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Efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse: systematic review and meta-analysis

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Running title: mesh/grafts for vaginal wall prolapse repair

Abstract

Background The efficacy and safety of mesh/graft in surgery for anterior or posterior pelvic organ prolapse is uncertain.

Objectives To systematically review the efficacy and safety of mesh/graft for anterior or posterior vaginal wall prolapse surgery.

Search strategy Electronic databases and conference proceedings were searched, experts and manufacturers contacted and reference lists of retrieved papers scanned.

Selection criteria Randomised controlled trials (RCTs), non-randomised comparative studies, registries, case series involving at least 50 women, and RCTs published as conference abstracts from 2005 onwards.

Data collection and analysis One reviewer screened titles/abstracts, undertook data extraction, and assessed study quality. Data analysis was conducted for three subgroups: anterior, posterior, and anterior and/or posterior repair (not reported separately).

Results Forty-nine studies involving 4569 women treated with mesh/graft were included. Study quality was generally high. Median follow up was 13 months (range 1 to 51). In anterior repair, there was short-term evidence that mesh/graft (any type) significantly reduced objective prolapse recurrence rates compared with no mesh/graft (relative risk 0.48, 95% CI 0.32-0.72). Non-absorbable synthetic mesh had a significantly lower objective prolapse recurrence rate (8.8%, 48/548) than absorbable synthetic mesh (23.1%, 63/273) and biological graft (17.9%, 186/1041), but a higher erosion rate (10.2%, 68/666) than synthetic mesh (0.7%, 1/147) and biological graft (6.0%, 35/581). There was insufficient information to compare any of the other outcomes regardless of prolapse type.

Conclusion Evidence for most outcomes was too sparse to provide meaningful conclusions. Rigorous long-term RCTs are required to determine the comparative efficacy of using mesh/graft.

(Word count: 249 < 250 as required by the Journal)

Keywords Systematic review, pelvic organ prolapse, mesh, safety, efficacy

Introduction

Pelvic organ prolapse (POP)[1] is common and is seen in 50% of parous women.[2] POP affects a woman's quality of life by its local physical effects (pressure, bulging, heaviness or discomfort) or its effect on urinary, bowel or sexual function. POP can be classified according to the compartment affected as: anterior vaginal wall prolapse (urethrocele, cystocele); posterior vaginal wall prolapse (rectocele, enterocele); prolapse of the cervix or uterus; and prolapse of the vaginal vault (which can only occur after prior hysterectomy). A woman can present with prolapse of one or more of these sites. The present review focuses on anterior and posterior vaginal wall prolapse.

Current treatment options for anterior and posterior vaginal wall prolapse include pelvic floor muscle training (PFMT), use of pessaries (mechanical devices such as rings or shelves), and surgery including anterior or posterior colporrhaphy and site-specific defect repair. Surgery can be augmented with implantation of mesh or graft materials which were first introduced in response to the high failure rate in both primary and secondary procedures: about 30% of women need an operation for recurrent prolapse.[3]

Mesh or graft repair is theoretically suitable for any degree of symptomatic anterior and/or posterior vaginal wall prolapse. In the UK, it has been most often used for women with recurrent prolapse.[4] The technique for inserting mesh or graft varies widely between gynaecologists. It can be individually cut, positioned and sutured using the surgeon's preferred technique over the fascial (a 'mesh inlay'), or the whole vagina can be surrounded by mesh/graft using introducers or commercial available kits ('total mesh').

However, the efficacy and safety of mesh or graft to augment surgery for anterior or posterior pelvic organ prolapse is uncertain[5], especially the occurrence and impact of mesh/graft erosion. The current study reports a rigorous systematic review of the evidence for efficacy and safety issues arising from the use of mesh/graft materials.

There are numerous types of mesh and graft materials available, which vary according to type of material, structure, and physical properties such as absorbability and pore size. In the present review, the term 'mesh' was used for synthetic material and 'graft' was used for biological material; and mesh/graft were classified into four groups: absorbable synthetic mesh (e.g. polyglactin); biological graft (e.g. porcine dermis,); combined absorbable/non-absorbable mesh/graft (termed 'combined' hereafter, e.g. polypropylene mesh coated with absorbable porcine collagen); and non-absorbable synthetic mesh (e.g. polypropylene).

The aims of the present systematic review were to compare: (a) efficacy and safety between procedures using mesh/graft and no mesh/graft, and (b) efficacy and safety between different types of mesh/graft.

This report is based on a systematic review commissioned and funded by the National Institute for Health and Clinical Excellence through its Interventional Procedures Programme.[6]

Methods

Search strategy

Extensive highly sensitive electronic searches were conducted to identify reports (both full text papers and conference abstracts) of published and ongoing studies on the safety and efficacy of mesh/graft used in the repair of pelvic organ prolapse. Searches were restricted to publications from 1980 onwards and to those published in the English language. Studies that reported only procedures without mesh/graft were not identified. Experts in the field were contacted and bibliographies of retrieved papers were scrutinised for additional reports. Eleven manufacturers were identified and contacted for properties of mesh/graft produced and for any studies related to mesh/graft. Full details of the search strategies used are available from the authors.

The databases searched were: Medline (1980-June week 3 2007), Medline In-Process (3rd July 2007), Embase (1980 – 2007 week 26), Biosis (1985- 5th July 2007), Science Citation Index (1980 – 2nd July 2007), Cochrane Controlled Trials Register (The Cochrane Library, Issue 2 2007), ISI Conference Proceedings (1990 – 27th June 2007) as well as current research registers (National Research Register (Issue 2, 2007), Current Controlled Trials (April 2007) and Clinical Trials (April 2007)). Additional databases searched for systematic reviews and other background information included the Cochrane Database of Systematic Reviews (The Cochrane Library, Issue 2, 2007), Database of Abstracts of Reviews of Effectiveness (June 2007) and the HTA Database (June 2007). Conference proceedings of major urogynaecological organisations (including American Urogynecologic Society, American Urological Association, European Association of Urology, European Society of Gynecological Endoscopy, Incontinence Society and International Urogynecological Association) for 2005 onwards were scrutinised for additional reports of randomised controlled trials (RCTs).

Inclusion and exclusion criteria

To try to ensure that all of the relevant studies wound be included, two reviewers (XJ & CG) screened the first 200 titles/abstracts independently. Any discrepancies between the screening results were discussed and consensus was reached. The main reviewer (XJ) then screened the remaining titles/abstracts using the agreed criteria. In cases of doubt, consensus was reached by discussing with the second reviewer (CG). Full text copies of all reports deemed to be potentially relevant were obtained and assessed by the main reviewer for inclusion.

Full-text RCTs, RCTs published as conference abstract from 2005 onwards, non-randomised comparative studies, registry reports, and case series using mesh/graft with at least 50 women were sought. Case series/registries with a mean follow up of at least one year

were included for both efficacy and safety. Case series/registries with a mean follow up of less than one year were included for safety outcomes only. One year was considered a minimum adequate period of time in which to assess the efficacy of prolapse repair.

The participants were women undergoing anterior and/or posterior vaginal wall prolapse surgery. Studies of women with prolapse caused by pelvic trauma, congenital disease, or prolapse after creation of a neovagina were excluded. Women undergoing other concomitant operations, such as hysterectomy or a continence procedure were considered providing the main indication for surgery was anterior or posterior prolapse.

The interventions considered were anterior and/or posterior vaginal wall prolapse repair with mesh/graft. There were no restrictions on type of mesh/graft or technique used. For RCTs and non-randomised comparative studies, the comparators were another operation technique using mesh/graft, or a type of surgery which did not involve mesh/graft.

Primary outcomes for efficacy included persistent prolapse symptoms (subjective failure) and recurrent prolapse at original site (objective failure). For objective failure, outcomes measured by different systems, such as Pelvic Organ Prolapse-Quantification (POP-Q) system and Baden-Walker system, were combined. Secondary outcomes for efficacy included new prolapse at other sites that were free of prolapse at baseline, need for further surgery for prolapse (both recurrent and new), persistent urinary symptoms, persistent bowel symptoms, and persistent dyspareunia. For persistent urinary symptoms, bowel symptoms, and dyspareunia, only women having these symptoms at baseline were considered.

Safety outcomes included blood loss, damage to surrounding organs during the operation, mesh/graft erosion, requirement for a further operation for mesh/graft erosion, new urinary incontinence, new bowel symptoms, new dyspareunia, infection, and other potentially serious adverse effects. For new urinary incontinence, bowel symptoms, and dyspareunia,

only women who were free of these symptoms at baseline were considered for these outcomes.

Data extraction and quality assessment

Data extraction and methodological quality assessment for the RCTs was conducted by two reviewers independently. The main reviewer extracted data and assessed the quality for the remaining studies. Two separate quality assessment checklists were used according to study design. Both checklists were developed by the Review Body for Interventional Procedures (ReBIP; Health Services Research Units at the University of Aberdeen and Sheffield), an independent review body that carries out systematic reviews for the Interventional Procedures Programme of the National Institute for Health and Clinical Excellence (NICE). The checklists were adapted from several sources.[7-9]

Data analysis

Data analysis was conducted for three subgroups of women according to the type of prolapse being repaired: anterior vaginal wall prolapse, posterior vaginal wall prolapse, and anterior and/or posterior vaginal wall repair (where the data were not reported separately).

