Adverse events following first, single, mesh and non-mesh surgical procedures for stress urinary incontinence and pelvic organ prolapse: a population-based cohort study using routinely collected data in Scotland, 1997-2016.

[short running title: Complications after incontinence and prolapse surgery in Scotland]

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Abstract

Background

Concerns have been raised about the safety of surgery for stress urinary incontinence (incontinence) and pelvic organ prolapse (prolapse) using transvaginal mesh. We assessed adverse outcomes following first, single mesh and comparable non-mesh procedures.

Methods

Women in Scotland aged ≥ 20 years undergoing a first, single incontinence or prolapse procedure during 1997/98-2015/16 were identified from a national hospitalisation database. Primary outcomes were immediate postoperative complications and subsequent (within 5 years) readmissions for later postoperative complications, further incontinence surgery, or further prolapse surgery. Poisson regression models were used to compare outcomes following procedures carried out with and without mesh.

Findings

16660 women underwent a first single incontinence procedure, 13133 (78·8%) using mesh. Compared to non-mesh open surgery (colposuspension), mesh procedures had a lower risk of immediate complications (adjusted rate ratio [aRR] 0·44 (0·36- 0·55)) and subsequent prolapse surgery (adjusted incidence rate ratio [aIRR] 0·30 (0·24-0·39)), and a similar risk of further incontinence surgery (aIRR 0·90 (0·73-1·11)) and later complications (aIRR 1·12 (0·98-1·27)) - all ratios for retropubic mesh.

18986 women underwent a first single prolapse procedure, 1279 (6·7%) using mesh. Mesh (compared to non-mesh) repair of anterior compartment prolapse was associated with a similar risk of immediate complications (aRR 0·93 (0·49- 1·79)); an increased risk of both further incontinence and prolapse surgery (aIRR 3·20 (2·06-4·96) and aIRR 1·69 (1·29-2·20) respectively); and a substantially increased risk of later complications (aIRR 3·15 (2·46-4·04)). Mesh (compared to non-mesh) repair of posterior compartment prolapse was associated with a similarly increased risk of repeat prolapse surgery and later complications. No difference in any outcome was observed between vaginal and, separately, abdominal mesh repair of vaginal vault prolapse compared to vaginal non mesh repair.

Interpretation

Mesh procedures for incontinence are associated with a lower risk of immediate complications and subsequent prolapse surgery than open colposuspension, the main alternative procedure. Mesh procedures are as effective as colposuspension (in terms of the risk of repeat incontinence surgery). Additionally, mesh procedures carry a similar risk of later complications, at least up to five years post surgery. These results therefore support the use of mesh procedures for incontinence, although further research on longer term outcomes would be beneficial.

Mesh procedures for anterior and posterior compartment prolapse (when performed as an isolated, first repair) are associated with poorer overall effectiveness and substantially increased later complications compared to similar non-mesh repairs. These procedures cannot be recommended for primary prolapse repair.

Both vaginal and abdominal mesh procedures for vaginal vault prolapse repair are associated with similar effectiveness and complication rates compared to non mesh vaginal repair. These results therefore do not clearly favour any particular vault repair procedure.

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Introduction

Female stress urinary incontinence (incontinence) and pelvic organ prolapse (prolapse) are common conditions causing substantial disability.(1,2) Women's lifetime risk (by age 80 years) of undergoing pelvic floor surgery for incontinence or prolapse has been estimated as 1 in 8 in the UK(3) and between 1 in 9(4) and, more recently, 1 in 5(5) in the US. Surgical repair for incontinence and prolapse has traditionally been performed using native tissue. However, over the past two decades alternative procedures involving the transvaginal placement of synthetic mesh tapes and implants have been developed for incontinence and prolapse respectively, as these were believed to be potentially less invasive, safer and/or more effective.

During the 1990s in the US and 2000s in the UK mesh tape procedures for incontinence were rapidly adopted,(6) due to perceived equivalent efficacy to open surgical approaches with the benefit of a minimally-invasive approach and cost savings.(7) Mesh tape procedures initially used a retropubic approach: transobturator approach procedures were subsequently developed in an attempt to reduce the risk of intraoperative bladder damage.(8) Transvaginal mesh implant procedures for prolapse were developed to reduce the high risk of prolapse recurrence following native tissue repairs,(9) and their use has gradually increased over the past decade.(10)

Despite a number of randomised controlled trials investigating the use of mesh in female incontinence and prolapse surgery, there is a lack of evidence on outcomes in routine practice, particularly long term outcomes.(7,11,12) Transvaginal mesh surgery, particularly for prolapse, is currently controversial. Patient advocacy groups have raised concerns about poor long term outcomes. Litigation brought by women who have experienced serious complications following mesh surgery is underway in many countries involving settled claims for over a billion US dollars and forcing manufacturers to withdraw mesh products or close down.(13-15) Enquiries into mesh surgery by the Scottish Government(16) and by NHS England(17) are ongoing. Several organisations have recently expressed reservations about transvaginal mesh surgery, in particular for prolapse,(18-21) although mesh surgery continues to be provided in many settings.(22) Procedures involving the transabdominal placement of mesh for uterine or vaginal vault prolapse have been available for many years and are less controversial than newer transvaginal mesh prolapse procedures.

We therefore aimed to compare long term effectiveness and complication rates following procedures with and without mesh for all first, single incontinence and prolapse operations

carried out in Scotland between 1997 and 2016, using a national healthcare utilisation database with complete population coverage.

Methods

Sampling and datasets

Data were extracted for all women aged ≥20 years undergoing incontinence and prolapse procedures during the period 1 April 1997 to 31 March 2016 from the Scottish hospital discharge dataset (SMR01) held by the Information Services Division (ISD) of NHS National Services Scotland.

Index procedures

Index procedures were restricted to first, single procedures. Combination procedures (i.e. an included procedure done at the same time as another incontinence or prolapse procedure) were excluded as were any procedures if the woman had undergone any incontinence or prolapse procedure in the preceding 5 years. Only the first index procedure performed during the study period was included for any individual woman.

The only exceptions were for mesh and non-mesh vaginal vault prolapse procedures (see below). These procedures inevitably follow prior hysterectomy hence women with prior hysterectomy were included. In addition these procedures are very rarely done as single procedures hence procedures done at the same time as non-mesh anterior and/or posterior colporrhaphy were included.

