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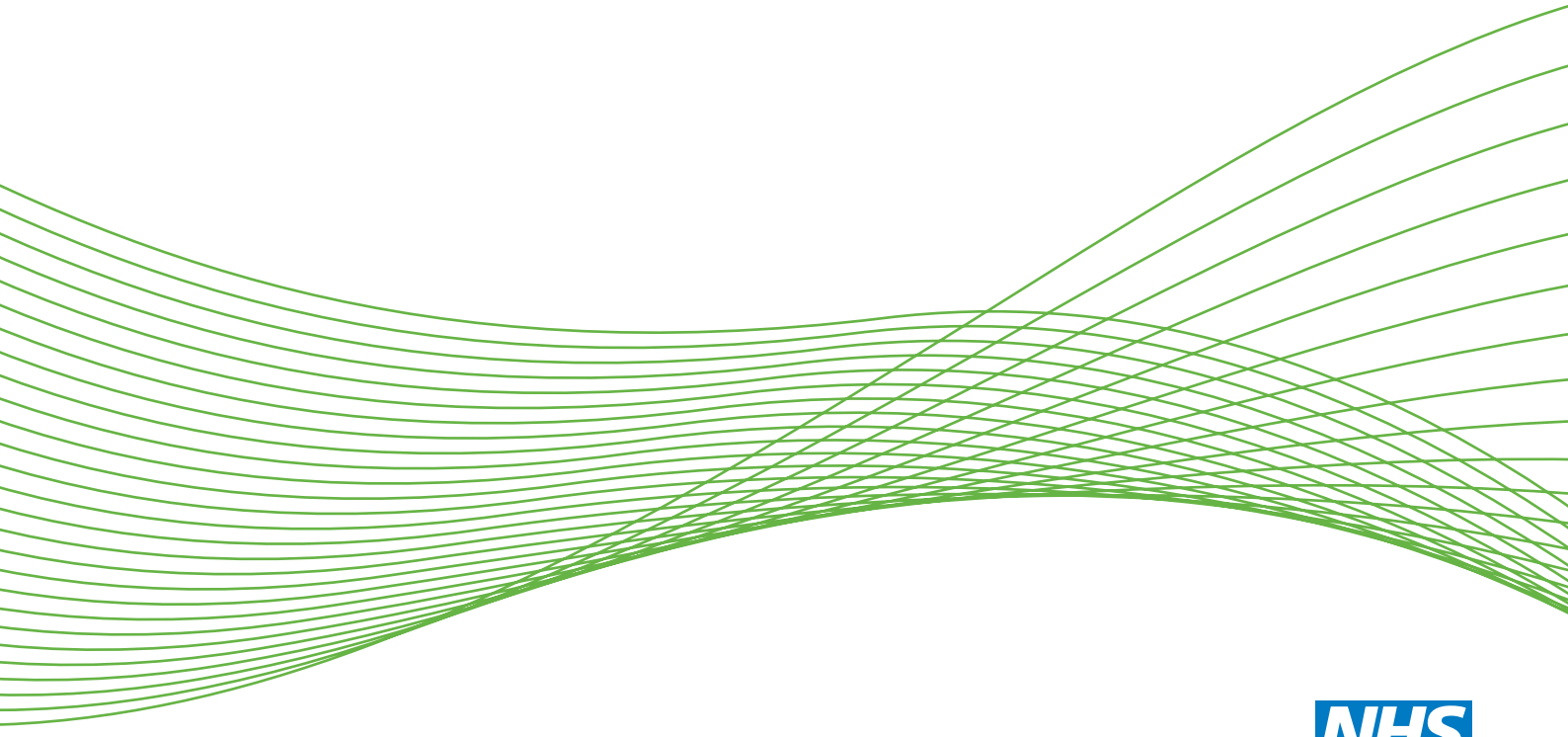

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Abstract

A randomised controlled trial of the clinical effectiveness and cost-effectiveness of different knee prostheses: the Knee Arthroplasty Trial (KAT)

David W Murray,[1]* Graeme S MacLennan,[2] Suzanne Breeman,[2] Helen A Dakin,[3] Linda Johnston,[4] Marion K Campbell,[2] Alastair M Gray,[3] Nick Fiddian,[5] Ray Fitzpatrick,[6] Richard W Morris[7] and Adrian M Grant[2] on behalf of the KAT group†

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Background: In the late 1990s, new developments in knee replacement were identified as a priority for research within the NHS. The newer forms of arthroplasty were more expensive and information was needed on their safety and cost-effectiveness.

Objectives: The Knee Arthroplasty Trial examined the clinical effectiveness and cost-effectiveness of four aspects of knee replacement surgery: patellar resurfacing, mobile bearings, all-polyethylene tibial components and unicompartmental replacement.

Design: This study comprised a partial factorial, pragmatic, multicentre randomised controlled trial with a trial-based cost–utility analysis which was conducted from the perspective of the NHS and the patients treated. Allocation was computer generated in a 1:1 ratio using a central system, stratified by eligible comparisons and surgeon, minimised by participant age, gender and site of disease. Surgeons were not blinded to allocated procedures. Participants were unblinded if they requested to know the prosthesis they received.

Setting: The setting for the trial was UK secondary care.

Participants: Patients were eligible for inclusion if a decision had been made for them to have primary knee replacement surgery. Patients were recruited to comparisons for which the surgeon was in equipoise about which type of operation was most suitable.

Interventions: Patients were randomised to receive a knee replacement with the following: patellar resurfacing or no patellar resurfacing irrespective of the design of the prosthesis used; a mobile bearing between the tibial and femoral components or a bearing fixed to the tibial component; a tibial component made of either only high-density polyethylene ('all polyethylene') or a polyethylene bearing fixed to a metal backing plate with attached stem; or unicompartmental or total knee replacement.

Main outcome measures: The primary outcome was the Oxford Knee Score (OKS). Other outcomes were Short Form 12; EuroQol 5D; intraoperative and postoperative complications; additional surgery; cost; and cost-effectiveness. Patients were followed up for a median of 10 years; the economic evaluation took a 10-year time horizon, discounting costs and quality-adjusted life-years (QALYs) at 3.5% per annum.

Results: A total of 116 surgeons in 34 centres participated and 2352 participants were randomised: 1715 in patellar resurfacing; 539 in mobile bearing; 409 in all-polyethylene tibial component; and 34 in the unicompartmental comparisons. Of those randomised, 345 were randomised to two comparisons. We can be more than 95% confident that patellar resurfacing is cost-effective, despite there being no significant difference in clinical outcomes, because of increased QALYs [0.187; 95% confidence interval (CI) –0.025 to 0.399] and reduced costs (–£104; 95% CI –£630 to £423). We found no definite advantage or disadvantage of mobile bearings in OKS, quality of life, reoperation and revision rates or cost-effectiveness. We found improved functional results for metal-backed tibias: complication, reoperation and revision rates were similar. The metal-backed tibia was cost-effective (particularly in the elderly), costing £35 per QALY gained.

Conclusions: The results provide evidence to support the routine resurfacing of the patella and the use of metal-backed tibial components even in the elderly. Further follow-up is required to assess the stability of these findings over time and to inform the decision between mobile and fixed bearings.

Trial registration: Current Controlled Trials ISRCTN45837371.

Funding: This project was funded by the NIHR Health Technology Assessment programme and the orthopaedic industry. It will be published in full in *Health Technology Assessment*; Vol. 18, No. 19. See the NIHR Journals Library website for further project information.

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List of abbreviations

ASA	American Society of Anesthesiologists
BMI	body mass index
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
CUA	cost–utility analysis
DVT	deep-vein thrombosis
EQ-5D	European Quality of Life-5 Dimensions
GP	general practitioner
HCHS	hospital and community health services (inflation index)
HES	Hospital Episode Statistics
HRG	Healthcare Resource Group
HTA	Health Technology Assessment
ice	imputation using chained equations
ICER	incremental cost-effectiveness ratio
IPW	inverse probability weighting
ISD	Information Services Division
KAT	Knee Arthroplasty Trial
MCID	minimal clinically important difference
MCS	mental component score
NIHR	National Institute for Health Research
OKS	Oxford Knee Score
OLS	ordinary least squares
ONS	Office for National Statistics
PCS	physical component score
PE	pulmonary embolism
QALY	quality-adjusted life-year
RCT	randomised controlled trial
SE	standard error
SF-12	Short Form questionnaire-12 items
TKR	total knee replacement
TOPKAT	Total Or Partial Knee Arthroplasty Trial

Scientific summary

Background

In the late 1990s, new developments in knee replacement were identified as a priority for research within the NHS. The newer forms of arthroplasty were more expensive and information was needed on their safety and cost-effectiveness. The Knee Arthroplasty Trial (KAT) was commissioned by the Health Technology Assessment (HTA) programme to address this need.

Objectives

The trial examined four key questions relating to knee replacement:

1. *Should the patella be resurfaced or not?* There is considerable variability in the use of resurfacing in the UK, with many surgeons routinely resurfacing the patella and many not. There is no clear evidence as to which approach is best.
2. *Should mobile or fixed bearings be routinely used?* Mobile bearings have the theoretical advantages of decreased wear and improved kinematics, which should result in an improvement in functional outcome and a decrease in the long-term failure rate. The main theoretical disadvantage is instability and dislocation of the bearing. It is not clear whether mobile bearings have clinical advantages or disadvantages.
3. *Should the tibial component be all polyethylene or have a polyethylene bearing supported by a metal backing?* Previous randomised controlled trials (RCTs) and meta-analyses of these trials found no difference in clinical outcome between the two types of tibial component. As all-polyethylene components are substantially cheaper than metal-backed components, the general recommendation is that all-polyethylene devices should be used in the elderly to reduce costs.
4. *Should unicompartmental or total knee replacement generally be used?* There is some evidence to suggest that unicompartmental replacement is associated with improved functional results, fewer complications, a faster recovery and lower costs than total replacements, but also a higher failure rate. It is not clear whether the advantages outweigh the disadvantages.

Methods

The trial was a partial factorial, pragmatic, multicentre RCT designed to assess clinical outcomes, complications and cost-effectiveness. The primary outcome measure was functional status as measured by the Oxford Knee Score (OKS). Other outcome measures were as follows: quality of life as measured by the Short Form 12 (SF-12) and EuroQoL 5D (EQ-5D); intraoperative and postoperative complications including the need for additional surgery; cost; and cost-effectiveness. Participants were followed up for a median of 10 years. A trial-based cost–utility analysis was conducted to evaluate whether patellar resurfacing, mobile bearings and all-polyethylene tibial components are cost-effective from the costing perspective of the NHS and the health perspective of the patients undergoing knee replacement. The economic evaluation took a 10-year time horizon, with future costs and quality-adjusted life-years (QALYs) discounted at 3.5% per annum.

