrospinous ligament fixation or sacrocolpopexy for vaginal prolapse or uterine procidentia or surgery for stress urinary incontinence or laparotomy or laparoscopy for any reason were excluded | traditional anterior colporrhaphy<br><br>N=97<br><br>Age: 65 ± 9<br>Parity: 2 (1-10)<br>BMI: 27.2 ± 4.1 | Parietene light, Sofradim Co. self-tailored low-weight polypropylene mesh<br><br>N=105<br><br>Age: 66 ± 9<br>Parity: 3 (0-11)<br>BMI: 26.5 ± 3.5 |
| Qatawneh, Jordan, 2012[135] | severe symptomatic pelvic organ prolapse (i.e. uterine or vaginal vault prolapse of stages 3 and 4) | <stage 3 prolapse, of any compartment or previous procedures with implants as a part of pelvic reconstructive | posterior fascial plication<br><br>N=63 | tension-free polypropylene mesh-reinforced (Gynemesh) anterior vaginal prolapse |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | surgery, known coagulation disorder, previous pelvic irradiation and women who wished to preserve their uterus | Age: 56±10<br>Parity: median, 6 (1-15)<br>BMI: 30±4 | with anterior colporrhaphy at the time sacrospinous colpopexy<br><br>N=53<br><br>Age: 57±7<br>Parity: median, 6 (3-14)<br>BMI: 30±3 |
| Rondini, Chile, 2015[136] | required reconstructive surgery, >18 years old, sexually active, and had a symptomatic stage 2–4 apical prolapse | history of previous apical reconstructive surgery, such as sacrospinous fixation, HUVS, or SCP | high uterosacral vault suspension<br><br>N=54<br><br>Age: 57.1±10.4<br>Parity: 4.0±2.0<br>BMI: 31.0±5.7 | abdominal sacrocolpopexy (with Prolene mesh)<br><br>N=56<br><br>Age: 57.3±10.1<br>Parity: 3.8±1.8<br>BMI: 29.0±4.4 |
| Rudnicki, Denmark, Norway, Sweden and Finland, 2013[137] | ≥ 55 years old, anterior wall prolapse ≥ stage 2 | previous major pelvic surgery, with the exception of a hysterectomy for reasons other than genital prolapse, previous vaginal surgery, or hysterectomy for POP, concomitant prolapse of the uterus or an enterocele of stage 1 or higher, previous incontinence sling surgery performed through the obturator membrane, current treatment with | anterior colporrhaphy<br><br>N=82<br><br>Age: 64.7±6.6<br>Parity: 2.3±1.0<br>BMI: 25.7±3.1 | collagen-coated transvaginal mesh (Avaulta Plus)<br><br>N=79<br><br>Age: 64.9±6.4<br>Parity: 2.4±1.0<br>BMI: 26.5±5.1 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | corticosteroids, or a history of genital or abdominal cancer | | |
| Sivaslioglu, Turkey, 2008[138] | diagnosed as having cystocoele | SUI or concomitant rectocoele or enterocoele or recurrent cystocoele | site-specific cystocele repair<br><br>N=45<br><br>Age: 50.1±9.9<br>Parity: 3.7±1.9<br>BMI: 30.3±5.6 | polyprolene mesh (Sofradim)<br><br>N=45<br><br>Age: 57.7±9.4<br>Parity: 3.1±1.4<br>BMI: 29.4±4.1 |
| Sokol, USA, 2012 (see Iglasia 2010[129], Gutman 2013[146])[150] | ≥ 21 years old, diagnosed with POP-Q stage 2-4 uterovaginal or vaginal prolapse who desired vaginal reconstructive surgery, available for 12 months follow-up, able to complete questionnaire | medical contraindications, current intermittent catheterization, pregnancy less than 12 months postpartum or desire for future fertility, uterus more than 12 weeks' size, adnexal mass, shortened vagina or other known Mullerian anomaly, other laparoscopic or abdominal/pelvic surgery in the previous 3 months, known neurologic or medical condition affecting bladder function, need for concurrent surgery requiring an abdominal incision | traditional vaginal reconstructive surgery<br><br>N=33<br><br>Age: 63.5 ± 8.9<br>Parity: 2.6 ± 0.9<br>BMI: 27.8 ± 6.4 | Prolift (Gynecare) transvaginal polypropylene mesh repair kit<br><br>N=32<br><br>Age: 64.4 ± 10.8<br>Parity: 2.4 ± 1.1<br>BMI: 27.4 ± 5.1 |
| Svabik, Czech Republic, 2014[139] | posthysterectomy patients with at least two-compartment prolapse (with affected apical/vault compartment, | patients with prolapse and uterus in place, those without levator ani avulsion and those | sacrospinous vaginal colpopexy (the Amreich–Richter procedure) with native tissue vaginal | Prolift mesh<br><br>N=36 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | stage ≥ 2) suffering from symptoms of prolapse, requesting pelvic floor reconstructive surgery, and diagnosed with a complete unilateral or bilateral avulsion injury | not requesting pelvic floor surgery | (anterior and posterior) repair<br><br>N=34<br><br>Age: 62.5 (10.85)<br>Parity: 2.2 (0.67)<br>BMI: 28.2 (4.18) | Age: 63.4 (8.61)<br>Parity: 2.1 (0.83)<br>BMI: 27.2 (3.21) |
| Tamanini, Brazil, 2013 (a) (see Tamanini 2013 (b)[140], Tamanini 2015[151])[140] | ≥ 45 years old, anterior vaginal wall prolapse stage ≥ 2, without previous surgical correction or with previous surgical treatment of AVWP without the use of polypropylene mesh | women who were previously treated (due to AVWP or SUI) using polypropylene mesh, who were receiving oncological treatment, with altered Papanicolau Smear exam or with uterine bleeding, with genital or acute urinary infection, patients who didn't commit to ambulatory follow-up or that refused the written informed consent | traditional colporrhaphy<br><br>N=55<br><br>Age: 63.4 ± 9.5<br>Parity: 4.2 ± 2.7<br>BMI: 27.8 ± 4.9 | NAZCA TC KIT (Promedon) polypropylene mesh<br><br>N=45<br><br>Age: 66.8 ± 9.2<br>Parity: 4.2 ± 2.6<br>BMI: 27.5 ± 5.4 |
| Tamanini, Brazil, 2015 (see Tamanini 2013 (a)[140] and (b)[140])[151] | ≥ 45 years old, anterior vaginal wall prolapse stage ≥ 2, without previous surgical correction or with previous surgical treatment of AVWP without the use of polypropylene mesh | women who were previously treated (due to AVWP or SUI) using polypropylene mesh, who were receiving oncological treatment, with altered Papanicolau Smear exam or with uterine bleeding, with genital or acute urinary infection, patients who didn't commit to | traditional colporrhaphy<br><br>N=55<br><br>Age: 63.4 ± 9.5<br>Parity: 4.2 ± 2.7<br>BMI: 27.8 ± 4.9 | NAZCA TC KIT (Promedon) polypropylene mesh<br><br>N=45<br><br>Age: 66.8 ± 9.2<br>Parity: 4.2 ± 2.6<br>BMI: 27.5 ± 5.4 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | ambulatory follow-up or that refused the written informed consent | | |
| Tamanini, Brazil, 2013 (b) (see Tamanini 2013 (a)[140], Tamanini 2015[151]) [141] | ≥ 45 years old, anterior vaginal wall prolapse stage ≥ 2, without previous surgical correction or with previous surgical treatment of AVWP without the use of polypropylene mesh | women who were previously treated (due to AVWP or SUI) using polypropylene mesh, who were receiving oncological treatment, with altered Papanicolau Smear exam or with uterine bleeding, with genital or acute urinary infection, patients who didn't commit to ambulatory follow-up or that refused the written informed consent | traditional colporrhaphy<br><br>N=55<br><br>Age: 63.4 ± 9.5<br>Parity: 4.2 ± 2.7<br>BMI: 27.8 ± 4.9 | NAZCA TC KIT (Promedon) polypropylene mesh<br><br>N=45<br><br>Age: 66.8 ± 9.2<br>Parity: 4.2 ± 2.6<br>BMI: 27.5 ± 5.4 |
| Turgal, Turkey, 2013[142] | grade 2-3 cystocele | urinary incontinence, previous gynaecological operation, concomitant rectocele or enterocele, or recurrent cystocele | anterior colporrhaphy<br><br>N=20<br><br>Age: 54.8 ± 9.9<br>Parity: 3.1 ± 1.4<br>BMI: 29.8 ± 3.7 | Sofradim (Parieten) polypropylene mesh<br><br>N=20<br><br>Age: 53 ± 12<br>Parity: 3.7 ± 1.9<br>BMI: 29.8 ± 3.7 |
| Vollebregt, The Netherlands, 2012 (see Vollebregt 2011[143])[152] | 40-80 years old, bothersome POP complaints, ≥ 2 predominant cystocele, indication for surgical correction | childbearing age were excluded if they had not completed their family or if they used inadequate birth control measures, history of urogynaecological surgery for pelvic organ prolapse or | anterior colporrhaphy<br><br>N=64<br><br>Age: 59 ± 8.3<br>Parity: 2.6 ± 1.1<br>BMI: 24.7 ± 3.1 | Avaulta anterior system (Bard)<br><br>N=61 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | incontinence, concomitant SUI with an indication for surgical correction, a history of cancer or chronic obstructive pulmonary disease, recurrent lower UTI (more than three culture-proven infections/year), maximum bladder capacity <300 ml, and an indication for hysterectomy | | Age: 60 ± 9.4<br>Parity: 2.5 ± 0.9<br>BMI: 25.2 ± 2.9 |
| Vollebregt, The Netherlands, 2011 (see Vollebregt 2012[152])[143] | 40-80 years old, bothersome POP complaints, ≥ 2 predominant cystocele, indication for surgical correction | childbearing age were excluded if they had not completed their family or if they used inadequate birth control measures, history of urogynaecological surgery for pelvic organ prolapse or incontinence, concomitant SUI with an indication for surgical correction, a history of cancer or chronic obstructive pulmonary disease, recurrent lower UTI (more than three culture-proven infections/year), maximum bladder capacity <300 ml, and an indication for hysterectomy | anterior colporrhaphy<br><br>N=62<br><br>Age: 59 ±8.6<br>Parity:2.7 ± 1.9<br>BMI: 24 ± 3.6 | Avaulta anterior system (Bard)<br><br>N=59<br><br>Age: 60 ± 9.1<br>Parity:2.4 ± 0.9<br>BMI: 24 ± 2.9 |
| Withagen 2011 (see Milani 2018[147])[34] | women with recurrent POP ≥ stage 2 of anterior wall, | pregnancy or contemplating future pregnancy, prior | anterior colporrhaphy | Prolift (Gynecare) transvaginal |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | posterior wall, or both, requiring surgical correction | vaginal prolapse repair with mesh, a compromised immune system or any other condition that would compromise healing, previous pelvic irradiation or cancer, blood coagulation disorders, renal failure, upper urinary tract obstruction, renal failure and upper urinary tract obstruction, or presence of large ovarian cysts or myomas. | N=99<br><br>Age: 64 ± 10.2<br>Parity: 2 (1-5)<br>BMI: 27 ± 4 | polypropylene mesh repair kit<br><br>N=95<br><br>Age: 64 ± 10.5<br>Parity: 2 (0-6)<br>BMI: 27 ± 6 |
| **Synthetic vs. Porcine** | | | | |
| Damiani, Italy, 2016[117] | POP-Q >2, symptoms specifically attributed to POP including vaginal bulging, protrusion or pelvic heaviness, and physical and mental ability to accomplish the 24-month follow-up | contemplating future pregnancy or had active/latent systemic infections, a compromised immune system, connective tissue disorders, uncontrolled diabetes mellitus or previous cancer | PelviSoft BioMesh; CR Bard<br><br>N=28<br><br>Age: 56.9 ± 4.4<br>Parity (vaginal): 2.0 ± 1.0<br>BMI: 26.7 ± 3.2 | Avaulta Solo; CR Bard<br><br>N=30<br><br>Age: 58.3 ± 6.5<br>Parity (vaginal): 2.0 ± 1.2<br>BMI: 27 ± 3.5 |
| Menefee, USA, 2011[133] | ≥18 years old, POP-Q ≥ 2 anterior vaginal wall prolapse, symptomatic, desired surgical correction, willing to be randomized | current pregnancy, plans for future pregnancy, a foreshortened vagina (as defined by a total vaginal length of 5 cm or less), a history of vaginal cancer, pelvic irradiation, an adverse reaction to porcine or synthetic materials, a history | paravaginal repair with porcine dermis graft<br><br>N=31<br><br>Age: 60 ± 10<br>Parity (vaginal): 3 (1–8)<br>BMI: 30 ± 5 | paravaginal repair with polypropylene mesh<br><br>N=36<br><br>Age: 65 ± 7.0<br>Parity (vaginal): 3 (1–7)<br>BMI: 28 ± 4 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | of graft-reinforced or mesh-reinforced anterior repair, or plans to move outside of the study area within the next 24 months | | |
| Natale, Italy, 2009[153] | women with recurrent POP ≥ stage 2 of anterior wall prolapse (Ba ≥-1) planning secondary pelvic reconstructive surgery | concomitant anti-incontinence procedure and patients with diabetes mellitus or collagen disease were excluded from our study | Pelvicol porcine dermis<br><br>N=94<br><br>Age: 67.0 ± 8.1<br>Parity: 2 (0-4)<br>BMI: 24.7 ± 4.5 | Gynemesh PS<br><br>N=96<br><br>Age: 62.5 ± 8.5<br>Parity: 2 (0-4)<br>BMI: 25.9 ± 5.5 |
| **Synthetic vs. Autologous/cadaver** | | | | |
| Culligan, USA, 2005 (see Tate 2011[155])[154] | women with post-hysterectomy vaginal vault prolapse scheduled for sacral colpopexy | NR | Tutoplast processed Suspend fascia lata; Mentor Corporation<br><br>N=50<br><br>Age: 57.5 ± 10.8<br>Parity (vaginal, median): 2<br>BMI: 27.3 ± 3.9<br>POP-Q: 2.4 ± 0.7 | synthetic mesh Trelex; Boston Scientific<br><br>N=50<br><br>Age:60.4 ± 10.1<br>Parity (vaginal, median): 3<br>BMI: 28.4 ± 4.7<br>POP-Q: 2.5 ± 0.5 |
| Tate, USA, 2011 (see Culligan 2005[154])[155] | women with post-hysterectomy vaginal vault prolapse scheduled for sacral colpopexy | NR | Tutoplast processed Suspend fascia lata; Mentor Corporation<br><br>N=29<br><br>Age: 57.5 ± 10.8<br>Parity (vaginal, median): 2 | synthetic mesh Trelex; Boston Scientific<br><br>N=29<br><br>Age:60.4 ± 10.1<br>Parity (vaginal, median): 3 |