A meta-analysis of RCTs, using Cochrane Collaboration Review Manager (RevMan 4.2) software, was conducted to directly compare the efficacy and safety of mesh/graft versus no mesh/graft and between different types of mesh/graft.

Crude event rates (and 95% confidence intervals calculated by using binominal distribution approximation) for each of the intervention categories were tabulated by summing across studies for all outcomes, and also according to study design (RCT, non-randomised comparative studies, case series/registries; data by study design not shown) to

facilitate qualitative assessment of potential heterogeneity of event rates across different study designs.

In addition, Bayesian meta-analysis models were used to model the objective failure rates for the different interventions for anterior repair. This was the only outcome with sufficient data to generate a model. RCTs and non-randomised comparative studies were included in the model. Case series were not included to avoid bias from the strong assumption of the equivalence of studies implicit in the crude event rates.[10] The specific type of model used was a (Bayesian) binomial random effects model. Differences between interventions, adjusted for study design, were assessed by the corresponding odds ratio and 95% credible interval (Crl). Crls are the Bayesian equivalent of confidence intervals. 'Head to head' indirect comparisons of the different mesh/graft types, adjusted for study design, was also conducted and reported as odds ratios and 95% CrIs. WinBUGS software was used to produce the models.[11]

Pre-specified subgroup analysis by different mesh types within non-absorbable mesh, i.e. Amid classification type I to IV,[12] was not conducted because most studies did not report the type of mesh, resulting in insufficient data for subgroup analysis. Pre-specified subgroup analysis by 'total mesh' (use of introducers/commercial available kits) and 'mesh inlay' was not conducted due to the lack of data. Potential differences between primary repairs and recurrent prolapse repairs were not assessed because only one study reported exclusively on women having recurrent repairs, and the remainder did not report these subgroups separately.

Results

Number, type and quality of included studies

From the initial 1633 publications identified by the literature search, 49 studies (reported in 67 publications) were included, of which six were full-text RCTs,[13-18] 11 were RCTs available

as conference abstracts,[19-29] seven were non-randomised comparative studies,[30-36] one was a prospective registry,[37] and 24 were case series with a minimum sample size of 50 women.[38-61] Six manufacturers provided data on mesh/graft properties and related studies, all of which had already been identified by our searches. The screening process is summarised in Figure 1. For the 17 RCTs, 14 compared mesh/graft with no mesh/graft, and three[13,22,26] compared different types of mesh/graft. Appendix 1 shows details of study design, methods, participants, and interventions. Seven ongoing RCTs[62-67] (Brandao: Personal communication, A Griffin, Johnson & Johnson, Aug 2007) and one ongoing registry[68] were also identified.

The included studies took place during the period 1996 – 2007 and in 12 countries. The median follow up was 13 months (range 1 to 51 months). In total, 4569 women were treated with mesh or graft. In studies providing this information, the mean age was 64 years (range 24 to 96 years). Seventy-two percent of repairs were primary procedures. The most common use of mesh or graft was for anterior repair (54%, 2472/4569). Overall, just over half of the studies used non-absorbable synthetic mesh (51%, 2320/4569) but for anterior repair alone and for posterior repair alone, biological graft was the most common alternative (46% (1124/2472) and 29% (121/417) respectively). The surgical techniques for implanting mesh/graft varied considerably across studies. Fifty-six percent (1404/2497) of women had a concomitant procedure for urinary incontinence and 37% (953/2583) had a hysterectomy.

The methodological quality was assessed for only the full text studies. For the six RCTs, adequate approaches to sequence generation for randomisation were reported in all studies except one;[13] concealment of treatment allocation was adequate in all RCTs except two;[13,17] all follow-up periods were one year or more; all studies used intention-to-treat analysis in that women were analysed in the groups to which they were randomised. For the seven included non-randomised comparative studies, mean follow up was less than one year

in two studies.[31,36] For the registry and case series, mean follow up was one year or more in 17 studies. The drop-out rates ranged from 0 to 30%.

Anterior vaginal wall prolapse repair

Thirty studies involving 2472 women provided data on the use of mesh/graft for anterior repair (five full text RCTs,[13-15,17,18] seven RCTs available as conference abstracts,[19,20,22-25,29] four non-randomised comparative studies,[30,33-35] one registry,[37] and 13 case series[38,44,46,49-52,55-60]). Four studies used absorbable synthetic mesh,[13,17,18,59] 14 studies used biological graft, [13-15,22,24,25,30,33,35,50-52,57,60] one study used combined mesh/graft,[38] and 14 studies used non-absorbable synthetic mesh.[19,20,22,23,29,33,34,37,44,46,49,55,56,58] The median follow-up time was 14 months (range 1 to 38 months). Two RCTs[13,22] and one non-randomised comparative study[33] compared different types of mesh/graft and the others compared mesh/graft with no mesh/graft.

Efficacy

There were too few data reported for most outcomes to draw reliable conclusions (Table 1).

However, in 10 RCTs involving 1148 women, there was some evidence that mesh/graft (any type) was better than no mesh for preventing objectively determined recurrence of anterior prolapse (77/557 vs. 179/591; RR 0.48, 95% CI 0.32 to 0.72, Figure 2). When evidence from other study types was also considered, there was a trend in the crude objective failure rates (Table 2) with procedures not using mesh/graft having the highest failure rate (184/640, 29%, 95% CI 25 to 32%), followed by procedures with absorbable synthetic mesh (63/273, 23%, 95% CI19 to 28%), biological graft (186/1041, 18%, 95% CI16 to 20%), and non-absorbable synthetic mesh (48/548, 9%, 95% CI 7 to 11%). Compared to

procedures not using mesh/graft, the numbers need to treat (NNT) were 17 for absorbable synthetic mesh, 9 for biological graft, and 5 for non-absorbable synthetic mesh.

Bayesian meta-analysis based on the evidence from the 10 RCTs and five non-randomised comparative studies showed that procedures without mesh/graft had significantly higher objective failure rates than procedures with biological graft or non-absorbable synthetic mesh. Comparisons between different types of mesh showed that non-absorbable synthetic mesh had statistically significantly lower objective failure rates than absorbable synthetic mesh (41/344 vs. 52/161; OR 0.23, 95% CrI 0.12 to 0.44) and biological graft (41/344 vs. 120/555; OR 0.37, 95% CrI 0.23 to 0.59) (Table 2).

This trend appeared to be supported by the need for re-operation (for recurrent and new prolapse) which was highest in women treated with absorbable synthetic mesh (9% (16/174)), compared with 3% (9/280) for biological grafts and 1% (3/234) for non-absorbable synthetic mesh (Table 1). However, counter-intuitively, the re-operation rate for women with no mesh was lower (2% (2/85)); this estimate is based on one small study with short follow up (one year) and as such should be interpreted with caution.

Safety

For anterior repair, there were too few data on safety outcomes to identify or rule out important adverse effects related to the use of mesh/graft either because the studies were not sufficiently large or the adverse effects were rare (Table 3).

There was some evidence to support the trends mentioned above (for objective failure rates and re-operation rates). Mesh/graft erosion increased from 0.7% (1/147, 95% CI 0.1 to 3.8) for absorbable synthetic mesh to 6.0% (35/581, 95% CI 4.4% to 8.3%) for biological graft, and to 10.2% (68/666, 95% CI 8.1 to 12.7%) for non-absorbable synthetic mesh. Women with a non-absorbable synthetic mesh repair were also most likely to require an

operation to remove it partially or completely because of mesh/graft erosion (23/347, 6.6%, 95% CI 4.5 to 9.7) than for either absorbable synthetic mesh (1/35, 2.9%, 95% CI 0 to 3.3) or for biological graft 2.6%, (4/154, 95% CI 1 to 6.5).

Posterior vaginal wall prolapse repair

Only nine studies involving 417 women treated with mesh/graft reported data on the use of mesh/graft in posterior repair (two full-text RCTs,[16,17] one RCT available as a conference abstract,[26] two non-randomised comparative studies,[31,32] one registry report,[37] and three case series[53-55]). Three studies used absorbable synthetic mesh,[17,26,32] three used biological graft,[16,31,53] two used combined mesh/graft,[26,54] and two studies used non-absorbable synthetic mesh.[37,55] No RCTs or non-randomised comparative studies compared different types of mesh/graft for posterior repair. The median follow up was 12 months (range 1 to 17 months).

There were too few data reported for any of the outcomes to draw reliable conclusions or to carry out further statistical analyses (Table 4 and 5).

Anterior and/or posterior vaginal wall prolapse repair

Fourteen studies involving 1680 women treated with mesh/graft reported data on the use of mesh/graft in anterior and/or posterior repair (three RCTs available as conference abstracts,[21,27,28] one non-randomised comparative study,[36] one registry report,[37] and nine case series[39-43,45,47,48,61]). One study used absorbable synthetic mesh,[21] none of the studies used biological graft, one study used a combined mesh/graft,[45] 10 studies used non-absorbable synthetic mesh,[27,28,37,40-43,47,48,61] and two studies used more than one of the above types of mesh/graft.[36,39] None of the RCTs or non-randomised comparative studies compared different types of mesh or grafts. The median follow up was 13 months (range 1 to 51 months).

