PROTOCOL FOR THE CLINICAL EFFECTIVENESS AND COST-EFFECTIVENESS OF LAPAROSCOPIC SURGERY FOR INGUINAL HERNIA REPAIR.

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B. Details of review team

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C. Full title of research question

Systematic review of the clinical effectiveness and cost-effectiveness of laparoscopic surgery for the repair of inguinal hernia (Update).

D. Clarification of research question and scope

This review will address two research questions to determine: 1) whether laparoscopic methods are more effective and cost-effective than open mesh methods of inguinal hernia repair; and 2) whether laparoscopic transabdominal preperitoneal (TAPP) repair is more effective and cost-effective than laparoscopic totally extraperitoneal (TEP) repair of inguinal hernia.

The analysis will focus on long term outcomes (e.g. hernia recurrence, persisting pain and numbness, and quality of life) but will also assess short term outcomes relating to the operative procedure (e.g. duration of operation, operative complications, length of hospitalisation, and time to return to usual activities) (see section **E 2.4** below). Cost-effectiveness will be assessed from the perspective of the NHS and Personal Social Services.

E. Report methods

E.1 Search strategy

Extensive electronic searches of the databases listed below will be conducted to identify both published and unpublished information. These searches will aim to identify existing systematic reviews and primary studies evaluating: 1) the effectiveness and cost-effectiveness of laparoscopic compared with open mesh

inguinal hernia repair; and 2) laparoscopic TAPP compared with laparoscopic TEP inguinal hernia repair. The search terms will be built upon work conducted as part of a previous HTA review of laparoscopic surgery for inguinal hernia repair and will involve the use of Medical Subject Headings (MeSH) as well as textword searching.

Table 1. Databases to be searched

Database	Years searched
Medline	1966- Present
Embase	1980-Present
Cinahl	1982-Present
HMIC	To present
Biosis	1985-Present
Science Citation Index	1981-Present
PreMedline	Present
Cochrane Controlled Trials Register	Cochrane Library 2003 Issue 2
Cochrane database of systematic reviews (CDSR)	Cochrane Library 2003 Issue 2
Database of abstracts of reviews of effectiveness (DARE)	To present
CRD NHS EED	To present
HTA	To present

Further citations will be sought from the reference lists of all retrieved studies. Current research registers will be searched and relevant professional and research organisations will be contacted. Specialists involved in research on the repair of inguinal hernia will be contacted through the EU Hernia Trialists Collaboration to ask for information on any other completed and ongoing trials known to them. There will be no language restrictions.

E.2 Inclusion criteria

E.2.1 Types of studies

An HTA systematic review (of which this report is an update), comparing laparoscopic with open methods of inguinal hernia repair and a Cochrane update of this review using, where possible, the results of IPD analyses have been conducted. We anticipate relying heavily on those sources when comparing laparoscopic methods with open mesh methods of inguinal hernia repair and will only include additional randomised controlled trials reported since 2000 (or additional data about trials included in existing reviews and published since 2000). Any new data to the original HTA review will be added to the original data in a meta-analysis where possible.

When comparing laparoscopic TAPP with laparoscopic TEP methods of inguinal hernia repair, all published and unpublished randomised controlled trials and quasi-randomised controlled trials will be eligible for inclusion. Where there is a scarcity of long term data, prospective comparative observational studies and case series will be considered.

E.2.2 Population

Adults with a clinical diagnosis of inguinal hernia for whom surgical management is judged appropriate. Where data allow, the patient population will be further split by whether or not the hernia is recurrent or bilateral and whether or not the patient is fit enough for general anaesthetic. Data from children aged 12 years and older will be included where these patients are included in a trial of adults. Data from paediatric trials will not specifically be sought.

E.2.3 Types of interventions

Methods of surgical repair of inguinal hernia:

a) Laparoscopic inguinal hernia repair (including TAPP and TEP).

b) Open mesh inguinal hernia repair (including open flat mesh, open pre-peritoneal mesh and open plug and mesh).