| Author, Country, Year | Inclusion criteria | Exclusion criteria | Control | Intervention |
|---|---|---|---|---|
| | | | BMI: 27.3 ± 3.9<br>POP-Q: 2.4 ± 0.7 | BMI: 28.4 ± 4.7<br>POP-Q: 2.5 ± 0.5 |
| **Synthetic vs. semi-dissolvable/dissolvable** | | | | |
| Bataller, Spain, 2018[156] | women requiring POP surgery, primary or recurrent symptomatic POP with predominant anterior vaginal wall descent (stage 2-3) | <21 years old, having a comorbidity or being at a high anesthetic risk requiring a particular approach, the inability to comprehend questionnaires or attend follow-up visits, previous colposacropexy or vaginal mesh procedure and a history of pelvic radiotherapy | laparoscopic sacrocolpopexy/cervicopexy with polyglactin mesh<br><br>N=60<br><br>Age: 60.8 ± 7.4<br>Parity (vaginal): 2.3 ± 1.1<br>BMI: 25.7 ± 3.2<br>POP-Q: 2-3 | anterior vaginal mesh; Elevate®Anterior and Apical<br><br>N=60<br><br>Age: 63.3 ± 7.2<br>Parity (vaginal): 2.4 ± 1.0<br>BMI: 26.9 ± 3.6 |
| Farthmann, Germany, 2013[42] | symptomatic cystocele > stage II or stage II in combination with a considerable lateral defect and risk factors for recurrent POP: chronic obstructive pulmonary disease, chronic obstipation, overweight | age <18 years, incomplete family planning, allergy to polypropylene, previous malignancy of the lower urinary tract, genital organs, or rectosigmoid, previous mesh implantation, missing informed consent, life expectancy <3 years, or patients that could not ensure follow-up visits over 3 years | absorbable polypropylene mesh<br><br>N=97<br><br>Age: 64.8 ± 8.1<br>BMI: 26.5 | conventional polypropylene mesh<br><br>N=101<br><br>Age: 67.4 ± 9.7<br>BMI: 26.7 |

## Appendix 6: Meta-Analysis Funnel Plots and Additional Forest Plots

Figure A1: Forest Plot of Bladder Injury in SUI Patients with Synthetic Mesh vs. Native Tissue

