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Hemiarthroplasty and total hip arthroplasty for treating primary intracapsular fracture of the hip: a systematic review and cost-effectiveness analysis

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 09/108/02. The contractual start date was in September 2010. The draft report began editorial review in March 2011 and was accepted for publication in May 2011. 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.

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Abstract

Hemiarthroplasty and total hip arthroplasty for treating primary intracapsular fracture of the hip: a systematic review and cost-effectiveness analysis

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Background: Hip fracture is a common problem in people aged > 60 years. The treatment options for individuals with high pre-fracture mobility, function and independence are hemiarthroplasty (HA) and total hip arthroplasty (THA).
Objective: The aim of this report is to assess the clinical effectiveness and cost-effectiveness evidence of THA compared with HA in patients with displaced intracapsular fracture who are cognitively intact with high pre-fracture mobility or function.
Data sources: A systematic search was made of 11 databases of published and unpublished literature from their inception to December 2010: MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, The Cochrane Library, Biological Science Citation Index, Social Science Citation Index, Conference Proceedings Citation Index – Science, UK Clinical Trials Research Network and the National Research Register archive, Current Controlled Trials and ClinicalTrials.gov.
Review methods: A systematic review of randomised controlled trials (RCTs) to assess the effectiveness of THA compared with HA in terms of dislocations, revisions, pain and function, and quality of life. Meta-analysis, independent subgroup analyses and exploratory cost-effectiveness modelling were performed.
Results: The literature search identified 532 unique citations, of which eight RCTs with almost 1000 participants satisfied the criteria for the effectiveness review. Meta-analysis found a statistically significant increased risk of dislocation for patients treated with THA compared with HA ($p = 0.01$), but a reduced risk of revision ($p = 0.0003$). There were no differences in terms of mortality. In all trials, individuals treated with THA reported better function and mobility and less pain than those treated with HA. Four trials reporting utility data found similar trends. Sensitivity analyses indicated that there were no statistically significant differences in outcomes based on follow-up, study quality, surgical approach taken, type of head or the use of cement. Four papers reported a cost–utility analysis or the cost-effectiveness of THA compared with HA. Exploratory modelling was undertaken that showed that THA is likely to be cost-effective compared with HA even when the limitations of the data and methodology are considered.
Limitations: The costs and disutilities associated with revisions and dislocations were not included in the economic evaluation.
Conclusions: THA appears to be more cost-effective than HA. It is likely that THA will be associated with increased costs in the initial 2-year period, but lower longer-term costs, owing to potentially lower revision rates. However, these longer-term costs have not been

modelled. The capacity and experience of surgeons to perform THA have not been explored and these would need to be addressed at local level were THA to become recommended for active, elderly patients in whom THA is not contraindicated. Further studies examining the impact of surgeon experience on performing the two procedures may offer more robust evidence on outcomes.
Funding: The National Institute for Health Research Health Technology Assessment programme.

Contents

List of abbreviations

CI	confidence interval
DVT	deep vein thrombosis
EQ-5D	European Quality of Life-5 Dimensions
EVPI	expected value of perfect information
HA	hemiarthroplasty
HHS	Harris Hip Score
NICE	National Institute for Health and Clinical Excellence
OHS	Oxford Hip Score
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	quality-adjusted life-year
RCT	randomised controlled trial
RD	risk difference
RR	relative risk
RRR	ratio of relative risks
SE	standard error
SF-36	Short Form questionnaire-36 items
THA	total hip arthroplasty

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Hip fracture is a common problem in people aged ≥ 60 years. The annual rate of hip fracture in women in the UK has been reported to be exponentially distributed and to be 20 per 10,000, 38 per 10,000 and 73 per 10,000 at 65, 70 and 75 years of age, respectively. Only 5% of fractures occur in men and women under the age of 60 years. Owing to increasingly ageing populations, the absolute number of hip fractures is expected to rise. Half of all hip fractures are displaced intracapsular fractures, i.e. unstable fractures in which the blood supply to the femoral head may be impaired, affecting the rate of fracture healing. The treatment for displaced intracapsular fractures is currently determined by the mobility and functional demands of the patient. There is no consensus regarding the optimal treatment for individuals who are cognitively intact and have high pre-fracture mobility or function: the two options are hemiarthroplasty (HA) or total hip arthroplasty (THA).

The principal outcomes associated with hip arthroplasty are dislocation, revision rates and quality of life. THA is particularly associated with higher rates of dislocation, whereas HA is particularly associated with pain, infection, loosening of the joint and acetabular erosion. Postoperative complications such as loosening and acetabular erosion can necessitate revision surgery. Revision rates may therefore be higher for HA than for THA.

Objectives

The purpose of this report is to assess the clinical effectiveness and cost-effectiveness evidence of THA compared with HA in patients with displaced intracapsular fracture who are cognitively intact and have high pre-fracture mobility or function.

Methods

A systematic review of the evidence for the clinical effectiveness and cost-effectiveness of THA compared with HA was performed. The primary outcomes of interest were dislocation, revision and reoperation rates. An information specialist made a systematic search of 11 databases of published and unpublished literature from their inception to December 2010. There was no restriction by language, date or study design. Two reviewers screened all titles and abstracts of the citations retrieved by the search to identify both clinical effectiveness and cost-effectiveness studies that satisfied the inclusion criteria, and extracted relevant data from all included studies. The references of all included studies were also checked for further relevant citations. Additionally, exploratory modelling was conducted using the differential costs and quality of life associated with THA compared with HA that were reported in a direct head-to-head randomised controlled trial (RCT) with 2-year follow-up.

Results

A single literature search was conducted for both clinical effectiveness and cost-effectiveness reviews and identified 532 unique citations. Fourteen citations satisfied the inclusion criteria

for the clinical effectiveness review. This represented eight separate trials with 972 participants. Meta-analysis of the six trials found a near significant increased risk of dislocation within 1 year for THA compared with HA [relative risk (RR) 3.98, 95% confidence interval (CI) 0.98 to 16.12, $p = 0.05$], but meta-analysis of seven trials found a statistically significant increased risk of dislocation for patients treated with THA (RR 2.40, 95% CI 1.41 to 2.76, $p = 0.01$) for all follow-up periods up to 13 years. Meta-analysis of five trials found a statistically non-significant 59% reduced risk of revision within 1 year for THA compared with HA (RR 0.41, 95% CI 0.16 to 1.03, $p = 0.06$), but meta-analysis of seven trials found a statistically significant 69% reduced risk of revision for patients treated with THA compared with HA (RR 0.31, 95% CI 0.17 to 0.59, $p = 0.0003$) for all follow-up periods up to 13 years.

Meta-analyses of the five and seven trials, respectively, found a statistically non-significant increased risk of any surgery (reduction of dislocations, revisions and all other surgical interventions) both within 1 year and for all follow-up periods for THA compared with HA ($p = 0.46$ and 0.75, respectively). Meta-analyses of five and seven trials, respectively, found a statistically non-significant 9% reduced risk of mortality within 1 year, and a non-significant 4% increased risk of mortality for all follow-up periods, for THA compared with HA ($p = 0.60$ and 0.81, respectively).

Independent subgroup analyses also indicate that study quality, the surgical approach taken (lateral or posterior), the use of cement and the use of unipolar or bipolar prostheses in HA are not statistically significant confounding variables affecting any of these outcomes, when comparing the data on THA and HA reported for the RCTs identified for this review.

Five studies reported Harris Hip Score (HHS). Two studies reported a statistically significant ($p < 0.05$) difference after 1 or 2 years in favour of THA, and the three other studies reported the average HHS for study survivors at all follow-up points to be higher (i.e. better) for individuals receiving THA than for those receiving HA. The three remaining studies also reported hip scores using different scales: two studies reported statistically significant differences in favour of THA compared with HA, one after 2 years and one after 3 years, and the third reported that individuals receiving THA reported less pain and better ambulation than those receiving HA. The only statistically significant differences between groups for peri- and postoperative adverse events or complications reported by any study were higher numbers of patients receiving blood transfusion for THA than for HA in one study and higher percentages of patients experiencing acetabular erosion or loosening for HA than for THA in two studies.

Three papers were found that reported the cost-effectiveness of THA compared with HA, although they performed only a cost–utility analysis. An additional paper reported the usage of resources and patient utility recorded in an RCT. The conclusion from the cost–utility analyses was that THA was more cost-effective than HA with an expected 1.53 quality-adjusted life-years (QALYs) being provided at a cost of US$3000. The cost per QALY ratio of US$1960 would be viewed as extremely cost-effective using standard UK cost-effectiveness thresholds. A further estimate of the cost-effectiveness of THA compared with HA was also calculated by the authors of this report using data from a published trial which had a follow-up period of 2 years. Even when the utility benefits are constrained to this 2-year horizon, the cost per QALY is < £25,000. When the time horizon is extrapolated to more realistic values, the cost per QALY decreases, reaching a value < £10,000 with a horizon of only 5 years. This value would be seen as cost-effective under current cost-effectiveness thresholds. Furthermore, longer-term consequences, such as the likely reduced rates of revision associated with THA compared with HA, have not been incorporated in the model. Therefore, the results presented are likely to be unfavourable to THA and the cost-effectiveness of THA is likely to be better than reported.

Discussion

This review conducted a comprehensive and sensitive search for relevant evidence and identified eight RCTs, as well as three ongoing studies. The evidence from the eight relevant RCTs identified indicates that the risk of dislocation is significantly increased for those patients treated with THA than for those with HA, and that the risk of revision is significantly reduced for those treated with THA compared with HA. Patients treated with THA are also more likely to report better function and mobility and less pain than those treated with HA. There are no significant differences in terms of other effectiveness or safety outcomes.

Exploratory modelling was undertaken that showed that THA is likely to be cost-effective compared with HA even when the limitations of the data and methodology are considered. The exploratory model did not consider future revisions or dislocations or differential mortality rates; however, these omissions are expected to strengthen the conclusion that THA is more cost-effective than HA.

Conclusions

Meta-analysis of eight RCTs indicates that THA is more effective than HA in terms of rates of revision, and also more effective in terms of function, pain and mobility, but less effective than HA in terms of rates of dislocation. THA appears to be more cost-effective than HA. It is likely that THA will be associated with increased costs in the initial 2-year period, but the longer-term costs, due to potentially lower revision rates associated with THA, have not been estimated. The capacity and experience of surgeons to perform THA have not been explored and these would need to be addressed at local level were THA to become recommended for active, elderly patients in whom THA is not contraindicated.

Funding

The National Institue for Health Research Health Technology Assessment programme.

Chapter 1

Background

Description of health problem

Hip fracture is a common problem in the population aged ≥ 60 years. The annual rate of hip fracture in women in the UK has been reported to be exponentially distributed and to be 20 per 10,000, 38 per 10,000 and 73 per 10,000 at 65, 70 and 75 years of age, respectively.[1] Only 5% of fractures occur in men and women under the age of 60 years.[2] Owing to increasingly ageing populations, the absolute number of hip fractures is expected to rise.[3–5] Half of all hip fractures are displaced intracapsular fractures, i.e. unstable fractures in which the blood supply to the femoral head may be impaired, affecting the rate of fracture healing.[2,6,7]

The treatment for displaced intracapsular fractures is currently determined by the mobility and functional demands of the patient. Individuals with a displaced intracapsular fracture and low pre-fracture mobility, cognitive impairment or low functional demands are generally treated with hemiarthroplasty (HA);[2,8,9] as many as 37% of individuals with hip fractures may be cognitively impaired.[10] Other patients with displaced intracapsular fractures, i.e. young patients and very frail elderly patients with limited mobility or cognitive impairment, tend to be treated with internal fixation.[8] However, there is no consensus regarding the optimal treatment for older individuals who are cognitively intact and have high pre-fracture mobility or function: the options are HA or total hip arthroplasty (THA).[8,9,11] The reported rate of THA in the Trent region of the UK for 1991–2004 was 2.3 per 100,000 diagnosed hip fractures.[12] The vast majority of mobile patients with a displaced intracapsular hip fracture are treated by HA rather than by THA.[13]

The principal outcomes associated with hip arthroplasty are dislocation, revision rates and resultant quality of life. THA has been associated with higher rates of dislocation, which may be due to the greater degree of mobility permitted.[4,14] It has also been reported that higher rates of dislocation are more likely if the surgical approach is posterolateral rather than anterolateral and if a smaller femoral head is used.[15–17] The incidence or recurrence of dislocation has been found to be significantly related to a reduction in an individual's quality of life.[18] HA is particularly associated with pain, infection, loosening of the joint and acetabular erosion.[6,19] Postoperative complications such as loosening and acetabular erosion, in particular, can necessitate revision surgery. Revision rates may therefore be higher for HA than for THA.

Current service provision

In the UK, the vast majority of mobile patients with a displaced intracapsular hip fracture are treated by HA rather than by THA.[13] A survey of 223 UK hospitals in 2000 reported that, for active patients, HA was undertaken at 73% of hospitals, THA at 16% and internal fixation at 37% (the proportions exceed 100% as some hospitals reported using more than one method of treatment). Cemented prostheses were used in 74% of arthroplasties for active patients.[11] The actual number of patients receiving only the two interventions for intracapsular hip fracture, and who were without cognitive impairment and were also independently mobile prior to the fracture, is not known. The National Joint Registry does not report these discrete data.

Description of technology under assessment

The technologies under assessment are HA and THA. HA involves replacing the femoral head, whereas THA replaces both the femoral head and the acetabular articular surface. HA may be unipolar (generally used for patients with lower functional demands[2]) or, more recently, the more mobile bipolar, which aims to reduce acetabular erosion.[6] These prostheses may or may not be cemented into place.[2]

Chapter 2

Definition of the decision problem

The purpose of this report is to perform a review of the evidence to determine the clinical effectiveness and cost-effectiveness of THA in comparison with HA.

Decision problem

What is the clinical effectiveness and cost-effectiveness of THA compared with HA?

Overall aims and objectives of assessment

1. To identify, appraise and synthesise relevant studies satisfying the inclusion criteria for an assessment of clinical effectiveness of THA compared with HA.
2. To identify relevant studies satisfying the inclusion criteria for an assessment of cost-effectiveness, and to summarise the available evidence.
3. To construct a mathematical model to estimate the cost-effectiveness of THA with HA.

Chapter 3

Assessment of clinical effectiveness

Methods for reviewing effectiveness

A review of the evidence for clinical effectiveness has been undertaken systematically following the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[20] English and non-English-language studies were included and there was no limit by date.

Identification of studies

A comprehensive search was undertaken in October and December 2010 to identify systematically both clinical effectiveness and cost-effectiveness literature comparing THA and HA in patients with fractures of the femoral neck. The search consisted only of combining terms for THA with terms for HA. The MEDLINE search strategy is reported in *Appendix 1*. The aim of the strategy was to identify all studies that reported on trials comparing THA with HA. No MeSH (medical subject heading) term was used as the only appropriate term, 'arthroplasty, replacement, hip' covers both HA and THA. The strategy using the MeSH term therefore retrieved many studies concerning only one of the procedures, e.g. either THA or HA, but few studies covered both, the study design required for the review. This search was developed by the reviewer (CC) and the information specialist (PE).

The following electronic databases and online conference proceedings were searched from inception for published and unpublished research evidence:

- MEDLINE (Ovid) 1950 to December 2010
- EMBASE 1980 to December 2010
- Cumulative Index to Nursing and Allied Health Literature (EBSCO) 1982 to December 2010
- The Cochrane Library including the Cochrane Systematic Reviews Database, Cochrane Controlled Trials Register, Database of Abstracts of Reviews of Effects, Health Technology Assessment and NHS Economic Evaluation Database 1991 to December 2010
- Biological Abstracts [via Institute for Scientific Information (ISI) Web of Science] 1969 to December 2010
- Science Citation Index (via ISI Web of Science) 1900 to December 2010
- Social Science Citation Index (via ISI Web of Science) 1956 to December 2010
- Conference Proceedings Citation Index-Science (via ISI Web of Science) 1990 to December 2010
- UK Clinical Trials Research Network and the National Research Register archive up to December 2010
- Current Controlled Trials up to December 2010
- ClinicalTrials.gov up to December 2010.

All citations were imported into Reference Manager Version 12 (Thomson Reuters, CA, USA) software and duplicates were deleted. Titles and abstracts of all unique citations were then double-screened by two reviewers (CC and AS) using the inclusion criteria outlined below. Any discrepancies were resolved by retrieving the full paper. The full papers of all potentially relevant citations were retrieved so that an in-depth assessment concerning inclusion could be made.

The reference lists of all included studies and relevant reviews were also screened to identify additional, relevant studies not retrieved by the search of electronic databases.

Inclusion criteria

Population

Patients eligible for hip replacement as a result of intracapsular fracture and who are able to give consent and were independently mobile prior to fracture.

Intervention

Total hip replacement.

Comparator

Hemiarthroplasty.

Settings

Secondary care.

Outcomes

Primary outcomes

1. Dislocation rate.
2. Revision rate: where possible, the data were analysed separately for early revision, i.e. up to 1 year of surgery or revision for the duration of follow-up as a whole. Revision indicates that the original implant was either replaced by a new prosthesis of the same type or changed for a different type, e.g. HA was revised to THA.
3. Non-revision surgery: (further surgical intervention relating to the affected hip, involving anaesthesia that does not involve the revision or removal of implant, e.g. reduction, removal of cement fragments or application of distal trochanteric transfer) where these data are reported separately from revisions. Analysis describes re-operation events relating to the operated hip only.
4. Any surgery: a combined outcome measure to include all forms of surgery, i.e. an intervention on the affected hip requiring anaesthetic. This includes open and closed reduction of dislocations, and revision and non-revision surgery. The aim was to accommodate event data that do not explicitly specify revision or non-revision surgery, but only 'additional surgery' or 'reoperations'.

Secondary outcomes

1. Hip ratings [e.g. Oxford Hip Score (OHS)].
2. Mobility.
3. Mortality.
4. Surgery duration (in minutes).
5. Hypotension during surgery.
6. Operative blood loss (in millilitres).
7. Postoperative blood transfusion (in units).
8. Postoperative complications, e.g. loosening, erosion, wound infection, pneumonia, deep-vein thrombosis (DVT).
9. Length of hospital stay.
10. Health-related quality of life.
11. Resource utilisation.
12. Cost–utility.

Follow-up

There was no minimum duration of follow-up.

Study design

Randomised controlled trials (RCTs) only, as a scoping report for this project (HTA 09/108/01) identified at least seven such trials.

Exclusion criteria

Population

Patients eligible for hip replacement as a result of intracapsular fracture who are cognitively impaired or who were not independently mobile prior to fracture.

Intervention

Internal fixation.

Data extraction strategy

Data were extracted independently from all included studies by one reviewer (CC) using a data extraction form developed for this review and piloted on two studies (see *Appendix 2*). All data extracted were checked thoroughly by a second reviewer (AS) and any discrepancies were resolved by discussion and reference to the full paper.

