Surgical treatments for women with stress urinary incontinence: the ESTER systematic review and economic evaluation

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Scientific summary

The ESTER systematic review and economic evaluation

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Scientific summary

Background

Urinary incontinence (UI) in women is a distressing and common condition that impairs quality of life and results in a large economic burden to both the NHS and women themselves. The prevalence of UI varies during life but is high in women who have had children and in older women (20–50%). The incidence of stress urinary incontinence (SUI) increases following menopause because of lowered oestrogen levels. Many women access conservative treatment with physiotherapy to deliver pelvic floor muscle training (PFMT) and bladder training initially but, if this fails, surgery is the mainstay of treatment.

Incontinence varies in degree of severity from several drops of urine to complete bladder emptying. It may occur daily, many times a day or only occasionally, perhaps once a month or related to a certain activity. It may be predictable or very unpredictable. These different factors – severity, frequency and predictability – all play a role in evaluating the impact of incontinence on behaviour, treatment choice, quality of life and economic burden. The precise economic burden has proved difficult to calculate.

There are several surgical treatment options for the management of women with SUI, with many variations on most options, but, essentially, they fall into nine distinct categories: anterior vaginal repair; bladder neck needle suspension; open abdominal retropubic colposuspension; laparoscopic retropubic colposuspension; traditional suburethral retropubic sling procedures; mid-urethral sling (MUS) procedures, comprising two distinct categories (retropubic MUS and transobturator MUS); single-incision sling procedures (‘mini-slings’); and periurethral injection (injectable bulking agents).

The high failure rates of early surgical techniques led to the development of colposuspension, but this approach, though efficacious, was associated with greater morbidity and a longer recovery time. The development of laparoscopic colposuspension, a more minimally invasive variation of colposuspension, was considered slightly less effective than the open surgery, but reduced morbidity and length-of-stay outcomes. Innovation and unmet need led to the development of traditional suburethral sling procedures in which a piece of material, which could be biological or synthetic, is placed under the urethra and the free ends secured in one of a number of different ways. The advent of a new minimally invasive technique that enabled the sling/mesh to be placed without tension ushered in a new era of simpler, potentially effective and cheaper treatment.

The number of women having surgery has increased and the choice of operation has changed over the last decade. In 2013–14, Hospital Episode Statistics (HES) data for England show that around 12,000 women had a MUS operation, with around 500 having another type of continence procedure (colposuspension ≈300, traditional slings ≈200) and just over 700 having periurethral injections. In contrast, 10 years earlier just under 7000 women had a MUS operation and ≈1400 had a colposuspension and ≈250 had a traditional sling. Records of how many vaginal mesh implants are implanted or removed per year in women with SUI are scant. However, until recently it would appear that the trend has shifted to the majority of women having a minimally invasive MUS, which in turn has led to a substantial increase in the total number of women having continence surgery. These trends are likely to be driven, in part, by the perception of improved effectiveness and safety. However, over the past decade safety concerns raised by patients over mesh implants have been growing. These concerns led to a patients’ campaign, which was followed by a non-mandatory recommendation by the Scottish Government not to use mesh implants. An independent enquiry followed within Scotland and the suspension of use of any vaginal mesh (including MUSs) was maintained, with UK parliamentary questions, a mandatory national audit and a national campaign, Hear Our Voice, joining the discussions. The debate encompasses the wider use of vaginal mesh in conditions not being considered in this report. There remains a lot of uncertainty surrounding the optimal choice of surgery,

especially related to long-term safety, with recent news and media headlines adding to the ambiguity faced by all involved. What is unclear is the strength of evidence to support the choice of any one surgery over another.

Objectives

The aim of this project was to evaluate the clinical effectiveness, safety and cost-effectiveness of surgical treatments for SUI and stress-predominant mixed urinary incontinence (MUI) in women based on published evidence.

The key objectives were to:

- undertake an evidence synthesis using systematic review methods, including a network meta-analysis (NMA) to estimate the relative clinical effectiveness of the different types of surgery
- undertake a review of safety/adverse effects associated with each type of surgical intervention
- develop a decision model to estimate the cost-effectiveness of surgical treatments for SUI and stress-predominant MUI
- utilise the decision model to undertake a value-of-information (VOI) analysis to assess the need and focus of further primary research
- undertake a discrete choice experiment (DCE) to explore the preferences of women.