Index incontinence procedures were defined using the Office of Population Censuses and Surveys Classification of Interventions and Procedures 4th revision (OPCS-4) classification system and grouped as: open colposuspension (non-mesh); urethral injection therapy (non-mesh); traditional suprapubic sling (non-mesh); unspecified mesh tapes (up to end March 2006); retropubic mesh tapes; and transobturator mesh tapes (both from April 2006 when specific codes became available) (Extra-Supplementary Material [ESM] 1).

Index prolapse procedures were defined using OPCS-4 as: anterior colporrhaphy with and without mesh for anterior compartment repair; posterior colporrhaphy with and without mesh for posterior compartment repair; sacrospinous fixation of the vagina (non-mesh), vaginal mesh

vault repair (mesh), and open sacrocolpopexy (abdominal mesh) for repair of vaginal vault prolapse; and vaginal hysterectomy (non-mesh) for repair of uterine prolapse.

Only colposuspensions and sacrocolpopexies done as open abdominal procedures were included: the small number of laparoscopic procedures provided in Scotland over the period of our analysis were excluded (ESM 1). Only vaginal hysterectomies done specifically for prolapse (as indicated by the diagnostic code recorded on the patient's hospital discharge record) were included in our analysis (ESM 1). Note that in Scotland it is routine clinical practice for surgeons performing a vaginal hysterectomy for uterine prolapse to perform some element of reconstruction (suspension of the vaginal vault) following uterine removal. This is generally not coded as a separate concurrent procedure as it is considered to be a standard component of the primary hysterectomy. Additional procedures (e.g. colpocleisis, sacrohysteropexy, vaginal mesh uterine suspension) were considered for inclusion but rejected as insufficient numbers were performed during the study period (Figure 1).

Outcomes

Outcomes were defined as follows:

Immediate (within the index admission record) and late procedural complications (within records of readmissions subsequent to the index admission and within 5 years) were identified via International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10) and OPCS-4 codes on hospital discharge records. Multiple complications within a single admission were counted as one complication, with multiple (re)admissions counted separately. Codes for complications included those for haemorrhage, relevant infections, pain, direct procedure related adverse events such as bladder perforation and urinary difficulties, and repeat surgery for mesh removal, with some specific codes only included in immediate or late complications as clinically appropriate (ESM 2).

Further surgery for incontinence or prolapse was similarly identified via OPCS-4 and ICD-10 codes from hospital discharge records within 5 years of the index admission with multiple readmissions for further surgery counted separately. Further incontinence surgery following an index incontinence procedure indicates failure of the initial procedure and hence provides a measure of procedure effectiveness. Conversely, further prolapse surgery following an index incontinence procedure can be considered as an additional late complication (and vice verse for index prolapse procedures). Full code lists for all outcomes are available in ESM2.

Covariates

The following covariates were extracted from the hospital discharge database: age at index procedure admission; Scottish Index of Multiple Deprivation (SIMD) rank, an area-based measure of material deprivation, derived from the postcode of residence at index admission and grouped into quintiles;(23) co-morbidity status, based on any of diabetes (ICD-9/10 codes 250, E10-E14), ischaemic heart disease (410-414, I20-I25) or chronic obstructive pulmonary disease (490-492, 496, J40-J44) recorded on the index hospital discharge record or records within the 5 years prior to the index record. Surgeon volume was based on the annual number of incontinence and, separately, included prolapse procedures performed by the consultant responsible for the index procedure. Incontinence/prolapse index procedures were categorised as performed by a low volume surgeon if the consultant was responsible for <20 included incontinence/prolapse procedures in that year.(24) National designations were used to categorise the index admission hospital as teaching; large general; general; community or other.(25)

Validation of index procedure and complication codes

The PROSPECT clinical trial, which recruited between 2010 and 2013, is comparing outcomes following mesh and non-mesh repair of anterior and posterior compartment prolapse.(26) Thirty three women in the trial had an index mesh procedure in a Scottish hospital and were known to have experienced subsequent mesh erosion complications by April 2015. Using these women as a validation dataset, we validated the OPCS-4 and ICD-10 codes recorded on the SMR01 records relating to their index procedure and subsequent admissions for repair of mesh erosion.

Eleven of the women underwent single anterior or posterior mesh colporrhaphy (included in this study) as their index procedure and all were correctly coded on the corresponding SMR01 record. The remaining 22 women underwent a combination index procedure (excluded from this study), of which 11 were fully correctly coded. The women underwent a total of 24 subsequent mesh erosion repair procedures as a day case or inpatient: the remainder were managed as outpatients. Twenty three of the anticipated 24 SMR01 records were identified. Twenty two of the 23 records included OPCS-4 and/or ICD-10 codes used in this study to identify late complications.

Analysis

Summary statistics for baseline characteristics and adverse outcomes were reported by procedure type and a visual inspection of the data made. Length of stay in days for each index procedure was reported as median and interquartile range.

Poisson regression was used to estimate the crude and adjusted rate ratio (denoted RR and aRR respectively) of all outcomes. For late procedural complications and repeat surgery, multiple events were allowed. Follow-up was censored at 5 years following the index procedure or at 31st March 2016. Covariates were selected for inclusion in the regression models if they were identified by the project steering committee as potential confounders (see ESM 3 for causal diagram). For immediate complications all counts occurred in the same period. For other complications an offset term was used to allow for differential follow-up periods.

Outcomes for each procedure were compared to those following a non-mesh reference procedure. For incontinence procedures, the non-mesh reference category was open colposuspension. Additionally, pre-specified subgroup analyses were undertaken to compare transobturator mesh procedures to retropubic mesh procedures for the period 2006/07 onwards (when procedure specific coding became available).

For prolapse procedures, the non-mesh reference category was anterior colporrhaphy. Additionally, subgroup analyses were undertaken to compare mesh to similar non-mesh procedures for anterior compartment repair (anterior colporrhaphy with and without mesh, 2007/08 onwards); posterior compartment repair (posterior colporrhaphy with and without mesh, 2007/08 onwards); and vault prolapse repair (vaginal mesh vault repair with mesh and, separately, open sacrocolpopexy with abdominal mesh versus sacrospinous fixation of the vagina without mesh from 2006/07 onwards). Further prolapse surgery following an index prolapse procedure was analysed overall and (for all index procedure types excluding vaginal hysterectomy) according to whether the repeat procedure was on the same or a different anatomical compartment to the index procedure. Vaginal hysterectomy was excluded from this analysis as uterine prolapse cannot recur once the uterus has been removed.