Quality assessment strategy

The quality assessment of included RCTs was undertaken using appropriate quality assessment criteria. There is no published surgical RCT checklist, so this review applied surgical-quality assessment criteria outlined in a relevant Cochrane review.[21] These are included in the *Appendix 3*. Critical appraisal was performed by one reviewer (CC) and checked thoroughly by a second reviewer (AS). Any discrepancies or differences were resolved by discussion and reference to the full paper.

Methods of analysis/synthesis

Meta-analysis of trials was performed using RevMan 5.0 (The Nordic Cochrane Centre, Copenhagen, Denmark). For discrete and numerical outcomes, relative risk (RR; also known as risk ratio) and risk difference (RD) were reported with 95% confidence intervals (CIs). For continuous outcomes, weighted mean differences were calculated using the inverse variance and reported with 95% CIs. The studies were appraised in terms of clinical validity and methodological heterogeneity to determine whether or not statistical pooling of trial data within a meta-analysis was appropriate. Where studies were meta-analysed, the more conservative random-effects model was used to account for clinical and methodological variations between trials.[22] Statistical heterogeneity was described using the I^2 statistic, and potential reasons for any heterogeneity were discussed. The level of heterogeneity was defined as low (< 25%), moderate (25–50%) or high (≥ 50%).[23] Only randomised participants for whom a valid outcome had been evaluated and reported were included in the analysis.[24] The denominators used were determined based on the intention-to-treat principle, i.e. follow-up denominators included individuals who had died, unless an outcome (e.g. hip score) required the patient to respond at a specific point in time (e.g. 1 year). Otherwise, individuals lost to follow-up and therefore without a possible evaluated outcome, e.g. missing data, were excluded. Forest plots are presented for all the analyses in which there was more than one relevant study and sufficient data to undertake a meta-analysis. Results for all analyses, including those of single studies, are presented in summary tables. One comparison is analysed and presented: THA versus HA. Separate analyses were performed both for early follow-up (≤ 1 year), where these data were available, and for all follow-up periods, for the outcomes of dislocations, revisions, any surgery and mortality. The possibility of a difference in outcome for surgical approach, cementing of the prosthesis and the use of unipolar or bipolar prosthesis in hemiarthroplasty has been suggested, but not conclusively addressed, by previous research using randomised trial evidence.[19,21,25,26] Subgroup analyses were therefore performed using Altman and Bland's[27] test of interaction, comparing treatment effects between independent

subgroups, applying a method for estimating the ratio of two relative risks. The aim was to determine whether or not differences in outcomes between THA and HA were sensitive to the following potentially confounding variables: approach (anterolateral vs posterior); the use of cement; the use of unipolar or bipolar HA prostheses; and study quality. The subgroups were defined by these variables.

Results

Quantity of research available

The search of electronic databases identified 532 unique citations. After screening, 13 citations representing seven published RCTs satisfied all of the inclusion criteria: Dorr *et al.*,[28] Skinner *et al.*,[29] Ravikumar and Marsh,[30] Baker *et al.*,[19] Keating *et al.*,[2,31] Blomfeldt *et al.*,[32,33] Macaulay *et al.*[34–36] and Mouzopoulos *et al.*[37] An eighth RCT, van den Bekerom *et al.*,[38] was identified by the clinical advisor (SB) shortly before completion of the report. This study had not been published and catalogued in the databases at the time at which the searches were performed. One further potentially relevant study was excluded because it was unclear whether or not it satisfied the population inclusion criteria (it was published as an abstract only), and it did not report any of the primary outcomes.[39] Three ongoing trials were also identified (ISRCTN70736853, NCT00556842 and NCT01109862). No additional relevant papers were identified from reference tracking. Details of the screening and inclusion process are provided in the PRISMA flow chart (*Figure 1*).

Summary of studies

Eight RCTs were identified that provided data on primary outcomes comparing THA with HA for adults with displaced intracapsular or subcapital hip fracture (*Table 1*).[2,19,28–36,37,38] The mean age of participants in the included trials ranged from 69 to 82 years, with an overall age range of 41–96 years. At least 68% of participants in each of the trials were women. The number of participants in the eight trials ranged from 40 to 252. Five studies compared THA with cemented[19,31,32,38] or uncemented HA[29,30] or with a mixture of both types of prosthesis fixture.[28,34] Mouzopoulos *et al.*[37] did not report whether or not the prosthesis was cemented or uncemented.[37] The surgery reported in the trials by Baker *et al.*[19] and Blomfeldt *et al.*[32] was undertaken using the direct lateral approach; the trials reported by Dorr *et al.*,[28] Skinner *et al.*,[29] and Ravikumar and Marsh[30] used the posterior approach; and the trials reported by Keating *et al.*,[31] Macaulay *et al.*[35] and van den Bekerom *et al.*[38] used a mixture of the two approaches, depending on surgeon's choice. The approach used was not reported by Mouzopoulos *et al.*[37] The time from fracture to treatment was reported in only three trials and ranged from within 24 hours of admission[29] to within up to 48 hours of trial entry.[19,31] Dorr *et al.*,[28] Skinner *et al.*,[29] Baker *et al.*,[19] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*[37] and van den Bekerom *et al.*[38] all reported follow-up data on a primary outcome for up to 1 year, and Dorr *et al.*,[28] Ravikumar and Marsh,[30] Baker *et al.*,[19] Keating *et al.*,[31] Mouzopoulos *et al.*[37] and van den Bekerom *et al.*[38] all reported data on these outcomes for follow-up points > 1 year. Some trials reported primary and secondary outcome data for a number of different follow-up periods.

Quality assessment

Randomisation and allocation concealment were considered adequate in the studies by Baker *et al.*,[19] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Keating *et al.*[31] and van den Bekerom *et al.*[38] (e.g. use of sealed envelopes or a computer-generated randomisation sequence). In the studies by Dorr *et al.*,[28] Skinner *et al.*,[29] and Ravikumar and Marsh,[30] randomisation was by hospital number only and allocation concealment was not reported. Mouzopoulos *et al.*[37] reported randomisation to intervention based on selection of every third admission; details of allocation concealment were unreported. All eight RCTs defined inclusion criteria for the study and reported follow-up of at least 1 year (*Table 2*). Only Dorr *et al.*[28] did not describe fully or compare intervention

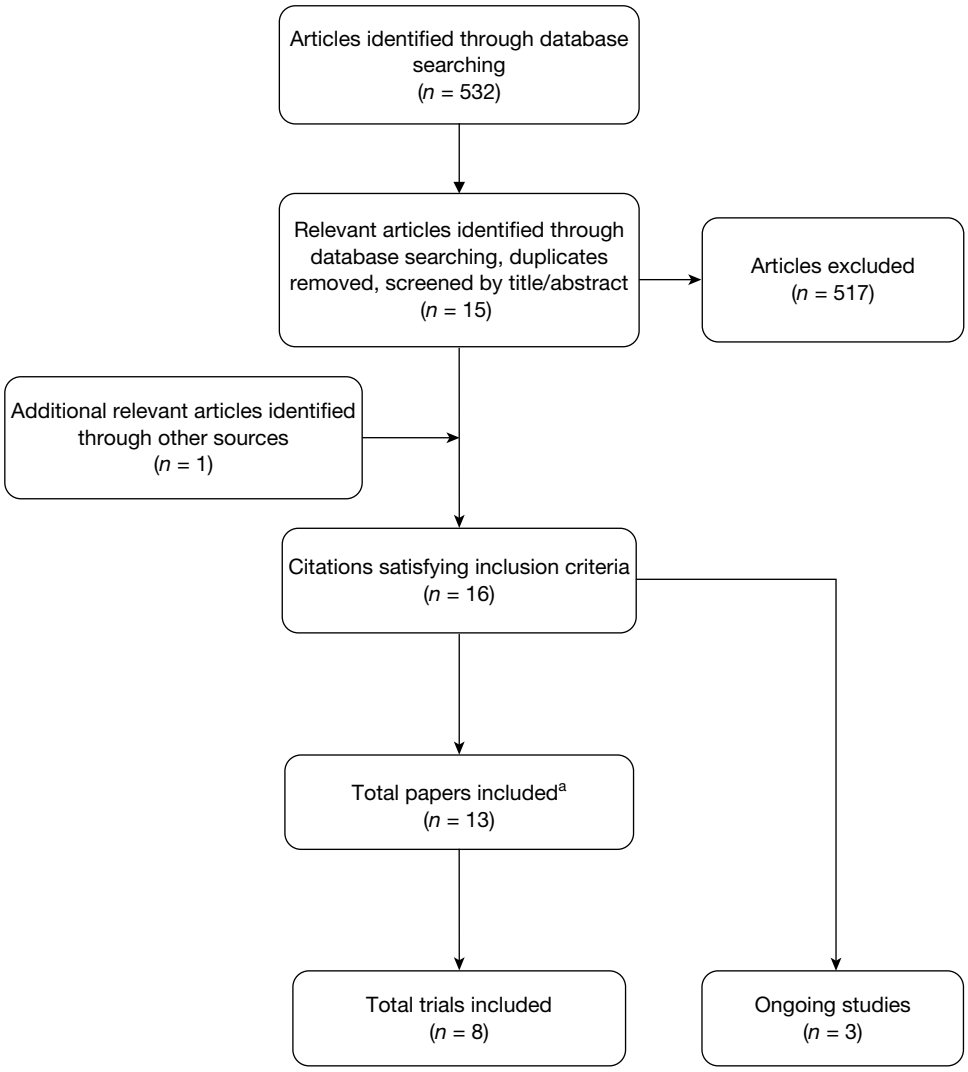

FIGURE 1 PRISMA flow diagram: clinical effectiveness. a: Multiple publications, including abstracts.

groups. van den Bekerom *et al.*[38] described both groups fully, but did not perform any tests to determine whether or not the differences in terms of cardiovascular, neurological and locomotive comorbidities, the taking of analgesics and pre-operation mobility were statistically significant. Four studies[19,31,32,35] clearly conducted intention-to-treat analyses, but this was unclear in the remaining four studies. Baker *et al.*,[19] Blomfeldt *et al.*,[32] Mouzopoulos *et al.*[37] and van den Bekerom *et al.*[38] also clearly reported comparable care for both intervention groups; this was unclear in the remaining four trials.

Only Blomfeldt *et al.*[32] reported that the surgeons involved were experienced in both procedures; Baker *et al.*[19] reported that the surgery in each trial arm was performed by surgeons with similar levels of training; and Keating *et al.*[31] reported that more patients were treated by consultants/senior surgeons in the THA group than in the HA group. The relative expertise of the surgeons conducting the two procedures was only reported in two studies.[19,38] Only in one study was it clear that the outcome assessors were blind to the intervention.[37] Keating *et al.*[31] and Macaulay *et al.*[35] both reported ≤ 5% loss to follow-up, and Blomfeldt *et al.*[32] reported a loss to follow-up of 6–8% across arms. The remaining studies all had an attrition rate of ≥ 10% or did not report whether or not any loss to follow-up had occurred.

TABLE 1 Study characteristics

Study author, date, country	Study design	Inclusion criteria	Exclusion criteria	Intervention (THA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery	Comparison (HA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery
Dorr *et al.*,[28] 1986, USA	RCT	Displaced femoral hip fractures (Garden grades III and IV);[40] ambulatory, oriented to time, place and person	Ambulation and mental status: ambulatory with confusion; non-ambulatory	Posterolateral approach; size of head = 28 mm (cemented); type of head NR *n* = 39 1. 69 (51–87) years; gender = 23/16 2. NR 3. NR	Approach = posterolateral; type of head NR *n* = 37 CHA (bipolar) *n* = 13 UHA (bipolar) 1. Mean age (range): CHA = 72 (53–79), UHA = 66 (41–85) gender = 35/15 2. NR 3. NR
Skinner *et al.*,[29] 1989; Ravikumar and Marsh,[30] 2000, UK	RCT	Displaced subcapital femoral neck fracture (Garden grades III and IV);[40] age ≥ 65 years (Note: includes unknown number of patients with 'compromised mental state': Ravikumar and Marsh,[30] p. 794)	Patients with old fractures, pathological fractures or those suffering from rheumatoid arthritis	Posterolateral approach; size of head = 32 mm (cemented); Howse II prosthesis [b]*n* = 89 (exact numbers not reported for 1-year data) 1. 81 years; gender = 90% women (overall) 2. NR 3. 'Usually within 24 hours of admission'[29]	Posterolateral approach; size of head = NR; Austin Moore prosthesis [b]*n* = 91 UHA (unipolar) (exact numbers not reported for 1-year data) 1. 82 years; gender = 90% women (overall) 2. NR 3. 'Usually within 24 hours of admission'[29]
Baker *et al.*,[19] 2006, UK	RCT	Displaced fracture of the femoral neck; age > 60 years, a normal Abbreviated Mini Mental Test score,[41] the ability to walk ≥ 0.5 miles (0.8 km), the ability to live independently (without reliance on a caregiver), a non-pathological fracture, and a hip with no or minimal osteoarthritic changes	Age < 60 years, medical or physical comorbidities that limited the walking distance to < 0.5 miles (0.8 km), a pre-existing hip abnormality requiring THA, or a pathological fracture secondary to malignant disease	Lateral approach; size of head = 28 mm (cemented); mean of outer diameter of acetabular component = 44–55 mm *n* = 40 1. 74.2 (63–86) years; gender = 32/8 2. NR 3. 1.75 days	Lateral approach; Endo femoral head (Zimmer); cemented *n* = 41 CHA (unipolar) 1. 75.8 years (range 66–86 years) Gender = 32/9 2. NR 3. 1.95 days
Keating *et al.*,[31] 2006, UK	RCT	Displaced intracapsular hip fracture; no formal age criteria, but protocol indicated that it was expected to be ≥ 60 years of age; normal cognitive function (a Mini Mental Test score[41] of > 6), the ability to be mobile, independent of another person prior to the fracture, and no serious concomitant disease (or other clinical reason for exclusion)	Undisplaced or valgus impacted intracapsular fracture	Direct lateral and posterior (60 vs 9); size of head NR; Charnley or Exeter head *n* = 69 (cemented) 1. 75.2 (SD 6) years; gender = 52/17 2. NR 3. Within 48 hours of trial entry	Approach: direct lateral and posterior (62 vs 7); size of head NR; predominantly Charnley or Exeter head *n* = 69 (cemented) (bipolar; two receive unipolar prosthesis) 1.75 years (SD 6 years) ; gender = 54/15 2. NR 3. Within 48 hours of trial entry

TABLE 1 Study characteristics *(continued)*

Study author, date, country	Study design	Inclusion criteria	Exclusion criteria	Intervention (THA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery	Comparison (HA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery
Blomfeldt *et al.*,[32] 2007, Sweden	RCT	Acute displaced intracapsular fracture of the femoral neck (Garden grades III and IV)[40] following a fall; age 70–90 years; absence of severe cognitive dysfunction, non-institutionalised independent living status and pre-injury independent walking capability with or without aids	Patients with pathological fractures and displaced fractures present for >48 hours before presentation; patients with rheumatoid arthritis or osteoarthritis	Lateral (modified Hardinge) approach; size of head ≥28 mm (cemented); modular Exeter femoral component *n* = 60 1. 80.5 years (range 70–90 years); gender = 47/13 2. Ceder A or B (i.e. full health or other illness not affecting rehabilitation): 88% 3. NR	Lateral approach; size of head ≥ 28 mm; modular Exeter femoral component *n* = 60 (cemented) (bipolar) 1. 80.7 years (range 70–89 years); gender = 54/6 2. Ceder A or B: 83% 3. NR
Macaulay *et al.*,[35] 2008, USA	RCT	>50 years of age; ability for independent ambulation before fracture; displaced fracture of the femoral neck (Garden grades III and IV);[40] ability to comprehend or read English or Spanish	Chronic-to-severe dementia (<23/30 on Folstein MMSE); pathologic fracture; other concomitatant bone fractures requiring surgical repair; pre-existing arthritis of the hip	Posterolateral or direct lateral (modified Hardinge) approach (surgeon's choice); size of head, ≥28mm; type of head, NR; cement vs 'press-fit stem' (surgeon's choice) [b]*n* = 18 1. NR; gender = NR 2. NR 3. NR	Posterolateral or direct lateral approach (surgeon's choice); size of head, NR; type of head, NR; bi- vs unipolar (surgeon's choice: 5 vs 18); cement vs 'press-fit stem' (surgeon's choice) [b]*n* = 23 1. NR; gender = NR 2. NR 3. NR
Mouzopoulos *et al.*,[37] 2008, USA and Germany	RCT	Patients with displaced subcapital hip fracture (Garden grade III or IV)[40] after falling down and having treatment in our hospitals from April 1999 to April 2002; (p. 372: aged ≥70 years, with good cognitive status and moderate dependency)	Previous hip fracture, history of cancer or Paget's disease, or rheumatic arthritis	Approach NR; size of head NR; type of head 'Plus'; cement: NR *n* = 37 1. 73 years (5 years) ; gender = 28/9 2. NR 3. 45 ± 7 (hours)	Approach NR; size of head NR; type of head 'Merete'; cement: NR *n* = 34 1. 74 years (4 years) ; gender = 24/10 2. NR 3. 46 ± 2 (hours)

continued

Summary of effectiveness

Numbers of patients experiencing dislocations

Six studies[19,28,29,32,35,38] (762 analysed participants) compared numbers of patients with dislocations within or up to 1 year post operation. A meta-analysis demonstrated a borderline statistically significant increased risk of dislocation for those receiving THA compared with HA (RR 3.98, 95% CI 0.98 to 16.12, $p = 0.05$), with a moderate level of statistical heterogeneity ($I^2 = 46\%$) (*Figure 2* and *Table 3*). There was a 4% increase in the absolute risk of dislocation for those receiving THA compared with HA (meta-analysed RD 0.04, 95% CI 0.00 to 0.09, $p = 0.05$, with a

TABLE 1 Study characteristics *(continued)*

Study author, date, country	Study design	Inclusion criteria	Exclusion criteria	Intervention (THA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery	Comparison (HA) characteristics Population characteristics *n* 1. Mean age, gender (f/m)[a] 2. Comorbidities 3. Time from fracture to surgery
van den Bekerom *et al.*,[38] 2010, Netherlands	RCT	≥ 70 years of age; displaced intracapsular fracture of the femoral neck; ability to give informed consent; no metastatic disease; no contraindications to anaesthesia before fracture; ability to understand written Dutch	Inability to fulfil inclusion criteria; advanced radiological osteoarthritis or rheumatoid arthritis in the fractured hip; significant senile dementia; suspected pathological fracture; patients who were bedridden or barely mobile from bed to chair	Approach was surgeon's choice (anterolateral/posterolateral = 93/22); size of head, 32 mm; type of head, Weber Rotationsprosthese (Sulzer AG, Winterthur, Switzerland) or Muller Geradschaftprosthese (Proteli AG, Münsingen, Switzerland); cemented *n* = 115 1. 82.1 years (range 70.1–95.6 years) ; gender = 90/25 2. Cardiovascular (33%), malignancies (5%), pulmonary (16%), neurological (29%), locomotive (27%), diabetes (10%) 3. NR	Approach was surgeon's choice (anterolateral/posterolateral = 132/5); size of head, NR; type of head, Weber Rotationsprosthese or Muller Geradschaftprosthese; (cemented) (bipolar) *n* = 137 1. 80.3 years (range 70.2–93.9 years) ; gender = 115/22 2. Cardiovascular (25%), malignancies (8%), pulmonary (12%), neurological (19%), locomotive (16%), diabetes (14%) 3. NR

CHA, cemented hip arthroplasty; F, female; M, male; MMSE, Folstein Mini Mental State Examination; NR, not reported; SD, standard deviation; UHA, uncemented hip arthroplasty.
a All values are mean (range) unless indicated otherwise.
b Differences between groups were not significant in terms of age, gender, function and comorbidities.

high level of statistical heterogeneity ($I^2 = 59\%$) (see *Table 3*). The presence of such heterogeneity may be because of the absence, or very small number, of events in some of the trial arms.