E.2.4 Types of outcome measures

The primary outcomes will be:

- Hernia recurrence
- Persisting pain

The secondary outcomes will be:

- Duration of operation (min)
- Opposite method initiated
- Conversion
- Post-operative pain
- Haematoma
- Seroma
- Wound/Superficial Infection
- Mesh/Deep Infection

- Port site hernia
- Vascular injury
- Visceral injury
- Length of hospital stay (Days)
- Time to return to usual activities (Days)
- Persisting numbness
- Quality of Life

E.3 Data extraction strategy

The titles and abstracts (if available) of all papers identified by the search strategy will be screened. Full text copies of all potentially relevant studies will be obtained and two reviewers will independently assess them for inclusion. Reviewers will not be blinded to the names of studies' authors, institutions or publications. Any disagreements will be resolved by consensus or arbitration.

A data extraction form will be developed to record details of trial methods, participants, interventions, patient characteristics and outcomes. The form will be based on one used in a recent systematic review of methods of surgical hernia repair.[1] Two reviewers will extract data independently. Where a difference of opinion exists that cannot be resolved through discussion, they will consult an arbiter.

Where the results of a trial are published in whole or in part, more than once, only the most recent data will be included. All other papers will be used to provide other necessary information but will not be included in the count of included papers. This is to prevent results from individual patients being included more than once and therefore introducing reporting bias.

E.4 Quality assessment strategy

Two reviewers working independently will assess all studies that meet the selection criteria for methodological quality. Any disagreements will be resolved by consensus or arbitration. The system for classifying methodological quality of controlled trials will be based on an assessment of the three principal potential sources of bias. These are: selection bias from insecure random allocation of treatments; selection bias from losses to follow-up, particularly if related to one or other surgical approaches; and biased ascertainment of outcome where knowledge of the allocation might have influenced the measurement of outcome.

[1] McCormack K, Scott NW, Go PMNYH, Ross S, Grant AM on behalf of the EU Hernia Trialists Collaboration. *Laparoscopic techniques versus open techniques for inguinal hernia repair*. In: **The Cochrane Library, Issue 1, 2003. Oxford: Update Software**.

E.5 Methods of analysis/synthesis

The review will be conducted using the standard Cochrane software 'Revman'. Quantitative synthesis is planned if more than one eligible study is identified. Where appropriate, a pooled estimate of treatment effect across similar studies will be calculated for each pre-specified outcome, using standard statistics such as odds ratios or weighted mean differences. 95% confidence intervals will be generated where possible. A fixed effects approach to the analysis will be undertaken unless there is evidence of heterogeneity across studies. Evidence of heterogeneity across studies will be determined from visual inspection of the data or from the Chi square test for heterogeneity. If evidence of significant heterogeneity is identified, potential sources of heterogeneity will be explored. If there is no clear reason for heterogeneity, a random effects approach to the analysis will be undertaken. A narrative review of eligible studies will be undertaken where statistical synthesis of data from more than one study is not possible or considered not appropriate. Possible differential effects will be explored in sub-group analyses stratified by whether recurrent or bilateral hernias.

Where possible, the results will be based on analyses of individual patient data obtained through the EU Hernia Trialists Collaboration.

E.6 Methods for estimating quality of life, costs and cost-effectiveness and/or cost per QALY

A model will be developed to estimate the relative cost-effectiveness of: 1) laparoscopic compared with open mesh inguinal hernia repair; and 2) laparoscopic TAPP compared with laparoscopic TEP inguinal hernia repair. This model will combine data on clinical effectiveness with cost data relevant to the UK NHS. Further details of the modelling and data requirements are summarised below.

E.6.1 Cost data

The primary perspective for the costing will be the NHS and Personal Social Services. Cost data will therefore include the direct health service costs associated with the treatment options.

Quantities of resources used will be identified from consultation with experts, primary data from relevant sources and the reviewed literature. We anticipate that unit cost data will be extracted from the literature or obtained from other relevant sources (e.g. manufacturer price lists, NHS reference costs). All cost data will be converted to a single year (2003) in pounds sterling.

The following data will be needed to estimate costs incurred by the NHS for a particular procedure.

- staff time costs, consumables, overheads and capital charges associated with the actual operative procedure
- length of hospital stay
- post operative secondary care treatment during the period of hospitalisation and convalescence
- staff time costs, consumables, overheads and capital charges associated with any subsequent re-operation.

In order to provide a wider societal perspective and to elicit the impact on patients and their families, those costs that fall upon patients and their carers will also be reported where data are available. Specifically, we shall consider:

1) Patients' time and travel costs (reported in natural units of resource use)
2) Changes in productivity of patient/carer due to differences in management strategy. Time to return to work is primarily a measure of benefit. Although the primary perspective is NHS and PSS, we shall also take a wider societal perspective including differences in productivity which may or may not reflect an earlier return to usual activities (including work).