In sensitivity analyses, readmissions for further incontinence and/or prolapse surgery were analysed as a single composite outcome, as were readmissions for any further surgery and/or late complications to assess the level of double counting between outcome categories. In addition, the possible effect of consultant level clustering was examined in general estimating

models with a log-link, Poisson distribution and exchangeable correlation structure. Final sensitivity analyses (covering procedures from 2006/07 onwards only because of data availability) examined the effect of restricting index procedures to those with no previous incontinence or prolapse surgery in the 15 (rather than 5) years prior to the index procedure to ensure more complete exclusion of repeat procedures.

Ethical approvals were obtained from the local Caldicott Guardian and the Scottish Privacy Advisory Committee.

Data were analysed using SPSS v21.0 (SPSS Inc, Illinois, USA) and R (Vienna Austria 3.2.0).

Results

Of 26 885 incontinence and 77 537 prolapse procedures carried out in Scotland between 1997/98 and 2015/16, 16 660 (62.0%) and 18 986 (24.5%) respectively were first single included procedures included in our main analysis (Figure 1). Characteristics of women undergoing first single included procedures are shown in Table 1. Characteristics of women undergoing first combined procedures (excluded from our main analysis) are shown for comparison in ESM4. Of the 16 660 incontinence and 18 986 prolapse procedures, 1 and 3 respectively were excluded from the multivariable analysis due to the patient dying on the day of surgery and a further 73 and 98 respectively were excluded due to missing data on area deprivation status (Figure 1). Trends in the provision of each included procedure are shown in Figure 2 and ESM5. Information on inpatient length of stay for each included procedure is provided in ESM6.

Incontinence procedures

Compared to women undergoing non-mesh open colposuspension, patients undergoing mesh procedures for incontinence were of similar age, were less likely to live in a deprived area, and had similar levels of co-morbidity. Women undergoing mesh procedures were less likely to have their procedure in a teaching hospital or to have their procedure performed by a consultant with low procedure volume (Table 1).

Immediate complications following incontinence surgery

Overall 815 (4·9%) women had an immediate procedural complication. After adjusting for age, deprivation, co-morbidity, hospital type and consultant volume, women undergoing retropubic and transobturator mesh procedures had a substantially lower risk of immediate complications than those undergoing the reference non-mesh procedure (open colposuspension), (aRR 0·44 (0·36- 0·55) and 0·31 (0·24- 0·40) respectively, Table 2a). Within the mesh group, transobturator procedures were associated with fewer immediate complications than retropubic procedures (Table 3a). Subgroups of immediate complications are summarised in ESM7. Model fit statistics for all results are provided in ESM8 and ESM9.

Late complications following incontinence surgery

There were 2 771 hospital readmissions for late procedural complications over 75 436 person-years (36·7/1000 person-years). Both retropubic and transobturator mesh procedures had a similar risk of late complications to colposuspension (Table 2b). There was no difference in the rate of late procedural complications between transobturator and retropubic mesh procedures (Table 3b). Subgroups of late complications are summarised in ESM7. In general most immediate and later complications were infection or directly procedure related (e.g. organ damage, urinary difficulties). In addition, in patients who had mesh index incontinence surgery, around a third of late complication readmissions contained a code indicating a subsequent mesh removal procedure.

Further surgery following incontinence surgery

Compared with non-mesh open colposuspension, mesh surgery was associated with a similar risk of subsequent incontinence surgery (Table 2c and 3c). Mesh surgery using both retropubic and transobturator methods was associated with a substantially lower risk of subsequent prolapse surgery however (aIRR 0·30 (0·24-0·39) and 0·26 (0·20-0·34) respectively) (Table 2d and 3d).

Prolapse procedures

The characteristics of women undergoing first, single, included prolapse procedures during the study period are shown in Table 1.

Immediate complications following prolapse surgery

Overall 799 (4·2%) women had an immediate procedural complication following prolapse surgery. The crude and adjusted risks of immediate complications following each procedure type compared to the reference non-mesh procedure (anterior colporrhaphy) are shown in Table 4a. For women undergoing repair of specific compartments, there was no significant difference in risk of immediate complications following a mesh compared to a non mesh repair (Table 5a). Subgroups of immediate complications are summarised in ESM7.

Late procedural complications following prolapse surgery

There were 2 186 late procedural complications over 80 309 person-years (27·2 /1000 person years). In general late complication rates were higher following vault prolapse repair than standard anterior repair (Table 4b). Mesh procedures for anterior and posterior compartment prolapse had much higher late complication rates than corresponding non-mesh procedures on the same compartment (aRR 3·15 (2·46-4·04) and 2.76 (2·11-3·61) respectively, Table 5b). There was no significant difference in the rate of late procedural complications following vaginal or abdominal mesh repair for vault prolapse compared to non mesh vaginal vault repair (Table 5b). Subgroups of late procedural complications are summarised in ESM7. In general most immediate and later complications were infection or directly procedure related. In addition, in patients who had mesh index prolapse surgery, up to around a half of all late complication readmissions contained a code indicating a subsequent mesh removal procedure.

Further surgery following prolapse surgery

Anterior colporrhaphy with mesh was associated with a higher risk of subsequent incontinence and prolapse surgery than anterior colporrhaphy without mesh. Posterior colporrhaphy with mesh was associated with a higher risk of subsequent prolapse surgery than posterior colporrhaphy without mesh. Subsequent incontinence and prolapse surgery rates were similar following vaginal and, separately, abdominal mesh repair for vault prolapse compared to non mesh vaginal vault repair (Table 5c and 5d). For patients undergoing repeat prolapse surgery, around one third of subsequent procedures were performed on the same compartment as the original surgery and two thirds were performed on a different or unspecified compartment (ESM10). Index anterior and posterior compartment repair was associated with an increased risk of further prolapse surgery on the same and different compartments, though the rate ratios for

reoperation on the same compartment were imprecisely estimated due to relatively small numbers of outcomes observed (ESM11).

Sensitivity analyses

Results when readmissions for incontinence and/or prolapse surgery, and readmissions for any further surgery and/or late complications, were analysed as single composite outcomes, indicated minimal double counting between categories. Performing the analyses using generalized estimating equation models accounting for clustering by consultant (ESM 12), and limiting the analyses to index procedures from 2006/07 onwards with no prior incontinence or prolapse procedure within the preceding 15 rather than 5 years, also yielded similar results (ESM 13-16).