Seven studies[19,28,30–32,35,38] (900 analysed participants) compared the number of patients with dislocations for all follow-up periods post operation, up to 13 years. A meta-analysis demonstrated a statistically significant increased risk of dislocation for those receiving THA compared with HA (RR 2.40, 95% CI 1.41 to 2.76, $p = 0.01$), with a low level of statistical heterogeneity ($I^2 = 13\%$) (see *Figure 3* and *Table 3*). The 1-year follow-up data may have also generated a statistically significant difference had the sample been larger. There was a 5% increase in the absolute risk of dislocation for those treated with THA compared with HA (meta-analysed RD 0.05, 95% CI 0.00 to 0.09, $p = 0.03$), with a high level of statistical heterogeneity ($I^2 = 64\%$) (see *Table 3*).

Number of patients experiencing revision surgery or any surgery

Revisions included revisions because of all causes, including dislocations. Five studies[29,32,35,38,39] (669 analysed participants) compared the number of patients who experienced revision surgery within or up to 1 year post operation. A meta-analysis demonstrated a statistically non-significant 59% reduced risk of revision for those receiving THA compared with HA (RR 0.41, 95% CI 0.16 to 1.03, $p = 0.06$), with no statistical heterogeneity ($I^2 = 0\%$) (see *Figure 4* and *Table 3*). There was a

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TABLE 2 Quality assessment outcomes

Study	Allocation concealment	Inclusion criteria defined	Intention-to-treat analysis	Intervention groups described and comparable	Surgeons experienced in both operations	Care identical other than intervention	Outcome measures defined	Outcome assessors blind	Follow-up of at least 1 year	Loss to follow-up reported and ≤5%
Dorr *et al.*[28]	No	Yes	Unclear	Unclear	No	Unclear	Yes	No	Yes	Unclear
Skinner *et al.*,[29] Ravikumar and Marsh[30]	No	Yes	Unclear	Yes	Unclear	Unclear	Yes	No	Yes	Unclear
Baker *et al.*[19]	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	No	Yes	No
Keating *et al.*[31]	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	No	Yes	Yes
Blomfeldt *et al.*[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Macaulay *et al.*[35]	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	No	Yes	Yes
Mouzopoulos *et al.*[37]	No	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	No
van den Bekerom *et al.*[38]	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	No	Yes	No

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Baker 2006[19]	3	40	0	41	15.2	7.17 (0.38 to 134.53)
Blomfeldt 2007[32]	0	60	0	60		Not estimable
Dorr 1986[28]	6	39	0	50	15.8	16.57 (0.96 to 285.54)
Macaulay 2008[35]	1	17	0	23	13.8	4.00 (0.17 to 92.57)
Skinner 1989[29]	11	89	10	91	39.6	1.12 (0.50 to 2.52)
van den Bekerom 2010[38]	5	115	0	137	15.5	13.09 (0.73 to 234.18)
Total (95% CI)		**360**		**402**	**100.0**	**3.98 (0.98 to 16.12)**
Total events	26		10			

Heterogeneity: $\tau^2 = 1.12$; $\chi^2 = 7.39$, df = 4 ($p = 0.12$); $I^2 = 46\%$
Test for overall effect: $z = 1.93$ ($p = 0.05$)

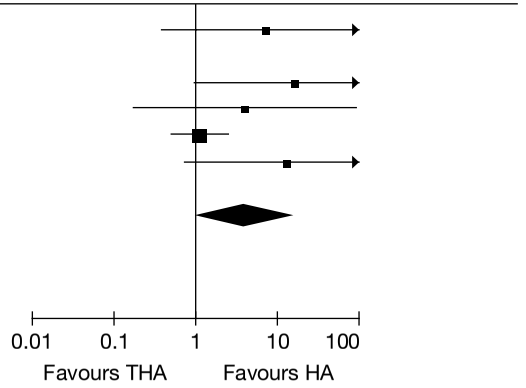

FIGURE 2 Risk of dislocations within and up to 1 year.

TABLE 3 Relative risks and RD for THA versus HA

Included studies	Number of studies	Follow-up	THA vs HA	RR (95% CI)	I^2 (%)	RD (95% CI)	I^2 (%)
Dislocations							
Dorr *et al.*,[28] Skinner *et al.*,[29] Baker *et al.*,[19] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] van den Bekerom *et al.*[38]	6	≤ 1 year	26/360 vs 10/402	3.98 (0.98 to 16.12), $p = 0.05$	46	0.04 (0.00 to 0.09), $p = 0.05$	59
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] van den Bekerom *et al.*[38]	7	Up to 13 years	40/429 vs 16/471	2.40 (1.41 to 2.76), $p = 0.01$	13	0.05 (0.00 to 0.09), $p = 0.03$	64
Revisions							
Skinner *et al.*,[29] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	5	≤ 1 year	5/320 vs 15/349	0.41 (0.16 to 1.03), $p = 0.06$	0	–0.02 (–0.06 to 0.02), $p = 0.35$	64
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Baker *et al.*,[19] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	7	Up to 13 years	12/399 vs 42/440	0.31 (0.17 to 0.59), $p = 0.0003$	0	–0.05 (–0.12 to 0.01), $p = 0.09$	80
Any surgery							
Skinner *et al.*,[29] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	5	≤ 1 year	24/320 vs 22/349	1.72 (0.41 to 7.21), $p = 0.46$	56	0.01 (–0.04 to 0.07), $p = 0.61$	57
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	8	Up to 13 years	50/468 vs 54/509	1.09 (0.65 to 1.83), $p = 0.75$	33	0.01 (–0.04 to 0.05), $p = 0.74$	40
Mortality							
Skinner *et al.*,[29] Blomfeldt *et al.*,[32] Keating *et al.*,[31] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	5	≤ 1 year	50/376 vs 58/400	0.91 (0.65 to 1.29), $p = 0.60$	0	–0.01 (–0.05 to 0.04), $p = 0.75$	0
Ravikumar and Marsh,[30] Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*,[35] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	7	Up to 13 years	176/433 vs 180/464	1.03 (0.80 to 1.32), $p = 0.81$	48	0.00 (–0.07 to 0.07), $p = 1.00$	52

2% reduction in the absolute risk of revision for those receiving THA compared with HA (meta-analysed RD –0.02, 95% CI –0.06 to 0.02, $p = 0.35$), with a high level of statistical heterogeneity ($I^2 = 64\%$) (see *Table 3*).

Seven studies[19,28,30,32,35,38,39] (839 analysed participants) compared the numbers of patients who experienced revision surgery for all follow-up periods post operation, up to 13 years. A meta-analysis demonstrated a statistically significant 69% reduced risk of revision for those receiving THA compared with HA (RR 0.31, 95% CI 0.17 to 0.59, $p = 0.0003$), with no statistical heterogeneity ($I^2 = 0\%$) (see *Figure 5* and *Table 3*). There was a 5% reduction in the absolute risk of

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Baker 2006[19]	3	40	0	41	5.2	7.17 (0.38 to 134.53)
Blomfeldt 2007[32]	0	60	0	60		Not estimable
Dorr 1986[28]	7	39	2	50	17.3	4.49 (0.99 to 20.41)
Keating 2006[31]	3	69	2	69	13.3	1.50 (0.26 to 8.70)
Macaulay 2008[35]	1	17	0	23	4.5	4.00 (0.17 to 92.57)
Ravikumar 2000[30]	18	89	12	91	54.2	1.53 (0.79 to 3.00)
van den Bekerom 2010[38]	8	115	0	137	5.5	20.22 (1.18 to 346.66)
Total (95% CI)		**429**		**471**	**100.0**	**2.40 (1.21 to 4.76)**
Total events	40		16			

Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 5.72$, df = 5 ($p = 0.33$); $I^2 = 13\%$
Test for overall effect: $z = 2.51$ ($p = 0.01$)

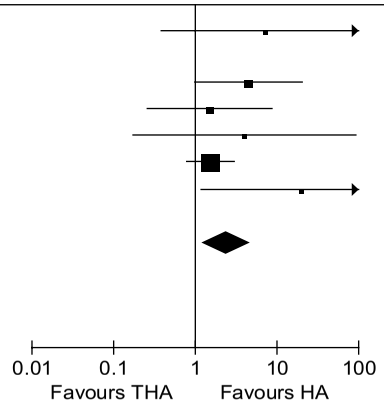

FIGURE 3 Risk of dislocations up to 13 years.

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Blomfeldt 2007[32]	0	60	0	60		Not estimable
Macaulay 2008[35]	1	17	0	23	8.8	4.00 (0.17 to 92.57)
Mouzopoulos 2008[37]	0	39	2	38	9.7	0.20 (0.01 to 3.93)
Skinner 1989[29]	4	89	12	91	72.9	0.34 (0.11 to 1.02)
van den Bekerom 2010[38]	0	115	1	137	8.6	0.40 (0.02 to 9.64)
Total (95% CI)		**320**		**349**	**100.0**	**0.41 (0.16 to 1.03)**
Total events	5		15			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.37$, df = 3 ($p = 0.50$); $I^2 = 0\%$
Test for overall effect: $z = 1.89$ ($p = 0.06$)

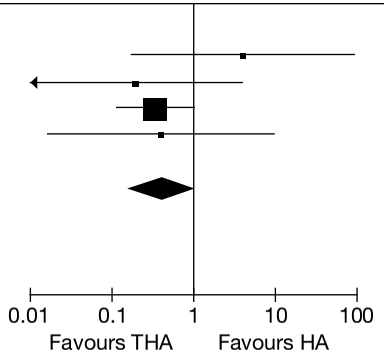

FIGURE 4 Risk of revision surgery within and up to 1 year.

Study or subgroup	THR Events	THR Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Baker 2006[19]	1	40	6	41	9.2	0.17 (0.02 to 1.36)
Blomfeldt 2007[32]	0	60	0	60		Not estimable
Dorr 1986[28]	1	39	3	50	8.0	0.43 (0.05 to 3.95)
Macaulay 2008[35]	1	17	0	23	4.0	4.00 (0.17 to 92.57)
Mouzopoulos 2008[37]	1	39	5	38	8.9	0.19 (0.02 to 1.59)
Ravikumar 2000[30]	6	89	22	91	54.1	0.28 (0.12 to 0.66)
van den Bekerom 2010[38]	2	115	6	137	15.8	0.40 (0.08 to 1.93)
Total (95% CI)		**399**		**440**	**100.0**	**0.31 (0.17 to 0.59)**
Total events	12		42			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.28$, df = 5 ($p = 0.66$); $I^2 = 0\%$
Test for overall effect: $z = 3.61$ ($p = 0.0003$)

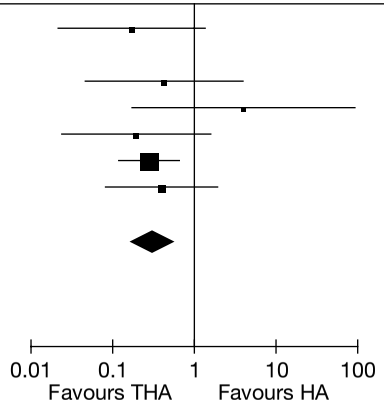

FIGURE 5 Risk of revision surgery up to 13 years.

revision for those exposed to THA compared with HA (meta-analysed RD –0.05, 95% CI –0.12 to 0.01, $p = 0.09$), with a high level of statistical heterogeneity ($I^2 = 80\%$) (see *Table 3*).

Five studies[29,32,35,38,39] (669 analysed participants) compared the number of patients who experienced any form of surgery (including open or closed reduction of a dislocation, revision or surgery for any other cause) within or up to 1 year post operation. A meta-analysis demonstrated a statistically non-significant increased risk of any surgery for those receiving THA compared with HA (RR 1.72, 95% CI 0.41 to 7.21, $p = 0.46$), with a high level of statistical heterogeneity ($I^2 = 56\%$) (see *Figure 6* and *Table 3*). There was a 2% increase in the absolute risk of surgery for those receiving THA compared with HA (meta-analysed RD 0.01, 95% CI –0.04 to 0.07, $p = 0.61$), with a high level of statistical heterogeneity ($I^2 = 57\%$) (see *Table 3*).

Eight studies[19,28,30–32,35,38,39] (977 analysed participants) compared the number of patients who experienced any surgery for all follow-up periods post operation, up to 13 years. A meta-analysis demonstrated a statistically non-significant increased risk of any surgery for those receiving THA compared with HA (RR 1.09, 95% CI 0.65 to 1.83, $p = 0.75$), with a moderate level of statistical heterogeneity ($I^2 = 33\%$) (see *Figure 7* and *Table 3*). There was a 1% increase in the absolute risk of surgery for those receiving THA compared with HA (meta-analysed RD –0.01, 95% CI –0.04 to 0.05, $p = 0.74$), with a moderate level of statistical heterogeneity ($I^2 = 40\%$) (see *Table 3*).

This analysis combined outcome data on patients with dislocations, revisions (not including dislocated revisions) and, where reported, other non-revision or dislocation surgery. Baker *et al.*,[19] Macaulay *et al.*,[35] Mouzopoulos *et al.*[37] and van den Bekerom *et al.*[38] reported only dislocation and/or revision event data, and no data on any other surgery. However, the exclusion of these four studies from the analysis, so that only studies reporting data on all three types of possible surgery were included, does not affect the result: RR 1.14, 95% CI 0.57 to 1.26, $p = 0.72$.

Hip scores and walking

All eight trials[19,28,30–32,35,38,39] reported patient-reported assessments of pain, function and mobility using hip scores. Only Macaulay *et al.*[35] and Mouzopoulos *et al.*[37] compared ratings using the same scale of the Harris Hip Score (HHS) at 1 year post operation, permitting meta-analysis (*Table 4*). However, because of the small number of studies, meta-analysis was not performed. Macaulay *et al.*[35] reported a non-significant difference in favour of THA using the HHS and pain and function subscales at 1 year, but statistically significant differences in favour of THA at 2 years for pain and function ($p < 0.05$). Blomfeldt *et al.*[32] reported a statistically significant ($p < 0.001$) difference after 1 year in favour of THA compared with HA, and Ravikumar and Marsh[30] and Mouzopoulos *et al.*[37] reported the average HHS to be higher for individuals treated with THA than for those treated with HA (p-values not reported). van den Bekerom *et al.*[38] also reported higher scores for THA than for HA for both 1 and 5 years, but the differences were not statistically significant. Three studies also reported hip scores using different scales (see *Table 4*).[19,28,31] Baker *et al.*[19] reported a statistically significant ($p = 0.033$) difference after 3 years in favour of THA compared with HA using the OHS. Keating *et al.*[31] reported a statistically non-significant ($p = 0.38$) difference after 1 year in favour of THA compared with HA using the Hip Rating Questionnaire, but a statistically significant ($p = 0.04$) difference after 2 years. Dorr *et al.*[28] reported two subscales of a modified version of the D'Aubigne/Postel hip score: individuals receiving THA reported less pain and better ambulation than those receiving HA, especially uncemented HA.

Six studies also reported additional mobility data (see *Table 4*).[19,28–31,35] Skinner *et al.*[29] and Ravikumar and Marsh[30] reported significant differences ($p < 0.05$) in favour of THA in the number of participants walking or mobile at 1 year and 13 years, respectively. Baker *et al.*[19] reported a statistically significant difference ($p = 0.039$) in favour of THA for mean walking

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Blomfeldt 2007[32]	2	60	0	60	14.3	5.00 (0.25 to 102.00)
Macaulay 2008[35]	1	17	0	23	13.6	4.00 (0.17 to 92.57)
Mouzopoulos 2008[37]	0	39	2	38	14.4	0.20 (0.01 to 3.93)
Skinner 1989[29]	13	89	19	91	36.1	0.70 (0.37 to 1.33)
van den Bekerom 2010[38]	8	115	1	137	21.6	9.53 (1.21 to 75.08)
Total (95% CI)		**320**		**349**	**100.0**	**1.72 (0.41 to 7.21)**
Total events	24		22			

Heterogeneity: $\tau^2 = 1.38$; $\chi^2 = 9.18$, df = 4 ($p = 0.06$); $I^2 = 56\%$
Test for overall effect: $z = 0.74$ ($p = 0.46$)

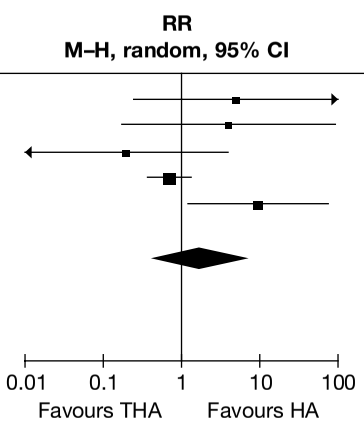

FIGURE 6 Risk of any surgery within and up to 1 year.

