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1. Title of the project

The clinical and cost-effectiveness of open mesh repairs in adults presenting with a clinically diagnosed unilateral, primary inguinal hernia who are operated in an elective setting: systematic review and economic evaluation.

2. Name of the TAR team and project lead

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3. Plain English summary

Inguinal hernia is the most common type of hernia. A hernia usually appears as a swelling or lump in the groin. The swelling may be painful and may affect day to day activities. If a hernia gets 'strangulated' (a section of bowel becomes trapped) it can be life threatening because of the reduction of blood supplied to the intestine. Hernias are commonly repaired using surgery where the abdominal bulge is pushed back into place and the weakness in the abdominal wall is strengthened. Rarely, inguinal hernias, which do not cause serious symptoms, are managed through watchful waiting as an alternative to surgical repair. Inguinal hernias occur mainly in men.

Repair of inguinal hernia is a very common surgical procedure. Various techniques and approaches are available for surgical hernia repairs. Recently 'tension-free' repairs, which are based on the use of 'mesh' (prosthetic and biological), are widely performed and considered superior to the traditional 'tissue-suture' repairs such as the Bassini or Shouldice technique. With regard to the tension-free repairs, meshes can be placed either through open surgery (e.g. Lichtenstein repair, pre-peritoneal repair) or laparoscopic (keyhole) surgery. The Lichtenstein technique is considered the gold standard among the open inguinal hernia repairs.

Recurrence rates after tension-free surgical procedures are usually low. Nevertheless, chronic pain, complications, and reduced quality of life have been reported after surgical repairs for inguinal hernia, especially after open repairs. There is a need to improve the current evidence on chronic pain, quality of life, and cost utility outcomes after open inguinal hernia repairs.

4. Decision problem

4.1 Background

An inguinal hernia is a protrusion of the contents of the abdominal cavity through a defect in the inguinal canal. It manifests as a lump or swelling in the groin that may cause discomfort and pain, and therefore limit daily activities and the ability to work. Occasionally the hernia sac contents may get incarcerated causing obstruction of the intestine or strangulation, leading to ischemia, necrosis and possible perforation of the intestine. Most of inguinal hernias are found in men due to the vulnerability of the male anatomy to the formation of hernias in this region.

In England 71,490 inguinal hernia procedures were carried out in 2012/13, [1] with over 100,000 NHS bed-days of hospital resources utilised, making the surgical repair of inguinal hernia the most common general surgical intervention in the UK.[2] Of these procedures, 92%

(65,759 repairs) were for the repair of primary hernias and 8% (5,731 repairs) for the repair of recurrent hernias.[1] The British Association of Day Surgery encouraged day surgery for the majority of inguinal hernia repairs to overcome the demand of hospital bed requirement.[2] Surgical repair (herniorraphy) is undertaken in most people presenting with inguinal hernia in order to close the defect, alleviate symptoms of discomfort, and prevent serious complications (such as obstruction or strangulation of the bowel). Most hernia repairs are undertaken as elective procedures.[3] Surgical treatments for inguinal hernia repair can be classified in three main categories: open repair with suture, open repair with mesh (e.g. Liechtenstein repair, pre-peritoneal repair) and laparoscopic repair with mesh. Severe chronic pain, wound infection, and recurrence are among the complications that occur after hernia repair.[4,5]

Published evidence has demonstrated low recurrence rate after mesh repair compared with the traditional sutured technique[6,7] and mesh repair is considered now the treatment of choice for the treatment of inguinal hernia.[8]

A lower risk of recurrence has been reported after open surgery than after laparoscopy for the treatment of painful primary hernias in adults.[9] Other relevant outcomes, including short-term recovery and long-term pain, seem to favour laparoscopic repair over open repair.[9] Different open repair procedures generally have produced similar results, and the pre-peritoneal repair has shown same or better outcomes compared with laparoscopic procedures.[9]

