

# **Effectiveness and cost-effectiveness of arthroscopic lavage in the treatment of osteoarthritis of the knee: a mixed methods study of the feasibility of conducting a surgical placebo-controlled trial (the KORAL study)**

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## ***Executive summary***

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## Executive summary

### Background

Osteoarthritis is the most common form of arthritis in Western populations. When medication for osteoarthritis of the knee does not sufficiently relieve symptoms, the surgical procedure of arthroscopic lavage may be undertaken. Arthroscopic lavage involves washing out the joint space during arthroscopy, with additional debridement (the mechanical removal of debris and the trimming of rough surfaces) if deemed necessary. The evidence for the effectiveness of arthroscopic lavage is variable, however, and the largest trial conducted to date showed no evidence of a benefit of arthroscopic lavage or debridement over placebo. The generalisability of the results of this trial has been questioned as all procedures were performed by a single surgeon, a significant proportion of patients had severe arthritis, and the primary outcome was based on a non-validated instrument. Given the widespread use, high cost and continuing uncertainty around the effectiveness of arthroscopic lavage for osteoarthritis of the knee, the Health Technology Assessment (HTA) programme sought to commission a similar placebo-controlled trial of arthroscopic lavage in the UK. Recognising that there might be difficulties of mounting such a trial (in terms of perceived acceptability of the placebo design) the research was commissioned with an integrated, yet discrete, feasibility study, which is described in this monograph.

### Objectives

The objectives of the feasibility study were two-fold: (a) to ascertain the acceptability of a randomised controlled trial comparing arthroscopic lavage with a placebo surgical procedure for the management of osteoarthritis of the knee; and (b) to assess the practical feasibility, through the conduct of a formal pilot study, of mounting such a multicentre placebo-controlled trial. This included assessing the acceptability of the proposed trial processes to patients and staff, to estimate the proportion of patients who would accept randomisation within the trial, and to examine the acceptability of the trial information material to patients.

### Methods

The initial exploration of acceptability comprised: focus groups with surgeons and anaesthetists; focus groups and interviews with potential participants; interviews with chairpersons of the UK Multicentre Research Ethics Committees (MRECs); and surveys of surgeons and anaesthetists.

The pilot study was designed as a two-centre, three-arm trial of arthroscopic lavage (with or without debridement at the clinical discretion of the surgeon); placebo surgery; and non-operative (i.e. medical) management with specialist reassessment.

### Results

There was broad acceptance across all stakeholder groups of the need to find out more about the effectiveness or otherwise of arthroscopic lavage. Despite this there was, however, variation in opinion within all the groups about how researchers should approach this and about whether or not it would be acceptable to investigate using placebo surgery. Within the health professional groups, there tended to be a split between those who were strongly opposed to the inclusion of a placebo surgery arm (on the grounds that it could lead to potential harms among individuals who could expect no personal benefit) and those who were more in favour on the grounds that they believed the small risks that relatively few people in a placebo surgery trial arm would be exposed to were justified because they were outweighed by the potential benefit (i.e. potential benefit to future patients and broader society through helping to ensure either that a demonstrably effective surgical procedure was used or that a demonstrably ineffective procedure was not). For prospective trial participants who had osteoarthritis of the knee, the acceptability of the trial was discussed from a more individual perspective – reflecting on their personal reasons for or against participating. The majority of this group said they would consider taking part. As well as expressing a desire to help others through their participation, there was a general tendency to down play any potential risk of harm from their participation whilst emphasising

the potential to gain some form of personal benefit. Given the nature of the proposed design, the health professionals and MREC chairpersons recognised that particular attention should be paid to the informed consent process when attempting to recruit participants.