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Baker 2006[19]	4	40	6	41	13.2	0.68 (0.21 to 2.24)
Blomfeldt 2007[32]	2	60	0	60	2.8	5.00 (0.25 to 102.00)
Dorr 1986[28]	8	39	5	50	15.8	2.05 (0.73 to 5.78)
Keating 2006[31]	6	69	5	69	13.9	1.20 (0.38 to 3.75)
Macaulay 2008[35]	1	17	0	23	2.6	4.00 (0.17 to 92.57)
Mouzopoulos 2008[37]	1	39	5	38	5.4	0.19 (0.02 to 1.59)
Ravikumar 2000[30]	18	89	27	91	29.6	0.68 (0.41 to 1.15)
van den Bekerom 2010[38]	10	115	6	137	16.8	1.99 (0.74 to 5.30)
Total (95% CI)		**468**		**509**	**100.0**	**1.09 (0.65 to 1.83)**
Total events	50		54			

Heterogeneity: $\tau^2 = 0.17$; $\chi^2 = 10.47$, df = 7 ($p = 0.16$); $I^2 = 33\%$
Test for overall effect: $z = 0.31$ ($p = 0.75$)

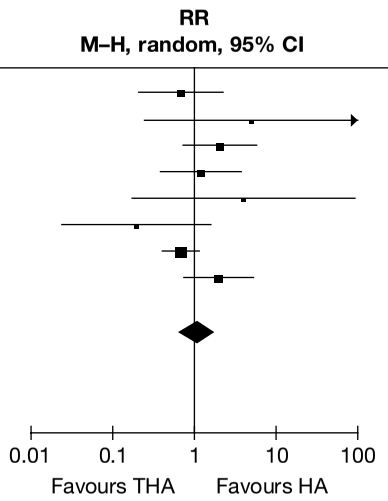

FIGURE 7 Risk of any surgery up to 13 years.

TABLE 4 Effectiveness outcomes

Study	Study duration/ follow-up	Primary outcomes (THA vs HA) 1. Number of patients with dislocations 2. Number of patients who had a revision 3. Number of patients who had a non-revision reoperation	Secondary outcomes Hip ratings (e.g. HHS) (THA vs HA)	Mobility, *n*, e.g. walking distance (THA vs HA)	Utility data 1. Quality of life 2. Length of hospital stay 3. Resource utilisation and/or cost–utility
Dorr *et al.*[28]	3, 12 and 24–48 months	1. 2–4 years unless stated: 7/39 (18%) vs 2/50 (4%) (at 'final follow-up'; six THA dislocations occurred immediately post operation or up to 3 months post operation; it is not reported when remaining dislocations occurred) 2. 2–4 years unless stated: THA 1/39 (3%) for loosening and heterotopic ossification at 3 years vs CHA 2/37 (5%) for heterotopic ossification and dislocation vs UHA 1/13 (8%) for femoral loosening 3. 1 year: THA 1/39 (3%) for recurrent dislocation in first month vs CHA 1/37 (3%) for removal of a cement fragment at 2 weeks	*Modified D'Aubigne/Postel hip score (higher better)* 1 year: pain = 5.5 (THA) vs 5.2 (CHA) vs 3.6 (UHA); ambulation = 4.1 (THA) vs 4.2 (CHA) vs 3.0 (UHA) 2 years: pain = 5.5 (THA) vs 5.1 (CHA) vs 3.0 (UHA); ambulation = 5.5 (THA) vs 4.0 (CHA) vs 3.0 (UHA)	Not walking at final follow-up: 1/39 vs 3/50	1. NR 2. 'There was no difference in the hospital time', pp. 22–3 3. NR
Skinner *et al.*[29] Ravikumar and Marsh[30]	1 year, 13 years	1. [a]1 year: 11/89 (12%) vs 10/91 (11%) (includes both 'fit' and 'unfit' patients; the latter were at significantly higher risk, $p < 0.05$) 13 years: 18/89 (20%), of which five had recurrent dislocations, four of which were revised vs 12/91 (13%) 2. 1 year: 4/89 (4%) for recurrent dislocation vs 12/91 (13%) for loosening, further fracture or ectopic calcification, $p < 0.01$ 13 years: 6/89 (7%) (two for infection and four recurrent dislocations) vs 22/91 (24%) for acetabular erosion, loosening, heterotopic ossification and deep infection Mean time to revision: 27.3 months (THA) vs 22.1 months (HA) 3. [a]1 year: 13/89 (15%) vs 19/91 (21%)[b] (reoperations, defined as second anaesthetic, includes reduction of a dislocation and/ or a revision) 13 years: 18/89 (20%) vs 27/91 (30%)[b] (reoperations, defined as second anaesthetic, includes reduction of a dislocation and or a revision)	*HHS (higher better)* 1 year: NR Average score among survivors at 13 years: 80 vs 55 Pain at 1 year (% of patients with highest pain score of 3–4, i.e. requiring analgesia): 0% vs 27% Pain at 13 years: 6% vs 45%	Patients with no loss of mobility at 1 year: 49% vs 30%, $p < 0.05$ Patients mobile at 1 year: 73% vs 66% At 13 years: 70% vs 53%%, $p < 0.05$	1. NR 2. NR 3. NR

continued

TABLE 4 Effectiveness outcomes *(continued)*

Study	Study duration/ follow-up	Primary outcomes (THA vs HA) 1. Number of patients with dislocations 2. Number of patients who had a revision 3. Number of patients who had a non-revision reoperation	Secondary outcomes Hip ratings (e.g. HHS) (THA vs HA)	Mobility, *n*, e.g. walking distance (THA vs HA)	Utility data 1. Quality of life 2. Length of hospital stay 3. Resource utilisation and/or cost–utility
Baker *et al.*[19]	3, 12 and 36 months (Data for 3 years from Baker *et al.*,[19] unless stated; mean follow-up was 39 months)	1. 30 days post operation only: 3/40 (8%) vs 0/41 (0%) ($p=0.116$, Fisher exact test) (1 month only) (no dislocation was revised) 2. 3 years (revisions or 'planned revisions'): 1/40 (3%) for pain due to femoral subsidence vs 6/41 (15%) for pain owing to acetabular erosion or periprosthetic fracture ($p=0.058$, Fisher's exact test) This includes a patient categorised for revision, but who 'declined additional intervention', p. 2587 (unclear how many events occurred before 1 year) 3. NR	*OHS (lower better) [mean (range)] THA (n = 36) vs HA (n = 33)* 18.8 (12–47) vs 22.3 (12–48) $p=0.033$ (Mann–Whitney) 18.8 vs 22.5 (Baker *et al.*[19])	Walking distance (km) [mean (range)]: THA ($n=36$) vs HA ($n=33$): 3.6 (0–40.2) vs 1.9 (0–6.4), $p=0.039$ (Student's *t*-test) 2.23 miles vs 1.09 miles (Baker *et al.*[42])	1. SF-36 [mean (range)] THA ($n=36$) vs HA ($n=33$) Not significant ($p=0.356$) Physical: 40.53 (16.2–56.5) vs 38.10 (16–58.8) Mental: 52.00 (24.2–68.4) vs 55.32 (39–66.6) 2. NR 3. NR
Keating *et al.*[31]	12 and 24 months	1. 2 years: 3/69 (4%) (all led to 'additional surgery') vs 2/69 (3%): OR 0.63 (95% CI 0.10 to 3.92), $p=0.62$ (unclear how many occurred before 1 year) 2. NR 3. 2 years ('Additional' or 'Further surgery': 'any procedure requiring general or regional anaesthesia. This included manipulative reduction of prosthetic dislocations'): 6/69 (9%) for dislocation ($n=3$), infection ($n=2$) and wound dehiscence ($n=1$) vs 5/69 (7%) (reasons not given): OR 0.81 (95% CI 0.25 to 2.65), $p=0.73$ (unclear how many events occurred before 1 year)	*Hip Rating Questionnaire (higher better); THA n = 66 vs HA n = 65* 1 year: 79.4 (17) vs 76.5 (13) (95% CI −8.00 to 3.09), $p=0.38$ 2 years: 79.9 (17) vs 73.8 (16) (95% CI −12.53 to −0.37), $p=0.04$	*Walking (note: included in Hip score): THR n = 66 vs HA n = 65* 1 year: 19.3 (6) vs 16.9 (5) (95% CI −4.15 to −0.03), $p=$NR 2 years: 19.3 (6) vs 16.2 (6) (95% CI −4.97 to −0.66), $p=$NR	1. EQ-5D at 2 years [mean (SD)]: (THR $n=66$ vs HA $n=65$): 0.69 (0.32) vs 0.53 (0.36) (95% CI −0.28 to −0.04), $p=0.008$ 2. 11.5 vs 12.3 days (post operation) 3. Hip-related re-admissions: 7 (10%) vs 8 (12%)
Blomfeldt *et al.*[32]	4 and 12 months (only 12-month data)	1. 1 year: 0/60 (0%) vs 0/60 (0%) 2. 1 year: 0/60 (1%) vs 0/60 (0%) 3. 1 year: 2/60 (3%) for a peri-prosthetic fracture post fall, fixed internally with a plate, and for a wound revision following infection vs 0/60 (0%)	*HHS (higher better)* [mean (range)] *(THA n = 56 vs HA n = 55) at 1 year* 87.2 (58.6–100.0) vs 79.4 (51.3–99.8), $p<0.001$ Pain subscale at 1 year: (THA $n=56$ vs HA $n=55$) 43.1 (30.0–44.0) vs 39.1 (20.0–44.0), $p<0.001$	NR	1. EQ-5D: 0.68 vs 0.63 ($p=0.636$) 2. NR 3. NR

Study	Study duration/ follow-up	Primary outcomes (THA vs HA) 1. Number of patients with dislocations 2. Number of patients who had a revision 3. Number of patients who had a non-revision reoperation	Secondary outcomes Hip ratings (e.g. HHS) (THA vs HA)	Mobility, *n*, e.g. walking distance (THA vs HA)	Utility data 1. Quality of life 2. Length of hospital stay 3. Resource utilisation and/or cost–utility
Macaulay *et al.*[35]	6, 12[35] and 24 months[34]	1. 1 year: 1/17 (5.9%) 5 months post surgery and revised vs 0/23 (0%) 2. 1 year: 1/17 (5.9%) due to dislocation vs 0/23 (0%) 3. NR	*At 1 year* HHS (higher better) [mean (SD)] (THA $n=17$ vs HA $n=23$): 84.2 (±12) vs 80.6 (±14.3), –3.6 (95% CI –15.3 to 8.3), $p=0.55$ *At 1 year* WOMAC function subscale (higher better) (mean ± SD): 75.9 ± 19.8 vs 78.7 ± 16.8, $p=0.71$ WOMAC pain subscale (higher better) (mean ± SD): 92.5 ± 14.6 vs 88.5 ± 13.6, $p=0.50$ *At 2 years* WOMAC function subscale (higher better) (mean ± SD): 81.8 ± 10.2 vs 65.1 ± 18.1, $p=0.03$ WOMAC pain subscale (higher better) (mean ± SD): 94.4 ± 6.8 vs 77.8 ± 20.9, $p=0.05$	At 6 months: TUG test: 14.2 seconds vs 20.7 seconds At 1 and 2 years: not statistically significant, but TUG indicates that THA patients complete the test about 2 seconds faster than the HA patients At 1 year: walking independently or with a cane 57% vs 41%	1. *At 1 year* SF-36 pain subscale (higher better) (mean ± SD): 53.2 ± 10.2 vs 42.4 ± 11.5, $p=0.02$ SF-36 mental health subscale (mean ± SD): 55.7 ± 15.8 vs 49.0 ± 12.0, $p=0.25$ *At 2 years* SF-36 pain subscale (higher better) (mean ± SD): 54.8 ± 7.9 vs 44.7 ± 10.5, $p=0.04$ SF-36 mental health subscale (mean ± SD): 54.9 ± 9.4 vs 40.9 ± 10.3, $p=0.006$ 2. NR 3. NR
[c]Mouzopoulos *et al.*[37]	1 year, 4 years	1. NR 2. 1 year: 0/39 (0%) vs 2/38 (5%) Up to 4 years: 1/39 (3%) vs 5/38 (13%) 3. NR	*HHS (higher better)* 1 year (THA $n=37$ vs HA $n=34$) (mean ± SD): 81.6 ± 4.9 vs 77.8 ± 9.6, $p=$NR 4 years (THA $n=33$ vs HA $n=30$) (mean ± SD): 83.7 ± 4.8 vs 79.5 ± 6.5; $p=$NR *Function using Barthel Index (higher better)* 1 year (THA $n=33$ vs HA $n=30$) (mean ± SD): 84.8 ± 14.8 vs 76.8 ± 6.8, $p=$NR 4 years (THA $n=23$ vs HA $n=20$) (mean ± SD): 85.3 ± 11.6 vs 79.6 ± 6.3, $p=$NR	NR	1. NR 2. THA (8.3 ± 6.2) vs HA (9.1 ± 3.4) (in days, mean ± SD) (p-value NR) 3. NR

continued

TABLE 4 Effectiveness outcomes *(continued)*

Study	Study duration/ follow-up	Primary outcomes (THA vs HA) 1. Number of patients with dislocations 2. Number of patients who had a revision 3. Number of patients who had a non-revision reoperation	Secondary outcomes Hip ratings (e.g. HHS) (THA vs HA)	Mobility, *n*, e.g. walking distance (THA vs HA)	Utility data 1. Quality of life 2. Length of hospital stay 3. Resource utilisation and/or cost–utility
van den Bekerom *et al.*[38]	1 year, 5 years	1. 1 year: 5/115 (4%) vs 0/137 (0%) 5 years: 8/115 (7%) vs 0/137 (0%) ($p=0.002$) *Note: dislocations: 3/93 (3%) anterolateral approach vs 5/22 (23%) posterolateral approach for THA; 0/132 (0%) vs 0/5 (0%) for HA* 2. 1 year: 0/115 (0%) vs 1/137 (1%) 5 years: 2/115 (2%) vs 6/137 (4%) ($p=0.29$) (for loosening, osteoarthritis of acetabulum and low-grade deep infection) 3. NR	*At 1 year* [mean (range)] HHS (higher better): (THA $n=115$ vs HA $n=137$)[d]: 76 (44–100) vs 73.9 (23–100), $p=0.40$ HHS (pain subscale): 40 (20–44) vs 37.5 (10–44), $p=$NR HHS (function subscale): 20.8 (0–36) vs 20.7 (0–36), $p=$NR *5 years (mean and range)* (THA $n=115$ vs HA $n=137$)[d]: 75.2 (45–98) vs 71.9 (33–99), $p=0.22$ HHS (pain subscale): 40.1 (20–44) vs 38.6 (10–44), $p=$NR HHS (function subscale): 20.1 (7–33) vs 18.6 (4–35), $p=$NR	NR	1. NR 2. THA: 18.4 (4–86) vs HA 17.1 (2–89) (days and range) 3. NR

CHA, cemented hip arthroplasty; EQ-5D, European Quality of Life-5 Dimensions; NR, not reported; OR, odds ratio; SD, standard deviation; SF-36, Short Form questionnaire-36 items; TUG, Timed Up and Go; UHA, uncemented hip arthroplasty; WOMAC, Western Ontario McMaster Osteoarthritis Index.

a Event data calculated from percentages and sample sizes reported.

b The percentages reported by Skinner *et al.*[29] for all second anaesthetic are less than the combined total of dislocations and revisions. This suggests that revised dislocations are treated as a single event. The event data used are those generated from the percentages reported for each outcome.

c The denominators used for this trial exclude randomised participants who did not actually satisfy the inclusion criteria: this was an implementation error by those applying the inclusion/exclusion criteria.[43]

d The number of participants given here has been extracted from the paper, but is incorrect: these are the numbers randomised and do not take into account loss to follow-up, e.g. due to mortality, which would have reduced the numbers at the point at which these data were collected from participants.

distance. Dorr *et al.*,[28] Keating *et al.*[31] and Macaulay *et al.*[35] also reported greater degrees of mobility among participants in the THA arms of trials (*p*-values not reported) for 4, 2 and 1 year(s), respectively.

Mortality

Five studies[29,31,32,38,39] (767 analysed participants) compared the number of patients who died within and up to 1 year post operation. A meta-analysis demonstrated a non-statistically significant 9% reduced risk of mortality for those treated with THA compared with HA (RR 0.91, 95% CI 0.65 to 1.29, $p = 0.60$), with no statistical heterogeneity ($I^2 = 0\%$) (see *Figure 8* and *Table 3*). There was a 1% reduction in the absolute risk difference (meta-analysed RD –0.01, 95% CI –0.05 to 0.04, $p = 0.75$), with no statistical heterogeneity ($I^2 = 0\%$) (see *Table 3*).

Seven studies[19,30–32,35,38,39] (888 analysed participants) compared the number of patients who died for all follow-up periods post operation, up to 13 years. A meta-analysis demonstrated a statistically non-significant 4% increased risk of death for those treated with THA compared with HA (RR 1.03, 95% CI 0.80 to 1.32, $p = 0.81$), with a moderate level of statistical heterogeneity ($I^2 = 48\%$) (see *Figure 9* and *Table 3*). There was no reduction in the absolute risk difference (meta-analysed RD 0.00, 95% CI –0.07 to –0.07, $p = 1.00$), with a high level of statistical heterogeneity ($I^2 = 52\%$) (see *Table 3*). It is commented that as the time period increases it is expected that the RR of mortality would become nearer to 1 as the patients are elderly and at risk of dying from causes other than those associated with either THA or HA.

Quality of life

Four trials reported scores on utility scales, or subscales, for THA compared with HA.[19,31,32,35] Blomfeldt *et al.*[32] and Keating *et al.*[31] both used the European Quality of Life-5 Dimensions (EQ-5D). Blomfeldt *et al.*[32] reported a slightly higher, statistically non-significant difference in favour of THA at 1 year (0.68 vs 0.63, $p = 0.636$), whereas Keating *et al.*[31] reported a statistically significant difference in favour of THA at 2 years (0.69 vs 0.53, $p = 0.008$). Using the Short Form questionnaire-36 items (SF-36), Macaulay *et al.*[35] reported a statistically significant difference at 1 year in favour of THA for pain (53.2 vs 42.4, $p = 0.02$) but not mental health (55.7 vs 49.0, $p = 0.25$), but statistically significant differences on both subscales at 2 years (54.8 vs 44.7 and 54.9 vs 40.9, respectively, $p < 0.05$). Baker *et al.*[19] reported a statistically non-significant difference between the two interventions at 3 years ($p = 0.356$) on the SF-36.

Peri- and postoperative outcomes and complications

Four studies reported data on surgery duration: Baker *et al.*[19] and Blomfeldt *et al.*[32] both reported that THA surgery took significantly longer ($p < 0.001$) than HA; Keating *et al.*[31] and van den Bekerom *et al.*[38] also reported that THA surgery was longer. Blomfeldt *et al.*[32] and van den Bekerom *et al.*[38] reported a significantly ($p < 0.001$) higher rate of intraoperative blood loss for THA surgery than for HA. Keating *et al.*[31] reported blood transfusions for a significantly ($p = 0.02$) higher number of patients receiving THA than for those receiving HA, although Blomfeldt *et al.*[32] reported no such statistically significant difference ($p = 0.322$) between groups in terms of the mean units of blood transfused.