For objective failure, there was a trend in the crude events rates (Table 6) with procedures not using mesh/graft having the highest failure rate (27/109, 25%, 95% CI 18 to 34%), followed by procedures with absorbable synthetic mesh (2/26, 8%, 95% CI 2 to 24%), combined mesh/graft (11/143, 8%, 95% CI 4 to 13%), and non-absorbable synthetic mesh (41/645, 6%, 95% CI 5 to 9%). Compared to procedures not using mesh/graft, the numbers need to treat (NNT) were six for absorbable synthetic mesh, six for biological graft, and five for non-absorbable synthetic mesh. There were too few data (only three RCTs) to conduct Bayesian meta-analysis and too few data on any of the other outcomes to identify or rule out important adverse effects related to the use of mesh/graft (Table 6 and 7).

Discussion

Summary of the evidence

In anterior vaginal wall prolapse repair, there was some short-term evidence suggesting that mesh/graft (any type) could reduce objective prolapse recurrence rates compared with no mesh/graft. In the comparison between different types of mesh/graft, non-absorbable synthetic mesh had statistically significantly lower objective failure rates than absorbable synthetic mesh and biological graft. However, there was no information about efficacy in the longer term.

While there might be some evidence of differences in objective efficacy related to the use of mesh, these must be considered alongside any safety concerns. There was some evidence to suggest that mesh/graft may cause problems with erosion and a subsequent need for operations to remove the foreign material. However, the numbers were too few to conduct statistical analyses to compare the erosion rates between different types of mesh or graft.

Methodology

315 In the present review, RCTs, non-randomised comparative studies, and large case series
316 (sample size ≥ 50) were included. The results were considered generalisable as the majority
317 of studies recruited participants from routine practice without restriction on the severity of
318 prolapse or other patient characteristics.

319 As this review focused on the efficacy and safety of treatments involving mesh/graft,
320 studies reporting only procedures without mesh/graft were not systematically searched for.
321 Data on no-mesh/graft treatments came only from the control groups of RCTs and non-
322 randomised comparative studies only. Therefore the results for 'no-mesh/graft' were not
323 derived from a comprehensive literature search and should be interpreted with caution.
324 However, considering that there was insufficient evidence for most outcomes involving
325 procedures with mesh/graft, including studies reporting only procedures without mesh/graft
326 would increase the accuracy of the estimates for the 'no mesh/graft' group, but would not
327 impact on the mesh/graft comparisons or change the conclusions of the review.

328 Categorising some of the reported outcomes was problematic. For instance, cut-off
329 points used to determine objective failure rates varied between studies. All types of infections
330 such as urinary tract infection, wound infection and pelvic abscess were grouped together.

331 Apart from conducting meta-analysis of the RCTs in RevMan to compare the efficacy
332 and safety between different types of mesh/graft, crude event rates from the RCTs and non-
333 randomised comparative studies were calculated by treating each arm in effect as a case series.
334 The rate from each arm was then combined with those from other such 'case series' derived
335 from comparative studies and from case series reporting mesh/graft. This was considered an
336 alternative way to compare all of the available mesh/graft types. The analyses were adjusted
337 to account for bias from non-randomised comparative studies and case series, which are more
338 prone to systematic biases than RCTs.

It was impossible to determine whether safety and efficacy of mesh differs between primary repair and recurrent prolapse repair. Of the 49 included studies, 12 reported a case mix (72% primary and 28% secondary operations) in 1359 women but no study reported the outcome data separately for the two groups. These data, however, suggest that many gynaecologists are already using mesh in women for primary repair. Only one[31] of the included studies reported exclusively on women having recurrent repair (a small comparative study of only 12 women in each of two arms).

Efficacy

One year was considered as an adequate minimum period of time to assess the efficacy of prolapse repair. However, even one year outcomes are too early to judge whether prolapse surgery is successful in the longer term. The mean time to first re-operation is reported in the literature as 12 years,[3] and therefore failure at one year should not be regarded as an adequate representation of efficacy. Prospective studies would require extended follow up to assess meaningful mesh/graft failure.

The conundrum in prolapse surgery is that objective prolapse recurrence is not necessarily related to continuation of prolapse symptoms (subjective failure). It is increasingly recognised that in prolapse surgery, subjective failure is a more appropriate outcome measure of efficacy than objective failure. It is also recognised that criteria for measuring such subjective prolapse outcomes are difficult to quantify and the most appropriate methods are still being evaluated. In the present review, only a few studies reported data on subjective prolapse symptoms and other genitourinary symptoms of importance to women (urinary, bowel and sexual function).

Safety

The clinical importance of mesh/graft erosion was difficult to assess. The diagnosis was both problematic as different authors used different definitions (mesh erosion, vaginal mesh extrusion, minor mesh exposure), and its clinical impact controversial as some gynaecologists operated on erosions[15,18,33,34,40-49,54,61] whereas others treated erosions with debridement, vaginal oestrogens, antiseptics or antibiotics.[36,41,48,57,60]

One of the anecdotally cited contra-indications for the use of mesh is the likelihood of dyspareunia. This outcome is more problematic to measure because some women are not sexually active, but not all studies take this factor into account when reporting their sexual function data. Secondly, some women may be sexually inactive because of their prolapse surgery (especially when the outcome is measured within 6 months of operation). Thirdly, many studies do not measure or report this outcome at all. Two outcomes were used in the present review to make the best estimates: persistent dyspareunia in women having dyspareunia at baseline (efficacy), and de novo dyspareunia in women without dyspareunia at baseline (safety). However, few studies reported such data.

Some adverse effects occurred infrequently: in consequence their estimated event rates may be prone to random error. Some of the safety outcomes, such as blood loss, may not be due only to the repair of vaginal wall prolapse, but also to concomitant procedures such as those for urinary incontinence or hysterectomy.

Although the numbers were not sufficient to perform meaningful sub-group analyses by 'total mesh' (use of introducers/commercial available kits) and 'mesh inlay', the use of blind introducers has given rise to some concern. These have only been used to date with non-absorbable synthetic mesh. In total, there were 6/476 (1.3%) events of damage to surrounding organs for anterior repair, 6/276 (2.2%) for posterior repair and 16/684 (2.3%) for anterior and/or posterior repair, giving a total of 28/1436 (1.9%). Of the 28 events, half were associated with an introducer kit.

Conclusions and implications

In general, the evidence for most efficacy and safety outcomes was too sparse to provide meaningful conclusions about the use of mesh/graft in anterior and/or posterior vaginal wall prolapse surgery.

Rigorous RCTs are required to determine the comparative efficacy of using mesh/graft and its optimal place in clinical practice. The RCTs should primarily compare the subjective failure rate in procedures using mesh/graft versus those without mesh/graft, and between different types of mesh/graft; use validated patient-reported outcome measures; have sufficient power to detect clinically meaningful differences in both efficacy and safety; and have the capacity to assess outcomes in the long term (at least 5 years), including cost-effectiveness.

In addition, prospective data collection should be considered in which the operative and clinical details of women undergoing prolapse surgery with mesh/graft can be recorded so that sufficient efficacy and safety data can be gathered to guide the use of mesh or grafts in the future.

(Word count: 4088)

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Disclosure of Interests

CG and CB were authors on one conference abstract that was included in the review.

Contribution to Authorship

XJ screened the search results, contacted manufactures, assessed studies for inclusion, undertook data abstraction and quality assessment, conducted meta-analysis, and drafted the review. CG drafted the scope, determined outcome categories, provided advice on assessing studies for inclusion, conducting meta-analysis, and on drafting of the review, drafted the discussion, and commented on drafts of the review. GM commented on the scope of the review, drafted letters for contacting mesh/graft manufacturers for additional information, supervised the conduct of the review, and commented on drafts of the review. GMac conducted the statistical analysis, drafted the data analysis section of the review, and commented on drafts of the review. CF developed and ran the literature search strategies, obtained papers, formatted the references, and drafted sections concerning search strategies and search results. CB provided specialist advice on classification of prolapse and mesh/graft

types, and commented on drafts of the review. JB supervised the conduct of the review, and commented on drafts of the review.

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References

1 Brubaker L, Bump R, Jacquetin B, Schuessler B, Weidner A, Zimmern P et al. *Pelvic organ prolapse.* Incontinence: 2nd International Consultation on Incontinence. Plymouth: Health Publication Ltd; 2002. p. 243-266.

2 Kohli N, Goldstein,DP. *An overview of the clinical manifestations, diagnosis, and classification of pelvic organ prolapse [webpage on the Internet].* Waltham, MA: UpToDate; 2007 [accessed September 2007] Available from: URL: http://patients.uptodate.com/topic.asp?file=pelvic_s/2164.

3 Hagen S, Stark D, Maher C, Adams EJ. Conservative management of pelvic organ prolapse in women. *Cochrane Database of Systematic Reviews* 2006;Issue 4. Art. No.: CD003882. DOI: 10.1002/14651858.CD003882.pub3.

4 Olsen AL, Smith VJ, Bergstom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol* 1997;89:501-6.

5 Jha S, Moran PA. National survey on the management of prolapse in the UK. *Neurourol Urodyn* 2007;26:325-31.

6 *Systematic review of the efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse [document on the Internet].* London: National Institute for Health and Clinical Excellence; 2008 [accessed May 2008] Available from: URL:http://www.nice.org.uk/guidance/index.jsp?action=download&o=39669.

7 Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Bouter LM et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998;51:1235-41.

8 *Undertaking systematic reviews of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews. CRD Report No 4*. University of York: Centre for Reviews and Dissemination; 2001.

9 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;52:377-84.

10 Sutton AJ, Abrams KR. Bayesian methods in meta-analysis and evidence synthesis. *Stat Methods Med Res* 2001;10:277-303.