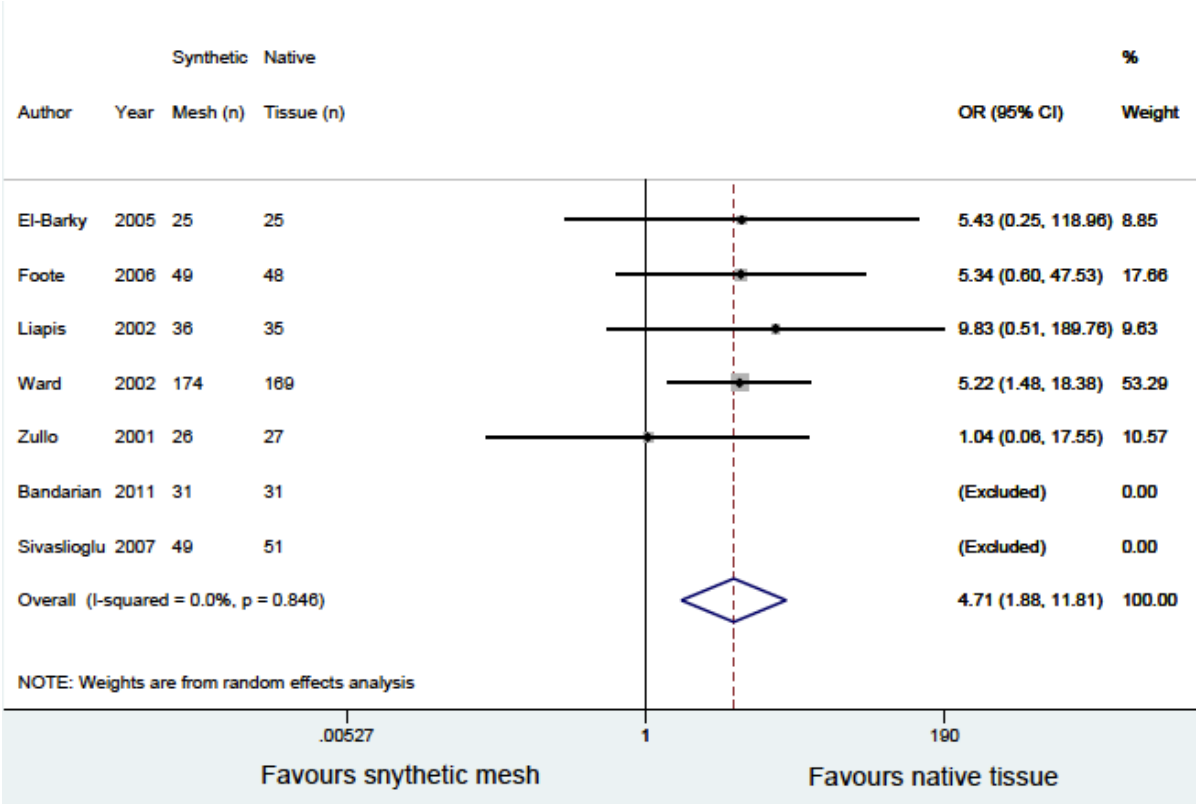

Figure A2: Forest Plot of Urinary Retention in SUI Patients with Synthetic Mesh vs. Native Tissue

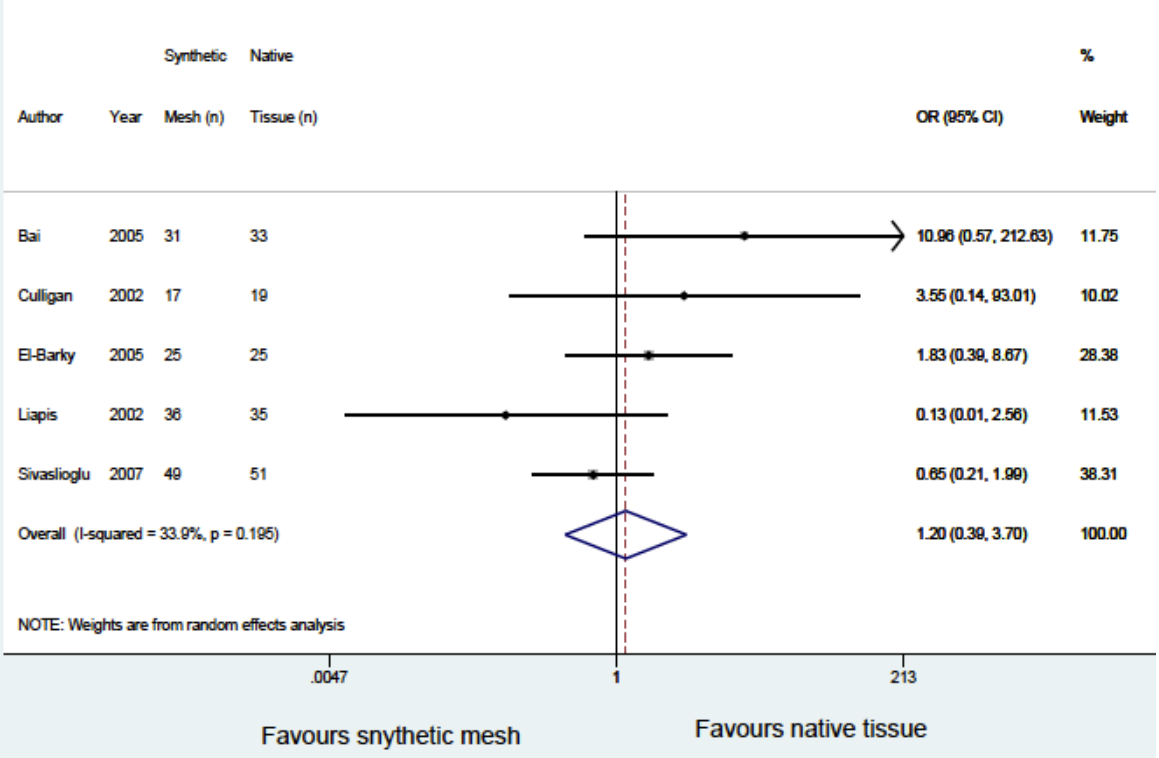

Figure A3: Forest Plot of UTI in SUI Patients with Synthetic Mesh vs. Native Tissue

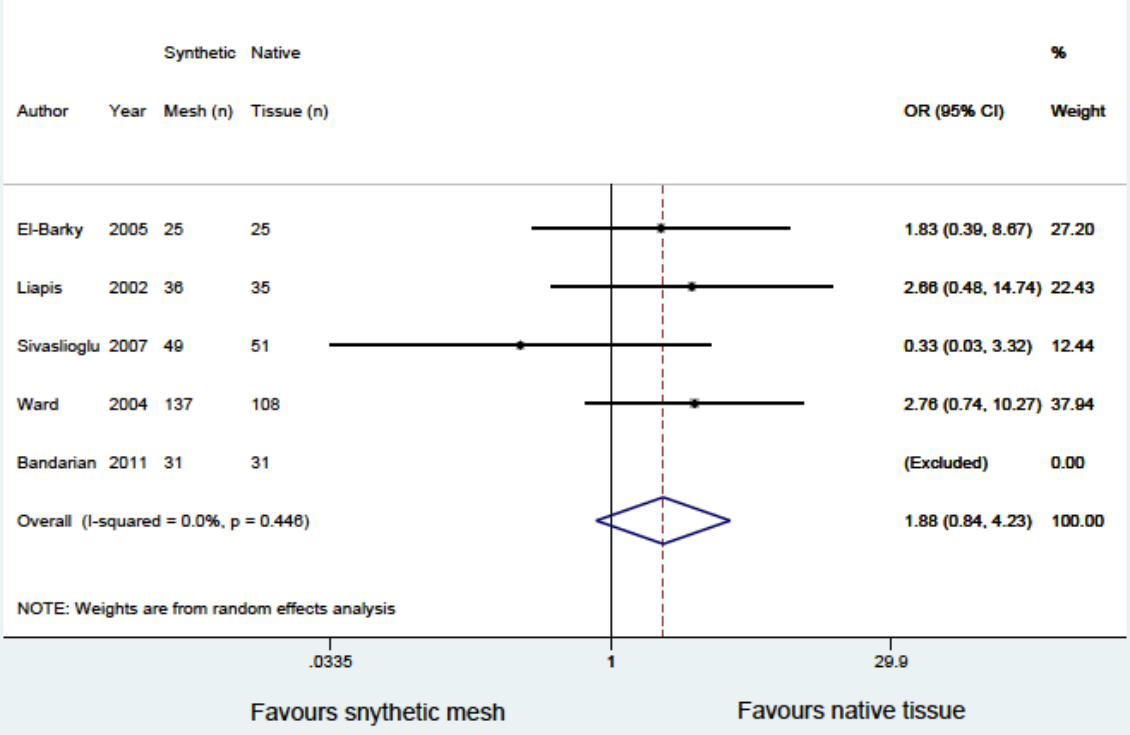


Figure A4: Forest Plot of Wound Infection in SUI Patients with Synthetic Mesh vs. Native Tissue

