



incontinence: systematic review and network meta-analysis of randomised controlled trials

Surgical interventions for women with stress urinary

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ABSTRACT

OBJECTIVES

To compare the effectiveness and safety of surgical interventions for women with stress urinary incontinence.

DESIGN

Systematic review and network meta-analysis.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES

Randomised controlled trials evaluating surgical interventions for the treatment of stress urinary incontinence in women.

METHODS

Identification of relevant randomised controlled trials from Cochrane reviews and the Cochrane Incontinence Specialised Register (searched May 2017), which contains trials identified from the Cochrane Central Register of Controlled Trials (CENTRAL), Medline, Medline In-Process, Medline Epub Ahead of Print, CINAHL, ClinicalTrials.gov, and WHO ICTRP. The reference lists of relevant articles were also searched. Primary outcomes were "cure" and "improvement" at 12 months, analysed by means of network meta-analyses, with results presented as the surface under the cumulative ranking curve (SUCRA). Adverse events were analysed using pairwise meta-analyses. Risk of bias was assessed using the Cochrane risk of bias tool. The quality of evidence for network meta-analysis was assessed using the GRADE approach.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Many surgical procedures, including open colposuspension and midurethral slings, are available to treat stress urinary incontinence

A large number of randomised controlled trials and several systematic reviews of randomised controlled trials have been conducted in this clinical area. The current evidence base is, however, fractured, focusing on pairwise comparisons with a lack of comparative data for all surgical interventions, making it difficult to judge which intervention is most effective overall

WHAT THIS STUDY ADDS

This review found that retropubic midurethral sling, transobturator midurethral sling, traditional sling, and open colposuspension are more likely to be effective than other surgical procedures for the treatment of women with stress urinary incontinence

The current evidence from randomised controlled trials is insufficient to establish long term effectiveness and safety of surgical interventions for stress urinary incontinence

RESILITS

175 randomised controlled trials assessing a total of 21 598 women were included. Most studies had high or unclear risk across all risk of bias domains. Network meta-analyses were based on data from 105 trials that reported cure and 120 trials that reported improvement of incontinence symptoms. Results showed that the interventions with highest cure rates were traditional sling, retropubic midurethral sling (MUS), open colposuspension, and transobturator MUS, with rankings of 89.4%, 89.1%, 76.7%, and 64.1%, respectively. Compared with retropubic MUS, the odds ratio of cure for traditional sling was 1.06 (95% credible interval 0.62 to 1.85), for open colposuspension was 0.85 (0.54 to 1.33), and for transobtrurator MUS was 0.74 (0.59 to 0.92). Women were also more likely to experience an improvement in their incontinence symptoms after receiving retropubic MUS or transobturator MUS compared with other surgical procedures. In particular, compared with retropubic MUS, the odds ratio of improvement for transobturator MUS was 0.76 (95% credible interval 0.59 to 0.98), for traditional sling was 0.69 (0.39 to 1.26), and for open colposuspension was 0.65 (0.41 to 1.02). Quality of evidence was moderate for retropubic MUS versus transobturator MUS and low or very low for retropubic MUS versus the other two interventions. Data on adverse events were available mainly for mesh procedures, indicating a higher rate of repeat surgery and groin pain but a lower rate of suprapubic pain, vascular complications, bladder or urethral perforation, and voiding difficulties after transobturator MUS compared with retropubic MUS. Data on adverse events for non-MUS procedures were sparse and showed wide confidence intervals. Long term data were limited.

CONCLUSIONS

Retropubic MUS, transobturator MUS, traditional sling, and open colposuspension are more effective than other procedures for stress urinary incontinence in the short to medium term. Data on long term effectiveness and adverse events are, however, limited, especially around the comparative adverse events profiles of MUS and non-MUS procedures. A better understanding of complications after surgery for stress urinary incontinence is imperative.

SYSTEMATIC REVIEW REGISTRATION PROSPERO CRD42016049339.

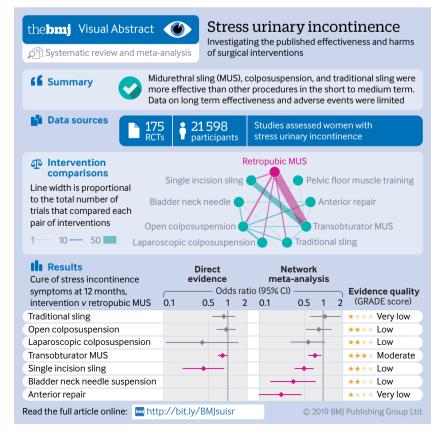
Introduction

Stress urinary incontinence-the leakage of urine resulting from increased intra-abdominal pressure during effort or exertion—is a common and distressing symptom that affects 25-45% of women.¹ Risk factors include previous pregnancy, vaginal delivery, obesity, and postmenopausal status.²⁻⁴ Stress urinary incontinence profoundly impairs quality of life and also imposes a financial burden on women and the healthcare system, although recent estimates are not available.5 6 Estimates from the financial year 1999/2000 of the annual spending on stress urinary incontinence vary from £117m (\$151m; €135m) for treatment costs incurred by the UK National Health Service⁷ to £818m for combined health, personal, and societal costs.8 A US study reported that women with stress urinary incontinence pay about \$750 each year out of pocket for routine care (2006 national resource costs), have a clinically significant reduction in health related quality of life, and are willing to pay nearly \$1400 each year for a cure.9 Although many women delay accessing care because of embarrassment, 10 11 a UK study has estimated that around 15% of women with stress urinary incontinence would seek help. 12 On presentation, care typically consists of initial recommendation to use conservative treatments (eg. pelvic floor muscle training) and advice on lifestyle changes such as weight loss. 13 If this initial approach fails, the next step is to offer surgery to decrease leakage.

Surgical treatment for stress urinary incontinence has evolved over the past two decades, with each procedure developed to overcome the limitations of previous procedures. 14 One of the earliest operations was anterior repair with urethral buttressing sutures. The high failure rate with this and another operation-bladder neck needle suspension-led to the development of open colposuspension, an open abdominal surgery to support the bladder neck and urethra with sutures. This approach was more effective than the other two procedures and for many vears was the standard surgical treatment for stress urinary incontinence. However, it was also associated with a higher perioperative and postoperative morbidity and a longer recovery time than the previous options. Laparoscopic colposuspension developed to overcome some of the problems with open colposuspension-was reported to be slightly less effective than open surgery. The high morbidity, longer recovery, and learning curve associated with laparoscopic colposuspension led to the development of traditional suburethral sling approaches, where a biological or synthetic sling is placed under the urethra and the free ends secured in several ways. These interventions were supplanted by mid-urethral sling (MUS) surgery in the late 1990s; a new minimally invasive, day case surgery that enabled a narrow strip of synthetic mesh (sling) to be placed with no fixation necessary (tension-free). The procedure has been adapted to include retropubic MUS (one vaginal incision and two lower abdominal incisions), transobturator MUS (one vaginal incision and two groin or thigh incisions), and, in recent years, a "minisling" procedure, with only one small vaginal incision (single incision sling). In the surgical treatment of stress urinary incontinence, MUS has become the most common procedure worldwide. 15 16

Since the introduction of MUS for the treatment of stress urinary incontinence, the number of surgeries has increased substantially.¹⁷ A study using NHS England data has shown that the number of surgeries for stress urinary incontinence increased from 8458 in 2000-01 to a peak of 13219 in 2008-09, before decreasing to 11845 in 2012.¹⁵ Similarly, a US study estimated a 27% increase in the rate of surgeries over a 10 year period (2000 to 2009),¹⁸ associated with a rapid adoption of MUS and a corresponding decrease in invasive procedures such as open colposuspension.^{15 18} The lifetime risk of surgery for stress incontinence or pelvic organ prolapse in the US has reportedly increased from 11% in 1995¹⁹⁻²¹ to 20% in 2011.^{21 22}

The safety of mesh implants for stress urinary incontinence and pelvic organ prolapse has, however, come under scrutiny owing to reports of women experiencing severe complications. ¹⁶ ²³ The growing international controversy around vaginal mesh has led to litigation against manufacturers worldwide, forcing withdrawal of some products. ²⁴ ²⁵ In the UK, the Scottish government initially recommended a suspension of vaginal mesh surgery in 2014 ²⁶ and then called for an immediate halt on its use in September 2018. Similarly, in July 2018 the NHS in England announced a national "pause" for vaginal mesh surgery until



enough evidence became available to support its use in clinical practice.²⁷ Ireland followed suit at the same time.²⁸ In all these restrictions, no distinction was made between mesh for prolapse repair and mesh for incontinence procedures.

The impact of the recent suspension on the numbers of women seeking help is currently unclear. It is possible that more invasive surgery could re-emerge as alternative surgical options to MUS. Women, healthcare professionals, and policy makers therefore should be aware of the relative effectiveness and adverse effects of the surgical options for stress urinary incontinence.