Considering the low recurrence rate reported in the literature after surgical repair of inguinal hernia, the key outcomes on which to measure the clinical success of hernia recovery should include chronic pain, complications, time to return to normal activities, and quality of life.[4,5] With incidence rates of 10% to 54%, chronic pain is the dominant complication after inguinal hernia repair, which considerably impacts upon patient's quality of life.[4,10,11] The reason for long-term postoperative pain after hernia repair is complex and often related to intra-operative nerve damage, which is often associated with technical aspects of the surgical procedures as well as with surgeon's dexterity and expertise.[12] The position of the mesh is probably another crucial factor. Recent systematic reviews and meta-analyses, which have assessed the effects of common surgical techniques (including open pre-peritoneal repair, Lichtenstein repair, and laparoscopic repair) in lowering chronic pain and improving major clinical outcomes, have produced conflicting results.[9,13-15] The overall low reported recurrence rate after inguinal hernia repair makes it difficult to determine which surgical procedure is the best[8] and there is a need to assess outcomes with regard to chronic pain, and quality of life, wound complications, and costs.

4.2 Purpose of the decision to be made

The objective of this appraisal is to assess the clinical and cost-effectiveness of surgical open mesh treatments for inguinal hernia in adults presenting with a clinically diagnosed unilateral, primary inguinal hernia who are operated in an elective setting. In particular, the effects of current open mesh surgical techniques with regard to chronic pain and patient's quality of life will be considered.

4.3 Clear definition of the intervention

Open mesh hernia repair methods include those involving mesh to strengthen the inguinal wall (e.g. open flat mesh, open pre-peritoneal mesh).

The following open mesh repairs of inguinal hernia will be considered for the purpose of this appraisal:

- **Anterior Lichtenstein repair:** Lichtenstein repair is a very common approach that involves the placement of flat mesh on top of the hernia defect through anterior dissection of the inguinal wall under local or general anesthesia.
- **Open pre-peritoneal mesh repair:** This procedure involves incision of the abdominal wall and implantation of the mesh in the space between the peritoneum and the muscle layers. The mesh is held in place with intra-abdominal pressure and requires less or no fixation. Open pre-peritoneal hernia surgery can be performed using different methods such as the Kugel patch, the Nyhus repair, the Read-Rives repair, the Transinguinal pre-peritoneal repair and the Stoppa repair.

Non-mesh techniques requiring suturing (e.g Shouldice, Bassini, McVay, Maloney darn and plication darn techniques) will not be considered in this appraisal as they have been proved to be inferior to current mesh techniques and hence no longer recommended.[16] Similarly, plug mesh repair and Prolene Hernia System will not be included in this assessment as they have not demonstrated to be superior to the standard Lichtenstein method (see section 4.5 below).

4.4 Populations and relevant subgroups

Adults presenting with a clinically diagnosed unilateral, primary inguinal hernia who are operated in an elective setting. No relevant subgroups identified.

4.5 Existing evidence/guidelines, and key factors to be addressed

The performance of open versus laparoscopic techniques has been assessed in a considerable number of randomised controlled trials (RCTs). A previous UK Health Technology Assessment included 37 RCTs published up to 2003 comparing open repairs versus

laparoscopic repairs.[14] A report commissioned by the USA Agency for Healthcare Research and Quality (AHRQ), which was published in 2012, compared the effectiveness and adverse effects of various surgical treatments for inguinal hernia in both adults and children.[9] The report identified 123 RCTs, 2 registries, and 26 non-randomised studies published between January 1990 and November 2011.[9] Thirty-six of the included 123 RCTs compared open mesh repairs versus laparoscopic mesh repairs for primary inguinal hernia (indicating that the size of the evidence base for this comparison has not significantly changed since 2003) and 20 RCTs assessed various open mesh repairs (some of which may no longer reflect the repairs commonly performed in clinical practice). Both these reports concluded that laparoscopic repair resulted in faster return to normal activities, less chronic pain and numbness and fewer post-operative complications (infection and haematoma) and that the open repair was associated with lower rates of serious complications (especially visceral injuries). With regard to recurrences, the USA AHRQ report found lower rates after open surgery while the UK report observed similar recurrence rates between laparoscopic and open procedures.