Where appropriate, costs and benefits will be discounted at 6% for costs and 1.5% for benefits, the rates recommended in the NICE guidance to manufacturers and sponsors of submissions.

The model will also require data on the following:

- Annual probability of death
- Annual probability of recurrence
- Length of operation
- Time to return to usual activities following an operation
- Probability of persisting pain

The impact of the costs related to other adverse events are likely to incorporated in other included cost estimates such as length of hospital stay.

E.6.2 Assessment of benefits

A balance sheet will be constructed to list possible benefits and costs of laparoscopic TAPP and laparoscopic TEP inguinal hernia repair compared with open mesh methods and between each other. We anticipate that the main measures of benefit will be: recurrence free; reduced persisting pain; faster return to usual activities; and fewer complications. If sufficient data are available from the literature, different outcomes will be ascribed utility values and QALYs will be estimated

Where the results of an analysis are published in whole or in part, more than once, only the most recent data will be included. All other papers will be used to provide other necessary information but will not be included in the count of included papers.

E.6.3 Modelling

A Markov model will be developed to estimate the cumulative costs, recurrences, and time away from usual activities associated with each method of hernia repair. The model will follow a cohort of patients from their initial operation through their convalescence (operation state) to their return to usual activities (successful operation state). The patients may remain in this state until they die or they may suffer a recurrence and therefore have a re-operation and move to the re-operation state. The cohort of patients could continue to move between the states of the model until they all eventually die. However, for the purposes of the analysis, the cohort will only be modelled for 5 years following the initial operation.

E.6.4 Sensitivity analysis

Probabilistic sensitivity analysis using Monte Carlo simulation will be performed to generate a distribution for the incremental cost-effectiveness estimates provided by the Markov Model. These sensitivity analyses will be repeated for two scenarios. The first will assume that laparoscopic surgery is predominantly performed using reusable equipment and the second will assume that predominantly disposable laparoscopic equipment is used.

A. Handling the company submission(s)

We shall develop the economic model to assess cost-utility and cost-effectiveness, using if necessary data contained in the company submission(s) to inform the estimates of effectiveness, cost-effectiveness and cost-utility. Any economic models contained within the company submission(s) will be assessed against the 35 point BMJ guidelines for reviewers. Strengths and weaknesses in terms of methodology adopted, reporting of results and conclusions will be described. It will then be compared with the results provided by the model we develop so that differences in results can be highlighted. If the model we develop differs substantively from that put forward by any company, we will justify any assumptions made. Any 'commercial in confidence' data taken from the company submission will be underlined in the HTA report (followed by an indication of the relevant company name e.g. in brackets) so that the NICE secretariat can negotiate (before and during the Institute's consultation process) with industry, the subsequent inclusion of such data in the HTA monograph publication or subsequent peer-review publications and so that confidentially sensitive information is not released into the public domain.

G. Project management

G.1 Timetable/milestones

Draft protocol: 10 June 2003

Final protocol: 1 July 2003

Progress report: 29 September 2003

The progress report will address the following areas:

- Whether progress is on schedule;
- Confirmation of external reviewers, including job title and institution;
- Confirmation of date of receipt of industry submissions (or notification if still outstanding);
- Indication of whether the extent of industry submission data marked 'in confidence' is unreasonable, for example if the whole of the submission is marked 'in confidence';
- Optional opportunity to comment on any problems encountered in producing the report.

Draft Assessment Report (DFR): 10 December 2003

G.2 Competing interests

There are no competing interests.

G.3 External reviewers

The Technology Assessment Report will be subject to external peer review by at least two experts. These reviewers will be chosen according to academic seniority and content expertise and will be agreed with NCCHTA. We recognise that methodological review will be undertaken by the NICE secretariat and Appraisal Committee, but if the TAR encounters particularly challenging methodological issues we shall organise independent methodological reviews. External expert reviewers will see a complete and near final draft of the TAR and will understand that their role is part of external quality assurance. All reviewers are required to sign a copy of the NICE Confidentiality Acknowledgement and Undertaking. We will send external reviewers' signed copies to NCCHTA. Comments from external reviewers and the Technical Lead, together with our responses to these will be made available to NCCHTA in strict confidence for editorial review and approval.