Cochrane Incontinence has published eight systematic reviews of randomised controlled trials evaluating nine surgical interventions for the treatment of stress urinary incontinence in women. ²⁹⁻³⁶ These reviews represent the most relevant body of evidence for assessing the effectiveness of the surgical interventions. The reviews are, however, comprised of sets of pairwise comparisons between alternative surgical approaches. Although the review is useful, the plethora of possible comparisons makes interpretation of current evidence by both women and healthcare professionals difficult.

This work is part of a broader National Institute for Health Research Health Technology Assessment funded project, including an economic evaluation and a discrete choice experiment.³⁷ In this paper, we report the clinical effectiveness component, which aimed to bring together all relevant randomised controlled trial evidence from the existing Cochrane reviews and more recently published randomised controlled trials. These data are incorporated into a network meta-analysis comparing the clinical effectiveness of the surgical procedures for stress urinary incontinence. We also reviewed the same evidence base to identify adverse events and complications associated with each type of surgical intervention.

Evidence acquisition

Search strategy and selection criteria

The methods of this evidence synthesis were prespecified in a research protocol; prospectively registered in the PROSPERO database.

We identified relevant randomised controlled trials from eight existing Cochrane reviews, 29-36 two obtained through personal communication (traditional suburethral slings: L Saraswat, 2016; laparoscopic colposuspension: MI Omar, 2016), and we performed an additional literature search (8 June 2017) of the Cochrane Incontinence Specialised Register,³⁸ which contains trials identified from the Cochrane Central Register of Controlled Trials (CENTRAL), Medline, Medline In-Process, Medline Epub Ahead of Print, CINAHL, ClinicalTrials.gov, and WHO ICTRP. We also hand searched journals and conference proceedings and perused the reference lists of relevant articles. No restriction was applied to publication status, year, or language of reports. Details of the search methods are available elsewhere.³⁷ One reviewer (SW) examined the titles and abstracts of studies identified by the literature searches. The same reviewer assessed the full text papers and conference abstracts for potentially relevant studies, and these were checked by another reviewer (MI or MS) using the following criteria for inclusion: randomised controlled trials or quasi-randomised controlled trials (eg, alternate allocation), women with stress urinary incontinence or mixed urinary incontinence with predominant symptoms of stress urinary incontinence (diagnosis as defined by trial investigators), and comparison of two or more surgical interventions. We grouped surgical interventions into nine categories: open retropubic colposuspension, retropubic MUS, transobturator MUS, single incision sling, traditional suburethral sling, laparoscopic colposuspension, bladder neck needle suspension, anterior vaginal repair, and urethral bulking agent treatment. Studies that compared a surgical intervention with a nonsurgical intervention were included if they contributed data to generate network plots of comparisons of interventions. We excluded studies comparing specific technical variations of the relevant surgical procedure (eg, inside-out versus outside-in transobturator MUS). Disagreements on study eligibility for inclusion were resolved by consensus or by an arbitrator.

Outcome measures

Primary outcomes were the number of women with cure, defined as resolution of incontinence symptoms, and the number of women with improvement, defined as any improvement in incontinence symptoms from baseline, including cure. As a variety of measures were used to define cure or improvement, we combined data based on a hierarchy of reported outcomes. For cure, women's self report (subjective measure) was given priority if available, followed by a composite measure of self report and objective indicators, and then by pad tests and urodynamic investigations (objective measures). For improvement, women's self report was preferred when available, followed by women's satisfaction, pad tests, and urodynamic investigations. Cough stress tests and diaries were not considered reliable measures and were excluded. We considered assessments performed at 12 months or closest to 12 months as well as longer term assessments when available. We excluded studies if they only reported assessments within two weeks post-surgery.

Secondary outcomes were the number of women having repeated surgery for incontinence symptoms, adverse events, length of hospital stay, and operation time during the study period as reported by the trial investigators.

Data extraction and assessment of risk of bias

Cochrane reviews provided outcome data from individual randomised controlled trials, study characteristics, and findings of risk of bias assessment. We cross checked the primary outcome data (cure and improvement) against primary trial reports, whereas all other data, including adverse events, were extracted verbatim from the Cochrane reviews. One reviewer (MI

or MS) extracted data from new studies identified by the literature searches, and another reviewer (MI or MS) independently verified these against primary trial reports for accuracy and completeness, with risk of bias assessed using the Cochrane risk of bias tool.³⁹ Authors of Cochrane reviews attempted to contact investigators of primary studies to obtain key missing data; this was not required for the new studies identified by the updated literature searches.

Data synthesis

For the assessment of primary outcomes (cure and improvement of symptoms), we conducted a network meta-analysis and combined direct evidence from headto-head comparisons and indirect comparisons, within a bayesian framework. The network meta-analysis was run in WinBUGS software (version 1.4.3), 40 and further analysis was undertaken using Stata version 14.41 Appendix 1 details the WinBUGS codes. Comparative effectiveness between interventions is reported as the median of posterior distribution of the odds ratio and the 95% credible intervals. Convergence was assessed using Brooks-Gelman-Rubin, trace, and autocorrelation plots. We also estimated the ranking probabilities of the different surgical treatments for cure and improvement using the surface under the cumulative ranking curves (SUCRA), which gives probabilities of each intervention being ranked the best (ie, having the highest proportion of women cured or improved). Consistency between the direct and indirect evidence was assessed by comparing the individual data point's posterior mean deviance contributions for the consistency and inconsistency model and node splitting analysis.42

We included eight surgical procedures in the network meta-analysis. Urethral bulking agent treatment was excluded, as no trials were available that compared bulking agents with other surgical interventions. Pelvic floor muscle training was included to enable indirect comparisons. Trials were excluded if they reported 100% events in all arms (three⁴³⁻⁴⁵ from the cure dataset and four⁴³⁻⁴⁶ from the improvement dataset), as they provided no evidence for the network meta-analysis.

The primary and secondary outcomes were summarised using direct comparison meta-analysis on pairs of interventions for which there was at least one trial. A random effects model was used to account for variability in reporting and timing of outcome measures. Effect sizes are reported as odds ratios with 95% confidence intervals for dichotomous outcomes, and as standardised mean difference with 95% confidence intervals for continuous outcomes. Heterogeneity was assessed using the I² statistic.⁴⁷ Analyses were performed using Stata (version 14).⁴¹

Quality of the evidence for cure and improvement was assessed using the GRADE approach for network meta-analysis⁴⁸ by one reviewer (MIO) and replicated by a second reviewer (MI). GRADE considers five criteria, including study design (judged according to the Cochrane risk of bias tool), inconsistency,

imprecision, indirectness, and publication bias, and has four levels of evidence: high, moderate, low, and very low.⁴⁸

We initially planned to analyse data according to relevant subgroups (ie, urodynamic or symptom based diagnosis of stress urinary incontinence, previous antiincontinence surgery, co-existing vaginal prolapse, and concomitant prolapse surgery). This was not feasible, however, because most trials did not provide information on these characteristics.

Patient and public involvement

This evidence synthesis directly involved two patient representatives. One patient representative (IM) actively contributed to the design (as an advisor for the grant application), conduct (including attendance at project and advisory group meetings), interpretation, and reporting of findings of this evidence synthesis. She is also included as co-author of this manuscript. Another patient representative (SB) was involved as a member of the advisory group for this project. Our work has also been shared with the National Institute for Health and Care Excellence to support the development of relevant guidelines. Other components of this project had a greater involvement of patients and it is planned to disseminate the results further through companion academic papers and directly to relevant health organisations.

Results

Characteristics of included studies

Data from 175 studies were included in the review; of those, 147 were from the Cochrane reviews and 28 from the additional searches. Figure 1 shows the study selection flowchart (PRISMA).

The included studies involved 21598 women and reported 21 treatment comparisons (table 1). Most involved MUS (retropubic or transobturator) as part of the interventions (97 studies). The most common intervention comparisons were transobturator MUS compared with retropubic MUS (58 studies) or compared with single incision slings (39 studies). This was followed by retropubic MUS versus open colposuspension (13 studies), open colposuspension versus laparoscopic colposuspension (12 studies), retropubic MUS versus traditional sling (9 studies), and retropubic MUS versus single incision slings (9 studies). For other comparisons, the number of available studies was small.

The included studies were published between 1978 and 2016. Reflecting the incremental development of surgical treatment for stress urinary incontinence, newer studies (those published after 2000) tended to include MUS as one of the study arms. Similarly, the 28 newly identified studies also focused on MUS (retropubic or transobturator) versus single incision sling (20 studies) or the comparison of two MUS surgeries (retropubic versus transobturator MUS, 4 studies). Thus, data for older procedures such as open colposuspension and traditional slings were derived from relatively older studies.