The Groin Hernia Guidelines published in 2013 included a meta-analysis of 8 RCTs with a total of 2912 patients on the effects of mesh plug repair versus Lichtenstein repair. Pooled data showed similar results in terms of post-operative complications and return to daily activity.[8] Another meta-analysis of 10 RCTs with a total of 2708 patients, compared mesh plug repair, Prolene® Hernia System and Lichtenstein repair. No significant differences in the number of recurrences were observed when Lichtenstein repair was compared with mesh plug repair or Prolene® Hernia System repair, respectively.[17] Another meta-analysis including six RCTs and a total of 1313 patients assessed the effects of Prolene® Hernia System and Lichtenstein for open inguinal hernia repair. Prolene® Hernia System was associated with higher rates of peri-operative complications compared with Lichtenstein repair and there was no significant difference in the duration of operation, time to return to work, chronic groin pain, and recurrence rate between the two techniques.[18] A recent clinical effectiveness report[9] based on 21 studies comparing Lichtenstein open mesh with various plug techniques, concluded that return to work was shorter after Lichtenstein repair but no other significant difference in terms of outcomes were observed. Two systematic reviews published in 2012 assessed the effects of open mesh repair (including open pre-peritoneal repair) versus Lichtenstein mesh repair. These reviews, which between them including a total of 13 RCTs, failed, however, to provide definitive and unequivocal results.[13,15]

In brief:

- Recent guidance from the British Hernia Society suggested that inguinal hernias should be repaired using a mesh technique.[8]

- The relevant mesh techniques commonly used for the treatment of primary inguinal hernia in the UK are open mesh repair (e.g. Lichtenstein repair, pre-peritoneal repair) or laparoscopic repair (e.g. TAPP repair, TEP repair).
- Laparoscopic repairs are associated with less chronic pain and numbness, and earlier return to normal activities. On the other hand, they require longer operation time, special equipments, and high surgeon's experience. For most of the short-term outcomes laparoscopic and open mesh repairs have demonstrated comparable effectiveness.[14] Laparoscopic repair is commonly used for recurrences and bilateral hernias. For adults with painful primary hernias, recurrence rates are reported to be lower after open surgery than after laparoscopy surgery.[9] In particular, open pre-peritoneal repairs have shown similar or better outcomes compared with laparoscopic procedures.[9]
- NICE guideline suggests that laparoscopic surgery should be considered one of the treatment options for inguinal hernia. A shared decision making model should be used for the choice of surgery by fully informing patients about the risks and benefits of open and laparoscopic repairs.[3] Laparoscopic surgery for inguinal hernia repair should only be performed by trained and experienced surgeons.[3]
- NICE uptake report published in 2010 suggests that of all surgical repairs of inguinal hernia performed in 2008/2009 in England; approximately 16% were performed using laparoscopic techniques.[19] In Scotland, the uptake of laparoscopic surgery in 2007/08 was lower with only 13% of inguinal hernia repairs performed using a laparoscopic approach.[20]
- The open mesh Lichtenstein repair is the most commonly performed procedure for hernia repair in the UK (96% of surgeons).[4] This method, however, is associated with pain and numbness due to the extensive dissection of the inguinal wall and the need for mesh fixation. The reason for the postoperative pain after Lichtenstein repair could be explained by the interaction between the mesh and the surrounding nerves.
- The open pre-peritoneal hernia repair is another open mesh approach where the mesh is held in place with intra-abdominal pressure, requiring no or less mesh fixation and less dissection of the inguinal wall. As the pre-peritoneal space lacks major nervous structures, the risk of pain after this surgical repair is reduced.