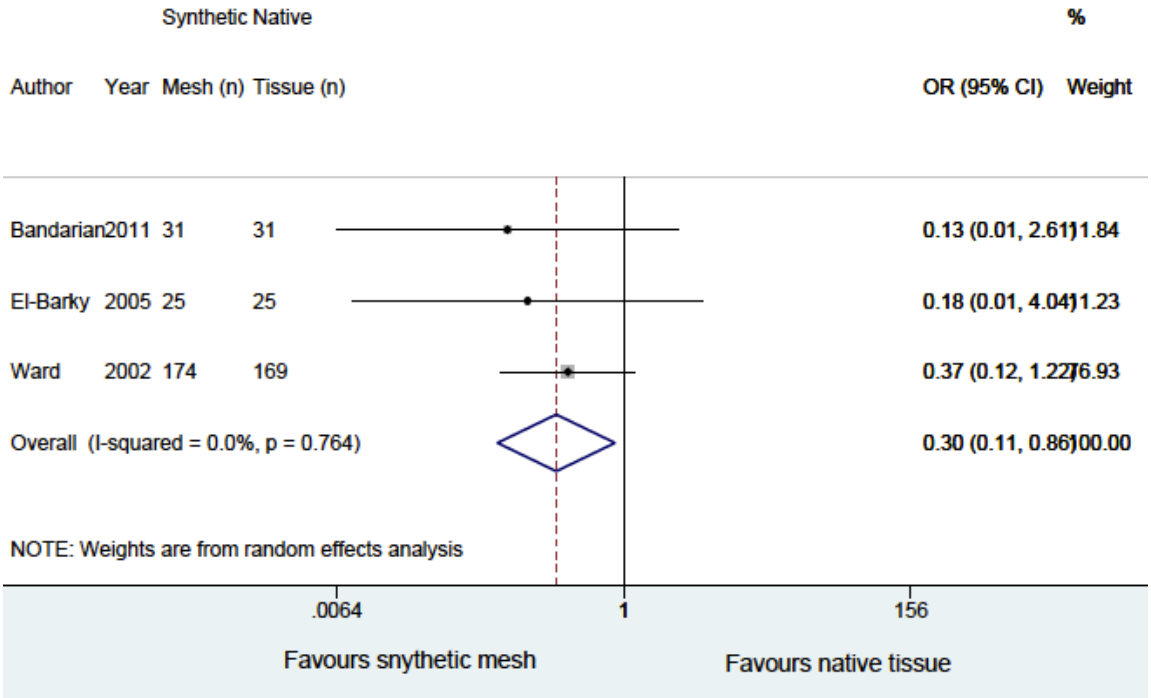

Figure A5: Funnel Plot with 95% Confidence Intervals to Test for Publication Bias in SUI Studies of Synthetic Mesh vs. Native Tissue

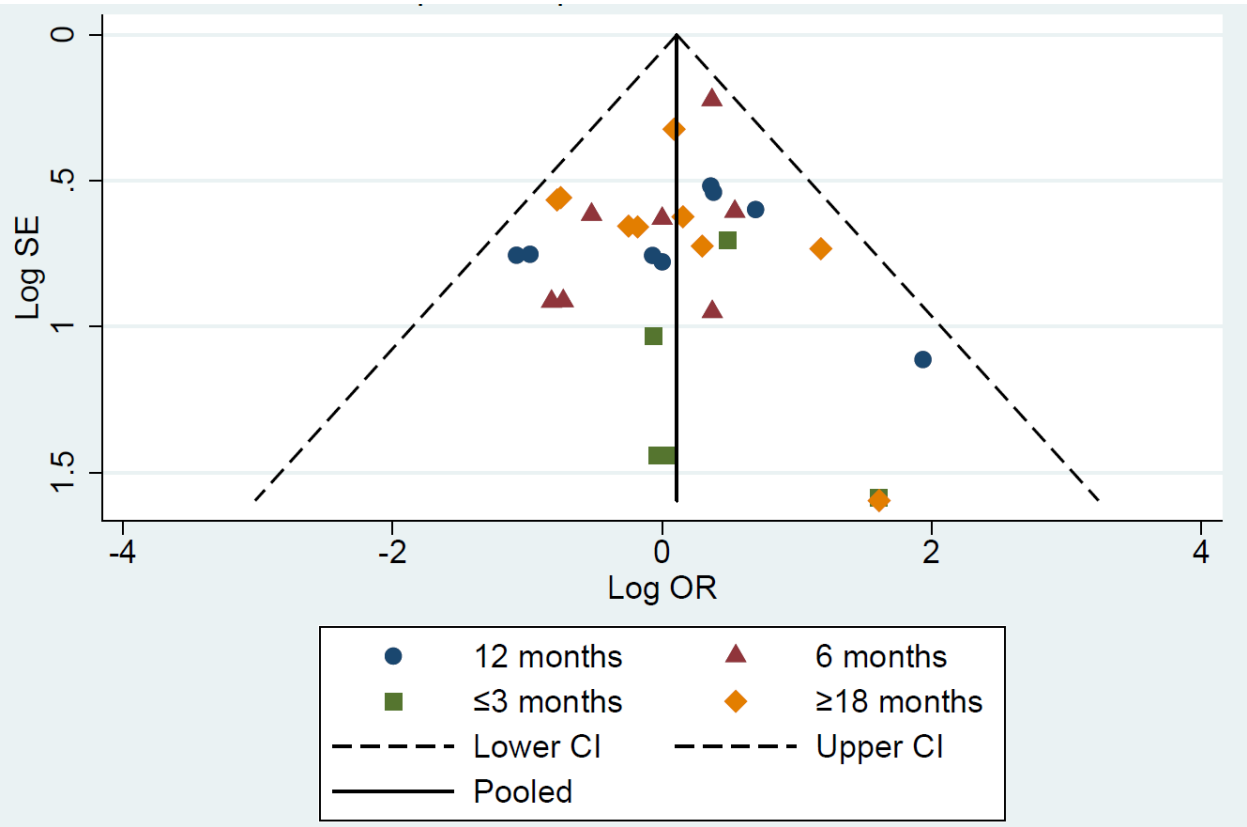

Figure A6: Funnel Plot with 95% Confidence Intervals to Test for Publication Bias in SUI Studies of Synthetic Mesh vs. AFS

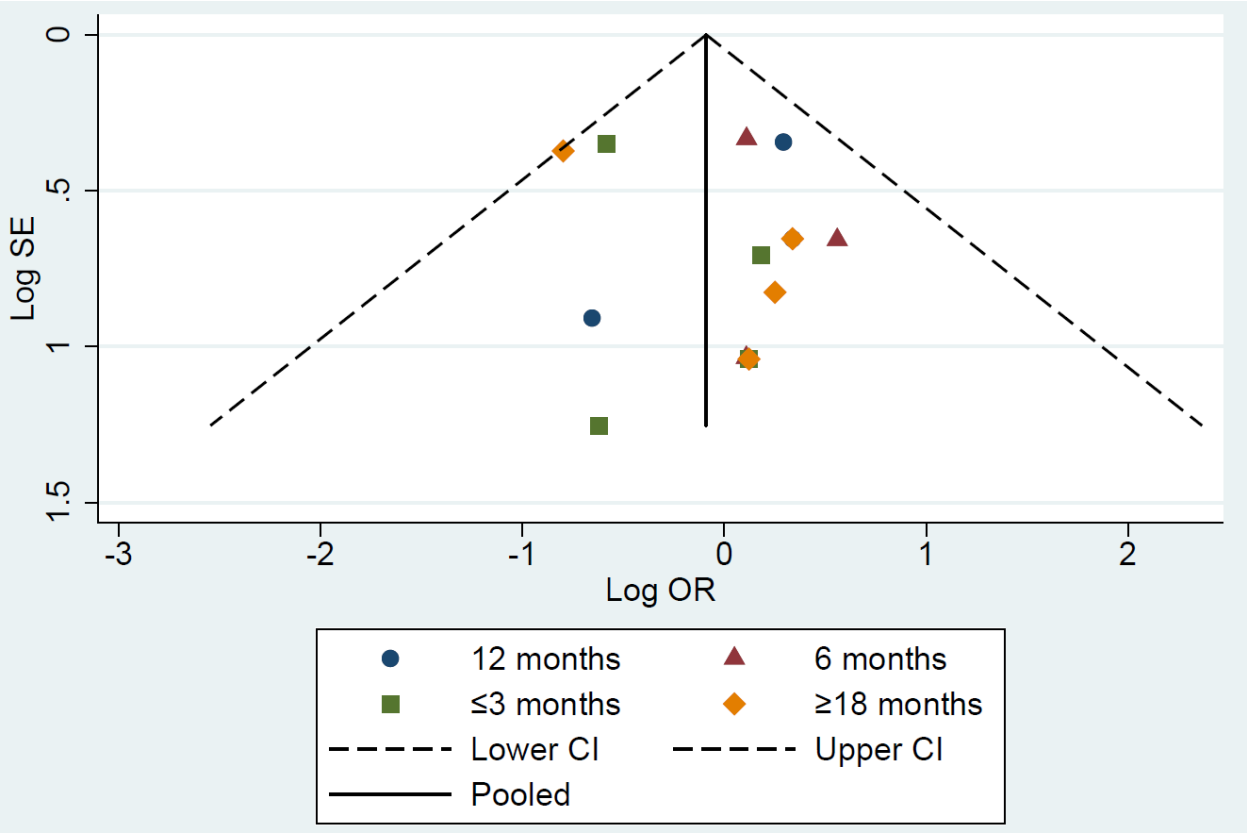

Figure A7: Funnel Plot with 95% Confidence Intervals to Test for Publication Bias in SUI Studies of Synthetic vs. Porcine Mesh