Results

In total, 116 surgeons in 34 UK centres participated in the trial. From July 1999 to January 2003, 4070 potentially eligible participants were identified and 2374 (58%) gave their consent and were randomised. Of these, 22 participants were subsequently found to have been randomised in error, which left 2352 participants formally in the trial: 1715 in the comparison assessing the patellar resurfacing; 539 in the comparison assessing the mobile bearing; 409 in the comparison assessing the metal backing; and 34 in the comparison assessing total versus unicompartmental knee replacement. There were 345 participants randomised to more than one comparison.

We found no significant difference in clinical outcome, in terms of pain and function, complications, readmission or reoperations, between participants with and without patellar resurfacing. However, there was a non-significant trend towards improved quality of life [mean QALY difference 0.187; 95% confidence interval (CI) –0.025 to 0.399; $p = 0.08$] and decreased costs (mean cost difference –£104; 95% CI –£630 to £423; $p = 0.70$) associated with resurfacing, suggesting that we can be more than 95% confident that patellar resurfacing is cost-effective compared with no resurfacing at a threshold of £7250 per QALY gained. Of the non-resurfaced cases, 2.8% had late resurfacing, which was of little benefit. This late resurfacing was done in the first 5 years. Of the resurfaced group, 1% had reoperations for complications of the resurfacing during the second 5 years. Our findings were independent of whether or not the trochlear design was anatomical.

We found no conclusive evidence of any risks or benefits associated with mobile bearings in terms of postoperative functional status, quality of life, reoperation and revision rates or cost-effectiveness. There was a 2% incidence of instability or bearing dislocation in the mobile bearing group and none in the fixed bearing group. Although mobile bearings were more expensive for the hospital than fixed bearings, these initial costs were partly offset by decreases in the cost of subsequent follow-up. Overall, mobile bearings increased costs by £85 (95% CI –£911 to £1081; $p = 0.87$) and QALYs by 0.051 (95% CI –0.333 to 0.435; $p = 0.79$) and had a 59% chance of being cost-effective.

We found that the functional results with a metal-backed tibia were better than with an all-polyethylene tibia. This difference was statistically significant with the EQ-5D and SF-12 but not with the OKS. The complication, reoperation and revision rates were not significantly different, although the major reoperation rate for the all-polyethylene tibia (3%) was more than twice that for the metal-backed tibia (1%). The group randomised to all-polyethylene tibial components accrued lower costs (mean difference –£10; 95% CI –£872 to £851; $p = 0.98$) and fewer QALYs (mean difference –0.293; 95% CI –0.706 to 0.119; $p = 0.16$) than those randomised to metal backing. The economic analysis showed that the metal-backed tibia was cost-effective compared with the all-polyethylene tibia, costing £35 per QALY gained for the population as a whole and being particularly cost-effective in those aged ≥ 70 years (95% probability).

Between designing and recruiting for KAT, the technique for unicompartmental replacement changed, as surgeons started using a minimally invasive approach. As a result, surgeons were keen to learn the new technique rather than randomise participants. Owing to the poor recruitment rate, recruitment to this comparison in KAT was stopped.

Conclusions

This trial is the largest RCT of knee replacement ever conducted and provides a wealth of data on the management and outcomes following knee surgery. It has achieved very high levels of follow-up, with a median of 10 years, and has important implications for clinical practice. The success of KAT has demonstrated that large pragmatic trials with economic evaluations are possible in orthopaedics and provides an exemplar for the conduct of such studies.

Evidence from KAT is supportive of routine resurfacing of the patella, whatever the design of the trochlea. If a patient has not undergone primary patellar resurfacing, the findings do not support late resurfacing, as this is of little, if any, benefit.

We found no evidence of a difference between mobile and fixed bearings in function and quality of life. Moreover, there was no significant difference in complication, reoperation or revision rates, and there was substantial uncertainty around estimated cost-effectiveness. We did, however, identify two disadvantages of mobile bearings that could encourage surgeons to use fixed-bearing devices. First, there was a 2% incidence of instability or bearing dislocation in the mobile bearing group. Second, although there was no significant difference in overall costs in the long term, there was a short-term saving for the hospital for fixed bearings, as they are appreciably cheaper.

The findings from KAT strongly suggest that the metal-backed tibias are beneficial and cost-effective. We believe that the previous recommendation that all-polyethylene tibias should be used to save money in the elderly is a false economy, as they are not only more costly in the elderly but also less effective.

Although recruitment to the comparison of unicompartmental knee replacement versus total knee replacement was stopped in KAT, the experience gained from KAT informed a new study, known as TOPKAT (Total Or Partial Knee Arthroplasty Trial). The TOPKAT study, funded by the National Institute for Health Research HTA board, finished its recruitment in September 2013 (HTA project reference number 08/14/08).

With the increasing longevity of knee replacement patients, longer follow-up is required to assess the long-term sustainability of these findings. Longer follow-up will also help to answer some important outstanding questions. In the patellar resurfacing trial there was, with increasing follow-up, an increasing number of reoperations for complications of resurfacing and a decreasing number of late resurfacings. If this trend continues, the data may no longer support routinely resurfacing the patella. In the mobile bearing trial, there was a trend towards increased cost-effectiveness of mobile bearings in patients aged < 70 years and fixed bearings in patients aged ≥ 70 years. Further follow-up is required to obtain clearer evidence to inform the use of mobile or fixed bearings. In the metal-backing trial, we found a trend towards an increased revision rate with all-polyethylene tibias. If this continues, the evidence will provide a strong clinical reason to avoid all-polyethylene tibias. We found some evidence of potential interactions between the various different randomisations. Further follow-up is required to determine if these are important.

We believe the 10-year KAT data set is the best knee replacement data set available, as it includes information about complications, revisions, patient-reported outcomes and health economics. Further work is needed to analyse the data set in detail to answer many of the current key issues in knee replacement surgery not related to the randomisations.

Trial registration

This trial is registered as ISRCTN45837371.

Funding

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Chapter 1 Introduction

Background to project

Health Technology Assessment programme-commissioned call

In the late 1990s, new developments in knee replacement were identified as a priority for research within the NHS. Although they held the promise of better results, the newer forms of arthroplasty were more expensive and information was needed on their safety and cost-effectiveness. This report describes the Knee Arthroplasty Trial (KAT), which was commissioned by the Health Technology Assessment (HTA) programme to address this need. When the trial was funded, it was recognised that any differential performance of the alternative prostheses that were to be compared would become apparent only after a long period of follow-up. Therefore, a plan to report findings after 10 years was built into the study from the start, and results up to a median of 10 years after surgery are described in this report.

Aims

The trial was designed to address questions about four developments in knee replacement surgery:

1. Is it better to resurface the patella as part of a knee replacement or not?
2. Are polyethylene moving components ('mobile bearing') between the tibia and femur better than standard designs with a fixed bearing?
3. Are tibial components made out of just high-density polyethylene ('all polyethylene') better than those with a metal backing plate and stem, and polyethylene bearing ('metal-backed')?
4. Is it better to replace a single compartment of the knee (unicompartmental replacement) or to replace the whole knee joint [total knee replacement (TKR)]?

Clinical background including updated review of evidence base

Total knee arthroplasty is now a common and established surgical procedure. Long-term observational studies have shown that there is variability in the failure rates of different designs of knee replacement, with the best having a 20-year survivorship of about 90%.[1–3] Overall, up to 20% of patients are not satisfied with the result of their knee replacement. Continued developments in design have aimed at further improving function and quality of life and increasing the duration of prosthetic survival.

A substantial proportion of patients have a poor functional result and persistent knee pain after knee replacement.[4,5] Many of these poor results are attributed to problems arising from the patellofemoral joint, and there is considerable debate regarding whether the patella should be resurfaced at the time of the primary total knee arthroplasty. Theoretically, patellar resurfacing should decrease the incidence of pain related to the patellofemoral joint, although the resurfacing can fail. Previous evidence in the form of non-randomised cohort studies, small randomised controlled trials (RCTs) and systematic reviews has not resolved the uncertainty regarding the benefits of patellar resurfacing.[6–21]

Many previous RCTs had insufficient sample sizes to detect clinically worthwhile differences in outcomes. There is great variability in the use of patellar resurfacing. Some surgeons routinely do not resurface, whereas others routinely do resurface. There is also a subgroup that sometimes resurfaces the patella, but there is no clear consensus as to which patients should undergo resurfacing.

Theoretically, by using mobile rather than fixed bearings between the tibial and femoral components the performance and longevity of knee replacement could be improved.[22,23] Mobile bearings are usually designed to be more congruent than fixed bearings and, therefore, have larger contact areas, which should reduce wear. However, as there are two bearing surfaces, the decrease in wear may be limited.

They also tend to have less constraint than fixed bearings, which should limit the shear stress at the bone–implant interfaces. Strong interfacial forces and osteolysis resulting from polyethylene wear debris are the most important causes of loosening, which is the most common cause of knee replacement failure. By allowing an appropriate amount of mobility, a mobile bearing design could optimise kinematics and thus improve function. However, mobile bearings can dislocate or be associated with instability. Previous non-randomised cohort studies, RCTs and systemic reviews did not resolve the benefits of using a mobile versus a fixed bearing.[24–29] Again, the evidence base suffers from limited evidence from RCTs with sufficient sample sizes to detect worthwhile differences.

Another common variation is the design of the tibial component. Use of a metal-backed base plate has theoretical advantages in that it distributes load more evenly across the implant–bone interface than an all-polyethylene tibia, and thus should decrease the risk of loosening. In addition, as the bearing is modular, the surgeon can select the thickness and constraints of the bearing after the components are fixed. However, metal backing reduces the thickness of the polyethylene that can be implanted in the available space, thus increasing the internal stresses within the polyethylene and increasing the risk of wear. Furthermore, metal backing is more expensive, and good medium- and long-term results have been reported for the use of non-metal-backed components.[30,31] Limited comparisons between non-metal-backed and metal-backed components have been performed, and to our knowledge no definitive difference has been determined.[4,32] As there is no apparent clinical advantage of metal-backed tibias and as they are more expensive, it is generally recommended that all-polyethylene tibias should be used in the elderly to save money.[33,34]

Overall, in the NHS about 7% of knee replacements are unicompartmental. There is, however, great variability: in different institutions unicompartmental knee replacements are used for between 0% and 70% of knee replacements. The results from specialist centres that implant large numbers of unicompartmental knee replacements have demonstrated that unicompartmental replacements give a faster recovery, lower morbidity, lower cost, better function and better pain relief than total replacements. However, in national registers, even though the risk of serious complications, such as death and infection, is lower with unicompartmental than with total replacement, the revision rate is about three times higher. There is clearly a need to establish the relative advantages and disadvantages of unicompartmental and TKRs so as to determine whether the use of unicompartmental replacement should or should not be encouraged. Although the only randomised study we are aware of did suggest that unicompartmental replacement is better than total, it was too small to form the basis of any strong recommendation.[13]

Outline of report

Reflecting the multiple research questions to be addressed, KAT was designed as a partial factorial, pragmatic, multicentre RCT to assess the clinical outcomes, complications and cost-effectiveness of the four aspects of knee replacements. The full details of the design and methods adopted are presented in *Chapter 2*. *Chapter 3* presents the results of the comparison of patellar resurfacing versus no resurfacing; *Chapter 4* presents the results of the comparison of the polyethylene moving component (mobile bearing) between the tibia and femur with standard designs with fixed bearing; *Chapter 5* presents the results of the comparison of the metal backing plate for the tibial component of the TKR with a single high-density polyethylene component; and *Chapter 6* presents the results of the comparison of unicompartmental replacement of the knee with TKR. *Chapter 7* discusses the implications of the project as a whole, finishing with a summary of the implications for practice and recommendations for further research.