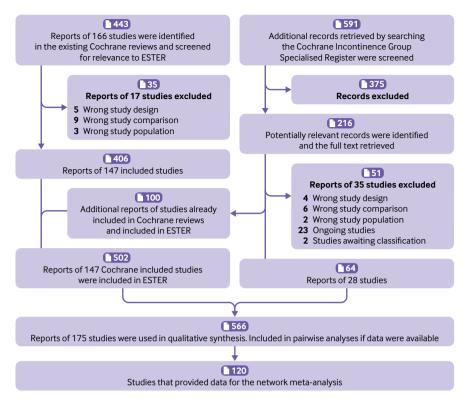


Fig 1 | PRISMA flowchart of study selection

Sample sizes were generally small (median 91 participants per trial, range 15-655). Most studies (134/175, 76%) also had a short duration of follow-up (median 12 months, range 1-126 months), with only 41 studies (23%) having a mean follow-up of three years or longer. Forty three studies (25%) were published only in abstract form.

Table 1 | Number of included studies by treatment comparison

Control group	Intervention group	Total No randomised	No of studies	No of studies from updated search
Retropubic MUS	Transobturator MUS	8876	58	4
Retropubic MUS	Open colposuspension	1240	13	0
Retropubic MUS	Laparoscopic colposuspension	651	8	0
Retropubic MUS	Traditional sling	868	9	0
Retropubic MUS	Single incision sling	1092	9	3
Retropubic MUS	Anterior repair	53	1	0
Transobturator MUS	Open colposuspension	272	4	0
Transobturator MUS	Laparoscopic colposuspension	35	1	0
Transobturator MUS	Traditional sling	141	3	1
Transobturator MUS	Single incision sling	4612	39	17
Transobturator MUS	Anterior repair	120	2	1
Transobturator MUS	Pelvic floor muscle training	460	1	1
Open colposuspension	Laparoscopic colposuspension	1402	12	0
Open colposuspension	Traditional sling	922	7	0
Open colposuspension	Bladder neck needle suspension	639	7	0
Open colposuspension	Anterior repair	690	8	0
Open colposuspension	Pelvic floor muscle training	45	1	0
Traditional sling	Single incision sling	72	1	1
Traditional sling	Urethral injection therapy	45	1	0
Traditional sling	Bladder neck needle suspension	20	1	0
Bladder neck needle suspension	Anterior repair	346	3	0
MUS=mid-urethral sling.				

Most of the included studies had high or unclear risk of bias across all risk of bias domains (table 2), but most notably for allocation concealment (selection bias). Blinding of participants and staff was not feasible owing to the nature of the intervention (surgery); inevitably limiting protection against performance and detection bias in most studies.

Effectiveness results: cure or improvement

Overall, 105 trials were available for the analysis of cure and 120 trials for the analysis of improvement. Figure 2 shows the network diagrams for cure and improvement.

Table 3 shows the results for direct (pairwise meta-analyses) and indirect comparisons (network meta-analysis) and the quality of evidence for cure of incontinence symptoms. The results of the network meta-analysis showed that traditional sling and retropubic MUS were more likely to be effective for curing (resolving) the symptoms of stress urinary incontinence, followed by open colposuspension and transobturator MUS (eg, compared with retropubic MUS, the odds ratio for traditional sling was 1.06 (95% credible interval 0.62 to 1.85), quality of evidence: very low; for open colposuspension was 0.85 (0.54 to 1.33), quality of evidence: low; for transobturator MUS was 0.74 (0.59 to 0.92), quality of evidence: moderate). The data for traditional sling and open colposuspension, however, were from only six studies; the 95% credible intervals around the estimates of effect were wide, and the overall quality of evidence was judged to be very low. The data for transobturator MUS were from 36 studies, and the quality of evidence was judged to be moderate.

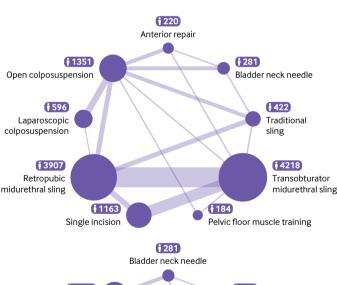
Study numbers do not add up to 175, as three arm trials are shown as pairwise comparisons.

Table 2 | Summary of risk of bias assessment in included studies. Values are numbers (percentages) unless stated otherwise

Assessment item		Risk level		
		Unclear	High	assessed
Random sequence generation (selection bias)	85 (49)	80 (46)	10 (6)	175
Allocation concealment (selection bias)	49 (28)	116 (66)	10 (6)	175
Blinding of participants and staff (performance bias)	8 (5)	123 (73)	37 (22)	168
Blinding of outcome assessment (detection bias): all outcomes	20 (15)	107 (81)	5 (4)	132
Blinding of outcome assessment (detection bias): patient reported outcomes	4 (11)	17 (47)	15 (42)	36
Blinding of outcome assessment (detection bias): clinician measured outcomes	8 (22)	20 (56)	8 (22)	36
Blinding (performance bias and detection bias)	1 (14)	6 (86)	0 (0)	7
Incomplete outcome data (attrition bias): all outcomes	54 (39)	76 (55)	9 (6)	139
Incomplete outcome data (attrition bias): patient reported outcomes	18 (50)	16 (44)	2 (6)	36
Incomplete outcome data (attrition bias): clinician measured outcomes	21 (58)	13 (36)	2 (6)	36
Selective reporting (reporting bias)	24 (65)	7 (19)	6 (16)	37
Other bias	0 (0)	82 (100)	0 (0)	82

Reflecting different publication dates of Cochrane reviews, different versions of Cochrane risk of bias tool were used. Risk of bias domains assessed were not consistent across Cochrane reviews included in this evidence synthesis.

Table 4 shows the results for the direct (pairwise meta-analyses) and indirect comparisons (network meta-analysis) and the quality of evidence for the number of women who experienced an improvement in incontinence symptoms. Retropubic MUS was, on average, more effective than the other surgical interventions (median odds ratio <1.0). In particular, transobturator MUS, traditional sling, and open colposuspension had the highest median odds ratios for improvement against retropubic MUS (eg,



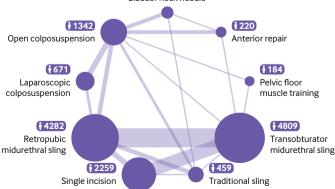


Fig 2 | Network plot for number of women showing cure (top panel) and improvement (bottom panel) of stress urinary incontinence symptoms. Circle size reflects number of women and line width reflects number of direct comparisons

compared with retropubic MUS, the odds ratio for transobturator MUS was 0.76 (95% credible interval 0.59 to 0.98), quality of evidence: moderate; for traditional sling was 0.69 (0.39 to 1.26), quality of evidence: low; for open colposuspension was 0.65 (0.41 to 1.02), quality of evidence: low), although the 95% credible intervals around the estimates of effect for traditional sling and open colposuspension were wide. The quality of evidence for traditional sling and open colposuspension was judged to be low, whereas the quality of evidence for transobturator MUS was judged to be moderate.

The network meta-analysis for cure showed no evidence of inconsistency (see appendix 2). With regard to improvement there was evidence of inconsistency for pelvic floor muscle training compared with transobturator MUS and for traditional sling and pelvic floor muscle training compared with open colposuspension suggesting that the direct and indirect evidence were not in agreement (see appendix 2).

The SUCRA results showed that the interventions with the best probability of achieving the highest cure rates (fig 3) were traditional sling, retropubic MUS, open colposuspension, and transobturator MUS, with an average probability of 89.4%, 89.1%, 76.7%, and 64.1%, respectively. For improvement (fig 4), the same four interventions were most likely to be the most effective, with an average probability of 97%, 76.1%, 67.7%, and 63.8%, for retropubic MUS, transobturator MUS, traditional sling, and open colposuspension, respectively. All the other surgical interventions in the model had less than 50% probability of being in the top rank for both cure and improvement.

Secondary outcomes

Limited data were available for the assessment of secondary outcomes. In particular, meta-analyses of adverse events were hampered by the dearth of available data and the lack of common outcome definitions across individual trials and Cochrane reviews. We summarise the results of meta-analyses when data were reported by more than five studies and for those procedures that were most likely to be most effective based on the results of the network