Considering the available evidence on surgical repairs of inguinal hernia and that chronic pain postoperative pain is more often associated with the Lichtenstein repair, we propose to assess the current evidence for the clinical and cost-effectiveness of **open pre-peritoneal repairs** versus standard anterior **Lichtenstein repair**.

The specific aims addressed by this appraisal will be the following:

- Systematically review the relative clinical-effectiveness of surgical **open pre-peritoneal mesh repairs** compared with standard **Lichtenstein repair** for the treatment of adults presenting with a clinically diagnosed unilateral, primary, inguinal hernia who are operated in an elective setting.
- Systematically review existing economic evaluations on surgical open mesh techniques for the treatment of adults presenting with a clinically diagnosed unilateral, primary, inguinal hernia who are operated in an elective setting.
- Develop a *de novo* economic model to assess the cost-effectiveness of surgical open mesh repairs for the treatment of adults presenting with a clinically diagnosed unilateral, primary, inguinal hernia who are operated in an elective setting.

5. Report methods for assessing the outcomes arising from the use of the interventions

An objective synthesis of the evidence for evaluating the clinical effectiveness of relevant open mesh surgical procedures for the repair of primary unilateral inguinal hernia will be considered. The evidence synthesis will be conducted according to the NICE methods of technology appraisal.[21] In particular, evidence on relevant outcomes will be obtained from a systematic review of the relevant literature. The systematic review will be conducted according to the general principles of the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care,[22] the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions[23] and the PRISMA statement for the reporting of systematic reviews and meta-analyses.[24]

5.1 Population

Adults presenting with a clinically diagnosed unilateral, primary inguinal hernia who are operated in an elective setting will be considered.

Children (<18 years old) and adults presenting with recurrent or bilateral inguinal hernia will not be deemed suitable for inclusion.

5.2 Setting

Any appropriate surgical setting.

5.3 Interventions

The interventions considered are **open pre-peritoneal mesh repairs** and **standard anterior Lichtenstein repair**. Open pre-peritoneal mesh repairs can be performed using various techniques including Kugel patch repair, Read-Rives repair, Transinguinal preperitoneal repair, Stoppa repair and Nyhus repair. The relative effectiveness of any of these techniques compared with the Lichtenstein repair will be assessed.

Open non-mesh techniques (including Shouldice, Bassini, Mcvay, Maloney darn and plication darn techniques) as well as mesh repairs that can be performed using both anterior and posterior approaches (such as the PROLENE hernia system and the mesh plug repair) will not be considered suitable for inclusion.

5.5 Outcomes

Studies will be selected for inclusion if they provide data on any of the following outcomes:

Patient reported outcomes:

- Chronic pain (>3 months after repair) (any measures)
- Chronic numbness (>3 months after repair) (any measures)
- Acute pain (<3 months after repair) (any measures)
- Acute numbness (<3 months after repair) (any measures)
- Quality of life (any measures)

Clinical and surgical outcomes:

- Mortality
- Complications (haematoma, seroma, wound/superficial infection, mesh/deep infection, vascular injury, visceral injury, port site hernia, other serious complications)
- Recurrence/re-operation rate
- Length of hospital stay (days)
- Time to return to normal activities (days)

5.6 Study design

Randomised controlled trials (RCTs) or quasi RCTs. Well-conducted systematic reviews will be considered as relevant sources of existing data and updated if necessary.

Exclusion criteria

We will exclude the following types of report:

- Biological studies;

- Editorials and opinions;
- Case reports;
- Conference abstracts.