Discussion

We report the first large-scale robust observational study of outcomes following surgical management of both incontinence and prolapse. We used high quality administrative data with complete population coverage to examine long term (up to five years) effectiveness and complications following specific mesh and comparable non-mesh procedures.

For stress urinary incontinence we found that in routine clinical practice mesh surgery was associated with a lower risk of immediate complications and subsequent prolapse surgery than the main alternative non-mesh open surgical procedure (colposuspension), and a similar risk of later complications and further incontinence surgery.

For prolapse we found that use of mesh in repair of anterior and posterior compartment prolapse was associated with both increased risk of complications and lower effectiveness. For example, anterior colporrhaphy with mesh was associated with a similar risk of immediate complications but a higher risk of later complications, subsequent incontinence surgery, and subsequent prolapse surgery compared to anterior colporrhaphy without mesh.

For patients undergoing repair of vaginal vault prolapse, we found no difference in any outcome (complications or further surgery) following vaginal mesh or, separately, abdominal mesh surgery compared to non mesh vaginal repair.

Strengths

This is the first study of incontinence and prolapse surgery to compare clinically relevant outcomes in routine clinical practice in a national study with complete population coverage, comparing mesh procedures with their corresponding non-mesh equivalents. It included large numbers of procedures provided over an extended period and examined outcomes up to 5 years following index surgery. We used high quality national datasets containing records of all routine NHS inpatient and day case care performed during the study period, and linked records belonging to individual patients across time using NHS Scotland's unique patient identifier.(27) We performed a range of sensitivity analyses which provided further support to our findings.

Limitations

As with all observational comparisons of treatment groups, confounding by indication is a possible explanation for our findings. It is plausible, for prolapse surgery in particular, that women with more severe disease were selected for mesh rather than non-mesh procedures. However, the women undergoing mesh procedures were similar in terms of age, deprivation, and comorbidity to those receiving non-mesh procedures (factors which we would except to be associated with worse post-operative outcomes). Moreover, confounding by indication is an unlikely explanation for the differential effect of mesh on immediate compared to late complications.

Our results are limited to women undergoing first, single incontinence or prolapse procedures. Prolapse frequently affects multiple anatomical compartments, and/or is accompanied by overt or occult incontinence. In addition, prolapse repair failure rates are relatively high leading to many women requiring repeat procedures. As a result, a relatively high proportion of the total volume of prolapse surgery carried out in Scotland involves multiple and/or repeat procedures and as such was excluded from our analysis. Our approach of focusing on first, single procedures allows clear comparisons of the outcomes seen after specific procedures however it means that we cannot directly comment on the outcomes of women undergoing multiple and/or repeat procedures. We would note however, that robust information on outcomes following specific procedures is likely to provide useful guidance for clinicians and patients considering appropriate procedures for women with prolapse affecting multiple compartments, in particular given the lack of other specific evidence on outcomes for these more complex groups.

Vaginal hysterectomy is not a reconstructive procedure and it can be performed for a range of indications including uterine prolapse. In recognition of this, we limited our analysis to vaginal hysterectomies recorded as done specifically for prolapse. In addition, we note that in Scotland it is routine clinical practice for surgeons performing a vaginal hysterectomy for uterine prolapse to perform some element of reconstruction (suspension of the vaginal vault) following uterine removal as an integral part of the procedure. We were unable to include some procedure types of interest in our analysis, in particular laparoscopic colposuspension, laparoscopic sacrocolpopexy, and mesh uterine suspension procedures, due to insufficient numbers of first, single procedures being performed in Scotland over our analysis period. We are therefore unable to comment on the outcomes of these procedures.

We were restricted in our ability to check the accuracy of coding for procedures and complications. However, the quality of Scottish hospital discharge records is generally high(28) and we undertook additional validation of the coding of index mesh prolapse procedures and their complications. This provided reassurance that the single procedures included in this study were highly likely to be correctly coded. In addition the extensive code lists used to identify subsequent readmissions for late complications were highly likely to pick up admissions relating to important complications such as mesh erosion.

Our classification of index procedure types was limited by the detail available within the OPCS4 coding system. This generally allows identification of specific types of index procedure, but not precise subgroups of procedures involving particular surgical techniques or particular types of mesh. For example, the available OPCS4 codes allowed us to distinguish retropubic and transobturator mesh incontinence procedures from 2006/07 onwards, but not procedure subtypes. Separate procedure codes for 'up-down' versus 'down-up' retropubic mesh insertion, or 'inside-out' versus 'outside-in' transobturator mesh insertion, are not available.

Our choice of primary outcomes focussed on diagnoses and procedures severe enough to require hospital (re)admission. Whilst detailed information is available for inpatient care, national level data on outpatient and community based care is sparser. It was therefore not possible to capture complications managed in outpatient or primary care settings, an issue other studies have also struggled to address.(29)

We developed an inclusive code list designed to capture all immediate and later complications. However coded data inevitably carries limited clinical detail so it was not possible to comment

on the severity of complications or their impact on patients' quality of life. Also, it was not possible to ensure that outcomes such as complication readmissions were a direct consequence of the index procedure of interest and not related to an alternative event. It should also be noted that whilst we used reoperation rates as an indication of effectiveness of the index procedure, this gives only a partial view of effectiveness as many factors in addition to the severity of persistent/recurrent symptoms may influence whether women undergo repeat surgery or not. Some women may choose more conservative treatment such as pelvic floor muscle training, which would not be captured by our methods. Additionally, further incontinence surgery following index prolapse surgery may reflect unmasking of occult incontinence following the initial anatomical repair which arguably may not be viewed as a complication.

Our initial 'look-back' period of 5 years to define 'first' procedures is relatively short. Sensitivity analysis involving an extended 15 year look-back suggested that a number of women in our cohorts had in fact had previous incontinence or prolapse surgery more than 5 years before their index procedure, so a number of repeat procedures will be included in the main analyses. The sensitivity analysis provided reassurance however that stricter exclusion of repeat procedures does not materially alter our results.

In general mesh procedures were carried out in the more recent years of the study period. If there were strong secular trends in the general risk of surgical complications this would influence the comparison of mesh and non-mesh procedures. However it is likely that background surgical risk has decreased over time, which would tend to conservatively bias results towards showing lower risk for the more recently provided mesh procedures.