Intervention 1	Table 5 Results for Hamber of	of women with cure of stress uri	•	· '	Nistronia materialista	
Transobturator MUS Retropubic MUS 36* 0.83 (0.71 to 0.97) 0.74 (0.59 to 0.92) Moderate				Direct evidence	Network meta-analysis	
Depen coliposuspension Retropubic MUS 6* 0.95 (0.68 to 1.32) 0.85 (0.54 to 1.33) Low					` '	• •
Aparoscopic colposuspension Retropubic MUS 2 0.40 (0.11 to 1.45) 0.58 (0.31 to 1.05) Low raditional sling Retropubic MUS 6* 0.87 (0.58 to 1.29) 1.06 (0.62 to 1.85) Very low insigle incision Retropubic MUS 6* 0.42 (0.20 to 0.87) 0.50 (0.66 to 0.70) Low Waladder neck needle suspension Retropubic MUS 0.42 (0.20 to 0.87) 0.50 (0.64 to 1.85) Very low with the company of the company o						Moderate
Traditional sling Retropubic MUS 6* 0.87 (0.58 to 1.29) 1.06 (0.62 to 1.85) Very low single incision Retropubic MUS 6* 0.42 (0.20 to 0.87) 0.50 (0.36 to 0.70) Low sladder neck needle suspension Retropubic MUS 0.34 (0.15 to 0.75) Low sladder neck needle suspension Retropubic MUS 0.22 (0.10 to 0.45) Very low selvic floor muscle training Retropubic MUS 0.22 (0.10 to 0.45) Very low selvic floor muscle training Retropubic MUS 0.22 (0.10 to 0.45) Very low selvic floor muscle training Retropubic MUS 0.22 (0.10 to 0.45) Very low selvic floor muscle training Retropubic MUS 0.29 (0.10 to 0.45) Very low selvic floor muscle training Retropubic MUS 1 0.90 (0.30 to 2.69) 1.16 (0.72 to 1.86) Low parasoscopic colposuspension Transobturator MUS 0.79 (0.42 to 1.46) Low discovered for the self-self-self-self-self-self-self-self-	Open colposuspension				0.85 (0.54 to 1.33)	Low
Single incision Retropubic MUS 6* 0.42 (0.20 to 0.87) 0.50 (0.36 to 0.70) Low	Laparoscopic colposuspension	Retropubic MUS		0.40 (0.11 to 1.45)	0.58 (0.31 to 1.05)	Low
Retropubic MUS 0.34 (0.15 to 0.75) Low	Traditional sling	Retropubic MUS		0.87 (0.58 to 1.29)	1.06 (0.62 to 1.85)	Very low
Netroin repair Retropubic MUS 0.22 (0.10 to 0.45) Very low	Single incision	Retropubic MUS	6*	0.42 (0.20 to 0.87)	0.50 (0.36 to 0.70)	Low
Pervict floor muscle training Retropubic MUS 1	Bladder neck needle suspension	Retropubic MUS			0.34 (0.15 to 0.75)	Low
Depart Colposuspension Transobturator MUS 1 0.90 (0.30 to 2.69) 1.16 (0.72 to 1.86) Low	Anterior repair	Retropubic MUS			0.22 (0.10 to 0.45)	Very low
Aparoscopic colposuspension Transobturator MUS 1 2.00 (0.17 to 23.96) 1.44 (0.81 to 2.62) Very low	Pelvic floor muscle training	Retropubic MUS			0.12 (0.04 to 0.32)	Low
Transobturator MUS 1 2.00 (0.17 to 23.96) 1.44 (0.81 to 2.62) Very low single incision Transobturator MUS 21* 0.74 (0.54 to 1.00) 0.68 (0.51 to 0.91) Low sladder neck needle suspension Transobturator MUS 1 0.50 (0.15 to 1.62) 0.30 (0.14 to 0.62) Very low slevic floor muscle training Transobturator MUS 1 0.50 (0.15 to 1.62) 0.30 (0.14 to 0.62) Very low slevic floor muscle training Transobturator MUS 1 0.20 (0.12 to 0.33) 0.16 (0.06 to 0.43) Low slevic floor muscle training Transobturator MUS 1 0.20 (0.12 to 0.33) 0.16 (0.06 to 0.43) Low slevic floor muscle training Open colposuspension 9 0.74 (0.43 to 1.30) 0.68 (0.42 to 1.08) Low slevic floor muscle suspension Open colposuspension 3* 2.47 (0.73 to 8.40) 1.24 (0.66 to 2.45) Very low slideder neck needle suspension Open colposuspension 3* 0.41 (0.25 to 0.68) 0.40 (0.20 to 0.78) Low slevic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low sleditional sling Laparoscopic colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low sleditional sling Laparoscopic colposuspension 1 0.88 (0.10 to 0.51) 0.14 (0.05 to 0.39) Low sleditional sling Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low sleditional sling Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low sleditional sling Laparoscopic colposuspension 0.88 (0.18 to 0.82) Very low sleditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low sleditional sling 0.47 (0.25 to 0.88) Very low sleditional sling 0.47 (0.25 to 0.88) Very low sleditional sling 0.47 (0.25 to 0.88) Very low sledition muscle training 0.47 (0.09 to 0.40) Very low sledition repair 0.49 incision 0.44 (0.00 to 0.34) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Very low sledition muscle training 0.44 (0.00 to 0.36) Ve	Open colposuspension	Transobturator MUS	1	0.90 (0.30 to 2.69)	1.16 (0.72 to 1.86)	Low
Single incision Transobturator MUS 21* 0.74 (0.54 to 1.00) 0.68 (0.51 to 0.91) Low	Laparoscopic colposuspension	Transobturator MUS			0.79 (0.42 to 1.46)	Low
Deladder neck needle suspension Transobturator MUS 1	Traditional sling	Transobturator MUS	1	2.00 (0.17 to 23.96)	1.44 (0.81 to 2.62)	Very low
Anterior repair Transobturator MUS 1 0.50 (0.15 to 1.62) 0.30 (0.14 to 0.62) Very low Pelvic floor muscle training Transobturator MUS 1 0.20 (0.12 to 0.33) 0.16 (0.06 to 0.43) Low aparoscopic colposuspension Open colposuspension 9 0.74 (0.43 to 1.30) 0.68 (0.42 to 1.08) Low aparoscopic colposuspension 3* 2.47 (0.73 to 8.40) 1.24 (0.66 to 2.45) Very low aparoscopic colposuspension Open colposuspension 0.59 (0.34 to 1.01) Low object of the color	Single incision	Transobturator MUS	21*	0.74 (0.54 to 1.00)	0.68 (0.51 to 0.91)	Low
Pelvic floor muscle training Transobturator MUS 1 0.20 (0.12 to 0.33) 0.16 (0.06 to 0.43) Low	Bladder neck needle suspension	Transobturator MUS			0.46 (0.21 to 1.02)	Very low
Agaroscopic colposuspension Open colposuspension 9 0.74 (0.43 to 1.30) 0.68 (0.42 to 1.08) Low raditional sling Open colposuspension 3* 2.47 (0.73 to 8.40) 1.24 (0.66 to 2.45) Very low slingle incision Open colposuspension 3* 0.41 (0.25 to 0.68) 0.40 (0.20 to 0.78) Low whaterior repair Open colposuspension 3* 0.20 (0.07 to 0.60) 0.26 (0.14 to 0.48) Very low relyic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low raditional sling Laparoscopic colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low raditional sling Laparoscopic colposuspension 1 0.87 (0.44 to 1.70) Low slinder neck needle suspension Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low slinder neck needle suspension 1 0.59 (0.26 to 1.33) Very low slinder neck needle suspension 1 0.59 (0.26 to 1.33) Very low slinder neck needle suspension 1 0.38 (0.18 to 0.82) Very low relationship Laparoscopic colposuspension 0.38 (0.18 to 0.82) Very low relationship Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low relationship Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low relationship Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low relationship Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low relationship 1 0.04 (0.25 to 0.88) Very low relationship 1 0.04 (0.25 to 0.88) Very low relationship 1 0.04 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low relationship 1 0.04 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low relationship 1 0.05 (0.05 to 18.56) Very lo	Anterior repair	Transobturator MUS	1	0.50 (0.15 to 1.62)	0.30 (0.14 to 0.62)	Very low
Traditional sling Open colposuspension 3* 2.47 (0.73 to 8.40) 1.24 (0.66 to 2.45) Very low slingle incision Open colposuspension 0.59 (0.34 to 1.01) Low slingle incision Open colposuspension 3* 0.41 (0.25 to 0.68) 0.40 (0.20 to 0.78) Low slingle incision Open colposuspension 3* 0.20 (0.07 to 0.60) 0.26 (0.14 to 0.48) Very low selvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low raditional sling Laparoscopic colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low slingle incision Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low slingle incision Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low slingle incision Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low slingle incision Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low slingle incision 1 Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low slingle incision 1 Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low slingle incision 1 Traditional sling 0.21 (0.09 to 0.49) Very low slingle incision 1 Traditional sling 0.21 (0.09 to 0.49) Very low slingle incision 1 Traditional sling 0.21 (0.09 to 0.34) Very low slingle incision 1 Traditional sling 0.21 (0.09 to 0.49) Very low slingle incision 0.67 (0.29 to 1.56) Very low slingle incision 0.67 (0.29 to 1.56) Low slingle incision 0.44 (0.20 to 0.96) Very low slingle incision 0.45 (0.20 to 0.65)	Pelvic floor muscle training	Transobturator MUS	1	0.20 (0.12 to 0.33)	0.16 (0.06 to 0.43)	Low
Single incision Open colposuspension 3* 0.41 (0.25 to 0.68) 0.40 (0.20 to 0.78) Low Anterior repair Open colposuspension 3* 0.20 (0.07 to 0.60) 0.26 (0.14 to 0.48) Very low Pelvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low Anterior repair Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low Anterior repair Laparoscopic colposuspension 1.83 (0.86 to 4.04) Very low Open colposuspension 1.83 (0.86 to 4.04) Very low Open colposuspension 1.84 (0.82) Very low Open colposuspension 1.85 (0.86 to 4.04) Very low Open colposuspension 1.85 (0.86 to 4.04) Very low Open colposuspension 1.86 (0.86 to 4.04) Very low Open colposuspension 1.87 (0.86 to 4.04) Very low Open colposuspension 1.88 (0	Laparoscopic colposuspension	Open colposuspension	9	0.74 (0.43 to 1.30)	0.68 (0.42 to 1.08)	Low