11 Spiegelhalter D, Thomas A, Best N. *WinBUGS: Bayesian inference using Gibbs sampling. User manual, version 1.4.* Cambridge: MRC Biostatistics Unit; 2003.

12 Amid PK. Classification of biomaterials and their related complication in abdominal wall hernia surgery. *Hernia* 1997;1:15-21.

13 De Ridder D. The use of biomaterials in reconstructive urology. *Eur Urol Suppl* 2002;1:7-11.

14 Gandhi S, Goldberg RP, Kwon C, Koduri S, Beaumont JL, Abramov Y et al. A prospective randomized trial using solvent dehydrated fascia lata for the prevention of recurrent anterior vaginal wall prolapse. *Am J Obstet Gynecol* 2005;192:1649-54.

15 Meschia M, Pifarotti P, Bernasconi F, Magatti F, Riva D, Kocjancic E. Porcine skin collagen implants to prevent anterior vaginal wall prolapse recurrence: a multicenter, randomized study. *J Urol* 2007;177:192-5.

16 Paraiso MFR, Barber MD, Muir TW, Walters MD. Rectocele repair: A randomized trial of three surgical techniques including graft augmentation. *Am J Obstet Gynecol* 2006;195:1762-71.

17 Sand PK, Koduri S, Lobel RW, Winkler HA, Tomezsko J, Culligan PJ et al. Prospective randomized trial of polyglactin 910 mesh to prevent recurrence of cystoceles and rectoceles. *Am J Obstet Gynecol* 2001;184:1357-62.

18 Weber AM, Walters MD, Piedmonte MR, Ballard LA. Anterior colporrhaphy: a randomized trial of three surgical techniques. *Am J Obstet Gynecol* 2001;185:1299-304.

19 Al-Nazer MA, Ismail WA, Gomma IA. Comparative study between anterior colporraphy versus vaginal wall repair with mesh for management of anterior vaginal wall prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:S49-S50.

20 Ali S, Han HC, Lee LC. A prospective randomized trial using Gynemesh PS for the repair of anterior vaginal wall prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:S221.

21 Allahdin S, Bain C, Glazener C. Feasibility study for a randomized controlled trial evaluating the use of absorbable mesh, polydioxanone and polyglactin sutures for anterior and posterior vaginal wall prolapse repairs. Annual Meeting, International Continence Society, Churchill, New Zealand, 27th Nov-1st Dec 2006. Abstract no 412.

22 Cervigni M, Natale F, Weir J, Antomarchi F. Prospective randomized controlled study of the use of a synthetic mesh (Gynemesho (R)) versus a biological mesh (Pelvicol (R)) in recurrent cystocele. *J Urol* 2007;177:423.

23 Hiltunen R, Nieminen K, Takala T, Hesikanen E, Niemi K. Transvaginal mesh repair of the anterior compartment prolapse; a randomized comparing prospective study. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:S142.

24 Hviid UH, Rudnicki M. A randomised controlled study of biomesh (Pelvicol) for vaginal anterior wall prolapse. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:S58.

25 Kocjancic E, Crivellaro S, Bernasconi F, Magatti F, Frea B, Meschia M. Cystocele repair with or without pelvicol implant: A two years follow-up. *Eur Urol Suppl* 2007;6:238.

26 Lim YN, Muller R, Hitchins S, Tang A, Naidu A, Greenland H. Is it worth incorporating mesh in pasterior colporrhaphy: a randomized study. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:S178-S179.

27 Lim YN, Carey MP, Higgs PJ, Goh J, Krause H, Leong A. Vaginal colporrhaphy versus vaginal repair with mesh for pelvic organ prolapse: a randomized controlled trial. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:S38-S39.

28 Meschia M, Baccichet R, Cervigni M, Guercio E, Maglioni Q, Narducci P. A multicenter randomized trial on transvaginal mesh repair of severe genital prolapse with the Perigee-Apogee system: the Perapo study. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:S10.

29 Nguyen JN, Burchette RJ. Anatomic support and visceral function following anterior colporrhaphy versus polypropylene mash transobturator prolapse repair: Avia trial. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:S51.

30 Chaliha C, Khalid U, Campagna L, Digesu GA, Ajay B, Khullar V. SIS graft for anterior vaginal wall prolapse repair--a case-controlled study. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:492-7.

31 Altman D, Mellgren A, Blomgren B, Lopez A, Zetterstrom J, Nordenstam J et al. Clinical and histological safety assessment of rectocele repair using collagen mesh. *Acta Obstet Gynecol Scand* 2004;83:995-1000.

32 Castelo-Branco C, Garrido JF, Ribas C, Iglesias X. Posterior vaginal wall repair with synthetic absorbable mesh: A new technique for an old procedure. *J Gynecol Surg* 1998;14:111-7.

33 Handel LN, Frenkl TL, Kim YH. Results of cystocele repair: a comparison of traditional anterior colporrhaphy, polypropylene mesh and porcine dermis. *J Urol* 2007;178:153-6.

34 Julian TM. The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall. *Am J Obstet Gynecol* 1996;175:1472-5.

35 Leboeuf L, Miles RA, Kim SS, Gousse AE. Grade 4 cystocele repair using four-defect repair and porcine xenograft acellular matrix (Pelvicol): Outcome measures using SEAPI. *Urology* 2004;64:282-6.

36 Vakili B, Huynh T, Loesch H, Franco N, Chesson RR. Outcomes of vaginal reconstructive surgery with and without graft material. *Am J Obstet Gynecol* 2005;193:2126-32.

37 Altman D, Falconer C. Perioperative morbidity using transvaginal mesh in pelvic organ prolapse repair. *Obstet Gynecol* 2007;109:303-8.

38 Cronje HS, Prollius A, de Beer JAA. Stage IV cystocele treated by sacrocolpopexy. *Int J Gynecol Obstet* 2006;92:153-4.

39 Achtari C, Hiscock R, O'Reilly BA, Schierlitz L, Dwyer PL. Risk factors for mesh erosion after transvaginal surgery using polypropylene (Atrium) or composite polypropylene/polyglactin 910 (Vypro II) mesh. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:389-94.

40 Amrute KV, Eisenberg ER, Rastinehad AR, Kushner L, Badlani GH. Analysis of outcomes of single polypropylene mesh in total pelvic floor reconstruction. *Neurourol Urodyn* 2007;26:53-8.

41 Collinet P, Belot F, Debodinance P, Ha DE, Lucot JP, Cosson M. Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:315-20.

42 Cosson M, Rajabally R, Bogaert E, Querleu D, Crepin G. Laparoscopic sacrocolpopexy, hysterectomy, and burch colposuspension: feasibility and short-term complications of 77 procedures. *J Soc Laparoendosc Surg* 2002;6:115-9.

43 Costantini E, Mearini L, Bini V, Zucchi A, Mearini E, Porena M. Uterus preservation in surgical correction of urogenital prolapse. *Eur Urol* 2005;48:642-9.

44 De Tayrac R, Deffieux X, Gervaise A, Chauveaud-Lambling A, Fernandez H. Long-term anatomical and functional assessment of trans-vaginal cystocele repair using a tension-free polypropylene mesh. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:483-8.

45 De Tayrac R, Devoldere G, Renaudie J, Villard P, Guilbaud O, Eglin G et al. Prolapse repair by vaginal route using a new protected low-weight polypropylene mesh: 1-year functional and anatomical outcome in a prospective multicentre study. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:251-6.

46 Deffieux X, De Tayrac R, Huel C, Bottero J, Gervaise A, Bonnet K et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: a comparative study. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:73-9.

47 Dwyer PL, O'Reilly BA. Transvaginal repair of anterior and posterior compartment prolapse with Atrium polypropylene mesh. *BJOG* 2004;111:831-6.

48 Fatton B, Amblard J, Debodinance P, Cosson M, Jacquetin B. Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolifttrade mark technique)-a case series multicentric study. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18:743-52.

49 Flood CG, Drutz HP, Waja L. Anterior colporrhaphy reinforced with Marlex mesh for the treatment of cystoceles. *Int Urogynecol J Pelvic Floor Dysfunct* 1998;9:200-4.

50 Frederick RW, Leach GE. Cadaveric prolapse repair with sling: intermediate outcomes with 6 months to 5 years of followup. *J Urol* 2005;173:1229-33.

51 Gomelsky A, Rudy DC, Dmochowski RR. Porcine dermis interposition graft for repair of high grade anterior compartment defects with or without concomitant pelvic organ prolapse procedures. *J Urol* 2004;171:1581-4.

52 Kobashi KC, Leach GE, Chon J, Govier FE. Continued multicenter followup of cadaveric prolapse repair with sling. *J Urol* 2002;168:2063-8.

53 Kobashi KC, Leach GE, Frederick R, Kuznetsov DD, Hsiao KC. Initial experience with rectocele repair using nonfrozen cadaveric fascia lata interposition. *Urology* 2005;66:1203-7.

54 Lim YN, Rane A, Muller R. An ambispective observational study in the safety and efficacy of posterior colporrhaphy with composite Vicryl-Prolene mesh. *Int Urogynecol J Pelvic Floor Dysfunct* 2005;16:126-31.

55 Milani R, Salvatore S, Soligo M, Pifarotti P, Meschia M, Cortese M. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh. *BJOG* 2005;112:107-11.