Chapter 2 Methods and practical arrangements

Study design

The trial was a partial factorial, pragmatic, multicentre RCT designed to assess the clinical outcomes, complications and cost-effectiveness of four aspects of knee replacements. The detailed protocol is included as *Appendix 1*.

The intention was to evaluate the newer designs as they would be used within the UK NHS setting. The plan was therefore to involve a large number of UK centres in which knee replacement was undertaken and to make comparisons based on outcomes important to people undergoing knee replacement and to those responsible for providing orthopaedic services. Eligible surgeons (see below) could recruit to any of the comparisons. However, the design acknowledged that some surgeons would have strong beliefs about some of the factors under investigation and that there would be some who would not wish to randomise between some factors but be comfortable to recruit to others. Surgeons could therefore choose which comparisons to contribute to [and which comparison(s) to randomise any given participant to] on the basis of equipoise, randomising participants to those aspects of component design for which they were not certain which arm was most suitable for that participant. Equipoise formed a central part of this recruitment strategy to help ensure that participants were randomised only when current evidence was insufficient to inform decisions about component design and to help boost recruitment of surgeons. Although most participants were enrolled into just a single comparison, surgeons could enrol an individual participant into more than one comparison, thereby decreasing the total sample size needed to achieve the necessary statistical power for each comparison. In particular, participants could be randomised to patellar resurfacing versus no resurfacing as well as to either all polyethylene versus metal-backed or mobile bearing versus fixed bearing. However, as all mobile bearing components are metal-backed, participants could be randomised in only one of these comparisons. Additionally, the design did not allow participants randomised in the unicompartmental versus TKR comparison to be randomised in any other comparison. For those participants randomised in two comparisons, a factorial design was used within the process for random allocation to ensure balance of allocation within and across comparisons (hence the description of the design as a partial factorial trial) (*Figure 1*).[35]

Important changes to the design after trial commencement

The rate of recruitment to the fourth comparison – unicompartmental versus TKR – proved to be very slow, despite efforts to encourage enrolment. Only 34 participants were recruited to this element of KAT, and, with the agreement of the data monitoring committee, a decision was taken to close recruitment to this component early in August 2002. The body of this report, therefore, describes in full only the three remaining comparisons, to which recruitment was successful. The very limited information gained from the unicompartmental versus TKR comparison is presented in *Chapter 6*.

Clinical centres

Orthopaedic surgeons within the UK were eligible to take part if they performed knee replacements routinely. To participate, they had to be prepared to allow the choice between the specific options in at least one of the trial comparisons to be decided by random allocation. Before participating in the trial, the surgeons formally chose the comparisons to which they would contribute – as expected, surgeons did differ in terms of which comparisons they would allow their patients' surgical management to be randomly allocated.

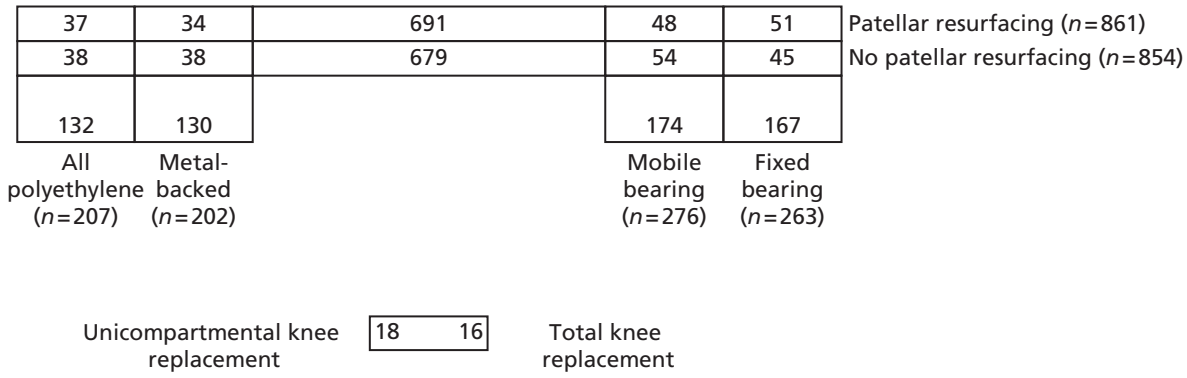

FIGURE 1 Diagrammatic representation of the partial factorial elements of KAT. *n* is the number of participants randomised to that intervention.

Study population

All patients under the care of a collaborating surgeon were potentially eligible for inclusion if a decision had been made to have primary knee replacement surgery. A patient was not eligible for a trial comparison if the surgeon considered that a particular type of operation was clearly indicated (e.g. if a patient required a highly constrained knee replacement to replace function of the collateral ligaments). A patient remained eligible only if the surgeon remained convinced that there was no indication for one particular choice within the trial; for example, a patient with a very thin patella would not be eligible for the patellar resurfacing comparison because the surgeon would not have chosen patellar resurfacing for such a patient.

As described above, individual patients could be recruited for more than one comparison if that was clinically appropriate. However, only a minority of participants were included in more than one comparison.

Consent to participate

Potential participants were sent information about the trial comparisons in which the surgeon responsible for their care had agreed to participate (patient information leaflets are reproduced in *Appendix 1*). Exact arrangements for recruitment depended on the local admission procedures, but, in general, information about the trial was given in two stages. A letter of invitation, together with information about the parts of the trial in which the surgeon had agreed to participate, was sent to potential participants at home. Information was also sent to their general practitioners (GPs) in case they were consulted. More detailed information concentrating on the options for which the patient was eligible was given to potential participants during discussions with a surgeon or research nurse at a pre-assessment clinic or when admitted before surgery.

All eligible patients who agreed to participate in the trial signed the KAT consent form (see *Appendix 1*). This form confirmed that the participant had been given the information they required and that the study had been explained to them. They also confirmed that they understood that they would be sent a postal questionnaire each year.

Health technology policies compared

The four comparisons made in KAT were:

- Patellar resurfacing versus no resurfacing – surgeons were randomised to resurface the patella or not, irrespective of the design of the prosthesis used.

- Mobile bearing between the tibial and femoral components versus standard designs without a mobile bearing – the surgeon was randomised to use the metal-backed cruciate-retaining or substituting design that he or she used routinely, or alternatively a mobile-bearing design that was essentially similar.
- Single high-density all-polyethylene component versus a tibial component with a polyethylene bearing fixed to a metal backing plate with a stem.
- Unicompartmental versus TKR.

Full information on the clinical details of each health technology under investigation is presented in more detail in the separate results chapters (see *Chapters 3–6*).

Treatment allocation

Participants were formally entered into the trial by telephoning an automated service within the trials office in Aberdeen. During this process, basic descriptive information was given first (surgeon; patient's name, sex and date of birth), followed by the patient classification part of the American Knee Society score (AKS) (unilateral, bilateral, generalised arthritis) and the comparison(s) to which the participant would be recruited. Once these details had been supplied, the random allocation was given in return. The allocation was computer generated in ratios of 1 : 1 after stratification by eligible comparisons and surgeon, and minimisation according to the patient's age (< 60 years, 60–79 years or ≥ 80 years), the patient's gender (male or female) and the site of disease (one knee, both knees or general arthritis).

Recruitment was carried out on the day before surgery (or sooner) to allow theatre staff to prepare appropriate equipment and prostheses. Each patient could be entered into the trial only once. In the event of a patient being admitted for bilateral knee replacements, the knee indicated by the patient to be the most painful was the knee that was considered for randomisation.

Clinical management

Within the randomised comparisons, all prostheses had suitable alternative designs, as outlined above. Surgeons followed their standard practice, that is the technique that they utilised did not require any modification for the purposes of the trial, and the outcomes were thus not influenced by a so-called learning-curve effect. We did not influence surgeons regarding whether they should utilise cruciate-retaining or substituting implants. All other aspects of care, such as prophylaxis against deep-vein thrombosis (DVT) and discharge from hospital, were left to the discretion of the responsible surgeon.

Data collection

Preoperative, intraoperative and postoperative data on surgery, knee components used, length of stay, operation time and complications were collected prospectively on standard forms (reproduced in *Appendix 1*). Data describing functional status [using the Oxford Knee Score (OKS)] and quality of life [using Short Form questionnaire-12 items (SF-12) and EuroQoL 5D (EQ-5D)] were collected directly from postal questionnaires completed by participants at baseline, 3 months after the operation, at 1 year and annually thereafter (see *Appendix 1*). Following one postal reminder, participants who had not returned the questionnaire were telephoned and offered the option of completing the questionnaire over the telephone. A number of other measures were taken to promote ongoing interest in, and commitment to, the trial including participant newsletters and annual Christmas cards.

Annual and 3-monthly questionnaires also included questions about GP, physiotherapy and outpatient consultations related to the study knee and any hospital admissions. Information on hospital admissions

and further surgery was supplemented with routinely collected information, when available, from the Hospital Episode Statistics (HES) database in England and Information Services Division (ISD) in Scotland. Although all participants consented to routine data on mortality being obtained from the Office for National Statistics (ONS) at the time of randomisation, in June 2006, it became necessary to obtain additional consent for all participants in Scotland to conduct routine mortality monitoring through the NHS Information Centre. In addition to obtaining participant consent to access medical information from routine sources at baseline, the Data Access and Advisory Group reviewed and approved the release of HES data at 5 and 10 years. Participants' case notes were reviewed if either questionnaires or routine data indicated further surgery or admissions.

Principal study outcome measures

The primary outcome measure was functional status as measured by the OKS,[36] which was developed specifically to measure outcomes of knee replacement and has been shown by a range of independent studies to perform well compared with alternative instruments.[37–39] Other outcome measures were as follows: quality of life as measured by the SF-12[40] and three-level EQ-5D;[41,42] intraoperative and postoperative complications including the need for additional surgery; cost; and cost-effectiveness. [SF-12 version 2 was used throughout the majority of the trial, although patients recruited early in the study completed version 1 at baseline.]