Interpretation in light of other evidence

Multiple trials on the short term outcomes following surgery for incontinence are available.(11,30-32) Trial results reporting lower risk of perioperative complications and subsequent development of prolapse following mesh surgery compared to non-mesh open surgical procedures are supported by our findings. Trial evidence that mesh and open surgical procedures have similar effectiveness over the short term is also supported by our results, and we provide new evidence that this comparable effectiveness is maintained over the longer term. Our finding of similar levels of later postoperative complications following mesh and open surgery for incontinence is reassuring, however we note that around a third of readmissions for later complications following mesh incontinence surgery involve mesh removal.(29)

Currently available trials on surgical management of prolapse are generally small, of moderate quality at best, and provide information on short term outcomes only.(12,33) The available trial evidence suggests that vaginal mesh surgery for prolapse of the anterior compartment is more effective (in terms of objective repair of the compartment operated on) over the short term than similar non-mesh surgery, but is associated with a higher risk of subsequent development of prolapse of other compartments and/or incontinence. Contrary to the available trials, we find no evidence that mesh surgery for anterior or posterior compartment prolapse provided in routine clinical practice is more effective than non-mesh surgery over the longer term. Rather, we find that mesh surgery is associated with an overall increased need for repeat prolapse surgery. There was an increased risk of further surgery on the same compartment as the index procedure (though the confidence interval was wide) and of further surgery on a different compartment.

Trial evidence also suggests that up to 10% of women experience mesh erosion through the vaginal mucosa following vaginal mesh surgery for anterior compartment prolapse. Our finding of the substantially higher risk of complications (and high proportion of complication readmissions involving mesh revision/removal) following mesh prolapse surgery is novel but in line with the evidence on mesh erosion rates.

Vaginal vault prolapse repair can involve mesh placement through the transvaginal (vaginal mesh vault repair) or abdominal (open sacrocolpopexy) routes. It is recognised clinically that the risks and benefits of abdominally compared to vaginally inserted mesh may be different.(21) However, in our analysis, we found no evidence that any outcomes following abdominal or vaginal mesh vault repair were better or worse than non-mesh vault repair (sacrospinous fixation of vagina), although confidence intervals were wide, reflecting the fact that both mesh vault procedures are relatively uncommonly performed (at least as first, single procedures) in Scotland.

Existing high quality observational evidence of outcomes following mesh and non-mesh prolapse surgery is very sparse. Welk(29) and Kelly(34) examined the incidence of repeat surgery for mesh complications/erosions following mesh surgery for incontinence and prolapse respectively using routinely available healthcare data on Ontario. The cumulative repeat surgery rate was found to be 3% and 5% by 10 years after index incontinence and prolapse procedures respectively. No information on other outcomes or comparison to non mesh surgery was provided. Chughtai examined short term outcomes following mesh and non-mesh vaginal

surgery for prolapse provided between 2008-2011 in New York State using routinely available healthcare data.(35) Women undergoing any mesh surgery (all procedure types considered together) were found to have a higher rate of reoperation for prolapse repair or mesh revision (both outcomes considered together) over the 12 months following surgery than those undergoing any non-mesh procedure. Our findings are in line with Chughtai's and substantially extend the available observational evidence by providing information on specific procedures and outcomes over a longer period of follow up.

Conclusion

Mesh procedures for incontinence are associated with a lower risk of immediate complications and subsequent prolapse surgery than open colposuspension, the main alternative procedure. Mesh procedures are as effective as colposuspension (in terms of the risk of repeat incontinence surgery). Additionally, mesh procedures carry a similar risk of later complications, at least up to five years post surgery. These results therefore support the use of mesh procedures for incontinence, although further research on longer term outcomes would be beneficial.

Mesh procedures for anterior and posterior compartment prolapse (when performed as an isolated, first repair) are associated with poorer overall effectiveness and substantially increased later complications compared to similar non-mesh repairs. These procedures cannot be recommended for primary prolapse repair.

Both vaginal and abdominal mesh procedures for vaginal vault prolapse repair are associated with similar effectiveness and complication rates compared to non mesh vaginal repair. These results therefore do not clearly favour any particular vault repair procedure.

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Disclosure of Interests

No conflicts of interest to declare.

Contribution to Authorship

JRM advised on study design, analysed the data, interpreted the data, drafted the manuscript, revised and approved the final manuscript. DAM advised on study design, analysed the data, interpreted the data, revised and approved the final manuscript. WA advised on study design, interpreted the data, revised and approved the final manuscript. CMF advised on study design, interpreted the data, revised and approved the final manuscript. CMAG advised on study design, interpreted the data, revised and approved the final manuscript. KG advised on study design, interpreted the data, revised and approved the final manuscript. LH extracted data, interpreted the data, revised and approved the final manuscript. RW designed the study, obtained governance approvals, oversaw the data analysis, interpreted the data and revised and approved the final version of the manuscript.

Details of Ethics Approval

Approvals were obtained from the local Caldicott Guardian and the Privacy Advisory Committee prior to undertaking data extraction and analysis. Data was held and analysed securely within ISD hence NHS ethical approval was not required.

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Table/Figure Caption List

Figure 1.

Caption:

Flow chart of patients undergoing stress urinary incontinence and pelvic organ prolapse surgery in Scotland, 1997/98-2015/16.

Figure 2.

Caption:

Numbers of first single included procedures performed in Scotland, 1997/98-2015/16.

Legend for 2A:

Specific codes for mesh incontinence procedures (retropubic and transobturator mesh) were introduced in April 2006. Prior to that date, a non specific OPCS4 code was used to denote all types of mesh incontinence procedures.

Legend for 2B:

Specific codes for mesh colporrhaphies and Vaginal mesh vault repair were introduced in April 2007 and April 2006 respectively.