56 Petros PEP, Richardson PA, Goeschen K, Abendstein B. The tissue fixation system provides a new structural method for cystocoele repair: A preliminary report. *Aust N Z J Obstet Gynaecol* 2006;46:474-8.

57 Powell CR, Simsiman AJ, Menefee SA. Anterior vaginal wall hammock with fascia lata for the correction of stage 2 or greater anterior vaginal compartment relaxation. *J Urol* 2004;171:264-7.

58 Rodriguez LV, Bukkapatnam R, Shah SM, Raz S. Transvaginal paravaginal repair of high-grade cystocele central and lateral defects with concomitant suburethral sling: report of early results, outcomes, and patient satisfaction with a new technique. *Urology* 2005;66:57-64.

59 Safir MH, Gousse AE, Rovner ES, Ginsberg DA, Raz S. 4-Defect repair of grade 4 cystocele. *J Urol* 1999;161:587-94.

60 Simsiman AJ, Luber KM, Menefee SA. Vaginal paravaginal repair with porcine dermal reinforcement: Correction of advanced anterior vaginal prolapse. *Am J Obstet Gynecol* 2006;195:1832-6.

61 Rozet F, Mandron E, Arroyo C, Andrews H, Cathelineau X, Mombet A et al. Laparoscopic sacral colpopexy approach for genito-urinary prolapse: experience with 363 cases. *Eur Urol* 2005;47:230-6.

62 Bombieri L. *A prospective randomised comparative study of posterior vaginal repair using pelvicol mesh versus standard repair. NO185139347.* National Research Register; 2007 [accessed June 2007] Available from: URL: http://www.nrr.nhs.uk/.

63 Fernandez H. *Comparative study of mesh versus no mesh in prolapse. ClinicalTrials.gov NCT00153257.* ClinicalTrials.gov; 2007 [accessed June 2007] Available from: URL: http://clinicaltrials.gov/ct/gui/c/r.

64 Nieminen K. *Low-weight polypropylene mesh for anterior vaginal wall prolapse: a prospective randomized study. ClinicalTrials.gov Identifier NCT00420225.* ClinicalTrials.gov; 2007 [accessed June 2007] Available from: URL: http://clinicaltrials.gov/ct/gui/c/r.

65 Sung VW. *Graft-augmented rectocele repair - a randomized surgical trial. ClinicalTrials.gov Identifier NCT00321867.* ClinicalTrials.gov; 2007 [accessed June 2007] Available from: URL: http://clinicaltrials.gov/ct/gui/c/r.

66 Verleyen P, Filip C, Bart K, Frank VD, Jan D, Dirk DR. A prospective randomised trial comparing Pelvicol and Vicryl for cystocoele repair in the raz-colposuspension. Joint Meeting of the International Continence Society and the International Urological Association, Paris, 23 - 27 August 2004. Abstract no 613.

67 Withagen M. *Performance of tension free vaginal mesh (Prolift) versus conventional vaginal prolapse surgery in recurrent prolapse. ClinicalTrials.gov Identifier NCT00372190.* ClinicalTrials.gov; 2007 [accessed June 2007] Available from: URL: http://clinicaltrials.gov/ct/gui/c/r.

68 Zylstra S. *Observational data collection of surgical outcomes in the treatment of vaginal prolapse with AMS products. ClinicalTrials.gov Identifier NCT00388947.* ClinicalTrials.gov; 2007 [accessed June 2007] Available from: URL: http://clinicaltrials.gov/ct/gui/c/r.

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Supplementary materials (online)

Appendix S1 Details of the included studies

Appendix S2 Checklist of quality assessment of randomised controlled trials

Appendix S3 Checklist of quality assessment of non-randomised studies

672 **Table 1** Efficacy of anterior repair, summary of crude event rates (95% CI, any study design), by type

673 of mesh/graft

	No mesh	Absorbable synthetic mesh	Biological graft	Non-absorbable synthetic mesh
Subjective failure	19/179 (10.6%, 6.9 - 16.0)	5/112 (4.5%, 1.9 - 10.0)	36/486 (7.4%, 5.4 - 10.1)	1/55 (1.8%, 0 - 6.5)
Objective failure	184/640 (28.8%, 25.4 - 32.4)	63/273 (23.1%, 18.5 - 28.4)	186/1041 (17.9%, 15.7 - 20.3)	48/548 (8.8%, 6.7 - 11.4)
De novo prolapse	-	-	8/58 (13.8%, 7.2 - 24.9)	8/45 (17.8%, 9.3 - 31.3)
Further operation needed*	2/85 (2.4%, 0.6 - 8.2)	16/174 (9.2%, 5.7 - 14.4)	9/280 (3.2%, 1.7 - 6.0)	3/234 (1.3%, 0.4 - 3.7)
Persistent urinary symptoms	9/10 (90.0%, 59.6 - 98.2)	5/49 (10.2%, 4.4 - 21.8)	13/14 (92.9%, 68.5 - 98.7)	17/44 (38.6%, 25.8 - 53.4)
Persistent bowel symptoms	-	-	-	-
Persistent dyspareunia	-	-	-	-

674 * surgery for prolapse (recurrent or de novo)
675 - No studies reported this outcome

Table 2 Bayesian meta-analysis models (above)[a] and indirect comparison (below)[a], anterior repair: objective failure (recurrent prolapse at original site)

Categories	n[b]	N[b]	OR (adjusted for study design)	95% CrI[c]
No mesh/graft	184	640	Reference technique	-
Absorbable synthetic mesh	52	161	0.82	0.50 to 1.32
Absorbable biological graft	120	555	0.51*	0.36 to 0.72
Non-absorbable synthetic mesh	41	344	0.19*	0.12 to 0.30

Comparisons	OR	95% CrI[c]
Absorbable biological graft *versus* absorbable synthetic mesh	0.64	0.36 to 1.06
Non-absorbable synthetic mesh *versus* absorbable synthetic mesh	0.23*	0.12 to 0.44
Non-absorbable synthetic mesh *versus* absorbable biological graft	0.37*	0.23 to 0.59

*Statistically significant

[a]Based on RCTs and non-randomised comparative studies only;

[b]n = cumulative number of patients experiencing the event, N = cumulative number of patients analysed by the studies.

[c]CrI. Credible interval with 95% probability of containing the true OR

688 **Table 3** Safety of anterior repair, summary of crude event rates (95% CI, any study design), by

689 type of mesh/graft

	No mesh	Absorbable synthetic mesh	Biological graft	Non-absorbable synthetic mesh
Blood transfusion	1/88 (1.1%, 0.2 - 6.2)	0/147 (0%, 0 - 2.5)	3/198 (1.5%, 0.5 - 4.4)	4/161 (2.5%, 1.0 - 6.2)
Damage to surrounding organs	0/19 (0%, 0 - 16.8)	0/112 (0%, 0 - 3.3)	0/94 (0%, 0 - 3.9)	6/251 (2.4%, 1.1 - 5.1)
Mesh/graft erosion	Not applicable	1/147 (0.7%, 0.1 - 3.8)	35/581 (6.0%, 4.4 - 8.3)	68/666 (10.2%, 8.1 - 12.7)
Operation for mesh/graft erosion	Not applicable	1/35 (2.9%, 0 - 3.3)	4/154 (2.6%, 1.0 - 6.5)	23/347 (6.6%, 4.5 - 9.7)
De novo urinary symptoms	-	0/63 (0%, 0 - 5.7)	3/42 (7.1%, 2.5 - 19.0)	3/44 (6.8%, 2.3 - 18.2)
De novo bowel symptoms	-	-	-	-
De novo dyspareunia	-	-	-	4/11 (36.4%, 15.2 - 64.6)
Infection	4/142 (2.8%, 1.1 - 7.0)	0/112 (0%, 0 - 3.3)	5/477 (1.0%, 0.4 - 2.4)	11/558 (2.0%, 1.1 - 3.5)
Other serious adverse effects	1/93 (1.1%, 0.2 - 5.8)	0/35 (0%, 0 - 9.9)	2/212 (0.9%, 0.3 - 3.4)	4/248 (1.6%, 0.6 - 4.1)

690

691 - No studies reported this outcome

692 **Table 4** Efficacy of posterior repair, summary of crude event rates (95% CI, any study design), by type

693 of mesh/graft

	No mesh	Absorbable synthetic mesh	Biological graft	Combined mesh/graft	Non-absorbable synthetic mesh
Subjective failure	9/60 (15.0%, 8.1 to 26.1)	-	9/78 (11.5%, 6.2 - 20.5)	-	-
Objective failure	18/142 (12.7%, 8.2 - 19.1)	6/70 (8.6%, 4.0 - 17.5)	19/93 (20.4%, 13.5 - 29.7)	-	2/31 (6.5%, 1.8 - 20.7)
De novo prolapse	-	-	-	-	-
Further operation needed*	3/70 (4.3%, 1.5 - 11.9)	-	2/29 (6.9%, 1.9 - 6.9)	-	-
Persistent urinary symptoms	-	-	-	-	-
Persistent bowel symptoms	19/58 (32.8%, 22.1 - 45.6)	-	14/82 (17.1%, 10.5 - 26.6)	5/43 (11.6%, 5.2 - 24.6)	-
Persistent dyspareunia	-	-	5/14 (35.7%, 16.3 - 61.2)	-	-

694 * surgery for prolapse (recurrent or de novo)

695 - No studies reported this outcome

696

Table 5 Safety of posterior repair, summary of crude event rates (95% CI, any study design), by type of mesh/graft