Sample sizes

The size of the effect on the OKS sought in each comparison (and hence the sample size chosen) was based on the size of the difference in the OKS that seemed likely, as judged on the basis of current experience, and the size of the effect that was likely to offset any adverse effects and cost differences of the prosthetic design variable. All power calculations assumed that there was no interaction between comparisons: that is that the impact of each comparison was unaffected by whether or not the participant also underwent patellar resurfacing (see *Statistical analyses of clinical end points*). The difference in OKS sought was three points for the comparisons involving the tibial all-polyethylene backing, the mobile bearing and the unicompartmental arthroplasty, with 350 participants providing 80% statistical power and 470 participants providing 90% power to detect this difference ($p < 0.05$). The difference sought was 1.5 points for the patellar resurfacing comparison, with 1400 participants providing 80% power to detect this difference ($p < 0.05$). All sample size calculations were based on a standard deviation of 10 points for the OKS.

The rationale for the three-point difference in OKS was based partly on anchoring evidence and partly on distributional or statistical evidence.[43] Evidence from an anchoring perspective came from a study in which patients completing the OKS were also assessed by an orthopaedic surgeon using the AKS.[44] Overall, the average difference in OKS between patients assessed by the surgeon, as in adjacent categories of the AKS, was 3.5 points. In terms of distributional evidence, an overview of statistical evidence of the performance of the OKS concluded that a minimal clinically important difference (MCID) was a third to a half of the standard deviation of OKS, that is three to five points.[45] Overall, three points was selected as a MCID for sample size calculations for the metal-backed and mobile bearing comparisons and a more conservative 1.5 points for the patellar resurfacing comparison.

Statistical analyses of clinical end points

The comparisons were analysed and reported as separate trials in order to estimate the 'main effects' of the alternative approaches within each comparison, as prespecified in the protocol (*Appendix 1*).

The database was closed for final analysis on 8 June 2012, by which point a median of 10 years of follow-up had been achieved. Participant flow through the trial is summarised using a CONSORT (Consolidated Standards of Reporting Trials) style diagram.[46] Baseline characteristics are tabulated using descriptive statistics reported as appropriate for type of variable being summarised.

The functional status and quality-of-life outcomes within each trial comparison were compared by linear mixed models that adjusted for baseline scores and minimisation factors; random effects for participant and surgeon; and time point, which was incorporated using a dummy variable for each year that interacted with treatment allocation to allow the treatment effect to vary over time. Data were analysed on the basis of the procedure allocated irrespective of the treatment actually received (intention-to-treat principle). Participants were included in the model if they received any surgery and provided at least one follow-up measurement of outcome. Participants were excluded from outcome-specific models if they died before surgery, received no surgery or provided no follow-up data for that outcome. Missing baseline data were imputed using surgeon-specific mean scores for that particular outcome. Analysis was carried out on all available follow-up data to 10 years; no attempt was made to impute missing follow-up data. Descriptive statistics are reported at each time point and represented graphically over time by allocated group. Estimated effects of the intervention and 95% confidence intervals (CIs) at each time point are also tabulated and graphed through time; a marginal estimate of treatment effect over the whole 10-year period is presented (with 95% CIs) to aid ease of interpretation. It was anticipated that differences in revision rates may have influenced the primary outcome. If a participant had a revision (defined using the strictest definition of failure in the paragraph below), then all that participant's observations post the revision date were replaced by the reported value prior to revision. The primary outcome analysis was then replicated to test the robustness of the results to potentially differential revision rates. All analyses were implemented using xtmixed in Stata 12.1 (StataCorp, College Station, TX).

Clinical outcomes on reoperation within the first 10 years are tabulated and described using appropriate summary statistics. These outcomes were analysed within a survival analysis framework with time to failure of knee prosthesis as the event. Time to failure of the knee prosthesis was defined in three different ways. The strictest definition of failure was time to first major reoperation or prosthetic-related reoperation (see tables in *Chapters 3*, *4* and *5* for comparison-specific definitions); second, time to any reoperation; and, third, the most liberal definition, time to any reoperation or OKS on an annual questionnaire dropping to below the level of the self-reported baseline score. All outcomes were plotted using Kaplan–Meier time-to-failure plots and analysed using parametric survival regression models using a Weibull distribution. Owing to the paucity of events for the first two definitions of failure, models with only treatment effect covariates were fitted. Additionally, for the models of the final definition of failure, adjustments for minimisation covariates and surgeon were run. For the final definition of failure, events were generated using a mixture of interval and non-interval censored data, the impact of which was explored by rerunning models using interval-censored regression. Proportional hazards were assumed for all models and participants were censored at time of death or 10 years if they had not experienced an event. The proportions of participants experiencing specific types of reoperation over the 10-year trial follow-up period were compared using exact logistic regression (owing to the small number of events). All estimates of treatment effects are presented as hazard ratios or odds ratios and 95% CIs. Analyses were implemented using streg, intreg and exlogistic in Stata 12.1.

All analyses assumed no interaction between patellar resurfacing and the other interventions: that is patellar resurfacing had no effect on the treatment effects for any other comparison. As no previous factorial trials have been conducted for knee replacement, there is a shortage of data on which to base assumptions about interactions. However, we are aware of no clinical or mechanical reason why any interaction between patellar resurfacing and other comparisons would be expected and, therefore, assumed no interaction. The partial factorial design provided an opportunity to conduct preliminary analyses to explore whether there is any interaction between patellar resurfacing and the other comparisons, which was conducted in sensitivity analyses by including an interaction term between interventions at each time point. This analysis included only those that were randomised to more than

one comparison. Results are plotted as a difference in differences through time to aid interpretation. Post-hoc subgroup analysis on age at time of operation (< 70 vs. ≥ 70 years) and patellofemoral groove shape (domed vs. anatomical) were conducted in a similar fashion to the partial factorial element by allowing an interaction between subgroup and allocation at each time point.

Avoidance of bias, including blinding

As described above, the randomisation process was concealed and an intention-to-treat approach used in all primary analyses. Surgeons undertaking the procedures were not 'blind' to the allocation for obvious reasons. The primary outcome measure was based on participant-completed questionnaires. Only participants who wished to know which type of prosthesis they had received were told this information. In principle, it is possible that this knowledge might have influenced responses to questionnaires, but any such effect would be likely to dissipate over such a long period of follow-up.

Health economic evaluation

Study question for economic evaluation

We aimed to assess the cost-effectiveness of the following types of knee prosthesis, in line with the comparisons addressed by the trial:

- patellar resurfacing versus no patellar resurfacing
- mobile versus fixed bearing
- all-polyethylene versus metal-backed tibial component
- unicompartmental versus TKR.

Following UK guidelines for economic evaluation,[47] the KAT economic evaluation was conducted from the costing perspective of the UK NHS and from the health perspective of the patients undergoing knee replacement. The analysis, therefore, excluded costs incurred by other sectors of the economy, such as lost productivity, informal care, participants' out-of-pocket expenses or home/residential/rehabilitation care.

As KAT was a pragmatic trial involving long-term follow-up of elderly participants, data collection was streamlined further to reduce the questionnaire burden on participants and maximise response rates to annual questionnaires. In particular, the amount of costing data collected from annual questionnaires was limited to the main NHS costs directly attributable to knee replacement.

Framework for economic evaluation

Cost–utility analysis (CUA) was used to evaluate cost-effectiveness in order to capture any differences in quality of life between randomised comparisons. The primary end point therefore comprised the cost per quality-adjusted life-year (QALY) gained. CUA was used regardless of whether functional status or quality of life differed between randomised comparisons, as our primary interest is in the joint distribution of cost and effect differences, and also because KAT was not powered to demonstrate equivalence, and thus assuming no difference in outcomes could give misleading conclusions and bias estimates of decision uncertainty.[48,49]

The base-case analysis comprised a within-trial economic evaluation using only data from KAT. Results were not extrapolated beyond the end of the trial, as the within-trial period was already substantial (up to 12 years). Attrition and administrative censoring (i.e. data from time points not yet reached as a result of staggered recruitment times) were dealt with using multiple imputation and inverse probability weighting (IPW), as described below. The economic evaluation included all participants formally included in the trial with the exception of 34 participants who died before surgery and 66 participants who were randomised to the total versus unicompartmental knee replacement comparison or withdrew from the trial prior to

surgery, giving a total sample of 2252 participants. In line with the clinical analysis, the economic evaluation includes all annual questionnaires received by 8 June 2012. Additional data on hospital readmissions were obtained from HES up to 31 March 2011 (for participants living in England) and from ISD up to 31 December 2010 (for participants living in Scotland).

The base-case economic evaluation took a 10-year time horizon and, therefore, included all data on quality of life and costs and readmissions that occurred within 10 years of primary TKR or before administrative censoring (if sooner). However, alternative time horizons are presented in the sensitivity analyses. Costs and QALYs accrued beyond year 1 were discounted to present values at 3.5% per annum.[50]

Collection of resource-use data and unit costs

Quantities of knee-related resources used in the primary admission and subsequent follow-up were collected prospectively for each trial participant. Data collection focused on resources associated with the study knee and excluded resource use from unrelated causes to simplify data collection and reduce the length of participant questionnaires. Focusing on resource use directly related to the study knee and the complications of knee surgery also avoids the risk of catastrophic episodes involving high health-care resource use unrelated to treatment (e.g. renal failure, cancer or extended psychiatric admissions) swamping the main effect of treatment on costs and, therefore, reduces uncertainty around incremental costs and cost-effectiveness.[51]

Data on quantities of NHS resources related to the study knee were identified from the surgeon's form (see *Appendix 1*), the hospital care form (see *Appendix 1*) and annual questionnaires (see *Appendix 1*) completed by participants, with additional data on hospitalisations being collected from HES and ISD (*Table 1*). Questionnaires focused on the main cost drivers (see *Table 1*), which were identified following discussions with clinicians and from evidence from previous publications. In line with clinical analyses, readmissions to hospital that were related to the study knee or that were considered (by clinical adjudication) relevant to the primary TKR procedure [e.g. readmissions for myocardial infarction, DVT or pulmonary emboli (PE) within 3 months of TKR] were included in the analysis, but all other readmissions (including readmissions for thromboemboli that occurred after revision procedures on the study knee) were excluded from the analysis. The assumptions used to estimate resource use and costs from questionnaire responses are listed in *Box 1*.

Mobility aids and medications used to manage pain and arthritis in non-hospitalised participants were excluded from the analysis to simplify questionnaires and reduce the burden on participants. Mobility aids are unlikely to comprise a large proportion of 5- or 10-year total costs; furthermore, they will often be funded from outside the NHS perspective taken in this analysis, and the need for mobility aids will also be affected by comorbid conditions. Similarly, pharmaceuticals are likely to account for only a small proportion of total costs: recent evidence suggests that analgesics and arthritis medication accounts for only around 2–3% of total health-care spending in participants who have undergone joint replacement.[62]

Additionally, the following resources were assumed to be included in other unit costs and not considered separately to avoid double counting:

- Drugs (e.g. antibiotics, anaesthetics, anticoagulants) and non-surgical treatments (e.g. urinary catheters) administered during knee-related hospital admission: assumed to be covered by the cost of a bed-day.
- Cement, time in recovery room, intraoperative complications and blood products transfused while in theatre: assumed to be included in the cost of theatre time and not accounted for separately to avoid double counting.
- Surgical instruments used in primary knee replacement: assumed to be supplied at no cost by prosthesis manufacturers.
- Diagnostic tests or postoperative complications other than imaging for DVT/PE, transfusion and admission to high-dependency unit: assumed to be covered by the cost of a bed-day/outpatient consultation and any associated increases in length of stay.