Baker *et al.*,[19] Keating *et al.*[31] and Blomfeldt *et al.*[32] reported numbers of both peri- and postoperative adverse events or complications in each trial arm (*Table 5*). The most frequently reported adverse events were pneumonia, pulmonary embolism, DVT, wound infection and urinary tract infection. Rates of DVT were higher in the THA arms and rates of pulmonary embolism were higher in the HA arms; rates of pneumonia, infection and urinary tract infection were similar across arms. None of the studies reported any statistically significant differences between groups. The only significant difference between groups reported for postoperative complications was for the number of patients with radiographic evidence of acetabular erosion

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Blomfeldt 2007[32]	4	60	3	60	5.6	1.33 (0.31 to 5.70)
Keating 2006[31]	4	69	6	69	7.9	0.67 (0.20 to 2.26)
Mouzopoulos 2008[37]	6	39	6	38	10.9	0.97 (0.34 to 2.76)
Skinner 1989[29]	20	89	25	91	45.4	0.82 (0.49 to 1.36)
van den Bekerom 2010[38]	16	115	18	137	30.1	1.06 (0.57 to 1.98)
Total (95% CI)		**372**		**395**	**100.0**	**0.91 (0.65 to 1.29)**
Total events	50		58			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.93$, df = 4 ($p = 0.92$); $I^2 = 0\%$
Test for overall effect: $z = 0.53$ ($p = 0.60$)

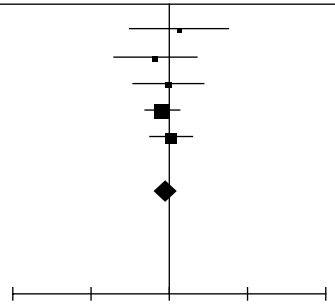

FIGURE 8 Risk of mortality up to 1 year.

Study or subgroup	THA Events	THA Total	HA Events	HA Total	Weight (%)	RR M–H, random, 95% CI
Baker 2006[19]	3	40	7	41	3.5	0.44 (0.12 to 1.58)
Blomfeldt 2007[32]	4	60	3	60	2.8	1.33 (0.31 to 5.70)
Keating 2006[31]	6	69	9	69	5.7	0.67 (0.25 to 1.77)
Macaulay 2008[35]	5	17	9	23	6.6	0.75 (0.31 to 1.84)
Mouzopoulos 2008[37]	15	39	13	38	12.5	1.12 (0.62 to 2.03)
Ravikumar 2000[30]	72	89	78	91	38.1	0.94 (0.83 to 1.08)
van den Bekerom 2010[38]	71	115	61	137	30.9	1.39 (1.10 to 1.76)
Total (95% CI)		**429**		**459**	**100.0**	**1.03 (0.80 to 1.32)**
Total events	176		180			

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 11.46$, df = 6 ($p = 0.08$); $I^2 = 48\%$
Test for overall effect: $z = 0.24$ ($p = 0.81$)

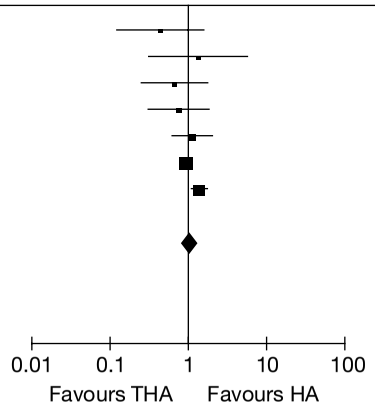

FIGURE 9 Risk of mortality up to 13 years.

TABLE 5 Adverse effects, complications and safety outcomes

Study	Mortality (THA vs HA)	Peri-operative outcomes (THA vs HA) Surgery duration (minutes)	Peri-operative complications (THA vs HA), e.g. hypotension, wound infection, pneumonia, DVT	Intraoperative blood loss (ml)	Blood transfusion (in units), THA vs HA	Postoperative complications, e.g. loosening, erosion
Dorr *et al.*[28]	'no difference in mortality between groups...' p. 23 (Overall $n=7$, but event data for each arm NR)	NR	Overall numbers only: PE ($n=3$); DVT ($n=2$); acute congestive heart failure ($n=1$); acute respiratory failure ($n=1$); pneumonia ($n=1$); UTI ($n=3$); wound haematoma ($n=1$); Gram-negative sepsis from cholelithiasis ($n=1$)	NR	NR	No infections; no differences between groups
Skinner *et al.*[29] Ravikumar and Marsh[30]	1 year[a]: 20/89 (22%) vs 25/91 (27%) 13 years[a]: 72/89 (81%) vs 78/91 (86%)	NR	Overall numbers only: PE ($n=2$); myocardial infarction ($n=3$); peroneal nerve palsy ($n=1$); iatrogenic femoral fracture ($n=1$)[31]	NR	NR	Acetabular erosion and loosening affected 0% (THA) vs 21% (HA) Overall superficial infection rate: 1.43% at 1 year; 3.3% (THA) vs 7.4% (HA) at 13 years
Baker *et al.*[19]	Approximately 3 years: 3/40 (8%) vs 7/41[b] (17%) ($p=0.194$) None related to the procedure	Mean (range): 93 (60–135) vs 78 (45–120), $p<0.001$	Up to 30 days post operation (no difference was significant): THA = 40 vs HA = 41: PE (0 vs 3); DVT (4 vs 0); pneumonia (3 vs 2); wound infection (3 vs 1); UTI (1 vs 0); atrial fibrillation (0 vs 1); haematemesis (0 vs 1); hyponatraemia (1 vs 0)	NR	NR	Only significant reported difference between groups was for radiographic evidence of acetabular erosion at a mean of 40 (range 12–66) months: 0/32 (0%) (THA) vs 21/32 (66%) (HA)
Keating *et al.*[31]	1 year: 4/69 (6%) vs 6/69 (9%) 2 years: 6/69 (9%) vs 9/69 (13%): OR 1.62 (95% CI 0.58 to 4.56) $p=0.36$	Mean (SD): 82.4 (25) vs 64.3 (15)	THA = 69 vs HA = 69: PE (1 vs 4); DVT (4 vs 0); pneumonia (3 vs 2); wound infection (3 vs 3); myocardial infarction (2 vs 3); septicaemia (1 vs 1)	NR	Numbers who received a transfusion: 23/69 (33%) vs 11/69 (16%), OR 0.38 (95% CI 0.17 to 0.86), $p=0.02$	No differences reported between groups
Blomfeldt *et al.*[32]	1 year: 4/60 (7%) vs 3/60 (5%), $p=0.697$	Mean (range): 102 (70–151) vs 78 43–131), $p<0.001$	THA = 60 vs HA = 60: DVT (0 vs 1); pneumonia (1 vs 0); wound infection (3 vs 2); myocardial infarction (1 vs 1); atrial fibrillation (0 vs 1); congestive heart failure (1 vs 0); decubitus ulcer (1 vs 0)	Mean: 460 (100–1100) vs 320 (50–850), $p<0.001$	Mean: 270 (0–1200) ml vs 200 (0–1200) ml, $p=0.322$	No differences between groups regarding hip or general complications; no signs of erosion or loosening in either group at 12 months

continued

TABLE 5 Adverse effects, complications and safety outcomes *(continued)*

Study	Mortality (THA vs HA)	Peri-operative outcomes (THA vs HA) Surgery duration (minutes)	Peri-operative complications (THA vs HA), e.g. hypotension, wound infection, pneumonia, DVT	Intraoperative blood loss (ml)	Blood transfusion (in units), THA vs HA	Postoperative complications, e.g. loosening, erosion
Macaulay *et al.*[35]	2 years: 5/17 (29%) vs 9/23 (39%), $p=0.53$[34] (mean 34 months; range 29–42 months)[c] 4/17 (24%) vs 7/23 (30%), $p=0.20$[35] (mean 19 months; range 3–33 months)	NR	THA = 17 vs HA = 23: anaemia (4 vs 3); pneumonia (0 vs 3); PE (0 vs 1); UTI (0 vs 3); wound infection (0 vs 1)	NR	NR	NR
Mouzopoulos *et al.*[37]	1 year: 6/39 (15%) vs 6/83 (7%) 4 years: 15/39 (38%) vs 13/38 (34%)	NR	NR	NR	NR	NR
van den Bekerom *et al.*[38]	1 year: 16/115 (14%) vs 18/137 (13%) ($p=0.86$) 5 years: 71/115 (62%) vs 61/137 (45%) ($p=0.09$)	< 60: 10% vs 35% 60–90: 57% vs 53% > 90: 20% vs 12% Unknown: 9% vs 16%	No differences reported between groups ($p=0.93$) in terms of general complications: cardiovascular, urological, neurological, respiratory, gastrointestinal, pressure ulcer, allergic reaction or kidney failure No differences reported between groups ($p=0.36$) in terms of local, in-hospital complications, including haematomas, infections, dislocations, wound dehiscence and superior gluteal palsy	< 500: 61% vs 81% > 500: 22% vs 6% Unknown: 17% vs 14% $p<0.001$ (X^2 test)	NR	No differences reported between groups (THA vs HA): loosening of femoral component (1% vs 4%); protrusio acetabuli (1% vs 3%); fissure at the acetabulum (1% vs 2%); heterotopic ossification (15% vs 10%)

NR, not reported; OR, odds ratio; PE, pulmonary embolism; UTI, urinary tract infection.

a Event data calculated from percentages and sample sizes reported.

b Baker *et al.*[19] reports 8/41 for HA, but we have used the 7/41 data for analysis as this figure was reported in the full paper; the eighth individual appears to have withdrawn.

c These data with the longer follow-up are used in the analysis.

at a mean follow-up of 40 months:[19] higher rates were reported for HA than for THA (66% vs 0%). Macaulay *et al.*[35] also reported peri-operative complications and found rates of pneumonia, pulmonary embolism, urinary tract infection and infection to be higher in the HA arm; it was not reported whether or not these differences were statistically significant. Ravikumar and Marsh[30] also reported a difference in the proportion of patients with evidence of acetabular erosion or loosening at a follow-up of 13 years: higher rates were reported for HA than for THA (21% vs 0%).

Subgroup analyses

A series of analyses were performed comparing treatment effects for dislocations, revisions, additional surgery and mortality for independent subgroups, defined by studies of different quality (*Table 6*), the different approach taken by surgeons (anterolateral or posterolateral, *Table 7*), whether or not cemented or uncemented prostheses were used (*Table 8*) and whether or not bipolar or unipolar hemiarthroplasty prostheses were used (*Table 9*). Studies were categorised as being of higher or lower quality based principally on reported methods of randomisation and allocation concealment and the explicit application of intention-to-treat analysis (see *Quality assessment* and *Table 2*). On this basis, Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*[32] and Macaulay *et al.*[35] were categorised as higher quality, and Dorr *et al.*,[28] Skinner *et al.*,[29] Ravikumar and Marsh,[30] Mouzopoulos *et al.*[37] and van den Bekerom *et al.*[38] were categorised as lower-quality studies. Meta-analysis of the lower-quality studies alone found a statistically significant reduced risk of revision for THA compared with HA ($p = 0.0004$); a similar but statistically non-significant relative risk was found in the analysis of the higher-quality studies. Neither lower- nor

TABLE 6 Subgroup analysis (higher-quality studies versus lower-quality studies for all the follow-up periods)

Included studies	Number of studies	Variable	THA vs HA, *n*	RR (95% CI)	I^2 (%)	RRR (95% CI)
Dislocations						
Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*[35]	4	Higher quality	7/182 vs 2/188	2.52 (0.65 to 9.82), $p = 0.18$	0	0.77 (0.12 to 5.08), $p = 0.78$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] van den Bekerom *et al.*[38]	3	Lower quality	33/243 vs 14/278	3.28 (0.88 to 12.16), $p = 0.08$	58	
Revisions						
Baker *et al.*,[19] Blomfeldt *et al.*,[32] Macaulay *et al.*[35]	3	Higher quality	2/113 vs 6/119	0.66 (0.03 to 13.98), $p = 0.79$	63	2.20 (0.09 to 59.12), $p = 0.62$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	4	Lower quality	10/232 vs 36/316	0.30 (0.15 to 0.58), $p = 0.0004$	0	
Any surgery						
Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*[35]	4	Higher quality	13/186 vs 11/193	1.12 (0.52 to 2.41), $p = 0.78$	0	1.08 (0.32 to 3.62), $p = 0.90$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	4	Lower quality	37/282 vs 43/316	1.04 (0.36 to 2.36), $p = 0.92$	63	
Mortality						
Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] Macaulay *et al.*[35]	4	Higher quality	18/186 vs 28/193	0.71 (0.41 to 1.23), $p = 0.22$	0	0.63 (0.33 to 1.20), $p = 0.16$
Ravikumar and Marsh,[30] Mouzopoulos *et al.*,[37] van den Bekerom *et al.*[38]	3	Lower quality	158/243 vs 152/266	1.13 (0.80 to 1.59), $p = 0.49$	80	

RRR, ratio of relative risks.

TABLE 7 Subgroup analysis (direct anterolateral approach versus posterolateral approach)

Included studies	Number of studies	Variable	THA vs HA, *n*	RR (95% CI)	I^2 (%)	RRR (95% CI)
Dislocations (all follow-up periods)						
Baker *et al.*,[19] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	3	Direct lateral	6/189 vs 0/228	8.42 (1.05 to 67.38), $p=0.16$	0	3.61 (0.33 to 39.97), $p=0.29$
Dorr *et al.*,[28] Skinner *et al.*,[29] van den Bekerom *et al.*[38]	3	Posterior	23/150 vs 12/156	2.33 (0.70 to 7.76), $p=0.17$	48	
Any surgery (all follow-up periods)						
Baker *et al.*,[19] Blomfeldt *et al.*[32]	2	Direct lateral	6/100 vs 6/101	1.14 (0.20 to 6.47), $p=0.88$	33	1.06 (0.14 to 8.11), $p=0.96$
Dorr *et al.*,[28] Ravikumar and Marsh[30]	2	Posterior	26/128 vs 32/141	1.08 (0.37 to 3.12), $p=0.89$	71	
Mortality at 1 year						
Baker *et al.*,[19] Blomfeldt *et al.*[32]	2	Direct lateral	6/100 vs 11/101	0.55 (0.21 to 1.45), $p=0.23$	0	0.67 (0.22 to 2.00), $p=0.47$
Skinner *et al.*[29]	1	Posterior	20/89 vs 25/91	0.82 (0.49 to 1.36), $p=0.44$	NA	

RRR, ratio of relative risks.

higher-quality study subgroups found a statistically significant risk of dislocation, any surgery or mortality. Meta-analysis of the lower-quality studies did find a statistically non-significant increased risk of mortality for THA compared with HA, and analysis of the higher-quality studies found a non-significant reduced risk of mortality for THA. However, despite these differences, there was no statistically significant difference between these study quality subgroups for any of the outcomes assessed (see *Table 6*).

There was no difference in the direction of effect, or any statistically significant difference, between the groups of studies reporting the use of either a direct lateral or a posterior surgical approach for any of the outcomes assessed (see *Table 7*), or for those subgroups of studies using cemented rather than uncemented or a mix of uncemented and cemented prostheses (see *Table 8*). When compared with bipolar HA, there was a statistically significant increased risk of dislocation for THA ($p=0.04$); this difference was not significant for THA compared with unipolar HA ($p=0.18$) (see *Table 9*). However, in a test of the ratio of RRs (RRR), this difference was found not to be statistically significant. When compared with unipolar HA, there was a statistically significant reduced risk of revision for THA ($p=0.0008$); this difference was not significant for THA compared with bipolar HA ($p=0.17$). However, again, in a test of the RRR, this difference was found not to be statistically significant. Meta-analysis of the bipolar HA studies found a statistically non-significant increased risk of mortality for THA compared with HA, and analysis of the unipolar studies found a non-significant reduced risk of mortality for THA. Again, despite these differences, there was no statistically significant difference in mortality between subgroups comparing individuals receiving either a unipolar or a bipolar hemiarthroplasty (see *Table 9*).

TABLE 8 Subgroup analysis (cemented THA and HA versus cemented and uncemented THA and HA) for all the follow-ups

Included studies	Number of studies	Variable	THA vs HA, *n*	RR (95% CI)	I^2 (%)	RRR (95% CI)
Dislocations						
Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	4	Cemented THA vs cemented HA	14/280 vs 2/302	4.39 (0.82 to 23.63), $p=0.08$	31	2.34 (0.39 to 13.91), $p=0.35$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Macaulay *et al.*[35]	3	Cemented or mixed THA vs uncemented or mixed HA	26/145 vs 14/164	1.88 (1.03 to 3.43), $p=0.04$	0	
Revisions						
Dorr *et al.*,[28] Baker *et al.*,[19] Blomfeldt *et al.*,[32], van den Bekerom *et al.*[38]	4	Cemented THA vs cemented HA	4/250 vs 13/270	0.34 (0.11 to 1.05), $p=0.13$	0	0.83 (0.16 to 4.36), $p=0.86$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Macaulay *et al.*[35]	3	Cemented or mixed THA vs uncemented or mixed HA	8/145 vs 23/147	0.41 (0.12 to 1.37), $p=0.15$	23	
Any surgery						
Dorr *et al.*,[28] Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	5	Cemented THA vs cemented HA	21/319 vs 19/339	1.15 (0.54 to 2.38), $p=0.71$	22	1.06 (0.30 to 3.03), $p=0.92$
Dorr *et al.*,[28] Ravikumar and Marsh,[30] Macaulay *et al.*[35]	3	Cemented or mixed THA vs uncemented or mixed HA	27/145 vs 28/127	1.08 (0.38 to 3.06), $p=0.89$	30	
Mortality						
Baker *et al.*,[19] Keating *et al.*,[31] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	4	Cemented THA vs cemented HA	83/284 vs 81/307	0.91 (0.49 to 1.66), $p=0.75$	48	0.97 (0.52 to 1.81), $p=0.92$
Ravikumar and Marsh,[30] Macaulay *et al.*[35]	2	Cemented or mixed THA vs uncemented or mixed HA	77/106 vs 87/114	0.94 (0.82 to 1.07), $p=0.34$	0	

RRR, ratio of relative risks.

Despite the absence of any statistically significant findings in these subgroup analyses, it cannot be excluded that this lack of difference may be owing to small samples in one or more of the groups.