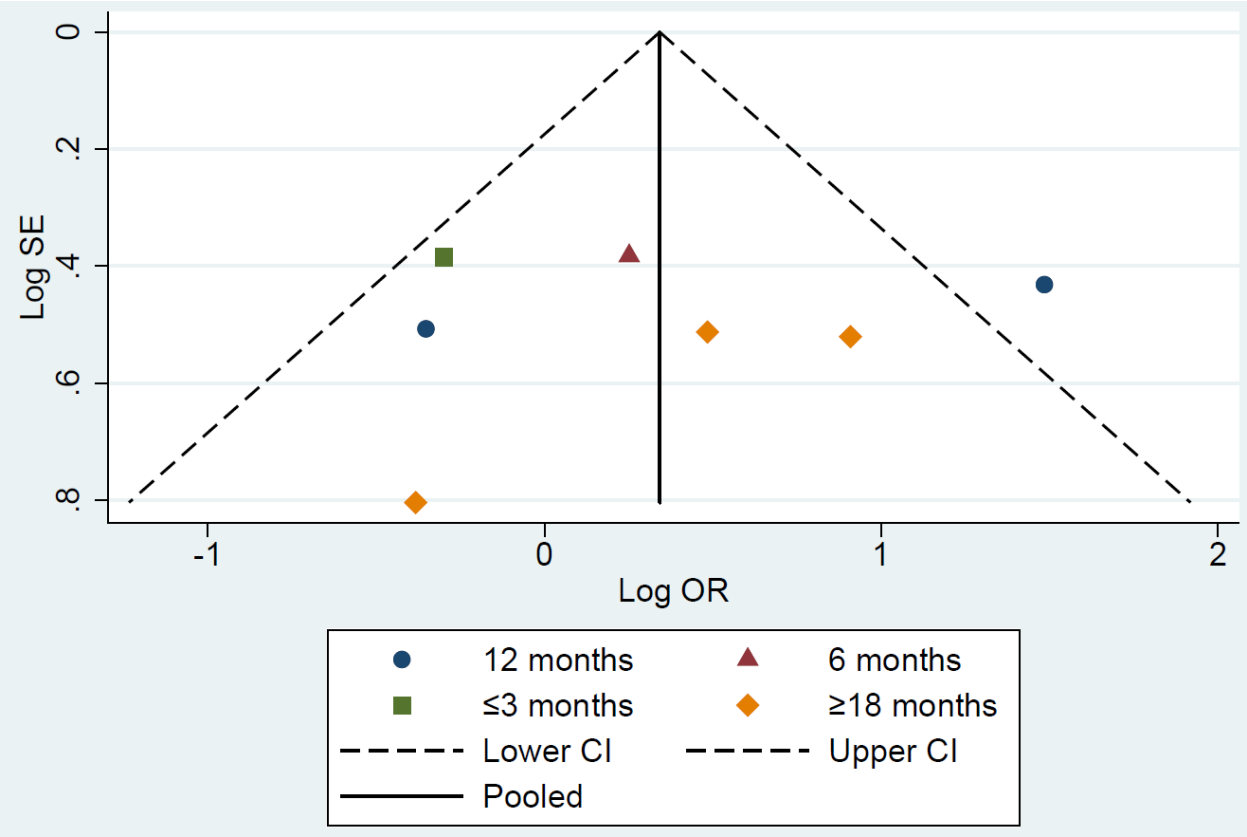

Figure A8: Forest Plot of Bladder Injury in POP Patients with Synthetic Mesh vs. Native Tissue

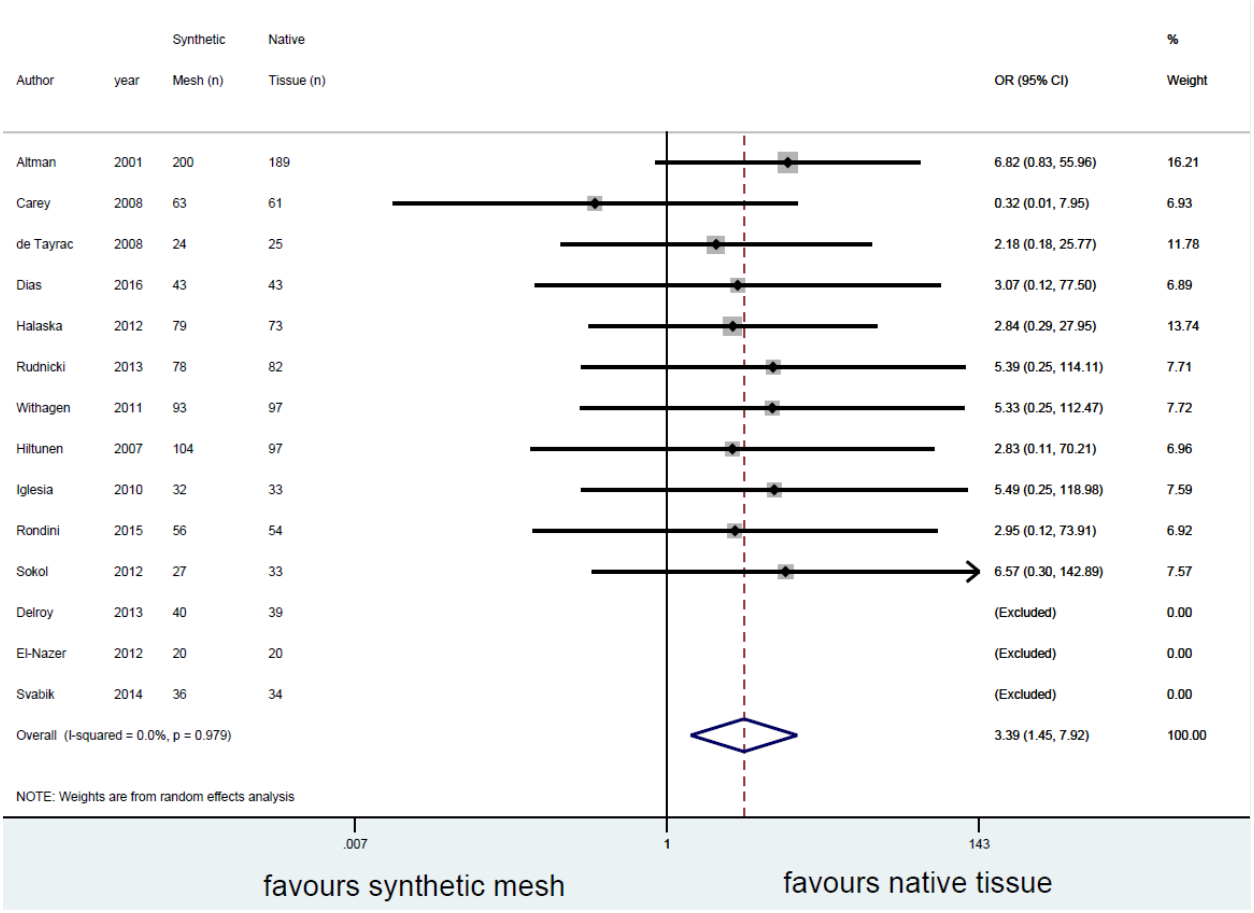

Figure A9: Forest Plot of Blood Loss in POP Patients with Synthetic Mesh vs. Native Tissue