Methods of the clinical effectiveness review

A systematic review was undertaken to evaluate the effectiveness and safety of surgical treatment options for SUI. The Cochrane Incontinence Group has published eight systematic reviews assessing nine distinct surgical procedures for the treatment of SUI in women. These existing Cochrane systematic reviews form the foundation of our work and were used to identify studies that meet our prespecified inclusion criteria. An additional search of the Cochrane Incontinence Group Specialised Trials Register was performed (date of last search 8 June 2017) to identify additional trials that met our inclusion criteria but had not been included in the published Cochrane reviews.

To be eligible for inclusion, studies had to compare two or more of the surgical interventions listed above. Studies that compared a surgical intervention with PFMT were also considered suitable for inclusion. The primary effectiveness outcomes of interest were the number of women cured (defined as resolution of clinical symptoms) and the number of women improved (defined as any improvement in clinical symptoms from baseline). Standard systematic review methods were applied. Both pairwise and network meta-analyses were undertaken for the primary outcomes. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was adopted to assess the quality of evidence of the primary outcomes. A number of adverse effect outcomes were also evaluated (i.e. repeat continence surgery, de novo symptoms of urgency or urgency incontinence, bladder or urethral perforation, tape/mesh extrusion or exposure, pain, infection and death) as well as outcomes assessing use of resources (i.e. length of hospital stay and operation time). Pairwise meta-analyses were undertaken for these outcomes.

Results of the clinical effectiveness review

Data from 175 studies were included in the review; 147 were from the Cochrane reviews and 28 were from additional searches. The included studies reported 21 treatment comparisons; the majority involved MUSs (retropubic or transobturator) as part of their interventions ($n = 97$). Open colposuspension versus other surgery was another common comparison (46 studies), followed by laparoscopic colposuspension (21 studies) and traditional sling (20 studies). Only one study comparing injectable bulking agents with

traditional slings was identified. The majority of included studies had high or unclear risk of bias across all risk-of-bias domains, but most notably for allocation concealment (selection bias).

The NMA, which combined evidence from direct head-to-head comparisons and indirect comparisons, included 120 studies that reported data on 'cure' or 'improvement'. The results suggest that retropubic MUS and transobturator MUS are more effective than other surgical procedures for both primary outcomes. Direct evidence was available mainly for the comparisons involving retropubic MUS, transobturator MUS or single-incision sling. Follow-up time was generally short (median of 12 months). However, assessment of adverse events for all procedures was hampered by sparse data. Transobturator MUS had a higher rate of further SUI procedures than retropubic MUS but a lower rate compared with single-incision sling. Rate of tape and mesh exposure was higher after transobturator MUS compared with after retropubic MUS or single-incision sling, whereas the rate of tape or mesh erosion or extrusion was similar between transobturator MUS and retropubic MUS. Retropubic MUS had a higher rate of major vascular complications, voiding difficulties and bladder or urethral perforation than transobturator MUS but a lower rate of groin pain. Rate of postoperative pain was higher after retropubic than single-incision sling whereas rate of unspecified 'pain' was higher after transobturator MUS than single-incision sling. Rate of infection (including urinary tract infection, wound infection and infection related to mesh) was similar between single incision sling and transobturator MUS.

Methods of the discrete choice experiment

An online survey containing a DCE was designed to explore women's preferences for different aspects of surgical treatments. Five attributes framed the hypothetical scenarios: adverse events, chronic pain, length of hospital stay, time to return to normal activities, and risk of recurrence during 12 months after surgery. The analytic approach considered conditional and mixed logit models to account for preference heterogeneity.

Discrete choice experiment results

Responses from a general population sample of women (n = 789) were collected by means of an online survey. The sample consisted of 436 non-patients and 353 patients with one or more types of UI. Results suggest that women in general would prefer a surgical treatment over no surgery. This preference was stronger for patients but was mediated by the respondent's health status. As expected, respondents preferred shorter hospital stays and surgical treatments that were associated with a lower risk of recurrence. Whereas preferences for chronic pain did not vary between groups, patients appeared to care less about adverse events and more about a shorter period to return to normal activities. Infections and pain during intercourse were preferred to the reference category of new urinary symptoms, whereas damage to organs or nerves and voiding difficulties were less preferred.