	No mesh	Absorbable synthetic mesh	Biological graft	Combined mesh/graft	Non-absorbable synthetic mesh
Blood transfusion	3/79 (3.8%, 1.3 to 10.6)	0/5 (0%, 0 to 43.4)	1/31 (3.2%, 0.6 to 16.2)	0/90 (0%, 0 to 4.1)	1/71 (1.4%, 0.2 to 7.6)
Damage to surrounding organs	2/79 (2.5%, 0.7 to 8.8)	0/5 (0%, 0 to 43.4)	1/31 (3.2%, 0.6 to 16.2)	0/90 (0%, 0 to 4.1)	3/71 (4.2%, 1.4 to 11.7)
Mesh/graft erosion	Not applicable	-	0/28 (0%, 0 to 12.1)	16/115 (13.9%, 8.7 to 12.1)	2/31 (6.5%, 1.8 to 20.7)
Operation for mesh/graft erosion	Not applicable	-	-	11/90 (12.2%, 7.0 to 20.6)	-
De novo urinary symptoms	-	-	-	-	-
De novo bowel symptoms	-	-	-	2/45 (4.4%, 1.2 to 14.8)	1/29 (3.4%, 0.6 to 17.2)
De novo dyspareunia	-	4/25 (16.0%, 6.4 to 34.7)	-	2/36 (5.6%, 1.5 to 18.1)	-
Infection	13/94 (13.8%, 8.3 to 22.2)	0/5 (0%, 0 to 43.4)	7/48 (14.6%, 7.2 to 27.2)	-	4/106 (3.8%, 1.5 to 9.3)
Other serious adverse effects	-	-	-	-	-

- No studies reported this outcome

Table 6 Efficacy of anterior and/or posterior repair, summary of crude event rates (95% CI, any study design), by type of mesh/graft

	No mesh	Absorbable synthetic mesh	Combined mesh/graft	Non-absorbable synthetic mesh
Subjective failure	14/34 (41.2%, 26.4 - 57.8)	14/32 (43.8%, 28.2 - 60.7)	-	0/148 (0%, 0 - 2.5)
Objective failure	27/109 (24.8%, 17.6 - 33.6)	2/26 (7.7%, 2.1 - 24.1)	11/143 (7.7%, 4.3 - 13.2)	41/645 (6.4%, 4.7 - 8.5)
De novo prolapse	-	-	-	-
Further operation needed*	-	-	-	7/161 (4.3%, 2.1 - 8.7)
Persistent urinary symptoms	-	-	-	46/203 (22.7%, 17.4 - 28.9)
Persistent bowel symptoms	-	-	-	1/21 (4.8%, 0.8 - 22.7)
Persistent dyspareunia	-	-	1/10 (10.0%, 1.8 - 40.4)	-

* surgery for prolapse (recurrent or de novo)

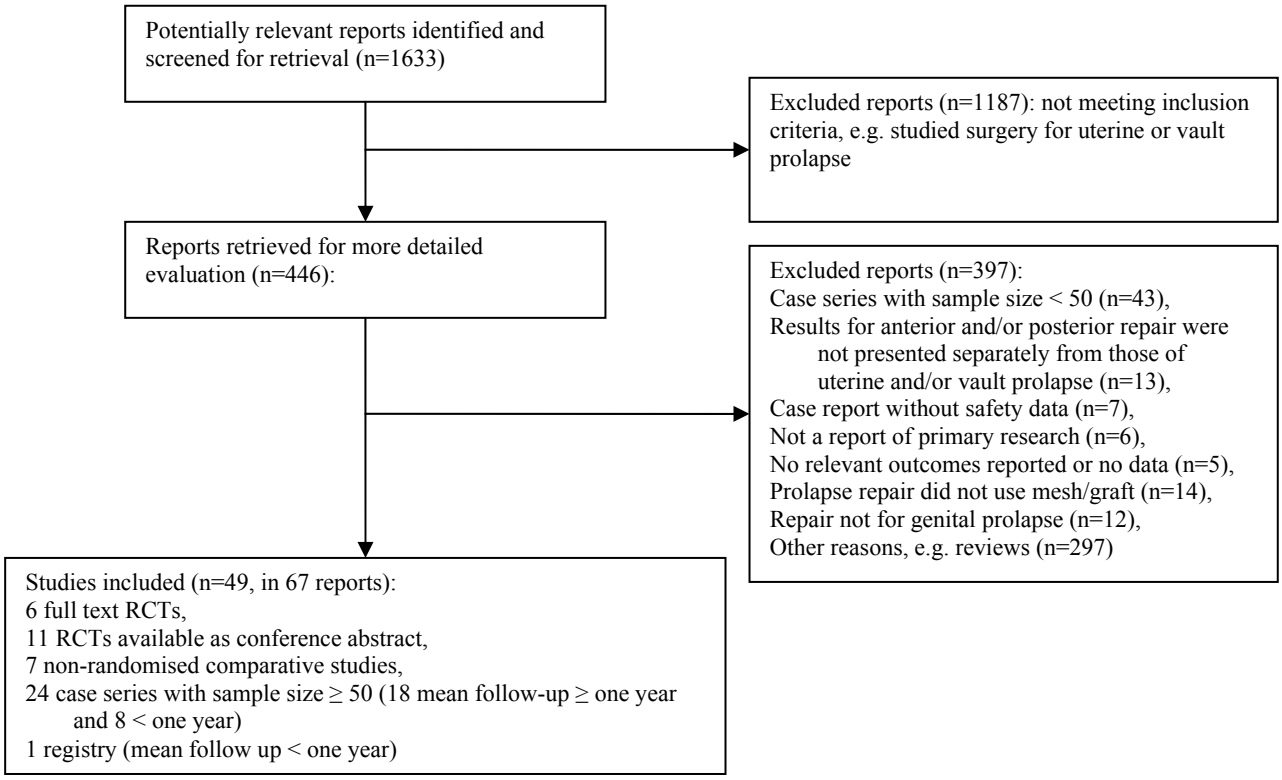
- No studies reported this outcome

Table 7 Safety of anterior and/or posterior repair, summary of crude event rates (95% CI, any study design), by type of mesh/graft

	No mesh	Combined mesh/graft	Non-absorbable synthetic mesh
Blood transfusion	1/35 (2.9%, 0.5 - 14.5)	-	11/810 (1.4%, 0.8 - 2.4)
Damage to surrounding organs	-	4/143 (2.8%, 1.1 - 7.0)	12/541 (2.2%, 1.3 - 3.8)
Mesh/graft erosion	Not applicable	9/143 (6.3%, 3.3 - 11.5)	62/1119 (5.5%, 4.3 - 7.0)
Operation for mesh/graft erosion	Not applicable	6/143 (4.2%, 1.9 - 8.9)	45/1098 (4.1%, 3.1 - 5.4)
De novo urinary symptoms	-	-	34/355 (9.5%, 6.9 - 13.1)
De novo bowel symptoms	-	-	1/47 (2.1%, 0.4 - 11.1)
De novo dyspareunia	-	10/78 (12.8%, 7.1 - 22.0)	3/42 (7.1%, 2.5 - 19.0)
Infection	-	-	33/661 (5.0%, 3.6 - 6.9)
Other serious adverse effects	-	-	3/278 (1.1%, 0.4 - 3.1)

- No studies reported this outcome

713 **Figure 1** Flow diagram for screening process.
714



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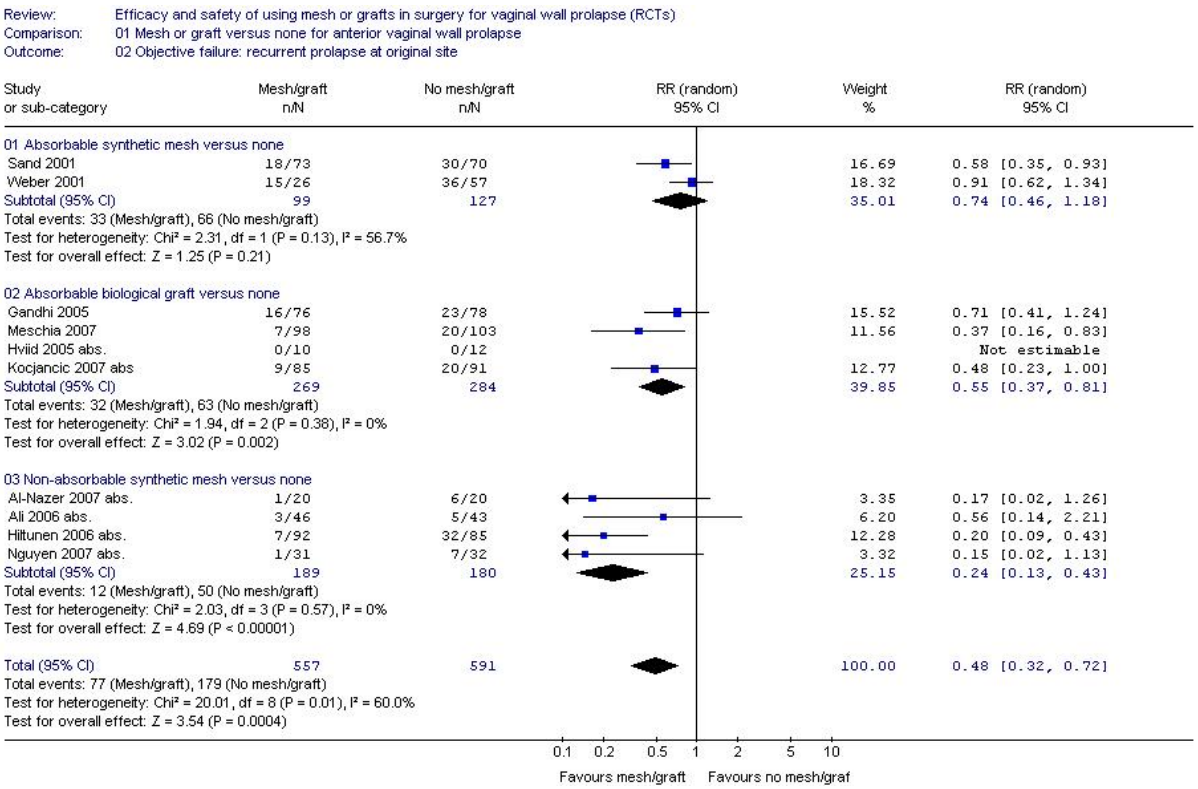
716 Figure 2