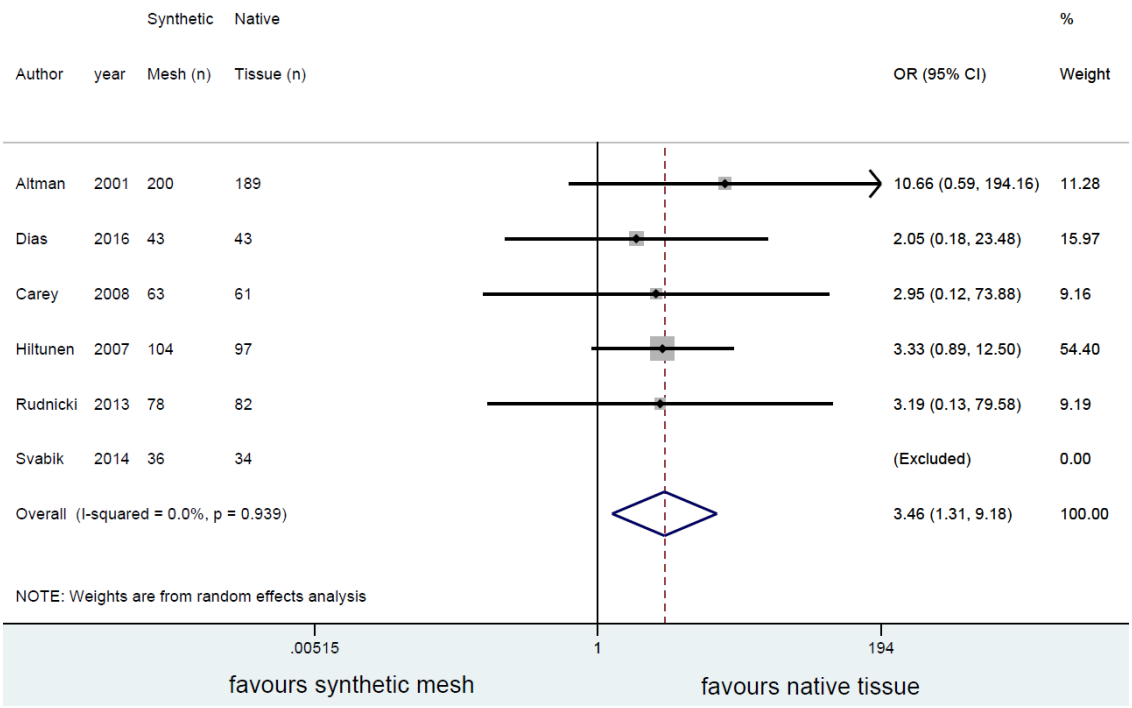

Figure A10: Forest Plot of Need for Blood Transfusion in POP Patients with Synthetic Mesh vs. Native Tissue

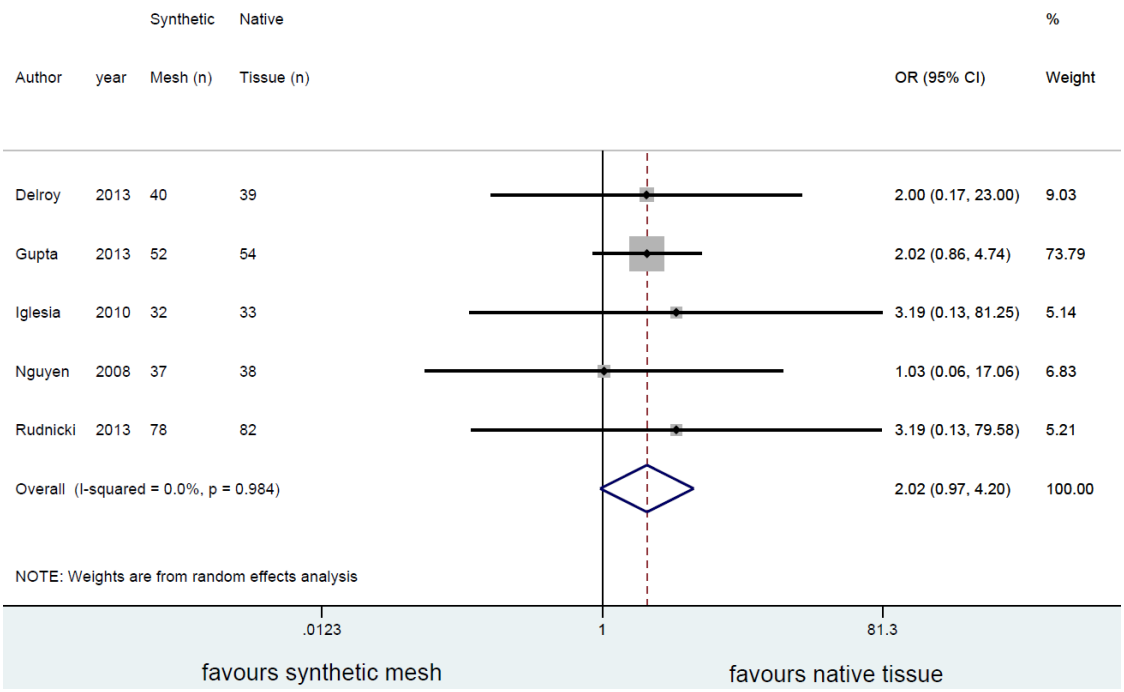

Figure A11: Forest Plot of Urinary Retention in POP Patients with Synthetic Mesh vs. Native Tissue

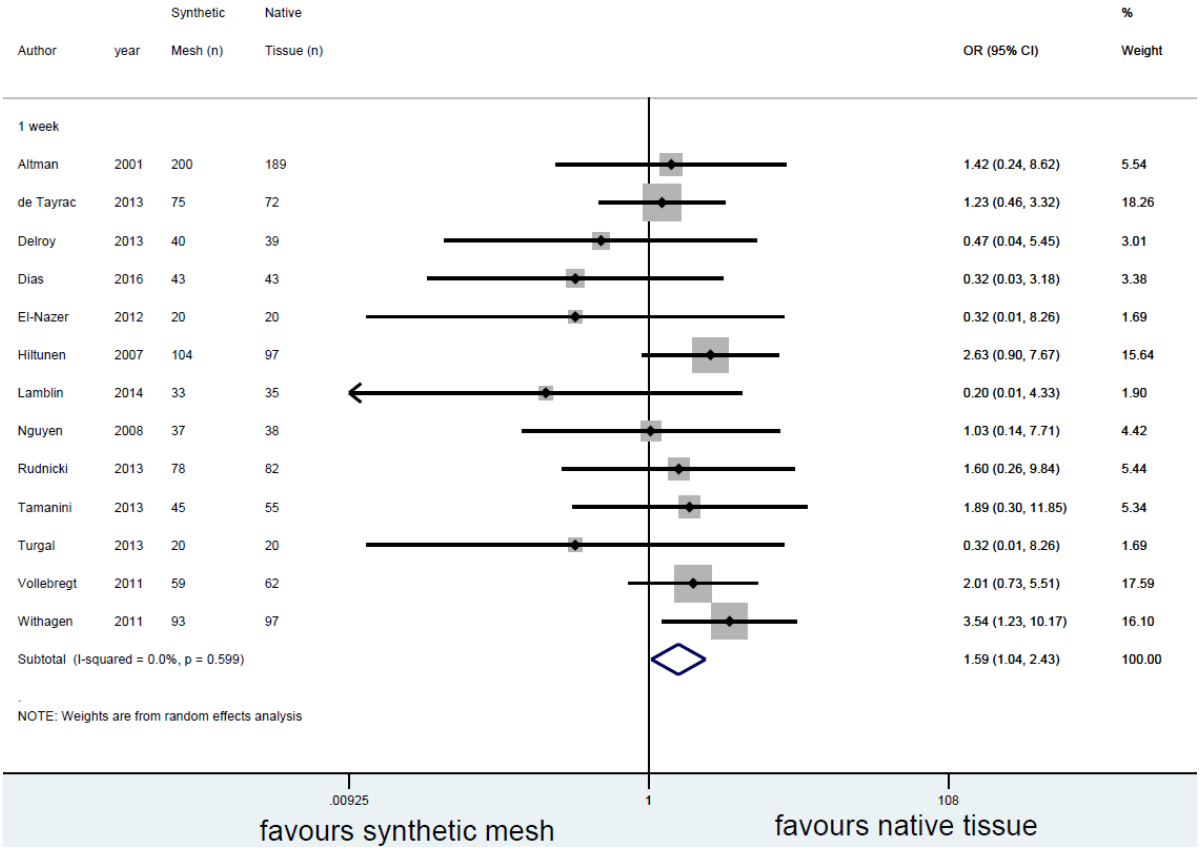

Figure A12: Forest Plot of UTI in POP Patients with Synthetic Mesh vs. Native Tissue