Bladder neck needle suspension Open colposuspension 3* 0.41 (0.25 to 0.68) 0.40 (0.20 to 0.78) Low Anterior repair Open colposuspension 3* 0.20 (0.07 to 0.60) 0.26 (0.14 to 0.48) Very low Pelvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low Pelvic floor muscle training Laparoscopic colposuspension 1.83 (0.86 to 4.04) Very low Single incision Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low Delvic floor muscle training Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low Delvic floor muscle training Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low Delvic floor muscle training Laparoscopic colposuspension 0.71 (0.07 to 0.63) Delvic floor muscle training 1.74 (0.25 to 0.88) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.49) Very low Delvic floor muscle training 1.75 (0.09 to 0.45) Low Delvic floor muscle training 1.75 (0.09 to 0.45) Delvic floor muscle training 1.75 (0.09 to 0.45) Very low Delvic floor muscle training 1.75 (0.09 to 0.45) Delvic floor muscle training 1.75 (0.09 to 0.45) Very low Delvic floor muscle training 1.75 (0.09 to 0.45) Delvic floor muscle training 1.75 (0.09	Traditional sling	Open colposuspension	3*	2.47 (0.73 to 8.40)	1.24 (0.66 to 2.45)	Very low
Anterior repair Open colposuspension 3* 0.20 (0.07 to 0.60) 0.26 (0.14 to 0.48) Very low Pelvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low Pelvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low Pelvic floor muscle training Caparoscopic colposuspension 1 0.87 (0.44 to 1.70) Low Pelvic floor muscle training Caparoscopic colposuspension 1 0.59 (0.26 to 1.33) Very low Pelvic floor muscle training Caparoscopic colposuspension 1 0.21 (0.07 to 0.63) Very low Pelvic floor muscle training Caparoscopic colposuspension 1 0.21 (0.07 to 0.63) Very low Pelvic floor muscle training 1 0.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low Pelvic floor muscle training Caparoscopic Capa	Single incision	Open colposuspension			0.59 (0.34 to 1.01)	Low
Pelvic floor muscle training Open colposuspension 1 0.08 (0.01 to 0.51) 0.14 (0.05 to 0.39) Low fraditional sling Laparoscopic colposuspension 1.83 (0.86 to 4.04) Very low single incision Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low sladder neck needle suspension Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low service floor muscle training Laparoscopic colposuspension 0.38 (0.18 to 0.82) Very low service floor muscle training Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low service floor muscle fraining 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.31 (0.09 to 0.49) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.31 (0.09 to 0.49) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.31 (0.09 to 0.34) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.31 (0.09 to 0.49) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.31 (0.09 to 0.49) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.32 (0.30 to 1.36) Very low service floor muscle training 1 1.00 (0.05 to 18.57) 0.35 (0.30 to 1.36) Very low service floor muscle training 1 1.00 (0.05 to 1.55) 0.65 (0.30 to 1.36) Very low service floor muscle training 1 1.00 (0.05 to 1.55) 0.35 (0.10 to 1.17) Low	Bladder neck needle suspension	Open colposuspension	3*	0.41 (0.25 to 0.68)	0.40 (0.20 to 0.78)	Low
Traditional sling Laparoscopic colposuspension 1.83 (0.86 to 4.04) Very low single incision Laparoscopic colposuspension 0.87 (0.44 to 1.70) Low sladder neck needle suspension Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low surferior repair Laparoscopic colposuspension 0.38 (0.18 to 0.82) Very low service floor muscle training Laparoscopic colposuspension 0.21 (0.07 to 0.63) Very low single incision Traditional sling 0.47 (0.25 to 0.88) Very low surferior repair 0.47 (0.25 to 0.88) Very low surferior repair 0.47 (0.25 to 0.88) Very low surferior repair 0.49 Very low service floor muscle training 0.41 (0.09 to 0.49) Very low surferior repair 0.41 (0.04 to 0.34) Very low surferior repair 0.44 (0.20 to 0.96) Very low surferior repair 0.45 (0.08 to 0.65) Low surferior re	Anterior repair	Open colposuspension	3*	0.20 (0.07 to 0.60)	0.26 (0.14 to 0.48)	Very low
Single incision Laparoscopic colposuspension Delvice floor muscle training Eladder neck needle Elevice floor muscle training Elaparoscopic colposuspension Elaparoscopic elapa	Pelvic floor muscle training	Open colposuspension	1	0.08 (0.01 to 0.51)	0.14 (0.05 to 0.39)	Low
Bladder neck needle suspension Laparoscopic colposuspension 0.59 (0.26 to 1.33) Very low on the property of th	Traditional sling	Laparoscopic colposuspension			1.83 (0.86 to 4.04)	Very low
Anterior repair Laparoscopic colposuspension Delvic floor muscle training Laparoscopic colposuspension Delvic floor muscle training Laparoscopic colposuspension Traditional sling Delvic floor muscle training Laparoscopic colposuspension Delvic floor muscle training Traditional sling Delvic floor muscle training Traditional sling Traditional sling Delvic floor muscle training Single incision Delvic floor muscle training Bladder neck needle suspension T* Delvic floor muscle training Bladder neck needle suspension Delvic floor muscle training Delv	Single incision	Laparoscopic colposuspension			0.87 (0.44 to 1.70)	Low
Pelvic floor muscle training Laparoscopic colposuspension 0.21 (0.07 to 0.63) Single incision Traditional sling 0.47 (0.25 to 0.88) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low 1.00 (0.05 to 18.57) 0.32 (0.05 to 0.49) Very low 1.00 (0.05 to 18.57) 0.67 (0.29 to 1.56) Very low 1.00 (0.05 to 18.57) 0.44 (0.20 to 0.96) Very low 1.00 (0.05 to 18.57) 0.24 (0.08 to 0.65) Low 1.00 (0.05 to 18.57) 0.05 (0.30 to 1.36) Very low 1.00 (0.05 to 18.57) 0.35 (0.10 to 1.17) Low 1.00 (0.05 to 18.57) 0.35 (0.10 to 1.17) Low	Bladder neck needle suspension	Laparoscopic colposuspension			0.59 (0.26 to 1.33)	Very low
Single incision Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low Anterior repair Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low Pelvic floor muscle training Traditional sling 0.21 (0.09 to 0.49) Very low Pelvic floor muscle training Traditional sling 0.11 (0.04 to 0.34) Very low Pelvic floor muscle suspension Single incision 0.67 (0.29 to 1.56) Very low Pelvic floor muscle training Single incision 0.24 (0.08 to 0.65) Low Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension Pelvic floor muscle training Bladder neck needle suspension Bladder neck needle suspension D.35 (0.10 to 1.17) Low	Anterior repair	Laparoscopic colposuspension			0.38 (0.18 to 0.82)	Very low
Bladder neck needle Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low Outerior repair Traditional sling 1 1.00 (0.05 to 18.57) 0.32 (0.13 to 0.79) Very low Outerior repair Traditional sling 0.21 (0.09 to 0.49) Very low Outerior repair Outerior Ou	Pelvic floor muscle training	Laparoscopic colposuspension			0.21 (0.07 to 0.63)	
Anterior repair Traditional sling O.21 (0.09 to 0.49) Very low O.11 (0.04 to 0.34) Very low O.67 (0.29 to 1.56) Anterior repair Single incision O.44 (0.20 to 0.96) Very low O.45 (0.30 to 1.36) Very low O.45 (0.30 to 1.36) Very low O.46 (0.30 to 1.36) Very low O.47 (0.30 to 1.36) Very low O.48 (0.30 to 1.36) Very low O.49 (0.35 to 1.55) O.55 (0.30 to 1.36) Very low O.49 (0.35 to 1.36) Very low O.49 (0.30 to 1.36) Very low O.49 (0.35 to 1.36) Very low	Single incision	Traditional sling			0.47 (0.25 to 0.88)	Very low
Pelvic floor muscle training Traditional sling 0.11 (0.04 to 0.34) Very low 0.67 (0.29 to 1.56) Sadder neck needle suspension Single incision 0.67 (0.29 to 1.56) Very low 0.44 (0.20 to 0.96) Very low 0.45 (0.30 to 1.36)	Bladder neck needle	Traditional sling	1	1.00 (0.05 to 18.57)	0.32 (0.13 to 0.79)	Very low
Bladder neck needle suspension Single incision 0.67 (0.29 to 1.56) Anterior repair Single incision 0.44 (0.20 to 0.96) Very low Pelvic floor muscle training Single incision 0.24 (0.08 to 0.65) Low Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Anterior repair	Traditional sling			0.21 (0.09 to 0.49)	Very low
Bladder neck needle suspension Single incision 0.67 (0.29 to 1.56) Anterior repair Single incision 0.44 (0.20 to 0.96) Very low Pelvic floor muscle training Single incision 0.24 (0.08 to 0.65) Low Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Pelvic floor muscle training	Traditional sling			0.11 (0.04 to 0.34)	
Anterior repair Single incision 0.44 (0.20 to 0.96) Very low Pelvic floor muscle training Single incision 0.24 (0.08 to 0.65) Low Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Bladder neck needle suspension	Single incision			0.67 (0.29 to 1.56)	
Pelvic floor muscle training Single incision 0.24 (0.08 to 0.65) Low Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Anterior repair	Single incision			0.44 (0.20 to 0.96)	Very low
Anterior repair Bladder neck needle suspension 1* 0.92 (0.55 to 1.55) 0.65 (0.30 to 1.36) Very low Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Pelvic floor muscle training				0.24 (0.08 to 0.65)	Low
Pelvic floor muscle training Bladder neck needle suspension 0.35 (0.10 to 1.17) Low	Anterior repair		1*	0.92 (0.55 to 1.55)		Very low
	Pelvic floor muscle training	Bladder neck needle suspension			0.35 (0.10 to 1.17)	Low
	Pelvic floor muscle training	Anterior repair			0.55 (0.17 to 1.77)	Very low