TABLE 9 Subgroup analysis (THA versus unipolar or bipolar HA) for all the follow-up periods

Included studies	Number of studies	Variable	THA vs HA, *n*	RR (95% CI)	I^2 (%)	RRR (95% CI)
Dislocations						
Dorr *et al.*,[28] [a]Keating *et al.*,[31] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	4	Bipolar	18/283 vs 4/316	3.87 (1.09 to 13.80), $p=0.04$	25	2.28 (0.51 to 10.09), $p=0.28$
Ravikumar and Marsh,[30] Baker *et al.*[19]	2	Unipolar	21/129 vs 12/132	1.70 (0.78 to 3.70), $p=0.18$	4	
Revisions						
Dorr *et al.*,[28] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	3	Bipolar	3/214 vs 9/247	0.41 (0.11 to 1.48), $p=0.17$	0	1.58 (0.35 to 7.18), $p=0.56$
Ravikumar and Marsh,[30] Baker *et al.*[19]	2	Unipolar	7/129 vs 28/132	0.26 (0.12 to 0.57), $p=0.0008$	0	
Mortality						
[a]Keating *et al.*,[31] Blomfeldt *et al.*,[32] van den Bekerom *et al.*[38]	3	Bipolar	81/244 vs 73/266	1.30 (0.97 to 1.74), $p=0.08$	6	1.60 (0.77 to 3.35), $p=0.21$
Ravikumar and Marsh,[30] Baker *et al.*[19]	2	Unipolar	75/129 vs 85/132	0.81 (0.41 to 1.58), $p=0.53$	40	

a Keating *et al.*[31] included as 67/69 are known to be bipolar hemiarthroplasty.

Chapter 4

Assessment of cost-effectiveness

Methods for reviewing cost-effectiveness

A review of the evidence for cost-effectiveness has also been undertaken. The searches performed were as described in *Chapter 3*, *Identification of studies*, but slightly different study selection criteria were applied to the results. Studies with either the outcomes of resource utilisation or cost–utility (as listed in *Chapter 3*, *Secondary outcomes*) or economic evaluations relating to the population and interventions specified in *Chapter 3*, *Inclusion criteria*, were included.

Results

Quantity of research available

The search of electronic databases identified 532 unique citations. Seven full papers were retrieved to determine whether or not they were relevant to this review. After screening, four studies satisfied the inclusion criteria.[31,44–46] Details of the screening and inclusion process are provided in the PRISMA flow chart (*Figure 10*). Three studies used mathematical models to perform an economic evaluation,[44–46] and one paper[31] reported the costs and utilities collected alongside an RCT.

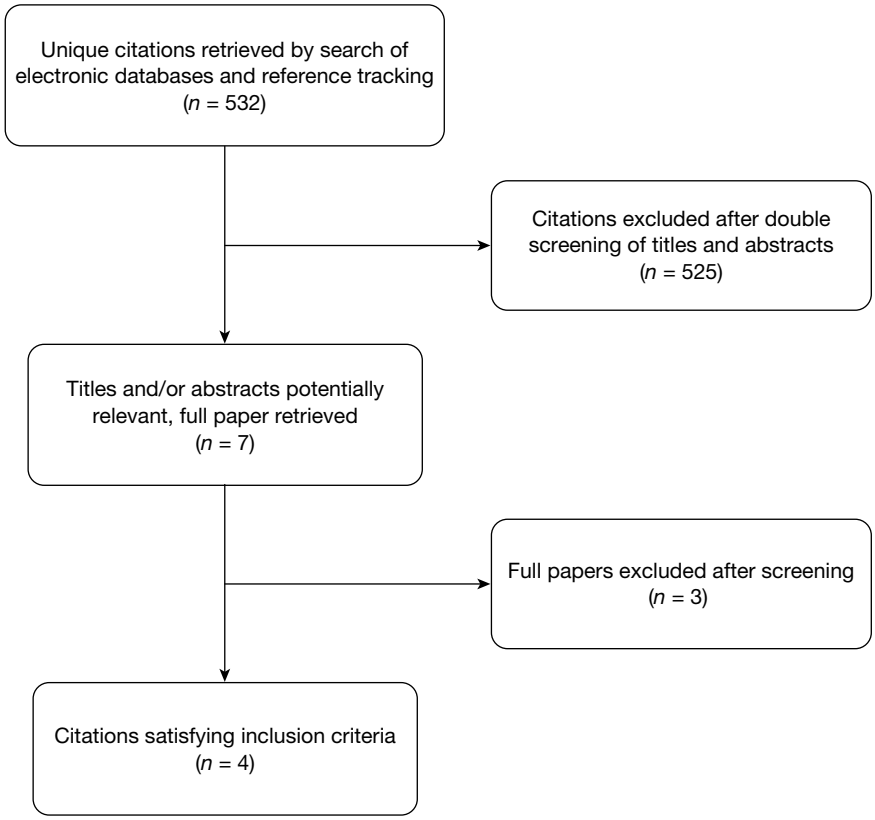

FIGURE 10 PRISMA flow diagram – cost-effectiveness.

A review of the cost-effectiveness literature

Four papers were identified as having an economic element, although only one took the form of a cost–utility analysis. This paper[46] evaluated a patient population with a displaced femoral neck fracture who were elderly and active and treated in an American setting. All costs associated with the surgical procedure and future revisions were included in a Markov model. The conclusion from the model was that THA was the more cost-effective treatment in the patient population with an expected 1.53 quality-adjusted life-years (QALYs) being provided at a cost of US$3000. The cost per QALY ratio of US$1960 would be viewed as extremely cost-effective using standard UK cost-effectiveness thresholds.[47] It was seen that the key driver of this result was the increased utility associated with patients who had undergone THA compared with those that had HA. These data were taken from Keating *et al.*,[31] with the difference in utility shown to be significant at 24 months ($p = 0.008$).

The study by Aleem *et al.*[45] did not include the costs associated with either surgical procedure and focused on the procedure that produced the greatest patient benefit, which implicitly assumes that costs are equal for THA and HA. The derivation of the utilities used within the model was far from ideal as these were derived from asking surgeons and hypothetical patients to rate model outcomes in terms of 0 (death) to 100 (perfect health), rather than using utilities reported directly from patients and with the derived utilities based on public preferences, using a choice-based method, as recommended by the National Institute for Health and Clinical Excellence (NICE).[47] Additionally, median values were used rather than mean values, which is incorrect in economic evaluations. The authors concluded that arthroplasty produces better patient outcomes than internal fixation and that THA had slightly better outcomes than HA.

The analysis of Iorio *et al.*[44] reported outcomes in terms of the cost per ambulatory patient at 2 years for four procedures (reduction with internal fixation, unipolar HA, bipolar HA and THA). As such, differences in the quality and length of life of patients during this period were ignored and the paper in essence reports a cost minimisation analysis. The authors concluded that THA was the most cost-effective of the four procedures.

Keating *et al.*[31] reported the costs and utility consequences from an RCT which compared THA and HA. The authors claim that THA is more cost-effective, but do not provide incremental cost-effectiveness ratios. The data contained within this manuscript could be used to calculate an estimate of the likely cost-effectiveness of THA compared with HA at the duration of follow-up (2 years) and at extrapolated time horizons. The authors of this report undertook this using a simple mathematical model that is detailed later (see *Chapter 4, The economic evaluation undertaken within this report*).

An assessment of Slover *et al.*,[46] using the Drummond *et al.*[48] checklist, is contained in *Appendix 4*. The remaining three papers with economic elements were not assessed as they were considered less appropriate owing to undertaking either a cost minimisation[44] or a benefit maximisation[45] approach or simply reported data from an RCT.[31]

The economic evaluation undertaken within this report

It was deemed that the Iorio *et al.*[44] and Aleem *et al.*[45] studies were too limited to inform the decision problem fully. The paper by Slover *et al.*[46] was a mathematical model of reasonable quality, but was based on a US setting rather than a UK one. The authors of this report decided to perform an economic evaluation based on the Keating *et al.*[31] RCT as this had high internal validity and was directly applicable to the study population. If the results from this analysis concurred with those from Slover *et al.*,[46] and to a lesser extent those of Iorio *et al.*[44] and Aleem *et al.*,[45] then this would support the conclusions that THA was more cost-effective than HA. The proposed modelling methodology was discussed with the clinical expert, who deemed that

this was an acceptable conceptual model. Given the resource constraints, a decision to employ a simplistic model was undertaken.

The Keating *et al.*[31] RCT is directly relevant to the decision problem as it was conducted in Scotland and compared the two interventions of interest. The data reported contained the utility of patients at 4, 12 and 24 months using the EQ-5D questionnaire and the mean costs associated with each intervention over the 2-year period. The EQ-5D is the utility measure preferred by NICE.[47] Costs were presented in five categories: initial inpatient episode; hip-related admissions; non-hip-related admissions; total hip-related costs; and total costs. Data concerning the characteristics of the Keating *et al.*[31] RCT are presented in *Table 1*. Owing to the direct relevance and high internal validity, the authors believed that these data were more appropriate to populate the economic model than the results produced by the meta-analyses undertaken earlier in this report.

An estimate of the cost-effectiveness of THA compared with HA was calculated assuming that the increased costs associated with THA were normally distributed with a mean of £3010 with a standard error (SE) of £2250. This cost differential is given some support by data from the American 2003 National Inpatient Survey reported in Slover *et al.*[46] that stated that the average hospital charges for THA compared with HA were US$4409 higher. The costs from Keating *et al.*[31] were inflated from the 2000–1 price year to a 2007–8 price year,[49] resulting in a mean increase in costs associated with THA compared with HA of £3937; the SE of this increase was assumed to increase to £2943. It was assumed that all costs were incurred in the first year and that costs would remain constant for both arms for the remainder of the model. This approach has support in research undertaken by Haentjens *et al.*,[50] which indicated that the type of surgical procedure (THA or HA) was not associated with differential costs in the year following hospital discharge. Given this methodology, costs were not discounted.

Based on distributions presented in Keating *et al.*,[31] it was assumed that the EQ-5D increase was 0.09 (SE 0.05), 0.05 (SE 0.05) and 0.16 (SE 0.06) at 4, 12 and 24 months, respectively. It was assumed that there was a linear change from zero to the sampled difference in utility at 4 months, a linear change between the sampled differences at 4 and 12 months and a linear change between the sampled differences at 12 and 24 months. The difference at 24 months was assumed to persist until the end of the modelling horizon. Utilities were discounted at 3.5% per annum as recommended by NICE.[47] In the analyses undertaken, time horizons of 2, 3 and 5 years were assessed as it was believed that the vast majority of patients who were alive at 2 years would survival an additional 3 years.

The incremental cost per QALY of THA was calculated as the incremental cost of THA divided by the incremental QALY. A plot of the modelled utilities is provided in *Figure 11* assuming that the midpoint estimates for both THA and HA are correct.

The mortality rates observed within the trial were considered. In the Keating *et al.*[31] RCT there was a greater proportion of deaths in the HA arm (13%) than in the THA arm (9%), although this was not statistically significant ($p = 0.36$). These data were pooled to form a risk of mortality in both arms of 11%, and it was assumed that the incremental QALY gain estimated for THA would be reduced by 11% to account for mortality.

In order to preserve consistency between the sampled utility differences when conducting the probabilistic sensitivity analyses, the same random number was used to select from the cumulative distribution function for each time point. This would ensure that if the value sampled for the difference at 4 months was higher than the median; the differences at 12 and 24 months would also be higher than the median value.

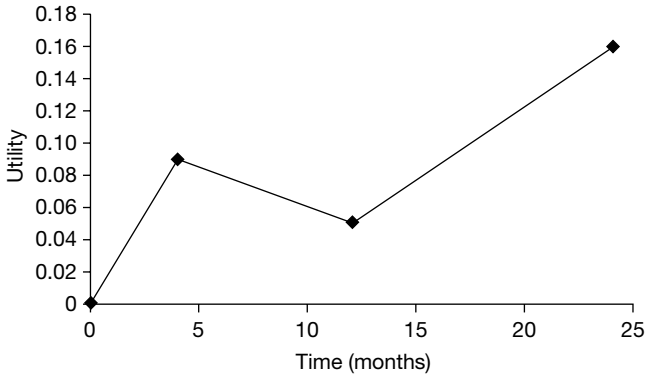

FIGURE 11 The assumed gain in utility associated with THA compared with HA.

For clarity, the parameter values used in the probabilistic sensitivity analyses are given in *Table 10*.

The results from this model are provided in *Table 11* and used 1000 Monte Carlo simulations. It is seen that even when the utility benefits are constrained to the 2-year horizon the cost per QALY is < £30,000. When the time horizon is extrapolated to more realistic values, the cost per QALY decreases, reaching a value < £10,000 with a horizon of only 5 years. This value would be seen as cost-effective under current cost-effectiveness thresholds.[47] It is seen that the results produced within our analyses concur with previous authors[44–46] in that THA is likely to be more cost-effective than HA.

The likelihood of THA being more cost-effective than HA can be displayed on a cost-effectiveness acceptability curve; this is shown in *Figure 12*. All time horizons are shown simultaneously on this figure for brevity; these are different modelling scenarios rather than competing strategies within one decision problem.

TABLE 10 The parameters used within the economic model

Parameter	Distribution used (mean, SE)	Note
Mean Incremental cost of THA compared with HA	Normal (£3937, £2943)	The Keating *et al.*[31] value at 2 years was inflated to 2007–8 prices. No other costs assumed
Mean incremental utility gain of THA compared with HA at:		
4 months	Normal (0.09, 0.05)	Taken from Keating *et al.*[31] The values were sampled using the same random number. Linear interpolation was assumed. For longer time horizons it was assumed that the utility gain at 24 months remained constant
12 months	Normal (0.05, 0.05)	
24 months	Normal (0.16, 0.06)	
Assumed mortality rate over the model horizon	11%	Data taken from Keating *et al.*[31] value at 2 years. No further mortality was considered

TABLE 11 The results from the model when comparing THA with HA

Time horizon (years)	Incremental costs (£)	Incremental QALYs	Incremental cost per QALY (£)
2	3989	0.147	27,023
3	3989	0.285	16,146
5	3989	0.580	7952

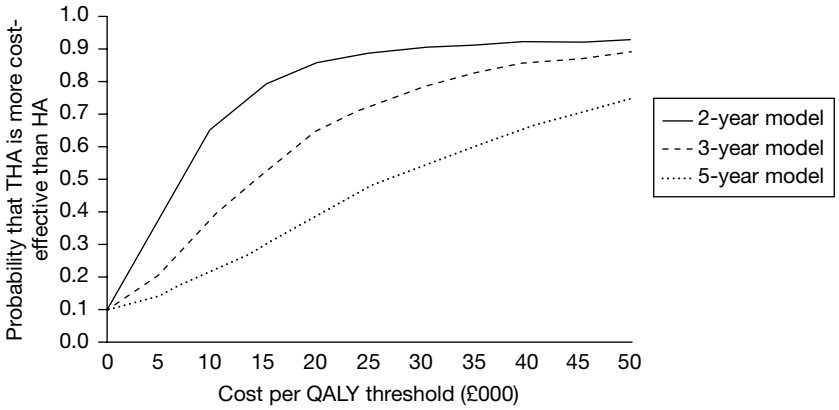

FIGURE 12 Cost-effectiveness acceptability curves depicting the likelihood that THA is more cost-effective than HA.

Limitations of the analyses

It is commented that longer-term consequences, such as the rates of revision and dislocation, have not been considered in this analysis. Data from studies with a follow-up to 13 years indicate that THA is associated with significantly fewer revisions (RR 0.31, 95% CI 0.17 to 0.59; see *Table 3*), whereas HA is associated with significantly fewer dislocations (RR 2.40, 95% CI 1.21 to 4.76; see *Table 3*). The impact of these omissions is likely to be unfavourable to THA as clinical advice indicates that the costs and disutility associated with revisions are far greater than those associated with dislocations. As such, this strengthens the conclusions that THA is more cost-effective than HA.

The effect of ageing on the incremental gain in utility has not been considered. There are no data to indicate whether or not the gain would increase, decrease or remain static as patients age; however, it is expected that the results may be more uncertain than presented.

Exploratory sensitivity analyses

Exploratory sensitivity analyses were undertaken assuming that the increased utility associated with THA compared with HA was equal to the midpoint reported by Blomfeldt *et al.*,[32] which was 0.05 (0.68 for THA and 0.63 for HA). Although this difference was statistically non-significant, the indication from Keating *et al.*[31] is that there is a real difference in utility. In this sensitivity analysis, the cost per QALY was £44,997, £30,511 and £18,932 at 2, 3 and 5 years, respectively. These values were was not as favourable to THA as the analyses based on Keating *et al.*,[31] but they still indicate that THA is likely to be more cost-effective than HA assuming a time horizon of ≥ 5 years using standard UK thresholds.[48]

However, the authors prefer the data from Keating *et al.*[31] as this study has a UK setting, has a slightly larger sample size, has a greater follow-up period and is consistent with the values used for increased costs associated with THA.

The cost data from Keating *et al.*[31] were inflated to 2007–8 prices, and it is uncertain whether or not the costs originally reported would have risen equally for both THA and HA, although it is likely there would have been some correlation regarding costs, such as inpatient costs that would be incurred in each operation.

Additionally, although there is some support for equal costs after the 2-year period,[50] it may be that the different rates of revisions and dislocations have a cost implication.

In order to explore the possibility that these incremental costs may differ from that used in the base case, sensitivity analyses were conducted varying the incremental cost of THA compared with HA (*Table 12*).

These sensitivity analyses indicate that even if the incremental cost of THA compared with HA increased to £8000 then it is likely that THA would still be cost-effective provided that the time horizon was ≥ 5 years, given current cost-effectiveness thresholds.[47]

The expected value of perfect information.

The expected value of perfect information (EVPI)[51] was calculated for the base-case model, assuming that the funders were prepared to pay a cost of £20,000 per QALY gained.[47] Population EVPI provides the maximum that a funder would be prepared to pay to eliminate all uncertainty in the decision problem and thus know with certainty which option was more cost-effective. If the cost of the research required to provide further information is greater than the population EVPI then the research should not be funded.

The estimated EVPI per patient is given in *Table 13* using time horizons of 3 and 5 years. At these time points the adoption decision would be THA. Population EVPI is calculated by the number of patients who are assumed to benefit owing to the greater certainty of which procedure is the more cost-effective.

As previously discussed, the omission of the costs and disutilities associated with revisions and dislocations is likely to strengthen the conclusion that THA is more cost-effective than HA. This would reduce the uncertainty in the decision and therefore it is likely that the EVPI is overestimated.

It is seen that the EVPI decreases as the modelling horizon increases. This is due to the greater certainty that THA is more cost-effective than HA when the time horizon is of larger duration. These values, however, are likely to change when trials currently under way report their findings and the evidence base expands.

TABLE 12 Sensitivity analyses exploring the impact of different assumed incremental costs of THA compared with HA on the cost per QALY gained (£)

	Time horizon		
Assumed incremental cost	2 years	3 years	5 years
£0	Dominates	Dominates	Dominates
£2000	13,550	7008	3451
£3937[a]	27,023	16,146	7952
£6000	40,659	21,023	10,354
£8000	54,198	28,031	13,805

a Base-case value.
'Dominates' indicates that THA provides a QALY gain at no additional cost.