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718 **Appendix S1 (online)** Details of the included studies

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Anterior vaginal wall prolapse repair								
RCT								
De Ridder 2002[13]	A, 65 B, 69	A, 70 (24-86) B, 70 (36-83)	NR	A, absorbable biological graft (porcine dermis) B, absorbable synthetic graft (polyglactin)	A, 55/0/10 B, 56/0/13	Hysterectomy: A, 38/65; B 41/69	A, 25m (5) B, 26m (6)	Efficacy
Gandhi 2005[14]	A, 76 B, 78	A, 65 (12) B, 66 (12)	NR	A, absorbable biological graft (cardaveric fascia lata) B, no mesh	A, 1/0/75 B, 5/0/73	Incontinence: A, 51/76; B, 43/78 Hysterectomy: A, 37/76; B, 37/78	13m (1 – 50)	Efficacy
Meschia 2007[15]	A, 98 B, 103	A, 65 (8) B, 65 (9)	A 100/0 B, 106/0	A, absorbable biological graft (porcine dermis) B, no mesh	A, 33/0/67 B, 39/0/67	Incontinence: A, 4/100; B 3/106 Hysterectomy: A+B, 188/206	1y	Safety Efficacy
Sand 2001[17]	A, 73 B, 70	A, mean 65 B, mean 63	A, 55/18 B, 49/21	A, absorbable synthetic mesh (polyglactin) B, no mesh	A, 8/0/65 B, 3/0/67	Incontinence: A, 58/73; B, 52/70 Hysterectomy: A, 36/73; B 39/70	1y	Safety Efficacy
Weber 2001[18]	A, 35 B, 39 C, 35	A, 66 (11) B, 66 (11) C, 62 (13)	NR	A, absorbable synthetic mesh (polyglactin) B, no mesh C, no mesh	NR	NR	23m (5 – 44)	Safety Efficacy
RCT (abs.)								
Al-Nazer 2007[19]	A, 20 B, 20	NR	NR	A, non-absorbable synthetic mesh (polypropylene, Gynemesh PS) B, no mesh	NR	NR	1y	Efficacy
Ali 2006[20]	A, 54 B, 54	NR	NR	A, non-absorbable synthetic mesh (polypropylene, Gynemesh PS) B, no mesh	NR	NR	6m	Safety Efficacy
Cervigni 2007[22]	A, 93 B, 87	A+B, mean 64	NR	A, non-absorbable synthetic mesh (polypropylene, Gynemesh) B, absorbable biological graft (human dermis)	NR	NR	6 – 28m	Safety Efficacy

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Hiltunen 2006[23]	A, 105 B, 97	NR	NR	A, non-absorbable synthetic mesh (polypropylene, Parietene light) B, no mesh	NR	NR	1y	Safety Efficacy
Hviid 2005[24]	A, 19 B, 20	A+B, 59 (40-84)	NR	A, absorbable biological graft (porcine dermis) B, no mesh	NR	NR	3m	Safety Efficacy
Kocjancic 2007[25]	A, 85 B, 91	NR	NR	A, absorbable biological graft (porcine dermis) B, no mesh	NR	NR	2y	Safety Efficacy
Nguyen 2007[29]	A, 31 B, 32	NR	NR	A, non-absorbable synthetic mesh (polypropylene, Perigee) B, no mesh	NR	NR	6m	Safety Efficacy
Non-randomised comparative studies								
Chaliha 2006[30]	A, 14 B, 14	A, 70 (51-86) B, 60 (47-79)	A, 12/2 B, 12/2	A, absorbable biological graft (small intestine submucosa) B, no mesh	A, 14/0/0 B, 14/0/0	Incontinence: A, 0/14; B, 0/14	2y	Safety Efficacy
Handel 2007[33]	A, 56 B, 25 C, 18	NR	A, 36/20 B, 24/1 C 17/1	A, absorbable biological graft (porcine dermis) B, non-absorbable synthetic mesh (polypropylene, not reported trade name) C, no mesh	A, 18/0/38 B, 7/0/18 C, 6/0/12	Incontinence: A 48/56; B, 20/25; C 9/18 Hysterectomy: A 46/56; B, 25/25; C, 18/18	All, 14m (2 – 46) A, mean 17m B, mean 13m C, mean 9m	Safety Efficacy
Julian 1996[34]	A, 12 B, 12	A, 63 (37-82) B, 66 (46-78)	A, 0/12 B, 0/12	A, non-absorbable synthetic mesh (polypropylene, Marlex) B, no mesh	NR	NR	2y	Safety Efficacy
Leboeuf 2004[35]	A, 24 B, 19	A+B, 65 (33-91)	NR	A, absorbable biological graft (porcine dermis) B, no mesh	A+B, 8/0/35	NR	Mean 15m	Safety Efficacy
Registry								
Altman 2007[37]	106	68 (10)	18/88	Non-absorbable synthetic mesh (polypropylene, Prolift)	106/0/0	NR	Registered in a 6m period	Safety
Case series								
Cronje 2006[38]	50	65	NR	Combined mesh/graft (polypropylene and polyglactine)	NR	NR	12m (1-50)	Safety Efficacy
De Tayrac 2006[44]	55	63 (11)	59/4	non-absorbable synthetic mesh (polypropylene, Gynemesh)	45/0/10	Incontinence: 22/63 Hysterectomy: 52/63	37 (10)	Safety Efficacy

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Deffieux 2007[46]	138	62 (30-83)	NR	Non-absorbable synthetic mesh (polypropylene, 89 Gynemesh, 49 Gynemesh-Soft)	118/0/20	Incontinence: 87/138 Hysterectomy: 103/138	6m	Safety
Flood 1998[49]	142	65 (37-87)	120/22	Non-absorbable synthetic mesh (polypropylene, Marlex)	NR	Hysterectomy: 94/142	3.2y (6w – 12y)	Safety Efficacy
Frederick 2005[50]	251	66 (31-90)	226/25	Absorbable biological graft (solvent dehydrated fascia lata)	158/0/90	Incontinence: 251/251 Hysterectomy: 28/248	22m (6 – 61)	Safety Efficacy
Gomelsky 2004[51]	70	NR	NR	Absorbable biological graft (porcine dermis)	NR	Incontinence: 65/70	24m (12 – NR)	Safety Efficacy
Kobashi 2002[52]	132	62 (35-90)	NR	Absorbable biological graft (solvent dehydrated fascia lata)	NR	NR	12m (6-28)	Safety Efficacy
Milani 2005[55]	32	63 (49-82)	NR	Non-absorbable synthetic mesh (polypropylene, Prolene)	32/0/0	NR	17m (3 – 48)	Safety Efficacy
Petros 2006[56]	98	65 (40-86)	42/48	Non-absorbable synthetic mesh (NR materia, multifilament, Tissue Fixation System)	NR	NR	8m (3 – 15)	Safety
Powell 2004[57]	58	NR	NR	Absorbable biological graft (donor or autologousfascia lata)	A, 17/0/22 B, 11/0/8	Incontinence: 41/58 Hysterectomy: 14/58	25m (12 – 57)	Safety Efficacy
Rodriguez 2005[58]	98	65 (40-86)	NR	Non-absorbable synthetic mesh (soft polypropylene, NR trade name)	6/0/92	Incontinence: 98/98	Assume 3m	Safety
Safir 1999[59]	112	65 (35-96)	70/60	Absorbable synthetic mesh (polyglacolic acid)	31/0/81	Hysterectomy: 22/112	21m (6 – 42)	Safety Efficacy
Simsiman 2006[60]	89	60 (26-82)	NR	Absorbable biological graft (porcine dermis)	NR	Incontinence: 41/89 Hysterectomy: 48/89	24m (6 – 44)	Safety Efficacy
Posterior vaginal wall prolapse repair								
RCT								
Paraiso 2006[16]	A, 31 B, 37 C, 37	A, 60 (11) B, 61 (12) C, 62 (9)	NR	A, absorbable biological graft (porcine dermis) B, no mesh C, no mesh	A, 0/12/19 B, 0/17/20 C, 0/11/26	Continence: A, 15/31; B, 17/37; C, 17/37 Hysterectomy: A, 13/31; B, 12/37; C 14/37	16m (4 – 34)	Safety Efficacy