TABLE 1 Health-care resources included in the economic evaluation and unit costs in 2010/11 pounds sterling

Resource included in economic evaluation	Source of data on resource-use quantities	Unit cost (£)	Reference for unit cost
Minute of theatre time	Primary TKR: HCF Readmissions and return to theatre: EO estimates (based on surgery classification identified from hospital/HES/ISD records)	16.87	Mean cost/minute across all orthopaedic operating theatres in Scottish NHS hospitals,[52] inflated from 2010–11 values to 2011–12 values using HCHS pay and prices inflation index.[53] Includes cost of staff, premedication/anaesthesia and recovery room. The cost of theatre time is also assumed to cover the cost of cement and blood transfusions delivered during the surgery. Although exact data on the duration of the primary TKR operation (from entry to anaesthesia room to leaving operating theatre) were available from the HCF, participant-level data on subsequent surgery (either during readmissions or later in the primary hospital admission) were not available. One of three orthopaedic surgeons estimated the typical duration of each type of surgery performed in the trial (and each combination of surgery types conducted in the same readmission) and this duration was applied to all participants undergoing that surgery type; the initial estimates were validated by one of the three surgeons to ensure consistency
Hospital bed-day	Primary: HCF Readmissions: HES/ISD, RF	328.73	Weighted average cost per excess bed-day for elective inpatient admissions for all procedures to the knee except those for trauma or for children,[54] inflated from 2009–10 values to 2011–12 values using HCHS pay and prices inflation index.[53,55] As the majority of admissions included in the analysis were for orthopaedics, the cost of orthopaedic bed-days was applied regardless of whether the reason for admission was non-orthopaedic (e.g. for PE). The length of stay calculated for each participant included time in hospital before the primary TKR procedure: even if this occurred before randomisation
Day-case stay in hospital	PAF, HES/ISD, RF	216.00	Owing to a lack of data on the hotel costs for participants who are admitted and discharged on the same day, such participants were assumed to accrue a cost mid-way between the cost of a bed-day (£328.73)[54] and the cost of an orthopaedic outpatient consultation (£103.27).[54] National average costs of day-case procedures cannot be used here, as they include theatre costs and components, which are costed separately
Knee components	SF and RF	Various	See text for details
Loan of instruments for revision surgery	N/A	500	Mean cost of hiring instruments for revision surgery for component manufacturers, which was applied to all one-stage revisions and the second stage of two-stage revisions. The average cost is based on a typical loan charge and is applied to 50% of procedures to allow for the fact that loan charges are waived for high-volume centres
Unit of whole blood	HCF[a]	119.00	National price charged per unit of whole blood in 2012–13,[56] deflated from 2012–13 to 2011–12 values using HCHS pay and prices inflation index[57]
Transfusion	HCF[a]	95.72	Cost of transfusion estimated by a previous economic evaluation, excluding the cost of blood and overnight stay,[58] inflated from 2004–5 values to 2011–12 values using HCHS pay and prices inflation index[53,55]

TABLE 1 Health-care resources included in the economic evaluation and unit costs in 2010/11 pounds sterling (*continued*)

Resource included in economic evaluation	Source of data on resource-use quantities	Unit cost (£)	Reference for unit cost
CT	HCF, RF	121.07	Based on the cost of CT (to diagnose PE), one area, pre and post contrast (RA10Z), averaged across outpatient, direct access and other,[54] inflated from 2009–10 values to 2011–12 values using HCHS pay and prices inflation index.[53,55] The cost of CT was applied to all participants for whom PE was recorded as a postoperative complication or for whom CT or VQ scan or tests/imaging for PE were recorded in free text fields
Leg ultrasound	HCF, RF	56.50	Based on the cost of an ultrasound scan (to diagnose DVT or haematoma) taking < 20 minutes (RA23Z), averaged across outpatient, direct access and other,[54] inflated from 2009–10 values to 2011–12 values using HCHS pay and prices inflation index.[53,55] The cost of a leg ultrasound was applied to all participants for whom DVT was recorded as a postoperative complication or for whom ultrasound, venogram or tests/imaging for DVT were recorded in free text fields
Spell in high-dependency/ critical care unit	HCF, RF[a]	992.70	Incremental cost of 24 hours spent in high-dependency unit: average cost of a bed-day in critical care unit (£1321.44; service codes XC01Z–XC07Z),[59] minus cost per bed-day in an orthopaedic ward (£328.73)[59]
Outpatient consultation	PAF	103.27	Weighted average across orthopaedic outpatient consultations (service code 110N),[54] inflated from 2009–10 values to 2011–12 values using HCHS pay and prices inflation index[53,55]
Physiotherapy consultation	PAF	43.33	Weighted average of consultations with hospital physiotherapists and community physiotherapists[60] (inflated from 2010–11 values to 2011–12 values using HCHS pay and prices inflation index[53]), assuming that 50% of participants would see a hospital rather than community physiotherapist.[61] The cost of NHS physiotherapy consultations was applied in all cases, as the proportion of consultations that were paid privately is not known
GP consultation	PAF	37.59	Unit cost per surgery consultation lasting 11.7 minutes, including direct care staff costs and qualification costs,[60] inflated from 2010–11 values to 2011–12 values using HCHS pay and prices inflation index[53]

CT, computed tomography; EO, expert opinion – typical operation time estimated by one of three orthopaedic surgeons based at one specialist orthopaedic centre; HCF, hospital care form (see *Appendix 1*); HCHS, hospital and community hospital services; N/A, not applicable; PAF, participant annual form (or 3-month form), completed by participant at 3 months and annually thereafter (see *Appendix 1*); RF, readmission form (see *Appendix 2*); SF, surgeon's form (see *Appendix 1*); VQ, ventilation/perfusion.

a Resource use was only included in costing analyses in cases in which this type of resource was explicitly mentioned on the hospital care form.

BOX 1 List of assumptions used in costing analyses

Costing analyses: component

- 30% fixed discount on all knee components.[a]
- Participants were assumed to not have received components other than patellas, femurs, tibial trays and tibial inserts unless component stickers or descriptions were attached to the form, although all 'other' components (e.g. stem extensions, augments, rods or blocks) recorded were also included in the analysis.
- Participants were assumed to use no more than one component of each of the four main types (patella, tibial insert, tibial tray and femur) per operation. Duplicate codes (e.g. for a second femur) were excluded from the analysis and assumed to be erroneous; in particular, duplicate codes may have been attached to participants' notes or hospital forms in error, relate to the other knee (in a bilateral operation) or have been ordered but returned to the manufacturer unused.
- All primary TKR procedures were assumed to require a tibial tray and femoral component (even if no corresponding component codes were included on the hospital form). Participants allocated to patellar resurfacing who received the allocated procedure were also assumed to have received a patella. All participants were assumed to require a tibial insert unless the tibial tray recorded was all polyethylene.
- All late patellar resurfacing and patella revision procedures were assumed to require a patella. All exchange of tibial insert procedures (whether conducted during or after the primary hospital stay) were assumed to require a tibial insert. Other components were assumed to be required during readmissions if readmission forms indicated that that component had been revised, or if codes and/or descriptions were recorded on the hospital form.
- First-stage revisions were assumed to require no knee components unless codes for cement spacer moulds were indicated on the readmission form or hospital notes.
- The cost of instruments for primary TKR was excluded from the analysis, as these are generally provided free of charge by component manufacturers. However, loan charges of £250 per operation were added to the cost of all one-stage revisions of the tibial and/or femur and all second-stage revisions. Although most high-volume centres will either own instruments for revision surgery or have them provided free of charge by manufacturers, smaller centres, which are assumed to account for 50% of revision procedures, will incur loan charges of around £500 per operation, giving an average cost of £250 (50% times £500) per revision.

Costing analyses: readmissions and ambulatory consultations

- The type of knee prosthesis used is assumed to have no effect on consumption of non-knee-related health-care resources, personal and social care services, mobility aids or medication.
- We assumed that annual questionnaires and HES/ISD provide complete data on all hospital readmissions up to the last questionnaire that participants return, or until the cut-off date for HES or ISD (if later).[a]
- All knee-related physiotherapy consultations were assumed to be funded by the NHS, with 50% occurring in hospital and the remainder in the community.
- The reporting periods of the 3-month questionnaire and the 1-year questionnaire overlap: the 3-month questionnaire asks participants to give the number of GP/physiotherapy/outpatient consultations they have attended 'since leaving the hospital', whereas the 1-year questionnaire asks for consultation numbers 'in the last year'. The number of consultations occurring in year 1 was, therefore, assumed to equal whichever was largest out of the number reported in the 1-year questionnaire and the number reported in the 3-month questionnaire. This ensures that consultation numbers during year 1 are always based on a 12-month period and allows for the potential discrepancies that could arise from participants answering the 1-year questionnaire > 1 year after hospital discharge, thereby missing the period of most intensive follow-up. Participants who did not return the 1-year questionnaire were assumed to have missing data on ambulatory consultations in year 1, even if the 3-month questionnaire was returned.

BOX 1 List of assumptions used in costing analyses (*continued*)

- Implausible or logically inconsistent data values recorded on questionnaires (e.g. participant weight < 10 kg) were treated as missing and imputed using multiple imputation (see *Methods for imputing missing data*).

Quality-adjusted life-year calculations

- EQ-5D utility was measured at baseline, 3 months, 1 year and annually thereafter. QALY calculations assumed that all quality-of-life measurements were taken at the scheduled time points: that is, 1-year EQ-5D utility was always measured exactly 12 months after the primary operation. This assumption simplifies QALY calculations and ensures that the initial increase in quality of life is always applied over the first 3 months after TKR, even if the EQ-5D questionnaire was completed much later.
- Quality of life was assumed to change linearly between baseline and 3 months, between 3 and 12 months and between annual questionnaires. For example, the number of QALYs accrued during year 2 was assumed to be the average of utility at year 1 and that at year 2. Similarly, utility at the time of death was estimated by linearly interpolating between participants' last observed utility and the utility imputed in place of the following annual questionnaire using multiple imputation (see *Methods for imputing missing data*).