Methods of the cost-effectiveness model

The review of cost-effectiveness studies identified 17 published modelling studies. However, none of the published models was deemed robust enough to be used within this analysis. Therefore, a new cost-effectiveness model was developed to assess the cost-effectiveness of the different surgical techniques and estimate the VOI to help inform decisions about further research. The model took a lifetime horizon and an NHS and personal social services perspective. A Markov microsimulation (MM) model, with 3-monthly cycles, was developed in TreeAge Pro® (TreeAge Software, Inc., Williamstown, MA, USA). Quality-adjusted life-years (QALYs) and costs were discounted at an annual rate of 3.5%. The model assumes that patients can receive a maximum of three surgical treatments for the treatment of SUI.

The main probabilities for the model were the success rates of the different interventions (i.e. subjective cure), rates of retreatment, complications/adverse events and mortality rates. The clinical evidence was based on the results of the systematic NMA. Long-term effectiveness estimates were extrapolated from these data. EuroQol-5 Dimensions (EQ-5D) utility estimates were derived from UK studies; however, utility decrements for complications were only available from a study based on elicitation from experts. Both deterministic and probabilistic sensitivity analyses were used to explore uncertainty surrounding estimates of cost-effectiveness.

Cost-effectiveness, expected value of perfect information and expected value of partial perfect information results

Over a lifetime time horizon, retropubic MUS is, on average, the least costly (£8099) and the most effective (24.22 QALYs) surgical treatment. With the exception of traditional sling, all other surgical treatments are dominated as they are more costly and less effective than retropubic MUS. Similarly, over a shorter time horizon (10 years), retropubic MUS remains the dominant strategy.

Over a lifetime time horizon, retropubic MUS has a > 26% probability of being cost-effective at a willingness to pay (WTP) threshold value of £20,000. Given the number of comparators, if all of the interventions were comparable we would expect each to have an 11% chance of being cost-effective. The only other strategies with reasonable size probabilities of being cost-effective are traditional sling (≈27% across all WTP values presented, suggesting little difference between retropubic MUS and traditional sling) and open colposuspension (≈14–16% across all WTP thresholds > £10,000). All other strategies have a < 10.5% probability of being cost-effective across all WTP values presented.

Seventeen individual sensitivity/scenario analyses were carried out on the base-case model results.

The expected value of perfect information (EVPI) per woman per year is £11,180. The EVPI for the population was also estimated based on an assumed 15,000 surgical interventions for SUI in the UK each year. Therefore, the population EVPI for 1 year is estimated to be £167.7M. Expected value of partial perfect information (EVPPI) analyses were conducted to estimate the value of removing uncertainty around particular parameters/groups of parameters. The largest value appears to be in removing uncertainty around the complications incidence rates, relative treatment effectiveness and health utility values.

Conclusions

The evidence for the effectiveness and safety of surgical treatments for SUI is limited, making robust conclusions difficult to draw. Overall, studies were rated as being at a high or unclear risk of bias. The NMA based on cure and improvement suggested that retropubic MUS, transobturator MUS and traditional sling were more effective, but this ranking does not consider the complication profile of these techniques. The short- to medium-term adverse event data were sparse. The DCE found that although women with a treatment history had a negative preference for surgical treatments, those with forms of UI that were extremely or moderately limiting in daily activities preferred a surgical treatment option. Further research investigating a woman's choice for or against surgery needs to explore treatment history in greater detail while considering more individual characteristics, including personal beliefs and perceptions that may act as a barrier to seeking professional advice. The economic model suggests that retropubic MUS is the most cost-effective technique based on the current evidence base, although sensitivity analysis to increase mesh complication rates and persistent pain after mesh surgery made traditional sling the more cost-effective option. The VOI analysis supports the need for further research to reduce the current uncertainty around complication rates. The wider literature and recent independent reviews have also highlighted the lack of robust adverse event long-term data.

Recommendations for research

Further robust evidence is required on long-term adverse effects and quality of life. Trials to ascertain these data may not be feasible; it would be more realistic to promote awareness as well as adequate reporting and monitoring of complications among surgeons and health professionals. In addition, more needs to be done to understand and quantify the relationship between different levels of severity of SUI and quality of life.

Most importantly, further research should focus on adverse events that, although infrequent, can have devastating impacts on women's quality of life when they occur.

Study registration

The study is registered as PROSPERO CRD42016049339.

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