Figures

Figure 1

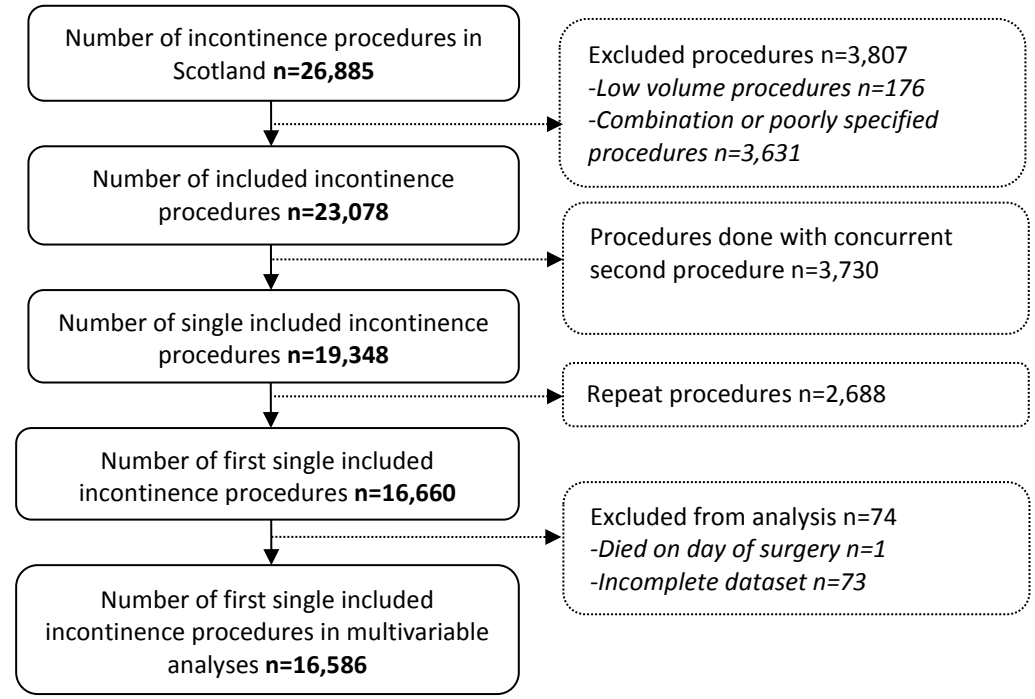

Figure 2

2A. First single incontinence procedure frequency in Scotland, 1997/98-2015/16.

2B. First single prolapse procedure frequency in Scotland, 1997/98-2015/16.

Tables

Table 1 Characteristics of patients undergoing first single included incontinence and prolapse procedures in Scotland, 1997/98-2015/16.

Incontinence surgery

	Open colposuspension (non mesh)	Urethral injection therapy (non mesh)	Suprapubic sling (non mesh)	Unspecified mesh	Retropubic mesh	Transobturator mesh
Number of patients	2367	685	475	3655	4628	4850
Years	1997/98-2015/16	1997/98-2015/16	1997/98-2015/16	1997/98-2005/06	2006/07-2015/16	2006/07-2015/16
Age, years, mean (SD)	50·8 (10·5)	56·6 (16·0)	53·2 (10·8)	51·8 (11·1)	50·8 (10·7)	51·1 (10·8)
Most deprived quintile, % (number)	23·5 (554)	24·2 (166)	35·4 (168)	17·0 (621)	18·0 (834)	23·1 (1109)
Co-morbidity, % (number)	5·9 (139)	14·7 (101)	10·9 (52)	7·5 (275)	4·9 (228)	7·0 (339)
Teaching hospital, % (number)	30·1 (713)	57·8 (396)	67·6 (321)	28·9 (1056)	24·8 (1147)	22·0 (1065)
Low volume consultant, % (number)	78·0 (1846)	66·0 (452)	56·6 (269)	40·2 (1468)	36·1 (1669)	27·8 (1347)

Prolapse surgery

	Anterior colporrhaphy (non mesh)	Anterior colporrhaphy with mesh	Posterior colporrhaphy (non mesh)	Posterior colporrhaphy with mesh	Sacrospinous fixation of vagina (non mesh)	Vaginal mesh vault repair (mesh)	Open sacrocolpopexy (abdominal mesh)	Vaginal hysterectomy (non mesh)
Number of patients	7643	278	6061	209	2058	112	680	1945
Years	1997/98-2015/16	2007/08-2015/16	1997/98-2015/16	2007/08-2015/16	1997/98-2015/16	2006/07-2015/16	1997/98-2015/16	1997/98-2015/16
Age, years, mean (SD)	62·1 (10·8)	62·1 (10·0)	58·6 (12·2)	59·0 (10·4)	64·9 (10·8)	63·5 (11·8)	63·3 (10·5)	56·7 (12·8)
Most deprived quintile, % (number)	16·3 (1241)	18·3 (51)	16·2 (976)	23·9 (50)	15·6 (321)	16·1 (18)	11·9 (81)	18·7 (363)
Co-morbidity, % (number)	8·2 (627)	10·1 (28)	7·8 (474)	12·4 (26)	11·6 (239)	14·3 (16)	9·0 (61)	5·2 (102)
Teaching hospital, % (number)	27·7 (2119)	52·5 (146)	32·2 (1952)	46·4 (97)	35·5 (731)	18·8 (21)	41·3 (281)	35·4 (688)
Low volume consultant, % (number)	72·5 (5538)	37·8 (105)	72·5 (4394)	39·7 (83)	52·7 (1085)	24·1 (27)	80·1 (545)	76·3 (1485)

Table 2 Adverse events following first single incontinence procedures in Scotland, 1997/98-2015/16.

	Open colposuspension (non mesh)	Urethral injection therapy (non mesh)	Suprapubic sling (non mesh)	Unspecified mesh	Retropubic mesh	Transobturator mesh
Number of patients	2367	685	475	3655	4628	4850
Years	1997/98-2015/16	1997/98-2015/16	1997/98-2015/16	1997/98-2005/06	2006/07-2015/16	2006/07-2015/16
Follow-up in months, median (interquartile range)	60·9 (60·9-60·9)	60·9 (45·3-60·9)	60·9 (60·9-60·9)	60·9 (60·9-60·9)	60·9 (43·8-60·9)	60·9 (48·9-60·9)
[A] Immediate postoperative complications						
Patients with a complication, % (n)	7·8 (185)	8·2 (56)	5·7 (27)	7·1 (258)	3·7 (169)	2·5 (120)
Unadjusted RR (95% CI)	1 (ref)	1·05 (0·78- 1·41)	0·73 (0·49- 1·09)	0·91 (0·75- 1·10)	0·47 (0·38- 0·57)	0·32 (0·25- 0·40)
Adjusted RR (95% CI)		1·01 (0·74- 1·37)	0·75 (0·50- 1·13)	0·84 (0·68- 1·02)	0·44 (0·36- 0·55)	0·31 (0·24- 0·40)
[B] Late postoperative complication admissions						
Patients with 1 or more admission	265	102	73	400	458	422
Total number of admissions within 5 years	391	251	113	612	698	706
Total person-years of follow-up	11454	2832	2090	18074	19608	21378
Crude incidence rate per 1,000 person-years	34·1	88·6	54·1	33·9	35·6	33·0
Unadjusted IRR (95% CI)	1 (ref)	2·59 (2·21-3·03)	1·58 (1·28-1·95)	0·99 (0·87-1·12)	1·04 (0·92-1·18)	0·97 (0·86-1·10)
Adjusted IRR (95% CI)		2·43 (2·07-2·86)	1·54 (1·25-1·91)	1·03 (0·91-1·18)	1·12 (0·98-1·27)	1·02 (0·89-1·16)
[C] Further incontinence surgery admissions						
Patients with 1 or more admission	131	199	53	241	200	258
Total number of admissions within 5 years	153	267	68	297	231	299
Total person-years of follow-up	11454	2832	2090	18074	19608	21378
Crude incidence rate per 1,000 person-years	13·4	94·3	32·5	16·4	11·8	14·0