Mortality

- For participants who died during the study, the date of death was obtained from routine monitoring by the NHS Information Centre, supplemented, when necessary, by contact with the participant's GP or details supplied by relatives on annual questionnaires sent out before quarterly ONS updates were received. In the very few cases in which the exact date of death was not known, death was assumed to have occurred half-way between the last date the participant was known to be alive (e.g. the date when they returned their last annual questionnaire) and the first date when they were known to be dead (e.g. when a questionnaire was returned by relatives).
- EQ-5D utility and the number of GP, physiotherapy and orthopaedic outpatient consultations were imputed for participants' last year of life using multiple imputation (see *Appendix 3*). Dummy variables indicating the year of death (relative to randomisation) were included in multiple imputation to allow for the effect of proximity to death on quality of life and resource use.
- To allow for the fact that participants who die during year *y* do not accrue a full year of resource use or QALYs, we multiplied the number of ambulatory consultations imputed for a complete year by the fraction of the year lived during year *y*. This adjustment implicitly assumes that ambulatory consultations related to the knee are evenly distributed across the last year of life. No adjustment was made for numbers of readmissions, as these are assumed to be complete up until the time of censoring or death.

Analysis

- The effect of each randomised comparison is assumed to be additive: that is the type of tibial component used is assumed to have no effect on the cost or QALY gain from patellar resurfacing (and vice versa).[a]
- Discounting for time preference was based on the number of whole years that had elapsed since the primary TKR operation date. Ambulatory consultations reported in the year *y* questionnaire were assumed to have occurred in that year even if the questionnaire was completed early or late. Readmissions were considered to have occurred in year *y* if the admission date was less than *y* years after the primary operation date (regardless of when the participant was discharged). To ensure consistency with the clinical analysis, the second stage of two-stage revisions was assumed to always occur in the same year as the primary stage.

a Assumption relaxed or varied in sensitivity analyses.

Unit cost data were collected from routinely available sources (see *Table 1*).[52,56,58,60] The index year for pricing was 2011/12 and prices from earlier (or later) years were inflated (or deflated) to 2011/12 values using the hospital and community hospital services (HCHS) pay and prices index.[53,55]

Stickers giving the product codes for the knee prosthesis components used in primary knee replacement and revisions were attached to the surgeon's form to indicate which brand and model was used in that operation. For all readmissions identified from participant questionnaires or HES/ISD that were deemed potentially related to knee surgery, the hospital was asked to provide a copy of participants' notes and/or complete the readmission form (see *Appendix 2*) including codes for all components used. Each component used was then valued using list prices obtained from manufacturers. List prices from 2008 were used for primary procedures when available and inflated to 2011/12 values. However, when such prices were not available (e.g. for components that have since been discontinued), list prices payable at the time of the KAT operations (1999–2002) were inflated to 2011/12 values using the HCHS pay and prices inflation index;[53,55] when the price of discontinued components at the time of operation was unavailable, prices were based on comparable components available today. Prices for revision components were obtained between 2008 and 2012 and inflated/deflated based on HCHS when necessary. The pay and prices index appears to be appropriate for knee replacement components, as those components for which list prices were available for 2001 and 2008 increased in price by 38.9% over that period (cf. 36.2% HCHS inflation).[53]

In practice, the prices hospitals pay for devices are substantially lower than list prices, as each hospital negotiates discounts with their supplier(s). Although actual discounts vary between hospitals and are commercially sensitive, we applied a fixed discount of 30% on all components in the base-case analysis; this discount was varied in sensitivity analyses.

Calculation of quality-adjusted life-years

Participants completed the three-level EQ-5D and SF-12 questionnaires preoperatively, 3 months after the primary TKR and annually thereafter as part of the participant annual form (see *Appendix 1*). In the base-case analysis, QALY calculations were based on EQ-5D utilities as prespecified in the trial protocol. EQ-5D is recommended[47] and widely used,[63] enabling the cost-effectiveness of trial interventions to be compared with other economic evaluations. EQ-5D health-state preference values were calculated using the UK N3 tariff, which is based on time trade-off valuations from 3395 members of the UK general public.[64] The number of QALYs that each participant accrued following TKR was calculated as the area under the utility curve, with linear interpolation between utility measurements (see *Box 1*).

Methods for imputing missing data

As the calculation of costs and QALYs requires summation of cost and utility data across numerous resource-use items and time points, missing data are a greater problem for economic evaluation than for clinical end points. Specifically within KAT, around 7% (12,102/173,404) of data points prior to administrative censoring were missing across the 77 variables included in the analysis, with 63% (1414/2252) of participants having missing data for at least one resource-use item or quality-of-life measurement, in addition to 884 participants (38%) who were administratively censored before the 10-year follow-up. A complete case analysis excluding all such participants would therefore have been highly inefficient. Furthermore, complete case analysis would also have been prone to bias,[65] as some missing data were not *missing completely at random*: for example, length of stay for revision procedures can be missing only for participants who underwent revisions and utility cannot be missing for participants known to have died in previous years. [The assumption that data are missing completely at random means that the probability of data being missing does not depend on either the values of observed data or the values of missing or unobserved data. Whereas complete case analysis assumes that data are missing completely at random, multiple imputation techniques assume that data are missing at random, i.e. that the probability that data are missing may depend on observed covariates included in the imputation model, but not on unobserved data.] Mean imputation and multiple imputation were used to ensure

complete data for all participants up to their date of administrative censoring.[66] IPW was then used to adjust for administrative censoring.

Mean imputation

Mean imputation was used for those variables that were not major cost drivers, had low levels of missingness and had limited data on which to base multiple imputation models (see *Appendix 3*). In particular, only 32 participants (1.4%) were transfused during their primary admission, 7 of whom had missing data on the number of units transfused; similarly, of the 324 readmissions, only 40 readmissions had missing component codes and 4 were missing length of stay. Imputing these variables using multiple imputation would have increased the complexity of the analysis and is unlikely to have provided stable estimates: particularly for components used in participants' second or subsequent readmission, for which very few data are available. For these variables, we therefore calculated the mean price or number of units across all participants who used such a component and applied this conditional mean to those with missing data. By assuming that all participants with missing data incurred exactly the same component cost, this method slightly underestimates the uncertainty around the mean, although this is unlikely to have affected the results significantly, as these resources are not major cost drivers.

Multiple imputation

Multiple imputation was used to impute all other missing data and propagate the uncertainty around imputed values through the analysis. Multiple imputation predicts missing values by iteratively estimating regression models on observed and imputed data.[66] This enabled missing data on specific resource items or EQ-5D utility measurements to be imputed based on participants' baseline characteristics and treatment allocation, other utility measurements and the quantities of other resources that they required, allowing for the correlations observed between these variables for other participants. Multiple imputation was conducted using the imputation using chained equations (ice) command (version 1.3.0) within Stata 12.0.[67–69] Default options within ice were used unless otherwise stated, which included running 10 cycles or iterations. Imputation was performed on the entire trial data set (excluding postrandomisation exclusions and participants randomised to total vs. unicompartmental knee replacement); imputation was run simultaneously on all three randomised comparisons in order to maximise the amount of data available to impute missing data and to ensure that all analyses used the same imputation model.

In line with current recommendations,[66] treatment indicators, demographic variables and cost components without missing data were included in the imputation function in addition to those variables with missing data to avoid bias and produce more accurate imputed values. *Appendix 3* gives the full list of variables included in multiple imputation and the imputation models used. Treatment allocation was coded using six dummies (patellar resurfacing, no patellar resurfacing, all polyethylene, metal-backed, mobile bearing and fixed bearing), which were equal to one if the participant was randomised to that treatment arm and zero if they were randomised to the other arm in that comparison or not included in that randomised comparison. This coding matched the way in which the partial factorial design was analysed. Conditional imputation was used to allow for mortality, ensuring that only participants alive at the start of that year were included in models to impute missing EQ-5D utilities and consultation counts. Year 11 data were included in the imputation model to improve predictions of utilities and resource use in earlier years and to facilitate sensitivity analyses using a longer time horizon. However, as year 12 data were available for only 78 living participants, year 12 variables were omitted from multiple imputation analyses to simplify the imputation function.

It is generally recommended that the number of imputations run is at least equal to the percentage of participants with missing data for at least one variable.[66] After conditional mean imputation was applied, 63% (1414/2252) of participants included in the analysis had some items of missing data before administrative censoring or 10 years (whichever was earlier). We therefore generated 100 imputed data sets to ensure that subsequent analyses give a reliable and replicable estimate of the posterior distribution around missing values. All analyses were repeated for each imputed data set and results combined using Rubin's rule.[66]

Multiple imputation was used to impute data for participants lost to follow-up or who declined further follow-up[70] as well as data from non-returned questionnaires or item non-response, as such data may not be missing completely at random, with dropouts potentially accruing higher costs and/or worse quality of life. Utilities and resource use after administrative censoring were imputed using multiple imputation to facilitate imputation of early observations; however, data imputed after administrative censoring were not used in the base-case analysis.

Adjustment for administrative censoring

Readmissions were identified from the participant annual form and from monitoring of routine admissions data via HES in England and ISD in Scotland. Readmission data from HES were available up to 31 March 2011 for participants living in England and data from ISD (for participants living in Scotland) were available up to 31 December 2010. It was assumed that HES, ISD and the participant annual form provided data on all readmissions related to the study knee that occurred before administrative censoring, including those in participants' last year of life and of participants who declined further follow-up or could not be contacted. This assumption is likely to be reasonable, as all participants consented to collection of readmission data from HES and/or ISD. Analysis of data up to year 5 suggested that HES/ISD picked up 82% of readmissions identified from participants' annual forms, whereas participants' forms identified 85% of readmissions identified through HES/ISD.[71]

However, no data are available for any participant after administrative censoring. Participants were considered to be administratively censored from the year when their last annual questionnaire was received or from the last annual follow-up point when both routine mortality data and HES/ISD data on readmissions were available (if this date was later than the participant's last questionnaire). Participants who died during the period for which HES and ISD data were available were considered not administratively censored. For example, a participant undergoing TKR on 1 December 2001 who completed annual questionnaires every year before the database was closed on 8 June 2012 would be censored at 10 years (the time the last annual questionnaire was completed, which is later than the latest available HES data, which ran up to 31 March 2011) and would contribute 10 years of complete data to the analysis. However, a participant with the same operation date who did not return questionnaires in years 9 and 10 would be considered to have been censored at 9 years (the last annual follow-up that occurred during the period up to 31 March 2011 for which HES data were available); missing data on quality of life and ambulatory care for this participant in year 9 would be imputed using multiple imputation.

Although all participants consented to routine data on mortality being obtained from the ONS at the time of randomisation, in June 2006, it became necessary to obtain additional consent for all participants in Scotland to conduct routine mortality monitoring through the NHS Information Centre. Of the 527 Scottish participants alive on 8 June 2006, 74 declined consent or were already lost to follow-up. Excluding 18 participants for whom death dates were available from other sources (e.g. annual questionnaires returned by relatives) and 20 participants who returned questionnaires in the last year for which HES/ISD data were available, 36 participants have unknown vital status. These participants were considered to have been administratively censored at the time when they last returned a questionnaire or had a recorded admission, or at their last annual follow-up before 8 June 2006 (whichever was later).