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Sand 2001[17]	A, 65 B, 67	NR	NR	A, absorbable synthetic mesh (polyglactin) B, no mesh	A, 0/0/65 B, 0/0/67	NR	1y	Safety Efficacy
RCT (abs.)								
Lim 2006[26]	A, 25 B, 9 C, 31	A, 58 (10) B, 67 (9) C, 55 (13)	NR	A, semi absorbable mesh/graft (polypropylene-polyglactin) B, absorbable synthetic mesh (polyglactin) C, no mesh	NR	NR	A, 14m (9) B, 12 (12) C, 12 (10)	Safety Efficacy
Non-randomised comparative studies								
Altman 2004[31]	A, 17 B, 15	A, 60 (42-75) B, 59 (43-68)	NR	A, absorbable biological graft (porcine dermis) B, no mesh	A, 0/16/1 B, 0/8/3	Hysterectomy: A, 2/17; B 2/15	6m	Safety Efficacy
Castelo-Branco 1998[32]	A, 5 B, 5	A, 57 (7) B, 56 (8)	NR	A, absorbable synthetic mesh (polyglacolic acid) B, no mesh	A, 0/3/2 B, 0/1/4	Incontinence: A, 1/5; B, 1/5 Hysterectomy: A, 1/5; B, 3/5	1y	
Registry								
Altman 2007[37]	71	68 (10)	48/23	Non-absorbable synthetic mesh (polypropylene, Prolift)	0/71/0	NR	Registered in a 6m period	Safety
Case-series								
Kobashi 2005[53]	73	31-86	NR	Absorbable biological graft (solvent-dried fascia lata)	NR	NR	14m (6 – 23)	Safety Efficacy
Lim 2005[54]	90	59 (31-85)	NR	Combined mesh/graft (polypropylene-polyglactin)	0/75/15	Incontinence: 69/90	6m	Safety
Milani 2005[55]	31	63 (50-80)	NR	Non-absorbable synthetic mesh (polypropylene, Prolene)	0/31/0	NR	17m (3 – 48)	Safety Efficacy

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Anterior and/or posterior vaginal wall prolapse repair								
RCT (abs.)								
Allahdin 2006[21]	A, 32 B, 34	NR	NR	A, Absorbable synthetic mesh (polyglactin) B, no mesh	NR	Hysterectomy: A+B,14/66	6m	Efficacy
Lim 2007[27]	A, 62 B, 60	NR	NR	A, non-absorbable synthetic mesh (polypropylene, Gynemsh PS) B, no mesh	NR	NR	1y	Safety Efficacy
Meschia 2007[28]	A, 36 B, 35	NR	A, 36/0 B, 35/0	A, total mesh: non-absorbable synthetic mesh (Perigee-Apogee system) B, no mesh	NR	NR	3m	Safety Efficacy
Non-randomised comparative studies								
Vakili 2005[36]	A, 98 B, 214	A, mean 65 B, mean 61	NR	A, absorbable biological graft or non-absorbable synthetic mesh (>=1 type) B, no mesh	A, 74/22/0 B, NR	Incontinence: A, 66/98; B, 142/214 Hysterectomy: A, 7/98; B, 23/214	9m (3 – 67)	Safety Efficacy
Registry								
Altman 2007[37]	71	NR	52/29	Non-absorbable synthetic mesh (polypropylene, Prolift, 51 had total mesh)	0/0/71	NR	Registered in a 6m period	Safety
Case series								
Achtari 2005[39]	198	63 (11.6)	NR	Non-absorbable synthetic mesh (Polypropylene, Atrium, total mesh) or combined mesh (polypropylene and polyglactin)	90/76/32	Incontinence: 67/198 Hysterectomy: 13/198	6w-6m	safety
Amrute 2007[40]	76	69 (11)	NR	Non-absorbable synthetic mesh (polypropylene, BioArc device, total mesh)	0/0/76	Hysterectomy: 36/76	31m (2)	Safety Efficacy
Collinet 2006[41]	277	64 (37-81)	NR	Non-absorbable synthetic mesh (polypropylene, 169 Prolene Soft, 108 Prolene)	63/46/166	Incontinence: 136/277 Hysterectomy: 164/277	2m	Safety

ID	N	Age, y, median (range) or mean (range)	Primary/ secondary repair, n	Mesh/graft	Anterior repair only/ posterior only/both, n	Concomitant operation	Follow-up, median (range) or mean (SD)	Outcomes reported
Cosson 2002[42]	83	47 (28-66)	NR	Non-absorbable synthetic mesh (polypropylene, Mersilene, total mesh)	0/0/83	Incontinence: 74/83 Hysterectomy: 60/83	Mean 343d	Safety
Costantini 2005[43]	72	61 (12)	NR	Non-absorbable synthetic mesh (polypropylene, Marlex, total mesh)	0/0/72	Incontinence: 58/72 Hysterectomy: 38/72	51m (12 – 115)	Safety Efficacy
De Tayrac 2007[45]	143	63 (37-91)	NR	Combined mesh/graft (polypropylene covered with atelocollagen)	67/11/65	NR	13m (10-19)	Safety Efficacy
Dwyer 2004[47]	97	61 (30-86)	NR	Non-absorbable synthetic mesh (polypropylene, Atrium, some women had total mesh)	47/33/17	Incontinence: 24/97 Hysterectomy: 10/97	29m (6-52)	Safety Efficacy
Fatton 2007[48]	110	63 (29-90)	88/22	Non-absorbable synthetic mesh (polypropylene, Prolene Soft, some women had total mesh)	22/29/59	Incontinence: 45/110 Hysterectomy: 15/110	25w (12-42)	Safety Efficacy
Rozet 2004[61]	325	63 (35-78)	NR	Non-absorbable synthetic mesh (polyester covered silicone, total mesh)	0/0/325	Incontinence: 163/325 Hysterectomy: 15/325	15m (6m-5y)	Safety

719

720 **APPENDIX 2Checklist of quality assessment of randomised controlled trials**

721

Criteria	Yes	No	Unclear	Comment
1. Was the assignment to the treatment groups really random?				
2. Was the treatment allocation concealed from those responsible for entering patients into trials, i.e. not knowing upcoming assignments in advance?				
3. Were the groups similar at baseline in terms of prognostic factors, e.g. age, duration of disease, disease severity?[1]				
4. Were the eligibility criteria specified?				
5. Was the intervention (and comparison) clearly defined?				
6. Were the groups treated in the same way apart from the intervention received?				
7. Was there a follow-up period ≥ 1 year?				
8. Was the outcome assessor blinded to the treatment allocation?				
9. If patient blind is possible, were the patients blinded?[2]				
10. If having primary outcome measures as continuous data, were the point estimates and measures of variability presented?[3]				
11. Were the withdrawals/drop-outs having similar characteristics as those completed the study and therefore unlikely to cause bias?[4]				
12. Did the analyses include all women according to randomised groups, i.e. intention-to-treat analysis?[5]				
13. Was the operation undertaken by somebody experienced in performing the procedure?[6]				

722

723 **Note:**

724

725 1. 'Yes' if two or more than two factors were similar.
726 2. If patient blinding is impossible, note 'impossible' in comment area and leave other
727 cells blank.
728 3. If having no primary outcome measures as continuous data, note 'no continuous
729 data' in comment area and leave other cells blank.

4. ‘Yes’ if no withdrawal/drop out; ‘No’ if drop-out rate ≥30% or differential drop-out.
5. ‘Yes’ if no withdrawals/drop out after enroll
6. ‘Yes’ if the practitioner received training on conducting the procedure before or conducted same kind of procedure before, i.e. no learning curve.

734 **APPENDIX 3Checklist of quality assessment of non-randomised studies**
735

Criteria	Yes	No	Unclear	Comments
1. Were participants a representative sample selected from a relevant patient population, e.g. randomly selected from those seeking for treatment despite of age, duration of disease, primary or secondary disease, and severity of disease?				
2. Were the inclusion/exclusion criteria of participants clearly described?				
3. Were participants entering the study at a similar point in their disease progression, i.e. severity of disease?				
4. Was selection of patients consecutive?				
5. Was data collection undertaken prospectively?				
6. Were the groups comparable on demographic characteristics and clinical features?				
7. Was the intervention (and comparison) clearly defined?				
8. Was the intervention undertaken by someone experienced at performing the procedure?[1]				
9. Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure? (E.g. access to back-up facilities in hospital or special clinic)				
10. Were all the important outcomes considered?				
11. Were objective (valid and reliable) outcome measures used, including satisfaction scale?				
12. Was the assessment of main outcomes blind?				
13. Was follow-up long enough (≥1y) to detect important effects on outcomes of interest?				
14. Was information provided on non-respondents, dropouts?[2]				
15. Were the withdrawals/drop-outs having similar characteristics as those completed the study and therefore unlikely to cause bias?[3]				

16. Was length of follow-up similar between comparison groups				
17. Were all the important prognostic factors identified, e.g. age, duration of disease, disease severity?[4]				
18. Were the analyses adjusted for confounding factors?				

The same form was adapted to assess the quality of case series after taking out question 6, 12, 16 and 18.

Note:

1. 'Yes' if the practitioner received training on conducting the procedure before or conducted same kind of procedure before, i.e. no learning curve.
2. 'No' if participants were from those whose follow up records were available (retrospective)
3. 'Yes' if no withdrawal/drop out; 'No' if drop-out rate ≥30% or differential drop-out, e.g. those having most severe disease died during follow up but the death was not due to treatment; no description of those lost.
4. 'Yes' if two or more than two factors were similar.