Unadjusted IRR (95% CI)	1 (ref)	7·03 (5·77-8·58)	2·43 (1·83-3·24)	1·23 (1·01-1·49)	0·88 (0·72-1·08)	1·04 (0·86-1·27)
Adjusted IRR (95% CI)		7·15 (5·83-8·76)	2·39 (1·79-3·20)	1·26 (1·03-1·54)	0·90 (0·73-1·11)	1·06 (0·86-1·30)
[D] Further prolapse surgery admissions						
Patients with 1 or more admission	165	9	19	109	96	99
Total number of admissions within 5 years	198	10	24	122	108	104
Total person-years of follow-up	11454	2832	2090	18074	19608	21378
Crude incidence rate per 1,000 person-years	17·3	3·5	11·5	6·8	5·5	4·9
Unadjusted IRR (95% CI)	1 (ref)	0·21 (0·11-0·39)	0·67 (0·44-1·02)	0·39 (0·31-0·49)	0·32 (0·25-0·41)	0·28 (0·22-0·36)
Adjusted IRR (95% CI)		0·20 (0·11-0·38)	0·68 (0·44-1·04)	0·37 (0·29-0·48)	0·30 (0·24-0·39)	0·26 (0·20-0·34)

Crude incidence rate per 1000 person-years = [total number of admissions within 5 years/total person-years of follow-up]*1000
RR relative risk; IRR incidence rate ratio

Table 3 Direct comparison of adverse events following specific mesh first single incontinence procedures, Scotland 2006/07-2015/16.

	Retropubic mesh	Transobturator mesh
Number of patients	4623	4801
Years	2006/07-2015/16	2006/07-2015/16
[A] Immediate postoperative complications		
Unadjusted RR (95% CI)	1 (ref)	0·69 (0·54-0·87)
Adjusted RR (95% CI)		0·71 (0·56-0·90)
[B] Late postoperative complication admissions		
Unadjusted IRR (95% CI)	1 (ref)	0·93 (0·84-1·03)
Adjusted IRR (95% CI)		0·90 (0·81-1·01)
[C] Further incontinence surgery admissions		
Unadjusted IRR (95% CI)	1 (ref)	1·19 (1·00-1·41)
Adjusted IRR (95% CI)		1·16 (0·97-1·38)
[D] Further prolapse surgery admissions		
Unadjusted IRR (95% CI)	1 (ref)	0·88 (0·67-1·16)
Adjusted IRR (95% CI)		0·86 (0·66-1·14)

RR rate ratio; IRR incidence rate ratio. Number of patients undergoing each procedure may be lower than that seen in Table 2 as patients with missing data were excluded from the regression models.

Table 4 Adverse events following first single prolapse procedures in Scotland, 1997/98-2015/16.

	Anterior colporrhaphy (non mesh)	Anterior colporrhaphy with mesh	Posterior colporrhaphy (non mesh)	Posterior colporrhaphy with mesh	Sacrospinous fixation of vagina (non mesh)	Vaginal mesh vault repair (mesh)	Open sacrocolpopexy (abdominal mesh)	Vaginal hysterectomy (non mesh)
Number of patients	7643	278	6061	209	2058	112	680	1945
Years	1997/98-2015/16	2007/08-2015/16	1997/98-2015/16	2007/08-2015/16	1997/98-2015/16	2006/07-2015/16	1997/98-2015/16	1997/98-2015/16
Follow-up in months, median (interquartile range)	60·9 (53·1-60·9)	60·9 (49·2-60·9)	60·9 (50·2-60·9)	59·3 (50·4-60·9)	39·3 (21·7-60·9)	60·9 (60·9-60·9)	60·9 (60·9-60·9)	60·9 (60·9-60·9)
[A] Immediate postoperative complications								
Patients with a complication, % (n)	4·5 (343)	3·6 (10)	3·3 (199)	1·4 (3)	4·4 (91)	4·5 (5)	6·3 (43)	5·4 (105)
Unadjusted RR (95% CI)	1 (ref)	0·80 (0·43-1·49)	0·73 (0·62-0·87)	0·32 (0·10-0·99)	0·98 (0·78-1·24)	0·99 (0·41-2·39)	1·40 (1·02-1·92)	1·20 (0·96-1·49)
Adjusted RR (95% CI)		0·78 (0·41-1·46)	0·74 (0·62-0·89)	0·31 (0·10-0·98)	0·94 (0·74-1·19)	0·95 (0·39-2·31)	1·32 (0·96-1·82)	1·24 (0·99-1·54)
[B] Late postoperative complication admissions								
Patients with 1 or more admission	504	49	477	42	184	17	78	150
Total number of admissions within 5 years	730	87	673	72	259	27	121	217
Total person-years of follow-up	33205	1236	26000	934	6562	518	3127	8726
Crude incidence rate per 1,000 person-years	22·0	70·4	25·9	77·1	39·5	52·1	38·7	24·9
Unadjusted IRR (95% CI)	1 (ref)	3·19 (2·55-3·98)	1·18 (1·06-1·31)	3·49 (2·74-4·44)	1·78 (1·55-2·05)	2·36 (1·61-3·46)	1·75 (1·44-2·12)	1·13 (0·97-1·31)
Adjusted IRR (95% CI)		3·18 (2·54-3·99)	1·15 (1·03-1·27)	3·23 (2·52-4·13)	1·79 (1·55-2·07)	2·22 (1·51-3·27)	1·86 (1·53-2·26)	1·09 (0·93-1·27)
[C] Further incontinence surgery admissions								
Patients with 1 or more admission	206	26	142	8	35	5	31	45
Total number of admissions within 5 years	228	28	159	9	39	5	33	50