Although administrative censoring is likely to be non-informative and the average follow-up time did not differ significantly between randomised comparisons, small differences in follow-up time could affect estimates of cumulative costs and QALYs. In line with current guidelines,[72] we therefore adjusted for censoring using IPW,[73,74] using the methods described below. The effect of adjusting for administrative censoring was evaluated in sensitivity analyses, which took a 9-year time horizon (using uncensored data for 93% of participants), took a within-trial time horizon (using all data available for each participant and making no adjustment for administrative censoring) or used multiple imputation estimates of utility and resource use after administrative censoring.

Statistical analysis, calculation of cost-effectiveness ratios and allowance for uncertainty

Although KAT is partially factorial, each randomised comparison was analysed separately, in line with clinical analyses. As a result, each comparison was assumed to address independent questions about separable aspects of knee replacement. In line with the clinical analysis (see *Statistical analyses of clinical end points*) and the study protocol (see *Appendix 1*), it was also assumed that there was no interaction between the different comparisons and that treatment effects were additive. The analysis, therefore, assumed that the cost-effectiveness of patellar resurfacing compared with no resurfacing was not affected by whether the tibial component was mobile versus fixed, or all polyethylene versus metal-backed, and that the decision about whether or not to resurface the patella was not affected by decisions about tibial component design. Interactions were not assessed in the base-case analysis, as the study is not powered to detect interactions and 85% of participants were randomised to only one comparison. However, a secondary regression analysis investigated interactions between randomised comparisons for the two subsets of participants randomised to two comparisons.

Following imputation of missing data on resource use, component prices and utilities, QALYs were calculated as the area under the utility profile and quantities of each type of resource were multiplied by unit costs to give the total QALYs and costs accrued by each trial participant in each of the 100 imputed data sets. Costs and QALYs accrued beyond year 1 were discounted at a rate of 3.5% per annum.[50]

Imbalances in baseline utility have been shown to introduce substantial bias into unadjusted economic evaluations, as baseline utility is directly included in QALY calculations and normally strongly predicts on-treatment utility.[75] We therefore adjusted for differences in baseline utility by estimating the number of QALYs accrued in each year using ordinary least squares (OLS) regression, controlling for baseline utility and treatment allocation and generating predictions for each study arm based on the mean baseline utility across both arms.

Total costs, resource use and QALYs across the 10-year time horizon were calculated using IPW[73,74] to allow for administrative censoring and differences in follow-up time among participants. To implement IPW, OLS regression estimates of the average costs and QALYs accrued in each study arm in each year across uncensored participants were multiplied by the number of participants who were alive and not administratively censored at that time point. Dates of censoring for each participant were identified as described above. Total costs and QALYs were divided by the Kaplan–Meier estimate of the probability of being administratively censored by that time point and then divided by the number of participants included in the analysis. Weighted costs and QALYs were summed across all time periods to give total costs.

Uncertainty around resource use, costs, QALYs and incremental cost-effectiveness ratios (ICERs) was quantified using bootstrapping. Bootstrapping was conducted separately for each randomised comparison (excluding participants not randomised to that comparison) and bootstrapping on each comparison was repeated for each of the 100 imputed data sets. For imputed data set m, bootstrapping[76] was used to sample participants with replacement from the trial data set; OLS regression was used to predict resource use, costs and QALYs in each year on that bootstrap replicate and the results of such regression analyses were combined in IPW with Kaplan–Meier estimates of the probability of being censored at each year in that bootstrap replicate. This procedure was repeated on 100 bootstrap replicates drawn (with replacement) from each of the 100 imputed data sets. The standard errors (SEs) around IPW estimates of total costs and QALYs for each imputed data set were calculated as the standard deviation across the 100 bootstrap replicates; results were combined across all imputed data sets using Rubin's rule to calculate SEs, CIs and *p*-values around resource use, costs and QALYs.[66]

Results are presented as mean ± SE for each group and mean ± 95% CI for between-group differences, with costs in pounds sterling at 2011 prices. The empirical distributions of 10,000 bootstrap estimates of incremental costs and QALYs for each comparison were plotted as scatter graphs on the cost-effectiveness plane. The net benefit method[77,78] was also used to estimate cost-effectiveness acceptability curves,[79,80]

which plotted the probability that each type of prosthesis refinement was cost-effective compared with its comparator against the ceiling ratio. The ceiling ratio represents the amount the NHS is assumed to be willing or able to pay per QALY gained. As the distributions of costs and QALYs for all three comparisons span all four quadrants of the cost-effectiveness plane, the 95% CIs around the ICERs are not defined and range from dominant to dominated. As a result, no 95% CIs are shown for ICERs.

Conclusions were based on the assumption that the NHS is willing to pay £20,000 per QALY gained, based on published social value judgements.[81] Prosthesis refinements generating more QALYs than their comparator were inferred to be cost-effective compared with their comparator if they cost < £20,000 per QALY gained, whereas less effective refinements were inferred to be cost-effective if they saved > £20,000 per QALY forgone compared with their comparator. We assumed that the NHS has symmetrical preferences with respect to losses and gains, as savings from one intervention will fund the cost of others within the largely fixed NHS budget and to ensure that conclusions are not affected by which treatment is designated the comparator.

Sensitivity and subgroup analyses

In total, 18 sensitivity analyses were conducted to relax the assumptions used in the base-case analysis and explore the effect of using alternative methodologies:

- Complete case analysis: excluding all participants with missing data on any component of QALYs or resource use before death or administrative censoring. To ensure complete data on costs and QALYs in participants' last year of life, EQ-5D utility at time of death was assumed to be equal to participants' last observed EQ-5D utility measurement and the number of ambulatory consultations attended in participants' last year of life was assumed to be equal to the number of consultations attended in the previous year, multiplied by the fraction of the year for which the participant was alive.
- Per-protocol analysis: excluding all participants who did not receive the procedure to which they were randomly allocated, or for whom it was unclear whether they had received the allocated procedure.
- Length of stay reduced by 46% for all primary KAT procedures to reflect the fact that mean length of stay for TKR is now 5.3 days,[82] compared with 10.0 days among KAT participants.
- 0% price discount applied to component prices (such that all component prices are based on list prices).
- 50% price discount applied to component prices.
- Varying cost per bed-day by ± 50% to reflect uncertainty around costs.
- Varying cost per minute of theatre time by ± 50% to reflect uncertainty around costs and the possibility of double-counting of knee components, which were (to a small degree) included in the cost of theatre time by aggregation of costs over all orthopaedic procedures.
- Alternative discount rates allowing for time preference [0% and 5% for both costs and QALYs and using differential discounting (0% for QALYs and 3.5% for costs)].
- No adjustment for baseline utilities.
- Within-trial time horizon: including all data collected before administrative censoring and making no adjustment for administrative censoring.
- 8-year time horizon.
- 9-year time horizon.
- 11-year time horizon.
- Using multiple imputation to adjust for administrative censoring, rather than IPW. This analysis used the multiple imputation estimates of utilities and resource use after administrative censoring that were excluded from the base-case analysis. For simplicity, this analysis assumed that no participants were readmitted after administrative censoring. Mean imputation was used to impute dates of death for participants who were administratively censored before year 10, assuming that the interval between censoring and death equalled their remaining life expectancy at the time of censoring (obtained from Government Actuary's Department estimates for age, sex and country of residence).[83]
- Participants receiving a femoral component with a patellofemoral joint that is shaped to accommodate an anatomic patella (conducted only for the patella comparison).

- Participants receiving a femoral component with a patellofemoral joint that is shaped to accommodate a domed patella (conducted only for the patella comparison).

All sensitivity analyses were based on 10,000 bootstrap replicates. Complete case analysis and per-protocol analyses were based on separate runs of bootstrapping, whereas all other sensitivity analyses were estimated from the raw data generated in the base-case bootstrapping analysis.

The partial factorial design permitted participants recruited to the patellar resurfacing versus no resurfacing comparison to also be randomised to either mobile versus fixed bearing or all-polyethylene versus metal-backed tibial components. In total, 338 participants were randomised in more than one comparison, 193 of whom were in the mobile versus fixed bearing comparison and 145 in the all-polyethylene versus metal-backed comparison. Although the base-case analysis assumed no interactions between randomised comparisons, interactions were evaluated in sensitivity analyses run on the subset of participants who were randomised to more than one comparison to evaluate whether interactions exist and (if so) what impact this has on the study conclusions. Linear regression was used to estimate the magnitude and statistical significance of interactions between patellar resurfacing and mobile versus fixed bearing and (separately) between patellar resurfacing and all-polyethylene versus metal-backed tibial components. OLS regression was used to predict the total annual cost and total annual QALYs as a function of the main effects for each comparison and an interaction term. For example, the explanatory variables within the analysis of mobile versus fixed bearing comprised a dummy indicating whether or not participants were randomised to patellar resurfacing, a dummy indicating whether or not participants were randomised to mobile bearing and an interaction term (the product of the other two dummies). Baseline EQ-5D utility was included as an additional predictor of annual QALYs. Regression analyses were repeated on 100 bootstrap replicates on each of the 100 imputed data sets, and predicted annual QALYs and annual costs for each treatment arm were adjusted for censoring using IPW and summed to give total costs and total QALYs over the first 10 years after TKR. As a secondary evaluation of interactions, subgroup analyses were conducted to estimate the costs and QALYs for each comparison on the subset of participants randomised to patellar resurfacing and on the subset randomised no patellar resurfacing. Both sets of analyses should be interpreted with caution, as they are based on small participant numbers.

Six post-hoc subgroup analyses were also conducted to explore whether or not differences between randomised comparisons varied between participant subgroups:

- participants < 70 years of age
- participants aged ≥ 70 years
- participants also randomised to patellar resurfacing (conducted only for the metal-backed and mobile bearing comparisons)
- participants also randomised to have no patellar resurfacing (conducted only for the metal-backed and mobile bearing comparisons).

Although no subgroups other than randomised patella allocation were prespecified in the protocol, there are strong a priori reasons to expect costs and/or outcomes of the KAT comparisons to differ by age and patellofemoral joint shape. In particular, age is currently an important factor taken into account in surgeons' decisions about which component type to use, as it predicts whether or not participants are likely to out-live their prosthesis. In particular, all-polyethylene tibial components are often used on cost grounds in older participants, who are unlikely to out-live the prosthesis. In the absence of prior data to inform the cut-off, the sample was divided into two approximately equal halves. Similarly, the shape of the patella button (anatomical or domed) may affect the cost and/or efficacy of patellar resurfacing. As patella buttons are usually matched to the patellofemoral groove in the femoral component (which is used regardless of whether the participant had patellar resurfacing), we therefore subgrouped by groove shape in the patella comparison.

Organisational set-up

Funding for the trial

The trial was funded by the National Institute for Health Research (NIHR) HTA programme (project number 95/10/01). Additional industry funding for research support in clinical centres was provided by the following: Howmedica Osteonics (Newbury, UK); Zimmer (Swindon, UK); J&J DePuy (Leeds, UK); Corin Medical (Cirencester, UK); Smith & Nephew Healthcare Ltd (Cambridge, UK); Biomet Merck Ltd (Bridgend, UK); and Wright Cremascoli (Woking, UK).