5.7 Search strategy

Highly sensitive search strategies will be designed, using appropriate controlled vocabulary and text word terms that reflect the surgical procedures under consideration for inguinal hernia repair. The Cochrane Highly Sensitive Search Strategy for identifying randomised trials[23] will be used in MEDLINE and adapted for other databases. There will be no publication date restriction and no language restriction (resources dependant). The following databases will be searched to identify relevant trials: MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Biosis, Science Citation Index, and the Cochrane Controlled Trials Register (CENTRAL). Scopus will be searched for *in press* articles. Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Review of Effects (DARE) and the HTA databases will be searched for evidence syntheses. Reference lists of all included studies will be perused in order to identify additional potentially relevant reports. We will also contact our panel of experts for details of any additional potentially relevant reports. A preliminary MEDLINE search strategy is detailed in Appendix 1

Ongoing studies will be identified through searching Current Controlled Trials, Clinical Trials and WHO International Clinical Trials Registry. Websites of manufacturers, professional organisations, regulatory bodies and HTA organisations will be searched to identify additional relevant reports.

5.8 Data extraction strategy

Two reviewers will independently screen the titles and abstracts of all citations identified by the search strategies. Full text copies of all potentially relevant studies will be retrieved, and assessed independently by two reviewers for eligibility. Any disagreements will be resolved by discussion or arbitration by a third reviewer.

A data extraction form will be developed and piloted for the purpose of this assessment. Information on study design, characteristics of participants, settings, characteristics of interventions and outcome measures will be recorded. One reviewer will complete the data extraction form for all included studies and a second reviewer will check the data extracted. Any disagreements will be resolved by discussion or arbitration by a third reviewer.

5.9 Quality assessment strategy

A single reviewer will assess the quality of the included studies and findings of the methodological assessment will be checked by a second reviewer. Any disagreements will be resolved by consensus or arbitration by a third reviewer. Studies will not be included or excluded on the basis of their methodological quality.

The quality of all the included RCTs will be evaluated using the Cochrane Risk of Bias tool.[23] Any relevant systematic reviews will be assessed using AMSTAR (assessing methodological quality of systematic reviews) tool.[25]

5.10 Methods of analysis/synthesis

The general approach recommended by the Cochrane Collaboration will be used. For binary outcomes the Mantel-Haenszel approach will be used to pool odds ratios derived from each study. For binary outcomes with rare events a sensitivity analysis using estimates derived using the Peto approach will also be considered. For continuous outcomes, mean differences will be pooled using an inverse variance approach. For time-to-event outcomes (recurrence and time to return to normal activities) an attempt will be made to pool hazard ratios when this information is available.

The statistical heterogeneity across studies will be explored using the Chi^2 and I^2 statistics. The primary analysis will use a fixed effect model to calculate the pooled estimates of effect. Where evidence of heterogeneity is detected, a random effects model will be used as a sensitivity analysis. If data permit, sensitivity analyses restricted to studies at low risk of bias will also be performed.

6. Report methods for synthesising evidence of cost effectiveness

An economic model based on open mesh techniques will be developed for the purpose of this appraisal. The model will be populated using data retrieved from the systematic review of clinical effectiveness (i.e. recurrence and re-operation rates), quality of life and chronic pain outcomes. We will consider the use of other study designs, such as observational studies to inform parameters of the model where no randomised data are available. We will conduct a review of currently published evidence on the cost-effectiveness of surgical techniques for inguinal hernia repair (see Section 6.1 below); and where published evidence is uncertain, clinical expert opinion will be consulted (e.g. regarding resource use required to perform surgical procedures) as appropriate.

6.1. Identifying and reviewing published cost-effectiveness studies

A review of existing economic evaluations assessing open pre-peritoneal mesh repairs versus standard Lichtenstein repair will be performed in accordance with the objectives detailed in Section 4.5.

The search strategies will be designed to identify economic evaluations of inguinal hernia repair. The following databases will be searched: NHS EED, HTA Database, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Science Citation Index, Health Management Information Consortium (HMIC) database, RePeC and CEA Registry. Websites of HTA organisations will be consulted for additional reports. Reference lists of all included studies will be scanned and appropriate experts will be contacted for details of additional reports. A draft MEDLINE search is detailed in Appendix 1.