Total person-years of follow-up	33205	1236	26000	934	6562	518	3127	8726
Crude incidence rate per 1,000 person-years	6·9	22·7	6·1	9·6	5·9	9·6	10·6	5·7
Unadjusted IRR (95% CI)	1 (ref)	3·28 (2·22-4·86)	0·89 (0·72-1·09)	1·40 (0·72-2·72)	0·86 (0·61-1·21)	1·40 (0·58-3·39)	1·53 (1·06-2·20)	0·83 (0·61-1·13)
Adjusted IRR (95% CI)		2·91 (1·95-4·34)	0·85 (0·69-1·04)	1·21 (0·62-2·36)	0·87 (0·62-1·23)	1·30 (0·53-3·18)	1·70 (1·18-2·47)	0·77 (0·56-1·05)
[D] Further prolapse surgery admissions								
Patients with 1 or more admission	863	52	526	27	285	18	139	215
Total number of admissions within 5 years	990	66	584	38	313	21	170	243
Total person-years of follow-up	33205	1236	26000	934	6562	518	3127	8726
Crude incidence rate per 1,000 person-years	29·8	53·4	22·5	40·7	47·7	40·5	54·4	27·8
Unadjusted IRR (95% CI)	1 (ref)	1·79 (1·39-2·30)	0·76 (0·68-0·84)	1·36 (0·99-1·88)	1·60 (1·41-1·82)	1·36 (0·88-2·09)	1·82 (1·55-2·14)	0·93 (0·81-1·08)
Adjusted IRR (95% CI)		1·62 (1·26-2·09)	0·73 (0·66-0·81)	1·19 (0·86-1·65)	1·55 (1·36-1·76)	1·24 (0·80-1·91)	1·93 (1·64-2·28)	0·90 (0·78-1·03)

Crude incidence rate per 1000 person-years = [total number of admissions within 5 years/total person-years of follow-up]*1000
RR relative risk; IRR incidence rate ratio

Table 5 Direct comparison of adverse events following specific mesh and non mesh first single procedures for prolapse, by anatomical compartment of index procedure, Scotland 2006/07-2015/16.

	Anterior compartment prolapse		Posterior compartment prolapse		Vaginal vault prolapse		
	Anterior colporrhaphy (non mesh)	Anterior colporrhaphy with mesh	Posterior colporrhaphy (non mesh)	Posterior colporrhaphy with mesh	Sacrospinous fixation of vagina (non mesh)	Vaginal mesh vault repair (mesh)	Open sacrocolpopexy (abdominal mesh)
Number of patients	3866	278	3086	209	1932	112	152
Years	2007/08-2015/16	2007/08-2015/16	2007/08-2015/16	2007/08-2015/16	2006/07-2015/16	2006/07-2015/16	2006/07-2015/16
[A] Immediate postoperative complications							
Unadjusted RR (95% CI)	1 (ref)	0·94 (0·50-1·78)	1 (ref)	0·50 (0·16-1·57)	1 (ref)	1·03 (0·42-2·53)	1·66 (0·89-3·12)
Adjusted RR (95% CI)		0·93 (0·49- 1·79)		0·49 (0·15-1·58)		1·14 (0·46- 2·84)	1·70 (0·89- 3·27)
[B] Late postoperative complication admissions							
Unadjusted IRR (95% CI)	1 (ref)	2·95 (2·33-3·73)	1 (ref)	2·84 (2·20-3·67)	1 (ref)	1·32 (0·89-1·97)	0·77 (0·48-1·25)
Adjusted IRR (95% CI)		3·15 (2·46-4·04)		2·76 (2·11-3·61)		1·23 (0·82-1·86)	0·88 (0·54-1·44)
[C] Further incontinence surgery admissions							
Unadjusted IRR (95% CI)	1 (ref)	3·49 (2·29-5·32)	1 (ref)	1·51 (0·76-3·02)	1 (ref)	1·59 (0·63-4·06)	0·84 (0·26-2·72)
Adjusted IRR (95% CI)		3·20 (2·06-4·96)		1·40 (0·68-2·86)		1·46 (0·55-3·85)	0·86 (0·26-2·84)
[D] Further prolapse surgery admissions							
Unadjusted IRR (95% CI)	1 (ref)	1·78 (1·37-2·30)	1 (ref)	1·77 (1·26-2·49)	1 (ref)	0·84 (0·54-1·30)	0·80 (0·53-1·23)

Adjusted IRR (95% CI)		1·69 (1·29-2·20)		1·70 (1·20-2·42)		0·83 (0·53-1·31)	0·77 (0·50-1·18)

RR relative risk; IRR incidence rate ratio. Number of patients undergoing each procedure may be lower than that seen in Table 4 as patients with missing data were excluded from the regression models.

Extra supplementary material

EMS 1 Index procedure coding

EMS 2 Outcome coding

ESM 3 Directed acyclic graph

ESM 4 Characteristics of patients undergoing first combined procedures

ESM 5 Index procedure frequency

ESM 6 Index procedure length of inpatient stay

ESM 7 Immediate and late complications by complication subgroups

ESM 8 Deviance and residual degrees of freedom for all Poisson regression models

ESM 9 Plots of predicted against observed rates from all Poisson regression models

ESM 10 Further prolapse surgery on same and different anatomical compartment following index prolapse procedure

ESM 11 Direct comparison of further prolapse surgery on same and different anatomical compartment following specific mesh and non mesh first single procedures for prolapse, by anatomical compartment of index procedure

ESM 12 Comparison of estimates from Poisson models and from generalized estimating equation models to accommodate clustering by consultant

ESM 13 Adverse events following first single incontinence procedures in Scotland, 2006/07-2015/16 with 15 year look back to define first procedures

ESM 14 Direct comparison of adverse events following specific mesh first single incontinence procedures, Scotland 2006/07-2015/16 with 15 year look back to define first procedures

ESM 15 Adverse events following first single prolapse procedures in Scotland, 2006/07-2015/16 with 15 year look back to define first procedures

ESM 16 Direct comparison of adverse events following specific mesh and non mesh first single procedures for prolapse, by anatomical compartment, Scotland 2006/07-2015/16 with 15 year look back to define first procedures