MUS=mid-urethral sling.

An odds ratio 1 favours the first treatment—ie, more events (cure) occur. An odds ratio 1 favours the second treatment—ie, fewer events.

meta-analysis (fig 5). Appendix 3 shows the full meta-analysis results for all included studies.

Repeat surgery for incontinence symptoms—rates of repeat surgeries were higher after transobturator MUS than after retropubic MUS at 12 months and more than 60 months, but the pooled analyses showed wide confidence intervals and considerable uncertainty around the estimates of effect (12 months, 21/585 (3.6%) v 14/641 (2.2%), odds ratio 1.37 (95% confidence interval 0.55 to 3.46); more than 60 months, 40/422 (9.4%) v 7/438 (1.5%), 4.06 (0.80 to 20.74)).

Major vascular complications—major vascular complications (as defined by the authors of Cochrane reviews) occurred less often after transobturator MUS than after retropubic MUS (10/2008 (0.5%) v 47/1966 (2.4%), odds ratio 0.36 (0.21 to 0.64)).

Bladder or urethral perforation—rates of bladder or urethral perforation were generally higher with retropubic MUS compared with transobturator MUS (5/3161 (0.2%) v 157/3171 (5.0%), odds ratio 0.15 (0.09 to 0.24)), open colposuspension (5/338 (1.5%) v 28/362 (7.7%), 0.23 (0.10 to 0.55)), and traditional sling (16/305 (5.2%) v 28/276 (10.1%), 0.50 (0.28 to 0.98)).

De novo symptoms of urgency or urgency incontinence—the incidence of de novo urgency and urgency incontinence was similar between transobturator MUS and retropubic MUS (172/2264 (7.6%) v 183/2321 (9.5%), odds ratio 0.93 (0.74 to 1.17)). The results for the comparisons between open colposuspension and retropubic MUS (28/249 (11%) v 22/287 (8%), 1.49 (0.81 to 2.75)) and between single incision sling and transobturator MUS (63/665 (9.5%) v 55/597 (9.2%), 0.98 (0.66 to 1.46)) did not favour either treatment and showed wide confidence intervals.

Voiding difficulties, including urinary retention—voiding difficulties were less common with transobturator MUS than with retropubic MUS (116/3110 (3.7%) v 234/3109 (7.5%), odds ratio 0.51 (0.40 to 0.64)). The summary estimates for open colposuspension versus retropubic MUS (29/374 (7.8%) v 31/413 (7.5%), 0.87 (0.41 to 1.82)) and traditional sling versus retropubic MUS (40/259 (15.4%) v 26/255 (10.2%), 1.46 (0.84 to 2.53)) did not favour one intervention over another and confidence intervals were wide.

^{*}These analyses are also informed by three arm trials, including one comparing retropubic MUS, transobturator MUS, and single incision, one comparing retropubic MUS, open colposuspension, and traditional sling, and two comparing open colposuspension, bladder neck needle, and anterior repair.

Table 4 Results for number of women with improvement of stress urinary incontinence symptoms					
			Direct evidence	Network meta-analysis	GRADE quality of evidence
Treatment 1	Treatment 2	No of trials	Odds ratio (95% CI)	Odds ratio (95% Crl)	
Transobturator MUS	Retropubic MUS	40*	0.86 (0.70 to 1.06)	0.76 (0.59 to 0.98)	Moderate
Open colposuspension	Retropubic MUS	6*	0.83 (0.55 to 1.24)	0.65 (0.41 to 1.02)	Low
Laparoscopic colposuspension	Retropubic MUS	4	0.49 (0.18 to 1.35)	0.52 (0.29 to 0.91)	Low
Traditional sling	Retropubic MUS	6*	0.62 (0.38 to 1.02)	0.69 (0.39 to 1.26)	Low
Single incision	Retropubic MUS	6*	0.42 (0.20 to 0.89)	0.50 (0.35 to 0.71)	Moderate
Bladder neck needle suspension	Retropubic MUS			0.25 (0.11 to 0.58)	Low
Anterior repair	Retropubic MUS			0.18 (0.08 to 0.39)	Very low
Pelvic floor muscle training	Retropubic MUS			0.43 (0.14 to 1.37)	Low
Open colposuspension	Transobturator MUS	1	0.90 (0.30 to 2.69)	0.85 (0.52 to 1.41)	Low
Laparoscopic colpo	Transobturator MUS			0.69 (0.37 to 1.26)	Low
Traditional sling	Transobturator MUS	1	2.00 (0.17 to 23.96)	0.91 (0.49 to 1.72)	Very low
Single incision	Transobturator MUS	28*	0.74 (0.57 to 0.96)	0.66 (0.49 to 0.89)	Moderate
Bladder neck needle suspension	Transobturator MUS			0.33 (0.14 to 0.79)	Very low
Anterior repair	Transobturator MUS	1	1.00 (0.26 to 3.89)	0.24 (0.10 to 0.53)	Very low
Pelvic floor muscle training	Transobturator MUS	1	0.18 (0.10 to 0.33)	0.56 (0.19 to 1.78)	Low
Laparoscopic colposuspension	Open colposuspension	9	0.93 (0.58 to 1.48)	0.81 (0.49 to 1.31)	Low
Traditional sling	Open colposuspension	3*	2.47 (0.73 to 8.40)	1.07 (0.54 to 2.15)	Low
Single incision	Open colposuspension			0.78 (0.44 to 1.36)	Low
Bladder neck needle suspension	Open colposuspension	3*	0.38 (0.22 to 0.63)	0.38 (0.18 to 0.81)	Low
Anterior repair	Open colposuspension	3*	0.20 (0.07 to 0.60)	0.28 (0.14 to 0.55)	Very low
Pelvic floor muscle training	Open colposuspension	1	8.87 (1.66 to 47.25)	0.66 (0.21 to 2.16)	Low
Traditional sling	Laparoscopic colposuspension			1.32 (0.62 to 2.98)	Low
Single incision	Laparoscopic colposuspension			0.97 (0.50 to 1.87)	Low
Bladder neck needle suspension	Laparoscopic colposuspension			0.47 (0.20 to 1.17)	Very low
Anterior repair	Laparoscopic colposuspension			0.34 (0.15 to 0.79)	Very low
Pelvic floor muscle training	Laparoscopic colposuspension			0.82 (0.25 to 2.88)	Very low
Single incision	Traditional sling	1	1.92 (0.65 to 5.64)	0.73 (0.37 to 1.39)	Low
Bladder neck needle suspension	Traditional sling	1	1.00 (0.05 to 18.57)	0.36 (0.13 to 0.95)	Very low
Anterior repair	Traditional sling			0.26 (0.10 to 0.65)	Very low
Pelvic floor muscle training	Traditional sling			0.62 (0.18 to 2.18)	Very low
Bladder neck needle suspension	Single incision			0.49 (0.20 to 1.24)	Very low
Anterior repair	Single incision			0.36 (0.15 to 0.82)	Very low
Pelvic floor muscle training	Single incision			0.84 (0.28 to 2.78)	Low
Anterior repair	Bladder neck needle suspension	1*	0.92 (0.55 to 1.55)	0.72 (0.31 to 1.63)	Very low
Pelvic floor muscle training	Bladder neck needle suspension			1.72 (0.45 to 6.89)	Low
Pelvic floor muscle training	Anterior repair			2.38 (0.65 to 9.30)	Very low

MIIS=mid-urethral slings.

*These analyses are also informed by two three arm trials comparing retropubic MUS, transobturator MUS, and single incision.