A health economist will assess the title and abstract of all citations identified by the search strategies for economic evaluations. Full-text papers will be obtained for those studies that appear to be potentially relevant and will be formally assessed for inclusion. Only full formal economic evaluations assessing the cost-effectiveness of the identified interventions will be deemed suitable for inclusion (i.e. cost minimisation, cost effectiveness, cost utility or cost benefit analyses). The quality of selected studies will be assessed by means of (i) the BMJ checklist for referees of economic analyses[27] for economic evaluations conducted alongside RCTs, and (ii), where appropriate, decision models will be reviewed against the NICE reference case. Studies that are most relevant to the scope of the appraisal will be identified. A narrative summary of the findings of economic evaluation studies will be presented, and will be grouped according to the main objectives of this appraisal. Data collected from the review of economic evaluations will be used, as appropriate, to inform the development of the *de novo* economic model. Additional data will be retrieved, as appropriate, to inform key model parameters (e.g. resource use, cost of surgical techniques and utilities).

6.2 Development of a health economic model

Health economic model

Current economic evidence is unlikely to be sufficient to answer the clinical decision problem of this assessment. Therefore, a *de novo* decision analysis model will be developed. The structure of the model will be dependent on the evidence derived from the clinical effectiveness review. We will seek advice from the Advisory Group and utilise current expertise available within the TAR team for modelling inguinal hernia repair and will develop a decision analytic model.[14] The structure and development of the model will be informed as appropriate using information collected from the review of economic studies.

The model will be structured to reflect the care pathways that patients with inguinal hernia repair will follow over time. The model will include an assessment of the initial intervention and any subsequent events experienced - including treatment of recurrent symptoms and/or complications. The final structure of the model and comparators for inclusion will be refined based on the available evidence obtained from the systematic review of clinical effectiveness, the review of current economic studies, and the availability of appropriate and robust data to populate the economic model.

Given the current care pathway, and the chronic nature of inguinal hernia conditions, with a likelihood of recurrence and re-operation over time, the most appropriate model to develop will likely to be a Markov state transition model. However, should it be deemed appropriate during the development of the model and data collection, we will consider adding further complexity, for example through a micro simulation model. This decision would be taken based on consultation with the Advisory Group and the TAR team. The model will be developed to capture the consequences of each strategy in terms of recurrence rates, health-related quality of life and costs to the NHS and PSS. The model will be based on a hypothetical cohort of patients treated with surgery for inguinal hernia, using open mesh techniques. This cohort will be followed up in the model over an appropriate time horizon of sufficient length to capture all of the costs and consequences attributable to open inguinal hernia repair. Each model cycle will likely to be of 1 year duration, with costs and benefits (consequences) accruing over time, to allow tracking of cumulative costs and consequences over the patient's lifetime (e.g. extrapolated recurrence rates, subsequent requirement for treatment / surgery, pain rates, health-related quality of life). Specifically relating to the stated decision problem, the model will incorporate, where evidence allows, health states which are appropriate to model the likely cost and utility implications of recovery, recurrence, re-operation and development of post-operative pain. Information to populate the model on risk of transiting to alternative states will be developed based on data retrieved from the systematic review of clinical effectiveness as well as from current available economic modelling evidence. If appropriate, and where sufficient data are available, sub-group analyses will be performed according to advise from the Advisory Group.

The economic perspective of the model will be the UK NHS and Personal Social Services. Costs and QALYs for the base case analysis will be discounted at a rate of 3.5% per annum and the impact of this tested appropriately in sensitivity analyses. All modelling work conducted will follow best practice methodology for the conduct of economic evaluation in health technology assessment.[28] Guidance on the appropriateness of included assumptions and

model structure will be sought from clinical experts in the field. The model will be developed using appropriate decision analysis software, such as Treeage Pro (TreeAge Software, Inc., Williamstown, MA, USA).