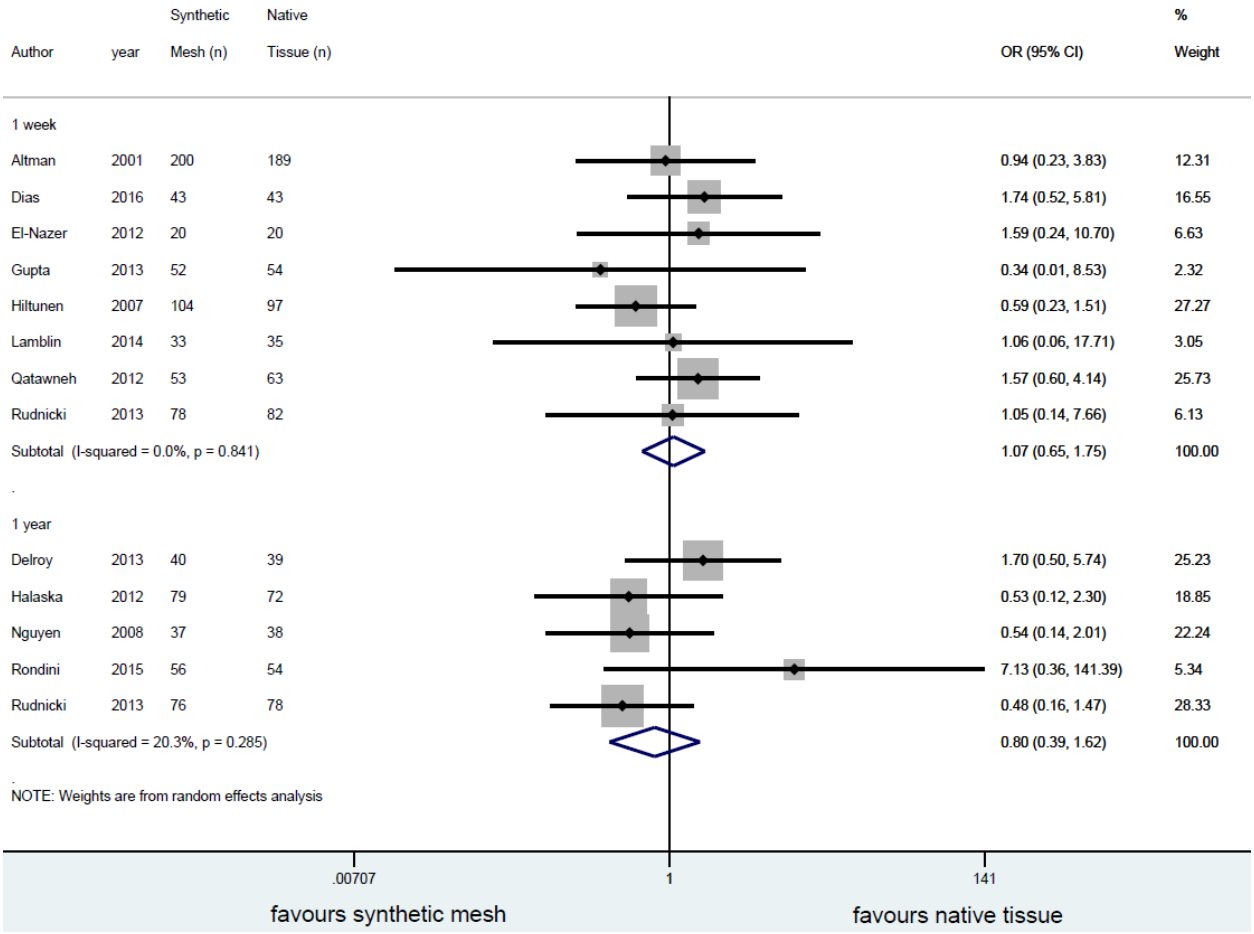

Figure A13: Forest Plot of Fever in POP Patients with Synthetic Mesh vs. Native Tissue

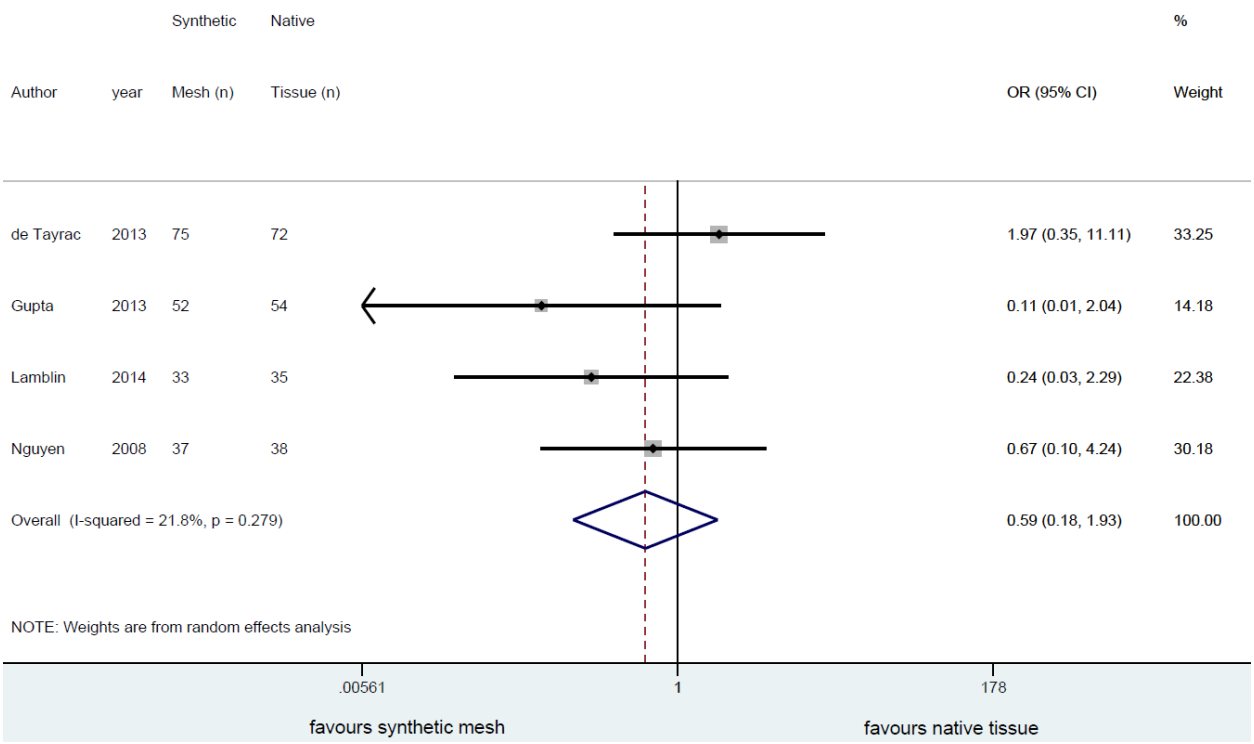

Figure A14: Forest Plot of De Novo Urinary Incontinence in POP Patients with Synthetic Mesh vs. Native Tissue

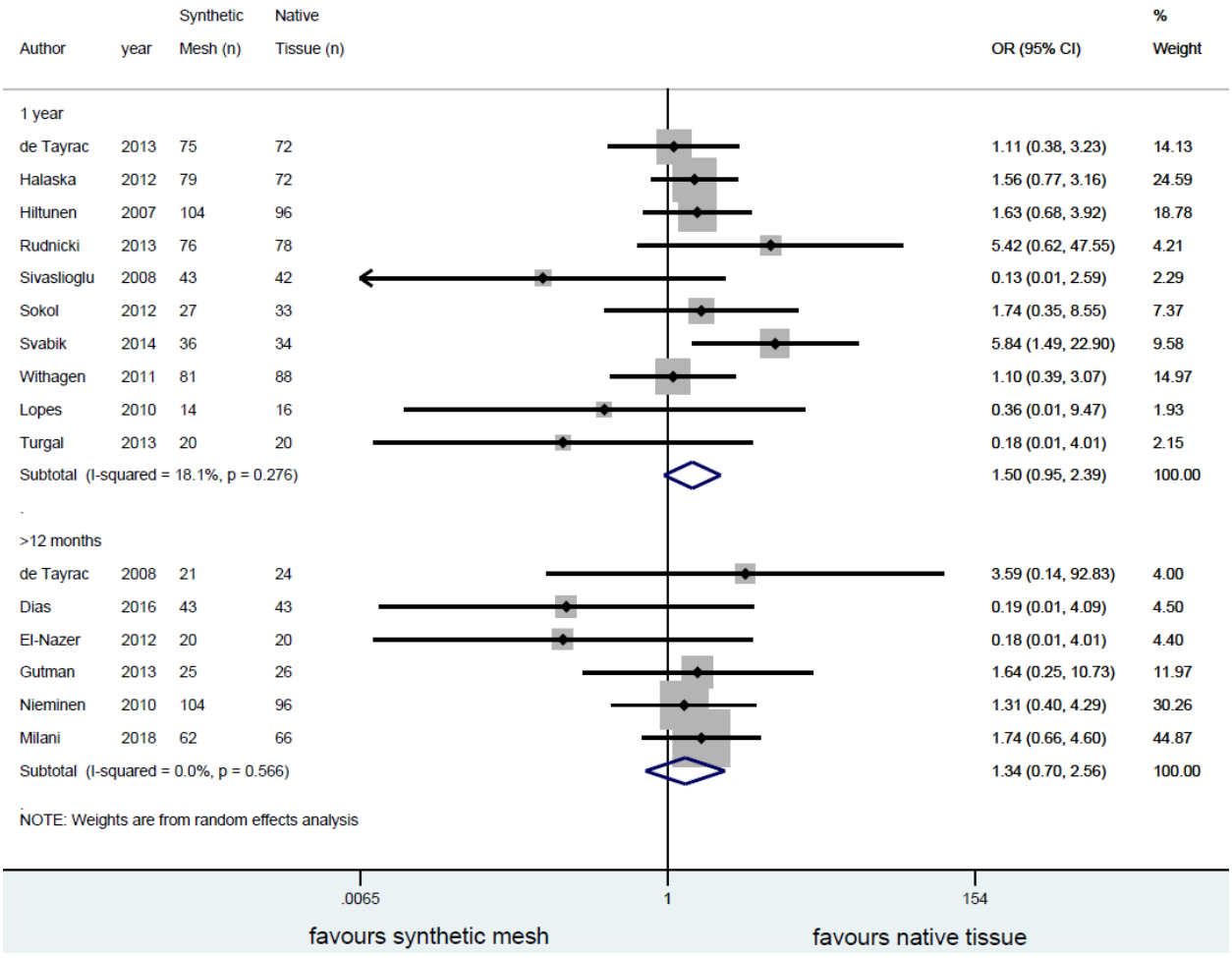

Figure A15: Forest Plot of Dyspareunia in POP Patients with Synthetic Mesh vs. Native Tissue