An odds ratio >1 favours the first treatment—ie, more events (improvement) occur. An odds ratio <1 favours the second treatment—ie, fewer events.

Tape/mesh extrusion or exposure—the rate of tape/mesh erosion or extrusion appeared similar between transobturator MUS and retropubic MUS (53/2225 (2.4%) v 48/2298 (2.1%), odds ratio 1.10 (0.70 to 1.70)), although confidence intervals were wide. The comparison of single incision sling versus transobturator MUS (19/399 (4.8%) v 13/354 (3.7%), 1.23 (0.57 to 2.68)) did not favour either treatment and showed wide confidence intervals. The rate of exposure to tape or mesh was higher after single incision compared with transobturator MUS, but the summary estimate showed wide confidence intervals (25/494 (5.1%) v 11/463 (2.4%), 1.74 (0.59 to 5.07)).

Pain—transobturator MUS was associated with a higher rate of groin pain compared with retropubic MUS (116/1833 (6.3%) v 24/1798 (1.3%), odds ratio 3.80 (2.45 to 5.89)), but with a lower rate of suprapubic pain (8/687 (1.2%) v 27/681 (4.0%), 0.37 (0.17 to 0.84)). The rate of postoperative pain was higher after retropubic MUS than after single incision sling (176/916 (19.2%) v 64/946 (6.8%), 0.21 (0.12 to 0.39)). The rate of unspecified pain

was higher after transobturator MUS than after single incision sling (17/328 (5.2%) v 4/412 (1.0%), 0.24 (0.06 to 0.92)).

Urinary tract infections—the rate of urinary tract infection was similar between single incision and transobturator MUS (36/544 (6.6%) *v* 26/447 (5.8%), odds ratio 1.11 (0.63 to 1.96)), although there was uncertainty around the summary estimate of effect.

Perioperative complications—perioperative complications were defined in different ways by the authors of Cochrane reviews and could include vascular events, bladder perforation, urinary tract infection, or pain, as well as other unspecified events. Results showed some degree of uncertainty for transobturator MUS versus retropubic MUS (127/1084 (11.7%) ν 150/1153 (13.0%), odds ratio 0.81 (0.55 to 1.19)) and open colposuspension versus retropubic MUS (97/338 (29%) ν 88/363 (24%), 1.19 (0.68 to 2.08)), and did not favour one treatment over the other.

Discussion

Using network meta-analyses we found that retropubic MUS, transobturator MUS, traditional sling, and open

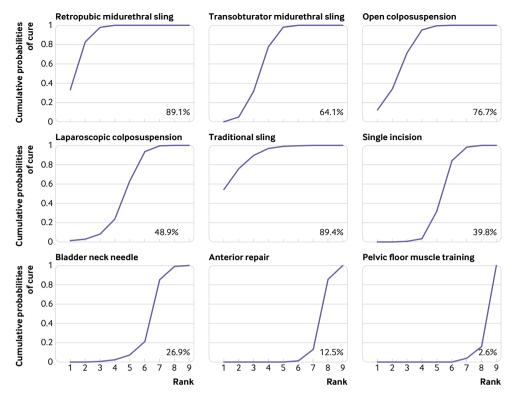


Fig 3 | Surface under cumulative ranking curves (SUCRA) for number of women showing cure of urinary incontinence symptoms

colposuspension are the surgical interventions likely to be most effective in terms of cure of stress urinary incontinence at 12 months or closest to 12 months.

Similarly, for improvement of incontinence symptoms, the same four interventions were likely to be the most effective.

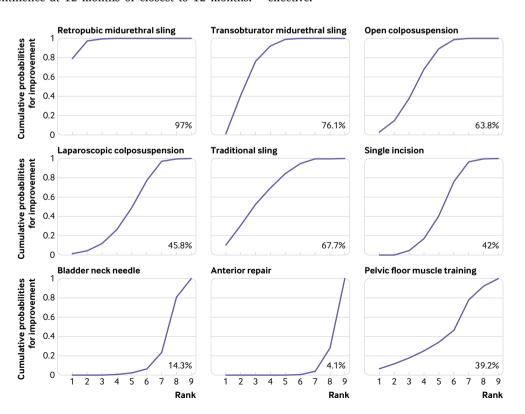


Fig 4 | Surface under cumulative ranking curves (SUCRA) for number of women showing improvement of urinary incontinence symptoms

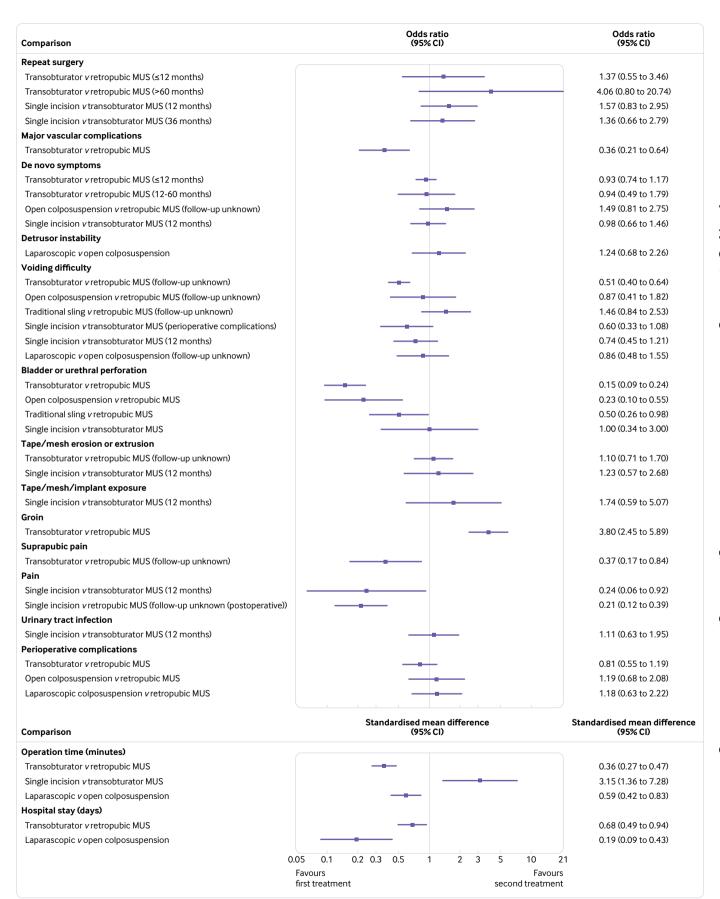


Fig 5 | Repeat surgery for stress urinary incontinence, adverse events, and resource use (only events reported by >5 studies). *Effect estimate is standardised mean difference. MUS=midurethral sling

The safety profile of these procedures showed that transobturator MUS had a higher rate of repeat procedures and a higher occurrence of groin pain than retropubic MUS. Conversely, retropubic MUS was associated with a higher rate of suprapubic pain, as well as a higher rate of major vascular complications, bladder or urethral perforation, and voiding difficulties than transobturator MUS. The rate of tape or mesh erosion or extrusion was similar between the two procedures. The rate of postoperative pain was higher after retropubic MUS than after single incision sling, whereas the rate of unspecified pain was higher after transobturator MUS than after single incision sling.

Retropubic MUS had higher rates of bladder perforation compared with open colposuspension and traditional slings. Available data showed no evidence that retropubic MUS was better or worse than open colposuspension and traditional slings in terms of de novo urgency or urgency incontinence, voiding difficulties, and complications, although confidence intervals were wide, indicating considerable uncertainty. Few studies (<5 studies) reported other intervention comparisons and therefore data were insufficient to draw any meaningful conclusions about relative safety.

Overall completeness and applicability of evidence

Overall, the quality of evidence for the primary outcomes (cure and improvement) was moderate for transobturator MUS versus retropubic MUS or transobturator MUS versus single incision, which were assessed by most of the included studies. The other comparisons had a limited number of studies and quality of evidence was judged to be low or very low. The evidence level was downgraded mainly for high or unclear risk of bias and imprecision of effect estimates.

The available evidence predominantly relates to comparisons involving retropubic MUS, transobturator MUS, and single incision sling. Randomised controlled trials evaluating these mesh procedures were generally carried out in recent years, whereas comparative evidence for previous mainstream procedures was limited and tended to rely on older studies. Indeed, our searches identified no new trials for open or laparoscopic colposuspension compared with traditional slings or MUS. Compared with recent trials on the use of mesh procedures for stress urinary incontinence, older publications referring to traditional procedures tended to be of poorer reporting quality, which could have contributed to lower the evidence level for traditional procedures.

Data for the assessment of complications were sparse for all surgical procedures included in this study, particularly over the long term. There was considerable uncertainty around the estimates of effect, reflecting that in most cases the sample size was small, the event rate was low, and the study period was relatively short.