Costs

Data will include the direct health service costs associated with each initial treatment (not likely to vary substantially) and subsequent management. It is unlikely that there will be any significant difference in surgical costs between open mesh repair techniques, as all procedures are likely to incur similar resource use in theatre and equipment required. We don't therefore envisage intervention costs to be a major driver of cost-effectiveness. Where possible, resource use required to perform respective surgical procedures will be obtained from the literature, and costed using standard national cost tariffs (e.g. for one hour in theatre). Where data from the literature are insufficient to develop a true picture of total costs, we will consult with clinical experts (within TAR team and the Advisory group) in the field to obtain the most appropriate resource use requirements to develop treatment costs.

Surgical procedures over follow up (as a result of recurrence) will be mapped to their appropriate HRG code, and costed using NHS reference costs or the payment by results national tariff. Further resource use events following initial treatment will be modelled using available evidence and valued using the same approach as described above, supplemented, where necessary, by other national sources such as the PSSRU Unit Costs of Health and Social Care and clinical expert opinion.

Utilities and QALYs

Data from the systematic review will be used to generate health state utilities where possible. In the event of gaps in the literature, a focused search of the literature, specifically deigned to obtain quality of life weights, particularly relating to hernia related pain and recurrence health states, together with scrutiny of existing sources such as the Harvard Database of Cost-utility Analyses, will be performed to ascertain whether relevant health state utility weights exist, and, if so, these will be applied to the health states within the model. If necessary, plausible assumptions will be made in order to use utility values derived from different patient population (e.g. using an additive model to combine the effects of disease progression and adverse events in one group to estimate the effect in another group). Quality of life data, preferably sourced from the EQ-5D, will be obtained from the systematic review of clinical effectiveness, and supplemented with any health state utility data obtained from the cost-effectiveness review as appropriate. Quality of life (utility) data will be combined with

mortality data outcomes (sourced from the review) to estimate Quality Adjusted Life Years (QALYs).

Cost-effectiveness

A cost utility analysis (CUA) will be performed and outcomes will be reported in terms of incremental cost per Quality Adjusted Life Year (QALY) gained. Treatment strategies will be ranked in ascending order of effectiveness (QALYs). Treatment strategies which are more costly, and less effective than other options, will be excluded on the principal of strict dominance. Incremental cost-effectiveness ratios (ICERs) will be reported and treatment strategies will be presented on the cost-effectiveness plane.

Uncertainty

Deterministic and probabilistic sensitivity analyses will be applied to the model in order to assess the robustness of the results to realistic variations in the values attached to model parameters. Uncertainty surrounding the cost-effectiveness of the alternative approaches to management will be presented in the form of cost-effectiveness acceptability curves (CEACs). Where the overall results are sensitive to a particular variable or assumption, deterministic sensitivity analysis will be reported. Such analyses may involve changes to the structure of the model or the parameter inputs (resource use, unit costs, utilities) used in the model. Subgroup analyses will be conducted as appropriate and in consultation with the Advisory group.

7 TAR team expertise

The TAR team are experienced in conducting reviews of this nature, in both the clinical and technical aspects required to address the commissioning brief. Miriam Brazzelli, Craig Ramsay, Rodolfo Hernandez, and Cynthia Fraser have been involved in a number of similar appraisals and the remaining TAR team members are familiar with the methods of systematic reviewing and economic modelling.

7.1 Team members' contribution

Miriam Brazzelli, Senior Research Fellow at the HSRU, and Craig Ramsay, lead of the Aberdeen Health Technology Assessment Group will oversee and co-ordinate all aspects of the appraisal and be the guarantors of the complete work. Pawana Sharma, Research Fellow at the Health Services Research Unit (HSRU), University of Aberdeen, will be responsible for the day-to-day running of the appraisal and will undertake the review of clinical effectiveness with advice and guidance from Miriam Brazzelli. Dwayne Boyers, Research Fellow, Health Economics Research Unit, University of Aberdeen, will undertake the economic evaluation.