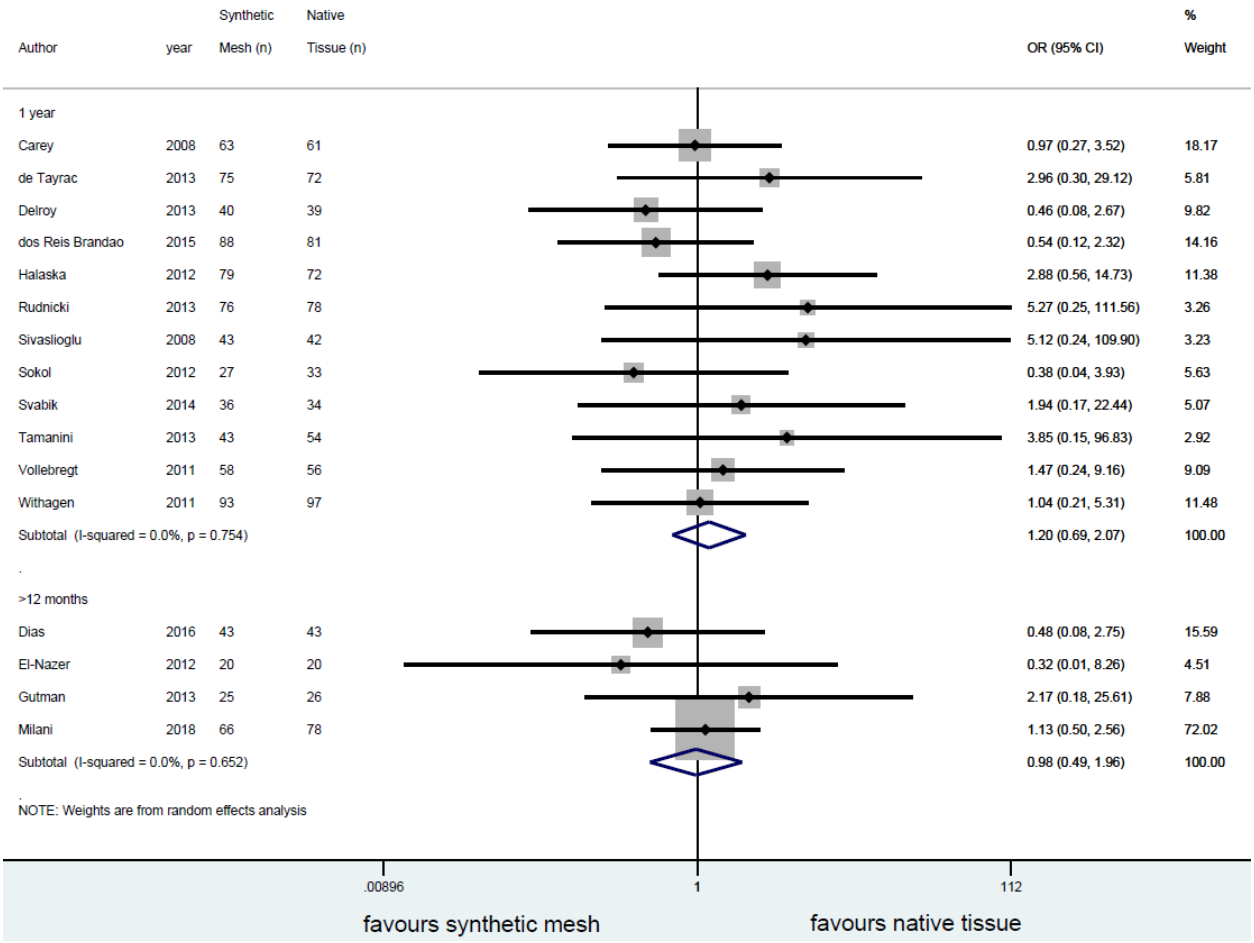

Figure A16: Forest Plot of Pain in POP Patients with Synthetic Mesh vs. Native Tissue

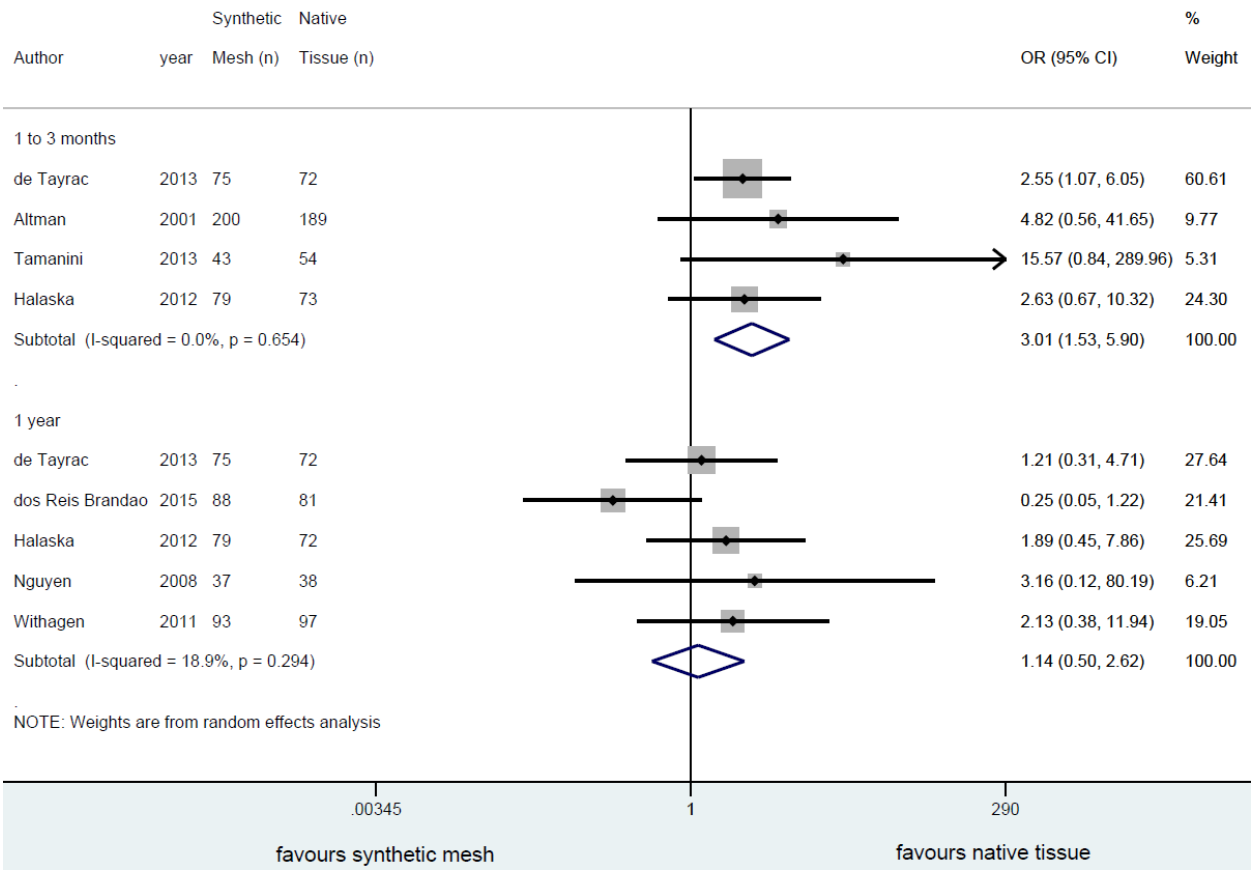

Figure A17: Funnel Plot with 95% Confidence Intervals to Test for Publication Bias in POP Studies of Synthetic Mesh vs. Native Tissue