The pilot study showed that, in principle, a placebo-controlled trial in surgery could be conducted. It showed that patients were willing to participate in a trial that would involve a placebo surgical arm, and that it was possible to undertake placebo surgery successfully and to blind patients to their allocation – although once patients knew their allocation, some patients allocated to surgery became more concerned about the possibility of undergoing placebo surgery, and withdrew. The experience of the pilot, however, showed that, despite full MREC approval, the study required major discussion and negotiation before local clinical approvals could be obtained. Many of the arguments raised at MREC level were raised again at local level, and the fact that ethics approval had been granted did not mean that clinicians would automatically accept that the process was ethical.

National trend data showed a slow decline in the usage of arthroscopic lavage over recent years.

## Conclusions

The feasibility study showed that, in principle, a placebo-controlled trial of arthroscopic lavage could be conducted in the UK, albeit with difficulty. Against this background and a falling use of arthroscopic lavage, the decision was taken not to proceed to full-scale trial for this particular procedure.

The study showed that the placebo-controlled design remains controversial, and for some health professionals the use of placebo surgery can never be justified. It highlighted the importance of the surgeon–anaesthetist relationship in this context and how acceptance of the trial design by both parties is essential to successful participation. It also highlighted the importance of informed consent for trial participants and the strength and influence of individuals' ethical perspectives in addition to collective ethics provided by MRECs.

The wider lesson from the study is that the most favourable circumstances for a placebo-controlled trial in surgery are those where: (a) alternative designs would provide inferior (and potentially

biased) results, particularly where the primary outcome is of a subjective nature and blinding cannot be sustained beyond the time of any placebo effect; (b) a placebo surgical procedure and type of anaesthesia can be devised that adequately mimic the active intervention with a level of intrusiveness and risk that is acceptable to surgeons, anaesthetists, ethics committees, and potential participants; (c) appropriate practical arrangements can be instituted in local centres to ensure that the delivery of such a design would be feasible; (d) sufficient numbers of potential participants (after assessment of clear descriptions and careful explanations in patient information leaflets of the advantages and disadvantages of taking part) judge for themselves that the risk-to-benefit ratio of participation is acceptable to them; and (e) levels of compliance with the allocation are sufficiently high to sustain scientific rigour.

## Implications for practice

- A placebo-controlled trial of arthroscopic lavage could be conducted in the UK, albeit with difficulty.
- Those conducting trials in surgery must consider surgeon–anaesthetist partnerships when planning clinical trials, especially trials including a placebo arm.
- People taking part in, and those responsible for, authorising the conduct of trials have their own individual ethical perspectives which can influence their attitudes to research (in addition to the collective ethics assessment provided by MRECs). Researchers need to be aware of these, and work with them when planning clinical trials – especially trials involving a placebo arm.
- Terminology referring to 'placebos', 'shams', 'dummies', etc. each have different connotations that may influence participation.
- The importance of including clear descriptions and careful explanations in patient information leaflets was reinforced in this study. All trials should ensure that any advantages and disadvantages of participation are explained as fully as possible.
- Patient information leaflets within placebo-controlled trials should explicitly state that whilst benefit might be seen within a placebo group, the underlying mechanism of the placebo has no known direct effect.
- National arrangements for indemnity and non-negligent harm should be clarified for all researchers involved in the conduct of clinical

trials, particularly those trials that might involve a placebo arm.

- The HTA programme should consider the routine use of staged funding (with integrated rapid decision-making) for more complex research projects.
- The optimal place for a placebo-controlled trial in surgery is likely to be where the strict conditions listed above can be satisfied.

## Implications for research

- Research is required into the impact of different terminology referring to placebos (e.g. placebo, sham, dummy) on the understanding of the role and function of a placebo.
- Research is required into the usefulness of formal decision aids to aid participant consent in the context of a placebo-controlled trial.

- Research is required into the impact of individual versus collective ethics on the conduct of placebo-controlled trials.

## Trial registration

This trial is registered as ISRCTN 02328576

## Publication

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The website also provides information about the HTA programme and lists the membership of the various committees.

# NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

## Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 03/48/01. The contractual start date was in July 2005. The draft report began editorial review in November 2008 and was accepted for publication in August 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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