Rodolfo Hernandez, Research Fellow, Health Economics Research Unit, University of Aberdeen, will conduct quality assurance of the model structure and outputs. Professor Luke Vale, Health Economics Research Unit, University of Aberdeen, will provide specialist advice for the economic modelling where required. Cynthia Fraser, Senior Information Specialist at the HSRU, will develop and run the search strategies and will be responsible for obtaining papers and managing references. Neil Scott, Medical Statistician at the Division of Applied Health Sciences, University of Aberdeen, will conduct statistical analyses. Irfan Ahmed, Consultant Surgeon, NHS Grampian, Aberdeen, will provide expert clinical advice on relevant surgical aspects.

7.2 Advisory Group

In addition to the TAR team, an Advisory Group comprising of surgeons, general practitioners and lay members will be set up to provide guidance on the care pathways, advise on important outcomes, and assist in the interpretation of the clinical effectiveness findings. The Advisory Group will be convened at least twice during the duration of the appraisal. Advisory Group members will include: Mr Yuen Soon, Consultant Surgeon, Royal Surrey County Hospital NHS Foundation Trust; Mr Ian Beckingham, Consultant surgeon, Nottingham University Hospitals; Dr Ewan Paterson, General Practitioner, Aberdeen, Dr David Stephen, Aberdeen, patient representative, together with all the members of the TAR team listed in the previous section.

8. Handling information from the companies

Following a request for information, any 'commercial in confidence' data provided by a manufacturer and specified as such will be highlighted in blue and underlined in the assessment report (followed by an indication of the relevant company name e.g. in brackets). Any academic-in-confidence data provided will be highlighted in yellow and underlined.

9. Competing interests of authors

Competing interests: None declared

10. Timetable/milestones

Milestone	Date to be completed
Draft protocol	21/05/14
Final protocol	TBC
Progress report	TBC
Assessment report	TBC

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12. Appendices

Appendix 1 Preliminary MEDLINE search strategies

Clinical Effectiveness Review

1 hernia,inguinal/su
2 hernia, inguinal/
3 (inguinal or groin).tw.
4 hernioplast$.tw.
5 herniorrhaph$.tw.
6 herniorrhaphy/
7 (hernia adj3 repair$).tw.
8 (2 or 3) and (4 or 5 or 6 or 7))
9 1 or 8
10 lichtenstein.tw.
11 (kugel or stoppa or nyhus or read-rives).tw.
12 (open adj3 mesh).tw.
13 (pre -peritoneal or preperitoneal).tw
14 or/10-13
15 randomized controlled trial.pt.
16 controlled clinical trial.pt
17 randomi?ed.ab.
18 placebo.ab
19 drug therapy.fs.
20 randomly.ab.
21 trial.ab.
22 groups.ab.
23 or/15-22
24 exp animals/ not humans/
25 23 not 24
26 9 and 14 and 25

B Cost Effectiveness Review

1 hernia,inguinal/su
2 hernia, inguinal/
3 (inguinal or groin).tw.

4 hernioplast$.tw
5 herniorrhaph$.tw.
6 herniorrhaphy/
7 (hernia adj3 repair$).tw.
8 (2 or 3) and (4 or 5 or 6 or 7)
9 1 or 8
10 exp "costs and cost analysis"/
11 exp economic evaluation/
12 economics/
13 exp economics,hospital/
14 exp economics,medical/
15 economics,pharmaceutical/
16 exp budgets/
17 exp models, economic/
18 exp decision theory/
19 monte carlo method/
20 markov chains/
21 exp technology assessment, biomedical/
22 cost$.ti.
23 (cost$ adj2 (effective$ or utilit$ or benefit$ or minimis$)).ab.
24 economics model$.tw.
25 (economic$ or pharmacoeconomic$).tw.
26 (price or prices or pricing).tw.
27 (value adj1 money).tw.
28 markov$.tw.
29 monte carlo.tw.
30 (decision$ adj2 (tree? or analy$ or model$)).tw.
31 Or/10-30
32 9 and 31.

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