Strength and limitations in relation to other studies The current debate on mesh surgery encompasses the treatment of both stress urinary incontinence

and pelvic organ prolapse. A statement issued by the US Food and Drug Administration⁴⁹ and the opinion expressed by the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)⁵⁰ acknowledge that mesh associated morbidity is higher when treating pelvic organ prolapse, which uses a greater amount of mesh compared with treating stress urinary incontinence. These statements also accept that MUS surgery for stress urinary incontinence is effective and safe in studies with up to one year of follow-up but acknowledge the lack of long term data. Single incision slings have since been removed from the market in Australia⁵¹ and New Zealand,⁵² but this does not affect MUS for the treatment of stress urinary incontinence.

The rate of long term adverse events for MUS has been investigated in recent cohort studies. A large retrospective cohort study in England published in 2017 investigated the rate of complications of vaginal mesh procedures (including retropubic and transobturator MUS) for the treatment of stress urinary incontinence in more than 92 000 women over a period of eight years. The study estimated that 9.8% of women experienced peri-procedural complications, within 30 days or five years, and 5.9% were readmitted at least once for a further mesh procedure within five years of the index procedure. ¹⁶

Another large observational study published in 2017,²³ as part of a Scottish independent review,²⁶ used routinely reported Scottish hospital inpatient data for more than 16000 women between April 1997 and March 2016. The findings showed that MUS procedures had a lower risk of immediate complications compared with open colposuspension (4%, 2%, and 8% for retropubic MUS, transobturator MUS, and open colposuspension, respectively). Compared with open colposuspension, MUS surgery had a similar risk of readmission for later complications (10%, 9%, 11%, respectively) and repeat surgery (4%, 5%, 6%, respectively) up to five years after the index surgery.²³ Infections and procedure related problems were the most common immediate and later complications after surgery. For procedures involving mesh, further surgery to remove the mesh was another later complication. Based on these findings, the Scottish independent review supports the use of mesh procedures for stress urinary incontinence but considers existing research evidence to be insufficient for safety and performance over the long term.

The NHS England Mesh Oversight Group report published in July 2017 reached a similar conclusion; that mesh procedures for the treatment of stress urinary incontinence are a safe option but evidence was insufficient to determine the extent of long term complications.⁵³ The Mesh Oversight Group made several recommendations to ensure better quality of care. These include improvements to surgical practice and training, raising awareness of possible postoperative complications, and offering quicker and improved access to clinical expertise for women with postoperative complications.⁵³

Such observations are in line with the present study based on published randomised controlled trials. Although our findings show the effectiveness of MUS surgery for stress urinary incontinence to be comparable or superior to traditional surgeries in terms of cure and improvement, evidence is insufficient to assess long term safety. In addition, comparative data on adverse events available for non-mesh procedures for stress urinary incontinence are limited. This raises the question as to whether previous gold standard procedures could and should be considered as valid surgical alternatives, if MUS were no longer an option for women with stress urinary incontinence. Our findings are thus in keeping with the recommendations by the Scottish and English national inquiries, which stressed the importance of better reporting of adverse events and better hospital statistics coding procedures to have a more complete picture of the level and seriousness of complications after surgery. 26 53 Previous systematic reviews have also highlighted this gap, and it is incumbent on future research to ensure that data on adverse events are properly assessed, collected, and analysed.

Strength and limitations of this study

To our knowledge, the current evidence synthesis is the first, comprehensive attempt to estimate the clinical effects and safety across all available surgical interventions for the treatment of women with stress urinary incontinence based on published clinical trials evidence. In particular, the strength of our study includes comprehensive coverage of all published randomised controlled trials on available surgery for stress urinary incontinence, and application of current best practice for undertaking systematic reviews. The network meta-analysis enabled comparison of any pair of surgical procedures under consideration, including those that were not directly compared in clinical trials. This greatly enhances the usefulness of the findings to patients, health professionals, and policy makers. Our multidisciplinary research team comprised clinicians, health service researchers, methodologists, statisticians, and patient representatives, who all contributed to the design and conduct of this evidence synthesis.

One limitation of this study was the lack of information on the severity of stress urinary incontinence in the included studies. The applicability of findings to women with varying degrees of severity is therefore uncertain. Heterogeneity of trial methodology among included studies, and, in particular, a lack of standard outcome measures, also restricted our ability to synthesise evidence. For example, type and definition of complications reported were not consistent across Cochrane reviews. We did not investigate the effects of specific variations in the use of the relevant surgical techniques (eg, inside-out versus outside-in transobturator sling insertion), or types of mesh material, as this was beyond the scope of this evidence synthesis. Another limitation of the

current evidence base is that data on adverse events are collected as part of randomised controlled trials. It is recognised that such trials, which tend to be limited in size and duration, might not be the most appropriate study design to identify long term adverse effects, and particularly rare complications. ⁵⁴ Although two reviewers independently extracted outcome data and risk of bias in the published Cochrane reviews, data extraction and the risk of bias assessment of the 28 new studies identified from the update literature searches were undertaken by one reviewer and verified by a second reviewer against the original trial reports. This was a pragmatic decision owing to time constraints.

Our literature search was conducted in May 2017. We conducted an updated search in November 2018 and identified an additional nine new studies that appeared to meet our inclusion criteria. Of these, only three small studies (<70 participants) include non-MUS procedures (open colposuspension, bladder neck needle suspension, and anterior repair), whereas the other studies focus on mesh procedures (MUS or single incision slings). Given the relatively large number of randomised controlled trials covering MUS or single incision slings already included in the present study, we believed that inclusion of these new studies would not substantially change the network meta-analysis results or overall findings and conclusions.

Implications for practice and research

The current main uncertainty relates to the long term effectiveness and safety of surgical procedures for the treatment of stress urinary incontinence. As with previous reviews, this study highlights the need for further research that pays attention to adverse events that might not be common but could have an important adverse impact on women's quality of life. Given our findings that MUS procedures are among the most effective surgical interventions for stress urinary incontinence, further research must identify which complications arise from the device itself (including type of mesh material used), insertion technique, or whole procedure. Training of surgeons and their ongoing surgical throughput may also need assessment. This would provide women with the necessary, broad range of evidence to help them understand the benefits and harms associated with the device and guide their choice of surgery. The assessment of long term safety and performance of mesh and non-mesh procedures would ideally require a large multicentre trial with an extended follow-up period (ie, a minimum of five years and possibly longer). A more realistic, less expensive, option would be to promote awareness of later complications associated with mesh among health professionals, as well as more precise reporting and recording of complications in national databases and registries to generate uniform and comprehensive data on surgery for stress urinary incontinence. Recently, the UK Royal College of Obstetricians and Gynaecologists welcomed the idea of a mandatory register to record outcomes in all women treated with vaginal mesh to properly monitor the adverse effects of

these implants and have a better understanding of how women are affected.⁵⁵ It has also been suggested that a publicly accessible registry of licensed mesh devices with details of the marketing authorisation and linked evidence would provide useful information on the characteristics and performance of these devices.⁵⁶ ⁵⁷

Another challenge in the current clinical practice is the lack of standardised data collection and the absence of a core outcome set for evaluation of surgery for stress urinary incontinence. This affects primary research and limits aggregation of data from primary studies for evidence synthesis. It is incumbent on stakeholders, incontinence related organisations, and researchers to develop core outcome sets and adverse events profile associated with surgery for stress urinary incontinence that are relevant to women, which will aid high quality, multicentre research.

Conclusions

In the short to medium term (12 months), retropubic MUS, transobturator MUS, traditional sling, and open colposuspension seem to be more effective than other surgical procedures for the treatment of stress urinary incontinence in women, although the quality of evidence was moderate at best and low or very low for most comparisons. Nevertheless, the comparative safety profile of these surgical procedures is still unclear. Evidence was also insufficient to assess the long term effectiveness and safety of surgical treatments. There is a clear need to address the current uncertainty around adverse events after surgery for stress urinary incontinence. Careful consideration of alternative surgical options and a better understanding of their associated risks and harms is a key requirement before opting for alternative, potentially less effective, non-MUS procedures.

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inclusion, and formatted the references. MI and MS evaluated full text papers with SW, extracted data, and assessed risk of bias. MI, MB, JH, and GML selected results for inclusion and planned the statistical analyses. JH performed all network and pairwise meta-analyses under supervision of GML. MIO and MI graded the quality of evidence. DC and LV provided methodological expertise. AM, LS, and PM provided clinical expertise. IM provided a patient perspective. MJ, EM, FB, and LT contributed to various aspects of the broader National Institute for Health Research (NIHR) Health Technology Assessment (HTA) project on which this manuscript is based. MI, MB, DC, and JH drafted the first version of the manuscript. All authors contributed to the revision of the first draft of the manuscript, critically checked its content, and approved its final version. MB was responsible for the integrity and accuracy of the data and is the guarantor. The corresponding author

attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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- $\begin{tabular}{ll} \textbf{Supplementary information:} & appendix 1, WinBUGS \\ code \end{tabular}$
- **Supplementary information:** appendix 2, inconsistency analysis and node-splitting analysis
- **Supplementary information:** appendix 3, full metaanalysis results for included studies