TABLE 13 The EVPI per patient at different modelling time horizons

Time horizon	EVPI per patient
3 years	£1043
5 years	£548

Chapter 5

Assessment of factors relevant to the NHS and other parties

Total hip arthroplasty appears to be more cost-effective than HA although it is likely that THA will be associated with increased costs in the initial 2-year period. The longer-term costs owing to potentially lower revision rates associated with THA have not been estimated. The capacity and experience of surgeons to perform THA have not been explored and these would need to be addressed at local level were THA to become recommended for active, elderly patients in whom THA is not contraindicated. Most orthopaedic surgeons would agree that THA is a more complex procedure than HA. According to clinical advice, the vast majority of HA cases are performed by a wide range of surgeons including more senior trainees. In contrast, THA procedures for fracture tend, in most units, to be performed by only trained, experienced joint replacement surgeons or under their direct supervision. If there was to be a significant increase in the use of THA for fracture of the femoral neck, there would need to be either a change in practice for these surgeons or extra training for the remainder to become confident in this procedure.

Chapter 6

Discussion

Statement of principal findings

Eight RCTs[19,28–30,32,37–39] satisfied the inclusion criteria. The number of participants in all of the trials was 972. Meta-analysis found a near significant increased risk of early dislocation within 1 year for THA compared with HA (RR 3.98, 95% CI 0.98 to 16.12, $p = 0.05$), but also found a statistically significant increased risk of dislocation for patients treated with THA compared with HA (RR 2.40, 1.41 to 2.76, $p = 0.01$) for all follow-up periods up to 13 years.

Meta-analyses of five trials[29,32,35,38,39] found a statistically non-significant 59% reduced risk of revision within 1 year for THA compared with HA ($p = 0.06$), but meta-analysis of seven trials[19,28,30,32,35,38,39] found a statistically significant 69% reduced risk of revision for patients treated with THA compared with HA (RR 0.31, 0.17 to 0.59, $p = 0.0003$) for all follow-up periods up to 13 years.

Meta-analyses of five trials[29,32,35,38,39] and eight[19,28,30–32,35,38,39] trials, respectively, found a statistically non-significant reduced risk of any surgery (dislocation reduction, revisions or other reoperations), both within 1 year and for all follow-up periods, for THA compared with HA ($p = 0.46$ and 0.75, respectively). Meta-analysis also found a statistically non-significant reduced risk of mortality both within 1 year and for all follow-up periods for THA compared with HA ($p = 0.60$ and 0.81, respectively). Subgroup analyses found that neither study quality, the surgical approach taken (lateral or posterior), the use of cement, nor the use of unipolar or bipolar prostheses were statistically significant confounding variables affecting any of these outcomes when comparing data on THA and HA from the RCTs identified for this review.

Eight studies[19,28–30,32,37–39] reported hip ratings, measuring function, mobility and level of pain experienced by participants post operation for between 6 months' and 13 years' follow-up. Five studies[30,32,35,37,38] used the HHS, one the OHS, one the Hip Rating Questionnaire and one a modified version of the D'Aubigne/Postel hip score. In all studies, individuals treated with THA reported better scores (i.e. more function and mobility and less pain) than those treated with HA. In four studies[19,31,32,35] this difference was reported to be statistically significant (Blomfeldt *et al.*[32] at 1 year; Keating *et al.*[31] and Macaulay *et al.*[35] at 2 years; Baker *et al.*[19] at 3 years). Clinical advice suggests that the hip scores used were designed and validated with reference to treatment of degenerative disease of the hip. There are no validated scores for the assessment and follow-up of patients with fractured neck of the femur. None of the scoring systems could be used after the fracture and before treatment as the factors involved in the score are not validated for this diagnosis. The best that can be said is that using these scoring systems prospectively after fracture will give a measure of improvement over time. The OHS would be seen as the most relevant as it is a patient-reported measure concerning hip health over the preceding 4 weeks and can be used in follow-up. The HHS may be considered less robust for this population as this includes clinician-led measures of movement and function.

Four trials[19,31,32,35] reported utility data using the EQ-5D and SF-36 measures: participants treated with THA reported statistically significantly better scores than those treated with HA in two studies;[31,35] the remaining two studies[19,32] reported no significant difference between groups.

The only statistically significant differences between groups for peri- and postoperative adverse events or complications reported by any study were higher intraoperative blood loss for THA by two studies;[32,38] higher numbers of patients receiving blood transfusion for THA than for HA in one study;[31] and higher percentages of patients experiencing acetabular erosion or loosening for HA than for THA in two studies.[19,24]

Five relevant reviews and meta-analyses have been published in the last 2 years.[21,26,52–54] Liao *et al.*[52] identified six of the eight RCTs analysed in the present review (only Mouzopoulous *et al.*[37] and van den Bekerom *et al.*[38] were omitted) and reported similar findings: the risk of dislocation was found to be significantly higher in THA than in HA (RR 3.45, 95% CI 1.29 to 9.19, $p = 0.01$), and the risk of revision was significantly lower (RR 0.28, 95% CI 0.12 to 0.66, $p = 0.003$); blood loss and surgery duration were significantly higher for THA than for HA; but mobility and pain were better for THA than for HA ($p < 0.05$). A review by Hopley *et al.*[26] had similar inclusion criteria, but included non-RCTs also. This review reported no difference between THA and HA in the risk of dislocation, although the 'tendency' favouring THA 'was most pronounced in studies with balanced patient baseline profiles and follow-up intervals of 2 or more years'.[26] THA was also associated with a lower, statistically non-significant risk ($p = 0.16$) of 're-operation' (this outcome was not defined, but appears to consist of revisions only in some cases and all additional surgery in others) across the RCT and non-RCT included studies. There was also no reported difference between treatments in terms of 1-year mortality, but 'Notable benefits [of THA] were observed in randomised trials'.[26] Independent subgroup analyses found no statistically significant effect of any confounding variables (including characteristics of study quality and surgeon experience) on dislocation and, for revision rates, significant differences only between cemented versus mixed prostheses, oriented and ambulatory versus mixed populations, and whether or not intention-to-treat analyses had been specified or unspecified. However, these findings were the result of pooling both RCTs and retrospective cohort studies. Despite the authors' argument that the inclusion of non-experimental studies substantially increased the overall sample size and enhanced the robustness of the resulting estimates, the pooling of data from studies using different study designs is questionable owing to the differing risk of bias inherent in the different designs.[22,55] Previous research in this subject area and population has also demonstrated significant discrepancies between the findings of randomised and non-randomised studies, concluding that the merits of non-randomised studies need to be considered very carefully.[56]

A recently updated Cochrane review by Parker *et al.*[21] with similar inclusion criteria to the present report undertook separate meta-analyses for both uncemented and cemented HA versus THA for the following outcomes of interest to the current review: dislocation rates, minor, major and 'any' 'reoperations', and mortality. The updated review included only full published data from six[19,28,31,32,35,37] of the eight RCTs identified by the present review. The Ravikumar and Marsh[30] paper, which reported follow-up data from the Skinner *et al.*[29] study, was not identified in the original review of 2006 and was also missed in subsequent updates. The updates could not have identified the study by van den Bekerom *et al.*,[38] but they did still fail to identify the Ravikumar and Marsh[30] paper, despite it being referenced in every trial published since 2006 and the authors stating explicitly that the reference lists of all included studies were checked. The uncemented HA analyses contained two trials,[28,29] and the cemented HA analyses contained four trials;[19,28,31,32] Macaulay *et al.*[35] and Mouzopoulous *et al.*[37] were included as mixed populations in the comparisons with THA only. All RR analyses were calculated using a fixed-effects model, which may be a questionable assumption. The review reported that THA had a statistically significantly higher likelihood of dislocation than HA, but found no statistically significant differences in terms of any 'reoperations' or mortality. The Parker *et al.*[21] review also performed analyses of the complications (e.g. infection rates, embolisms and medical complications) reported by the trials and found no significant differences between the two interventions.

A series of analyses by Goh *et al.*[53] applied the same inclusion criteria as the present review, but identified only four of the eight relevant RCTs. Goh *et al.*[53] did not combine these trials in a meta-analysis, but reported the difference in the RRs of dislocation or revision between THA and HA, using a fixed-effects model only, only for the individual trials. The findings of four of the eight relevant RCTs were also summarised in a review by Schmidt *et al.*:[54] Dorr *et al.*,[28] Skinner *et al.*,[29] Keating *et al.*[31] and Blomfeldt *et al.*[32] This was not a systematic review and no formal analysis or meta-analysis was performed.

Three papers were found that reported economic evaluations of THA compared with HA,[44–46] with a further paper reporting cost and utility data from an RCT.[31]

The data in the RCT were used in exploratory modelling work undertaken by the authors. All modelling exercises concluded that THA was likely to be cost-effective compared with HA.

Strengths and limitations of the assessment

Strengths

- This review developed a sensitive search strategy combining only terms for THA and HA, rather than limiting the search further by using terms for population, outcomes or study design. This search identified studies satisfying the inclusion criteria for both clinical effectiveness and cost-effectiveness.
- The search was comprehensive. There were no limitations of language or date (e.g. non-English-language studies have been included), reference tracking was applied to all included studies and an expert was consulted on other potentially relevant studies. Unpublished studies and ongoing trials were also identified. This suggests that the likelihood of publication bias in this review is relatively small.
- The review process: all titles and abstracts of citations retrieved by the search of electronic databases were screened independently for inclusion and exclusion by two reviewers; and all data extraction and quality assessment of included studies were checked thoroughly by two reviewers and any discrepancies identified and resolved.
- The impact of possible confounding variables, such as study quality, surgical approach, the use of cement and unipolar of bipolar prostheses, have been tested for.
- Exploratory modelling has been undertaken that shows that THA is highly likely to be cost-effective compared with HA even when the limitations of the data and methodology are considered. This concurs with previously published economic analyses.

Weaknesses

- Despite efforts to identify all published and unpublished research satisfying the inclusion criteria, publication bias as a result of the non-publication of trials demonstrating no effect cannot be entirely discounted.
- The costs and disutilities associated with revisions and dislocations were not included in the economic evaluation undertaken by the authors. However, this omission strengthens the conclusion that THA is more cost-effective than HA.

Uncertainties

- This review identified eight RCTs with a total of 972 participants in THA and HA treatment arms. The overall sample is therefore not very large.

- There was moderate or high statistical heterogeneity in some meta-analyses, which therefore increases the risk of uncertainty regarding some of the findings reported in this review.
- There was some clinical heterogeneity between studies in terms of surgical approach, type and size of prostheses used, outcome measures applied (i.e. revisions, 'reoperations', second anaesthetic and hip scores) and length of follow-up, which prevented the pooling of results from all eight RCTs for all outcomes. Some analyses of the primary outcomes therefore combined data from only four or five trials.
- The relative experience of surgeons in performing the two procedures is also not reported in seven[19,28,30–32,35,38] of the eight trials. This is a potential confounding variable and may have affected outcomes.
- The majority of independent subgroup analyses to test for the potential confounding effect of certain variables included only three or four trials.
- Revision of THA may present a more complex complication as clinical advice suggests that it is sometimes easier to revise a HA to a THA than it is to revise a THA to a further THA. There may have been greater reluctance to revise THAs, which might explain the smaller incidence of THA revisions within these trials; however, this is not always the case. Each revision must be viewed on its merits and a blanket comment cannot be made.
- The exploratory analyses did not consider the costs of future revisions or dislocations or of any differential rates of mortality, although, other than for dislocations, there was a trend for THA to have better outcomes. The inclusion of such factors is likely to strengthen the conclusion that THA is more effective than HA, but the reduction in the cost per QALY gained is uncertain.

Other relevant factors

None.

Chapter 7

Conclusions

Implications for service provision

Total hip arthroplasty appears to be more cost-effective than HA, although it is likely that this will be associated with increased costs in the initial 2-year period. The longer-term reduction in costs owing to potentially lower revision rates associated with THA have not been estimated. The capacity and experience of surgeons to perform THA have not been explored and these would need to be addressed at local level were THA to become recommended for active, elderly patients who were not contraindicated for THA.

Suggested research priorities

Eight head-to-head RCTs of THA and HA have currently been published. The EVPI per patient has been estimated, although it is expected that there is limited value in conducting a new trial comparing THA and HA as three such trials are ongoing at the time of writing. The biggest of these trials [Comparing Total Hip Arthroplasty and Hemi-Arthroplasty on Revision Surgery and Quality of Life in Adults With Displaced Hip Fractures (the HEALTH study): NCT00556842] has an estimated enrolment of 306 participants. Some of the published trials may also report more data as they become available. Furthermore, the findings of these trials are generally consistent regarding the relative efficacy and trends of the two interventions in terms of dislocation rates, revision rates, hip scores and quality of life. These findings do not appear to be affected by potential confounding variables identified in the literature (i.e. study quality, surgical approach, the use of cement and unipolar of bipolar hemiarthroplasty prostheses), as far as these data were available and permitted relevant subgroup analysis. However, further studies examining the impact of surgeons' experience in performing the two procedures (i.e. THA and HA each being performed by surgeons equally experienced in the respective procedures) may offer some more robust evidence on outcomes.

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Contributions of authors

Christopher Carroll acted as the principal investigator for this assessment, and designed, performed and wrote the review; Christopher Carroll and Philippa Evans designed search strategies and Philippa Evans undertook the searches; Alison Scope contributed to the review; and, Matt Stevenson reviewed the economic literature and constructed, populated and interpreted the results from the mathematical model. Simon Buckley provided expert clinical advice.

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Appendix 1

Literature search strategies

Example search strategy:

Database: Ovid MEDLINE(R) from 1950 to September Week 3 2010

Search strategy:

1. ((large adj femoral adj head adj3 replac$) or (total hip adj3 replac$) or (total hip arthroplasty)).mp.
2. ((hemi adj5 arthroplasty) or hemiarthroplasty or hemi?arthroplasty).mp.
3. 1 and 2

Appendix 2

Data extraction tables

Characteristics of included studies

Reference Manager ID	Study reference Author, date, country	Study design	Inclusion criteria (inclusion criteria for diagnosis)	Exclusion criteria (including number excluded)	Intervention group (THA) population characteristics *n* 1. Age, gender (f/m) 2. Comorbidities 3. Time from fracture to surgery	Comparison group (HA) and population characteristics *n* 1. Age, gender (f/m) 2. Comorbidities 3. Time from fracture to surgery

F, female; M, male.

Study outcomes

Reference Manager ID	Study reference Author, date	Study duration/ follow-up	Primary outcomes (THR vs HA) 1. Dislocation rate 2. Revision rate 3. Non-revision operations	Secondary outcomes (THA vs HA) Mobility, e.g. walking distance	Hip ratings (e.g. OHS)	Mortality	Quality of life Other outcomes (e.g. pain)	Resource utilisation Cost–utility	Complications Descriptions and frequency

Appendix 3

Critical appraisal quality assessment criteria for a surgical randomised controlled trial (based on Parker *et al.*[21])

Yes/No/Unclear

(1) Was there clear concealment of allocation? If allocation clearly concealed (e.g. numbered sealed opaque envelopes drawn consecutively). No or unclear if the method of allocation concealment or randomisation was not stated, unclear or if allocation concealment was clearly not concealed such as those using quasi-randomisation (e.g. even or odd date of birth).

(2) Were the inclusion and exclusion criteria clearly defined?

(3) Were the outcomes of participants who withdrew or excluded after allocation described and included in an intention-to-treat analysis? Yes (including if text states that no withdrawals occurred or data are presented clearly showing 'participant flow' which allows this to be inferred. Otherwise no.

(4) Were the treatment and control groups adequately described at entry and if so were the groups well matched, or an appropriate covariate adjustment made?

(5) Were the surgeons experienced at both operations prior to commencement of the trial?

(6) Were the care programmes other than the trial options identical?

(7) Were all the outcome measures clearly defined in the text with a definition of any ambiguous terms encountered?

(8) Were the outcome assessors blind to assignment status?

(9) Was the timing of outcome measures appropriate? A minimum of 12 months' follow-up for all surviving participants with active review of participants at set time periods.

(10) Was loss to follow-up reported and if so were less than five per cent of surviving participants lost to follow-up?

Appendix 4

Quality assessment of the economic evaluation undertaken by Slover *et al.*[46] through use of the Drummond *et al.*[48] checklist

1. Was a well-defined question posed in answerable form?	
1.1. Did the study examine both costs and effects of the service(s) or program(s)?	Yes
1.2. Did the study involve a comparison of alternatives?	Yes
1.3. Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	The viewpoint although not stated, could be determined as the hospitalisation costs were borne per patient within the USA, with benefits incorporating the longevity and quality of life of the patient. The decision-making context was for a patient aged 65–75 years in whom an arthroplasty (either THA or HA) would be performed
2. Was a comprehensive description of the competing alternatives given (i.e. can you tell who did what to whom, where and how often)?	
2.1. Were there any important alternatives omitted?	No
2.2. Was (should) a *do-nothing* alternative be considered?	No, displaced femoral neck fractures would always be treated
3. Was the effectiveness of the program or services established?	
3.1a. Was this done through an RCT?	No
3.1b. If so, did the trial protocol reflect what would have happened in regular practice?	Not applicable
3.2. Was the effectiveness established through an overview of clinical studies?	No
3.3. Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?	It was reported that data are lacking. In the base case the survival rates for THA and HA were assumed to be equal. Revision rates were assumed to be identical for THA and HA as was the risk of mortality following a revision. If these assumptions are incorrect then the conclusions presented could change
4. Were all the important and relevant costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, life-years gained)?	
4.1. Was the range wide enough for the research question at hand?	Yes, long-term costs and the utility of the patient were considered
4.2. Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers. Other viewpoints may also be relevant depending upon the particular analysis)	Yes, the key outcomes were the costs borne by the hospitals and the longer time utility and survival of the patient
4.3. Were the capital costs, as well as operating costs, included?	Unclear. The costing data were taken from the 2003 National Inpatient Survey.[a] It is not stated whether or not these include capital costs
5. Were costs and consequences measured accurately in appropriate physical units (e.g. hours of nursing time, number of physician visits, lost work-days, life-years gained)?	
5.1. Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	The costing data were taken from the 2003 National Inpatient Survey.[a] It is expected that these would include all relevant costs
5.2. Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	No

6. Were costs and consequences valued credibly?	
6.1. Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy-makers' views and health professionals' judgments)	Partly. The costing data were taken from the 2003 National Inpatient Survey.[a] Longer-term utility data were taken from an RCT. The utility decrement assumed because the procedure was not referenced
6.2. Were market values employed for changes involving resources gained or depleted?	Yes
6.3. Where market values were absent (e.g. volunteer labour), or market values did not reflect actual values (such as clinic space donated at a reduced rate), were adjustments made to approximate market values?	Not applicable
6.4. Was the valuation of consequences appropriate for the question posed (i.e. has the appropriate type or types of analysis – cost-effectiveness, cost–benefit, cost–utility – been selected)?	Yes. A cost–utility approach was deemed reasonable
7. Were costs and consequences adjusted for differential timing?	
7.1. Were costs and consequences that occur in the future 'discounted' to their present values?	Yes. Both future costs and future benefits were discounted at 3% per annum
7.2. Was there any justification given for the discount rate used?	Yes. This was in accordance with current US practice
8. Was an incremental analysis of costs and consequences of alternatives performed?	
8.1. Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?	Yes
9. Was allowance made for uncertainty in the estimates of costs and consequences?	
9.1 If data on costs and consequences were stochastic (randomly determined sequence of observations), were appropriate statistical analyses performed?	Stochastic analyses were not performed. Threshold analyses were performed to indicate when the conclusion in terms of cost-effectiveness would alter
9.2. If a sensitivity analysis was employed, was justification provided for the range of values (or for key study parameters)?	Threshold analyses were performed. No justification was provided for the ranges analysed, but these appeared appropriate. The threshold analyses varied the utility following THA or HA, the costs of THA and HA and the RR of revision between THA and HA
9.3. Were the study results sensitive to changes in the values (within the assumed range for sensitivity analysis, or within the CI around the ratio of costs to consequences)?	Yes, the results were sensitive to the change in values. Although, in the majority of cases THA was estimated to be more cost-effective than HA assuming a cost per QALY gained threshold of US$50,000
10. Did the presentation and discussion of study results include all issues of concern to users?	
10.1. Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	Yes. A cost per QALY gained ratio was presented. However, from the manuscript it was not possible to indicate why the incremental cost of the THA strategy was not equal to the incremental cost of the THA procedures given that all transition probabilities and future costs were assumed equal. Also, the interpretation of the threshold analyses appears incorrect in the figure legend (for example Figure 3[a])
10.2. Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?	No
10.3. Did the study discuss the generalizability of the results to other settings and patient/client groups?	No
10.4. Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?	No
10.5. Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g. distribution of costs and consequences, or relevant ethical issues)?	No

a As cited in Slover *et al.*[46]

Appendix 5

Hemiarthroplasty and total-hip arthroplasty for treating primary intracapsular fracture of the hip protocol

26 August 2010

1. Title of the project

What is the clinical and cost effectiveness of total hip-arthroplasty compared to hemi hip-arthroplasty?

2. Project lead

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3. Plain english summary

Hip fracture is a common problem in the population aged 60 years or more. The annual rate of hip fracture in women in the UK has been reported to be exponentially distributed and to be 20 per 10,000, 38 per 10,000 and 73 per 10,000 at 65, 70 and 75 years of age respectively.[1] Only 5% of fractures occur in men and women under the age of 60 years.[2] Due to increasingly aging populations the absolute number of hip fractures is expected to rise.[3,4,5] Half of all hip fractures are displaced intracapsular fractures, i.e. unstable fractures in which the blood supply to the femoral head may be impaired, affecting the rate of fracture healing.[2,6,7]

The treatment for displaced intracapsular fractures is currently determined by the mobility and functional demands of the patient. Individuals with a displaced intracapsular fracture and low pre-fracture mobility, cognitive impairment or low functional demands are generally treated with hemiarthroplasty (HA);[2,8,9] as many as 37% of individuals with hip fracture may be cognitively impaired.[10] By contrast, there is no consensus regarding the optimal treatment for individuals who are cognitively intact and with high pre-facture mobility or function: the options are HA or total hip arthroplasty (THA).[8,9,11]

The principal outcomes associated with hip arthroplasty are dislocation, revision rates and resultant quality of life. THA is particularly associated with higher rates of dislocation, which may be due to the greater degree of mobility permitted.[4] It has also been reported that rates of dislocation are more likely if the surgical approach is posterolateral rather than anterolateral and

if a smaller femoral head is used.[12,13,14] The incidence or recurrence of dislocation has been found to be significantly related to a reduction in an individual's quality of life.[15] HA is particularly associated with pain, infection, loosening of the joint and acetabular erosion.[6,16] Post-operative complications such as loosening and acetabular erosion, in particular, can necessitate revision surgery. Revision rates may therefore be higher for HA than for THA. In the only head-to-head trial of THA versus HA the quality of life was shown to be significantly higher at 24 months in patients following a THA.[17]

4. Decision problem

4.1 Purpose of the decision to be made

The assessment will address the question: What is the clinical and cost effectiveness of total hip-arthroplasty compared to hemi hip-arthroplasty?

4.2 Clear definition of the intervention

Total hip arthroplasty (THA). THA involves replacing both the femoral head and acetabular articular surface. These prostheses may or may not be cemented into place.[2]

4.3 Place of the intervention in the treatment pathway(s)

This review will focus on the use of interventions in the treatment of intracapsular hip fractures.

4.4 Relevant comparators

Hemiarthroplasty (HA). HA involves replacing the femoral head and may be unipolar (generally used for patients with lower functional demands[2]), or, more recently, the more mobile bipolar, which aims to reduce acetabular erosion.[6] These prostheses may or may not be cemented into place.[2]

4.5 Population and relevant sub-groups

Patients eligible for hip replacement due to intracapsular fracture, who are able to give consent and are independently mobile prior to fracture.

4.6 Key factors to be addressed

1. Evaluate the clinical and cost-effectiveness of THA versus HA.
2. Evaluate the safety of THA versus HA.
3. Identify any key areas for further research.

5. Report methods for synthesis of evidence of clinical effectiveness

A review of the evidence for clinical effectiveness will be undertaken systematically following the general principles recommended in the PRISMA statement.[18] English and non-English language studies will be included and there will be no limit by date.

5.1 Population

Adult patients eligible for hip replacement due to intracapsular fracture, who are able to give consent and are independently mobile prior to fracture.

5.2 Intervention

THA.

5.3 Comparator

HA.

5.4 Settings

Secondary care.

5.5 Outcomes

5.5.1 Primary outcome

1. Dislocation rate.
2. Revision rate. Where possible, the data will be analysed separately, for early revision, i.e. within 1 year of surgery, or revision for the duration of follow-up as a whole.
3. Non-revision reoperations (re-operations that do not involve revision or removal of implant). Where these data are reported separately from revisions.

5.5.2 Secondary outcomes

1. Hip ratings (e.g. Oxford Hip Score).
2. Mobility.
3. Mortality.
4. Surgery duration (in minutes).
5. Hypotension during surgery.
6. Operative blood loss (in millilitres).
7. Post-operative blood transfusion (in units).
8. Post-operative complications, e.g. loosening, erosion, wound infection, pneumonia, DVT.
9. Length of hospital stay.
10. Health-related Quality of life.
11. Resource utilisation.
12. Cost utility.

5.6 Follow-up

There is to be no minimum duration of follow-up.

5.7 Study design

Randomised Controlled Trials (RCTs) only, as a scoping report for this project identified seven such trials (09/108/01).

5.8 Search strategy

The search strategy will comprise the following main elements:

- Searching of electronic databases
- Contact with experts in the field
- Scrutiny of bibliographies of retrieved papers.

5.8.1 Electronic searches

A comprehensive search will be undertaken to identify systematically both clinical and cost-effectiveness literature comparing THA and HA in patients with fractures of the femoral neck. The search will involve the combining of terms for THA with terms for HA. An example MEDLINE search strategy is reported in *Appendix 10.1*. The aim of the strategy is to identify all studies that report on trials or studies comparing THA with HA. All searches will be done by an Information Specialist (PE). These searches will update the searches performed for the scoping report (09/108/01).

5.8.2 Databases

The following electronic databases will be searched from inception for published and unpublished research evidence:

- MEDLINE (Ovid) 1950–
- EMBASE 1980–
- CINAHL (EBSCO) 1982–
- The Cochrane Library including the Cochrane Systematic Reviews Database, Cochrane Controlled Trials Register, DARE, HTA and NHS EED databases 1991–
- Biological Abstracts (via ISI Web of Science) 1969–
- Science Citation Index (via ISI Web of Science) 1900–
- Social Science Citation Index (via ISI Web of Science) 1956–
- Conference Proceedings Citation Index- Science (CPCI-S)– (via ISI Web of Science) 1990–
- UK Clinical Trials Research Network (UKCRN) and the National Research Register archive (NRR)
- Current Controlled Trials
- Clinical Trials.gov up

All citations will be imported into Reference Manager software and duplicates deleted.

5.9 Inclusion criteria

The inclusion criteria are as reported in 5.1-5.7 above. Titles and abstracts of all unique citations will be screened independently by two reviewers using the inclusion criteria outlined below. Disagreement will be resolved by consensus, or with reference to a third reviewer when necessary. The full papers of all potentially relevant citations will be retrieved so that an in-depth assessment concerning inclusion could be made. Reference-tracking of all included studies and relevant reviews will also be performed to identify additional, relevant studies not retrieved by the search of electronic databases.

5.10 Exclusion criteria

Reviews of primary studies, and non-RCT evidence which otherwise satisfies the criteria, will not be included in the analysis, but will be retained for discussion and identification of additional trials.

5.11 Data extraction strategy

Data will be extracted independently from all studies by two reviewers using a standardised data extraction form (see *Appendix 10.2*). Discrepancies will be resolved by discussion, and with reference to a third reviewer if necessary. Authors will also be contacted for relevant missing data, as far as time allows.

5.12 Quality assessment strategy

The quality assessment of included RCTs will be undertaken using an appropriate quality assessment criteria. This is no published surgical RCT checklist, so this review will apply surgical quality assessment criteria outlined in a relevant Cochrane review.[21] These are included in *Appendix 10.3*. Critical appraisal will be performed by two reviewers independently. Discrepancies will be resolved by discussion, with involvement of a third reviewer when necessary.

5.13 Methods of analysis/synthesis

Data will be tabulated and relative risks (RRs) using both fixed and random effects models will be calculated where possible (if they were not published).[19] Included studies will be combined in a meta-analysis if clinical advice suggests that the included trials are sufficiently, clinically

homogenous. Two previous reviews comparing THA with HA have clearly applied different criteria when choosing to combine or not combine included trials, but the rationale behind the approaches taken was not reported in either review.[20,21] Clinical advice will therefore dictate whether trials of unipolar and bipolar, or cemented and uncemented HA can be justifiably combined, and whether trials employing different surgical approaches (anterior or posterior) may be meaningfully combined. Statistical heterogeneity between trials will also be tested using the I^2 statistic.[19] If clinical advice dictates that the combining of all studies is not appropriate, then sub-group and sensitivity analyses will be performed based on type of prostheses or surgical approach.

6. Report methods for synthesising evidence of cost-effectiveness

A systematic review of the existing literature studying the cost-effectiveness of THA compared to HA will be undertaken. In addition, a new economic model will be developed to compare a treatment strategy which incorporates THA with a strategy that uses HA (i.e. which is the approach most frequently used in current practice).

6.1 Identifying and systematically reviewing published cost effectiveness studies

The search strategy and sources detailed in *Section 5* will be used to identify studies of cost effectiveness. The approach described is very sensitive as no study design filters are being used and will retrieve any relevant cost-effectiveness studies. Identified economic literature will be critically appraised and assessed using the Drummond checklist.[22] Existing cost effectiveness analyses will also be used to identify sources of evidence to inform structural modelling assumptions and parameter values for the economic model.

6.2 Development of a health economic model

A *de novo* economic evaluation will be constructed, with the primary outcome from the model being an estimate of the incremental cost per additional quality adjusted life year (QALY) gained associated with use of echocardiography for newly diagnosed AF patient. The time horizon of our analysis will be a patient's lifetime in order to reflect the chronic nature of the disease and potential mortality. The perspective will be that of the National Health Services and Personal Social Services. Both costs and QALYs will be discounted at 3.5%.[23]

The model structure will be determined in consultation with clinical experts. It will incorporate the costs of each intervention and that of subsequent events that are dependent on the rates of adverse events associated with intervention. The health impacts of these events will also be simulated, which will allow an analysis of whether THA is more cost effective than HA for selected patient groups. Modelling assumptions will be taken from the literature, supplemented by clinical expert opinion where necessary.

Ideally, health related quality of life estimates will be available from the reviewed literature. In the absence of such evidence, the economic model may use indirect evidence on quality of life from alternative sources. Quality of life data will be reviewed and used to generate the quality adjustment weights required for the model. National sources (e.g. NHS reference costs,[24] national unit costs[25]) as well as the reviewed literature will be used to estimate resource use and costs for use in the economic model.

It is anticipated that there may be limited evidence for some of parameters that will be included in the economic model. Therefore the uncertainty around the parameter estimates

will be modelled to take account of this. The uncertainty in the central value for each required parameter will be represented by a distribution, enabling probabilistic sensitivity analysis to be undertaken on the model results. This will allow an assessment of the uncertainty to be made, and the results will be interpreted accordingly. Through expected value of perfect information analysis[26] and, if resources allow, expected value of partial perfect information analyses[27] we will identify whether further research is valuable, and in which areas further research is likely to be particularly valuable.

7. Expertise in this TAR team

TAR Centre

The ScHARR Technology Assessment Group (ScHARR-TAG) undertakes reviews of the effectiveness and cost effectiveness of healthcare interventions for the NHS R&D Health Technology Assessment Programme on behalf of a range of policy makers in a short timescale, including the National Institute for Health and Clinical Excellence. A list of our publications can be found at: http://www.sheffield.ac.uk/scharr/sections/heds/collaborations/scharr-tag/reports.

Much of this work, together with our reviews for the international Cochrane Collaboration, underpins excellence in healthcare worldwide.

Team members' contributions

Christopher Carroll, Research Fellow, ScHARR: has extensive experience in systematic reviews of health technologies. CC will lead the project and undertake the review of effectiveness. He will co-ordinate the review process, protocol development, abstract assessment for eligibility, quality assessment of trials, data extraction, data entry, data analysis and review development of background information and clinical effectiveness.

Matt Stevenson, Reader in Health Technology Assessment, ScHARR: has extensive experience in performing health technology assessments and has been the lead, or co-author on over ten full Health Technology reports. MS is also a NICE committee member and is the technical director of ScHARR-TAG. MS will construct, operate and interpret the results from the mathematical model.

Alison Scope, Research Associate, ScHARR: has experience in systematic reviews of health technologies. AS will assist CC with the abstract assessment for eligibility, quality assessment of trials, data extraction, data entry and data analysis for the clinical effectiveness review.

Philippa Evans, Systematic Reviews Information Officer, ScHARR: has experience of undertaking literature searches for the ScHARR Technology Assessment Group systematic reviews and other external projects. PE will be involved in developing the search strategy and undertake the electronic literature searches.

Gill Rooney, Project Administrator: will assist in the retrieval of papers and in preparing and formatting the report.

Clinical and expert advisors

Simon Buckley, Consultant, Northern General Hospital, Sheffield: Simon is a consultant surgeon in primary and revision hip and knee arthroplasty. He gained the FRCS (Tr & Orth) qualification in 2000, was previously the Cavendish Hip Fellow in Sheffield, and President of the British Orthopaedic Trainees Association (2001-2002). He is the audit lead for the Orthopaedic department at Sheffield Teaching Hospitals.

8. Competing interests of authors

The authors do not have any competing interests.

The clinical advisor does not have any competing interests

9. Timetable/milestones

The project is expected to run from 31 August to 31 December 2010

Milestone	
Draft protocol	31 August 2010
Final protocol	15 September 2010
Start review	16 September 2009
Progress report	16 November, October 2010
Assessment report	31 December 2010

10. Appendices

10.1 Draft Medline search strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) < 1950 to Present >

Search Strategy:

1. ((femoral adj head) or total hip replacement).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (5092)
2. hemiarthroplasty.mp. (1129)
3. (hemi adj5 arthroplasty).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (103)
4. hemi hip arthroplasty.mp. (1)
5. 2 or 3 or 4 (1217)
6. 1 and 5 (90)

10.2 Data extraction forms

TABLE Characteristics of included studies

Ref Man ID	Study ref Author, date, country	Study design	Inclusion criteria (incl. criteria for diagnosis)	Exclusion criteria (incl. number excluded)	Intervention group (THA) population characteristics *N*= 1.Age, gender (f/m) 2.Co-morbidities 3.Time from fracture to surgery	Comparison group (HA) and population characteristics *N*= 1.Age, gender (f/m) 2.Co-morbidities 3.Time from fracture to surgery

TABLE Study outcomes

Ref Man ID	Study ref Author, date	Study duration/ follow-up	Primary outcomes (THA vs HA) 1. Dislocation rate 2. Revision rate	Secondary outcomes (THA vs HA) Mobility, eg. walking distance	Hip ratings (eg. Oxford hip score i.e. OHS)	Mortality	Quality of life Other outcomes (eg. pain)	Resource utilisation Cost utility	Complications Descriptions and frequency

10. 3 Critical appraisal quality assessment criteria for a surgical RCT (from Parker *et al.* 2006[21])

Though the scores of the individual items may be summed, the principal aim is to gain an overall impression of quality, rather than for quantitative purposes.

1. Was there clear concealment of allocation?Score 3 (and code A) if allocation clearly concealed (e.g. numbered sealed opaque envelopes drawn consecutively). Score 2 (and code B) if there was a possible chance of disclosure before allocation. Score 1 (and code B) if themethod of allocation concealment or randomisation was not stated or was unclear. Score 0 (and code C) if allocation concealment was clearly not concealed such as those using quasirandomisation (e.g. even or odd date of birth).
2. Were the inclusion and exclusion criteria clearly defined? Score 1 if text states type of fracture and which patients were included and excluded. Otherwise score 0.
3. Were the outcomes of participants who withdrew or excluded after allocation described and included in an intention-to-treat analysis? Score 1 if yes or text states that nowithdrawals occurred or data are presented clearly showing 'participant flow' which allows this to be inferred. Otherwise score 0.
4. Were the treatment and control groups adequately described at entry and if so were the groups well matched, or an appropriate co-variate adjustment made? Score 1 if at least four admission details given (e.g. age, sex, mobility, function score, mental test score) with either no important difference between groups or an appropriate adjustment made. Otherwise score 0.
5. Were the surgeons experienced at both operations prior to commencement of the trial? Score 1 if text states there was an introductory period or all surgeons were experienced in both operations. Otherwise score 0.
6. Were the care programmes other than the trial options identical? Score 1 if text states they were or this can be inferred. Otherwise score 0.
7. Were all the outcome measures clearly defined in the text with a definition of any ambiguous terms encountered?Score 1 if yes. Otherwise score 0.
8. Were the outcome assessors blind to assignment status? Score 1 if assessors of anatomical restoration, pain and function at follow up were blinded to treatment outcome. Otherwise score 0.
9. Was the timing of outcome measures appropriate?A minimum of 12 months follow up for all surviving participants with active review of participants at set time periods. Score 1 if yes. Otherwise score 0.
10. Was loss to follow up reported and if so were less than five per cent of surviving participants lost to follow up? Score 1 if yes. Otherwise score 0.

References

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