The project management group

The trial was overseen by a project management group (see *Appendix 4* for membership). This group met at variable intervals, typically 4-monthly, usually by teleconference, through the course of the study.

The data monitoring committee

Accumulating trial data were periodically reviewed by a data monitoring committee, independent of the trial organisers (see *Appendix 4* for membership). The committee had three members: a statistician with experience of monitoring accumulating RCT data (who also acted as chairperson); an orthopaedic surgeon who was not involved in the trial; and a clinician with experience of RCTs.

The committee met four times between February 2002 and March 2005 at approximately yearly intervals, as decided by the committee. The committee's terms of reference were guided by the Peto approach to data monitoring in RCTs (see protocol in *Appendix 1*). Using this to recommend a change in the protocol (such as stopping recruitment in one or all elements) requires both (1) proof beyond reasonable doubt that for all or some types of participants one particular type of prosthesis is clearly indicated or contraindicated (often taken as three SEs difference in the primary outcome) and (2) evidence that might reasonably be expected to influence materially the care of people who require knee replacement by clinicians who know the results of this and comparable trials. On each occasion, the committee recommended continuation of the trial with no change of protocol. All other people, including the project management group, clinical collaborators and trial staff (except those who supplied the confidential analyses), remained ignorant of the interim results considered by the committee. The committee stood down once the initial trial results up to 2 years after surgery were analysed.

Participating centres

In total, 116 surgeons in 34 centres in the UK participated in KAT (*Table 2*).

Numbers recruited to each comparison

From July 1999 to January 2003, 4070 potentially eligible participants were identified and 2374 (58%) gave their consent and were randomised (*Figure 2*). The main reasons for non-randomisation were the participant's refusal to take part in the trial (546; 32%); the surgeon not wanting the participant to be randomised (462; 27%); a missed opportunity to recruit a scheduled participant (351; 21%); cancellation or deferral of the surgery or non-attendance on the part of the participant (84; 5%); the surgeon undertaking the procedure not being registered to participate in the trial (38; 2%); unavailability of necessary equipment (24; 1%); and unknown reasons (45; 3%). Subsequently, 22 participants were found to have been randomised in error: 14 were randomised twice, 3 were not eligible, 3 were treated by surgeons who were not registered to participate in the comparison and 2 were excluded for other reasons. This left 2352 participants formally in the trial: 1715 were included in the comparison assessing the patellar resurfacing; 539 in the comparison assessing the mobile bearing; 409 in the comparison assessing the metal backing; and 34 in the comparison assessing total versus unicompartmental knee replacement. There were 345 participants randomised in more than one comparison (see *Figure 1*). Separate CONSORT diagrams are presented for each comparison in the individual comparison chapters (see *Chapters 3–6*).

TABLE 2 Participating centres

Centre	Patellar resurfacing	Mobile bearing	All polyethylene	Unicompartmental	Participants recruited
Aberdeen	Yes	No	No	No	130
Barnstaple	Yes	No	No	No	85
Basildon	Yes	Yes	No	No	68
Birmingham	No	Yes	No	No	19
Bournemouth	Yes	No	No	Yes	122
Bury	Yes	No	No	No	24
Chester	Yes	No	Yes	No	122
Dundee	Yes	Yes	No	No	146
Exeter	Yes	No	No	No	198
Glasgow	Yes	Yes	No	No	63
Gloucester	Yes	No	No	No	19
Grimsby	Yes	No	Yes	No	21
Hairmyres	Yes	No	No	No	60
Halifax	No	Yes	No	No	72
Hartlepool	Yes	No	Yes	No	40
High Wycombe	Yes	No	No	No	8
Hull	Yes	No	No	No	36
Huntington	Yes	No	No	No	6
Leeds (Leeds General Infirmary)	No	No	Yes	No	69
Leeds (St James's University Hospital)	No	No	Yes	No	94
Liverpool	No	Yes	Yes	No	18
Macclesfield	Yes	No	No	Yes	19
Middlesbrough	Yes	Yes	No	Yes	41
Oxford	Yes	Yes	No	Yes	198
Perth	Yes	No	No	No	56
Redditch	Yes	Yes	No	No	46
Scunthorpe	Yes	Yes	No	No	69
Sidcup	Yes	No	No	No	52
Stracathro	Yes	Yes	Yes	No	140
Swansea	Yes	Yes	No	No	41
Swindon	Yes	No	No	No	73
Whiston	No	Yes	No	No	28
Wirral	No	No	Yes	No	87
Worcester	Yes	Yes	No	Yes	82

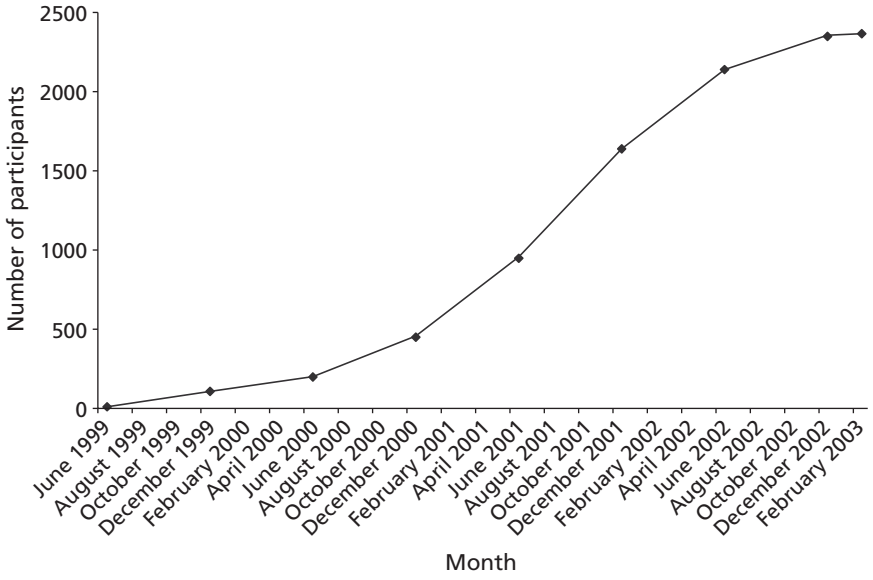

FIGURE 2 Recruitment graph.

Chapter 3 Patellar resurfacing versus no patellar resurfacing

Description of the groups at trial entry

Of the 2352 participants randomised, 1715 were recruited to the comparison assessing patellar resurfacing.

The two randomised groups were well matched at baseline (*Table 3*). In both groups the mean age was 70 years. In the patellar resurfacing group, 45% were male and in the non-resurfacing 44%. In both groups the mean body mass index (BMI) was 30 kg/m^2, and 96% of both groups had osteoarthritis. Participants were also well matched on the American Society of Anesthesiologists (ASA) classification system and previous knee surgery.

Surgical management

In total, 116 surgeons in 34 centres in the UK participated in KAT, 99 (85%) of whom recruited participants to the patellar resurfacing comparison. Of the 1715 randomised in this comparison, 1420 (83%) received the allocated procedure; 42 were subsequently withdrawn and received no surgery; 2 participants died prior to surgery; 8 received a unicompartmental replacement, which was not evaluated within this comparison; and for 21 the procedure received was unknown (*Figure 3*). The remainder, for various reasons, either had the patellar resurfaced when they were allocated to non-resurfacing (11%, 93 of 854) or, conversely, did not have a resurfacing when allocated to resurfacing (15%, 129 of 861). The most common reasons for non-compliance were clinical decision at time of operation or logistical constraint such as prostheses being unavailable at time of operation.

In-hospital care and short-term complications

Information on intra- and postoperative complications was returned for 1634 (99%) operations. Intraoperative complications were observed in only a small percentage of the participants (2.1%; 35 of 1634), and the operative procedure caused problems in few participants (0.9%; 15 of 1634). Overall, there were no differences between the randomised groups in these respects. Postoperative complications were reported in 15.1% (248) of 1638 participants; however, specific problems, such as wound infection, septicaemia, DVT or PE, cerebrovascular accident, and myocardial infarction, were rare (*Table 4*). Overall, 2.0% (33) of 1638 participants had additional knee surgery.

Four had knee dislocations. One participant allocated to be treated with both patellar resurfacing and a fixed-bearing prosthesis, but who actually received a mobile-bearing prosthesis, required closed reduction of the joint because of dislocation of the rotating insert 4 days after the initial operation. The participant had another dislocation 2 weeks later and was readmitted for revision of the spacer and femoral component. One participant, allocated to the patellar resurfacing group but who crossed over to the no-resurfacing group, had a subluxation of the bearing and required a reoperation for replacement of the platform insert. The remaining two participants who had dislocations (one allocated to both the no-patellar-resurfacing group and the mobile bearing group and the other allocated to the no-patellar-resurfacing group only) required manipulation under anaesthesia. Six participants died in the intermediate postoperative period: two died from a PE; one from a myocardial infarction; one from ischemic heart disease; one from pneumonia; and one from a cerebrovascular accident. Overall, 94.7% (1551) of 1638 participants were discharged directly to their home. The median length of hospital stay was 9 days. There were no differences between the randomised groups with regard to any of the above factors.

TABLE 3 Description of groups at trial entry for patella comparison

Characteristic	Patellar resurfacing (*n* = 861)		No patellar resurfacing (*n* = 854)	
Age (years) (mean, SD)	70	8	70	8
Female	474	55.1	481	56.3
BMI (kg/m^2) (mean, SD)	29.5	5.5	29.8	5.2
ASA classification				
Completely fit and healthy	153	17.8	143	16.7
Some illness but has no affect on normal activity	500	58.1	497	57.7
Symptomatic illness present but minimal restriction	144	16.7	136	15.8
Symptomatic illness causing severe restriction	5	0.6	5	0.6
Missing	59	6.9	73	8.5
Primary type of knee arthritis				
Osteoarthritis	800	92.9	789	92.4
Rheumatoid	29	3.4	37	4.3
Both	2	0.2	1	0.1
Missing	30	3.5	27	3.1
Extent of knee arthritis affecting mobility				
One knee	225	26.1	229	26.8
Both knees	366	42.5	342	40.0
General	270	31.4	283	33.1
	n = *831*		**n = *820***	
Other conditions affecting mobility	101	12.2	127	15.5
Medical	61	7.3	66	8.0
Locomotor/musculoskeletal	55	6.6	78	9.5
	n = *829*		**n = *824***	
Previous knee surgery	281	33.9	268	32.5
Ipsilateral osteotomy	11	1.3	13	1.6
Ipsilateral patellectomy	0	0.0	0	0.0
Contralateral previous knee replacement	112	13.5	94	11.4
Other previous knee surgery	167	20.1	172	20.9
Arthroscopy	146	17.6	150	18.2
Other related surgery	26	3.1	23	2.8

ASA, American Society of Anesthesiologists; SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

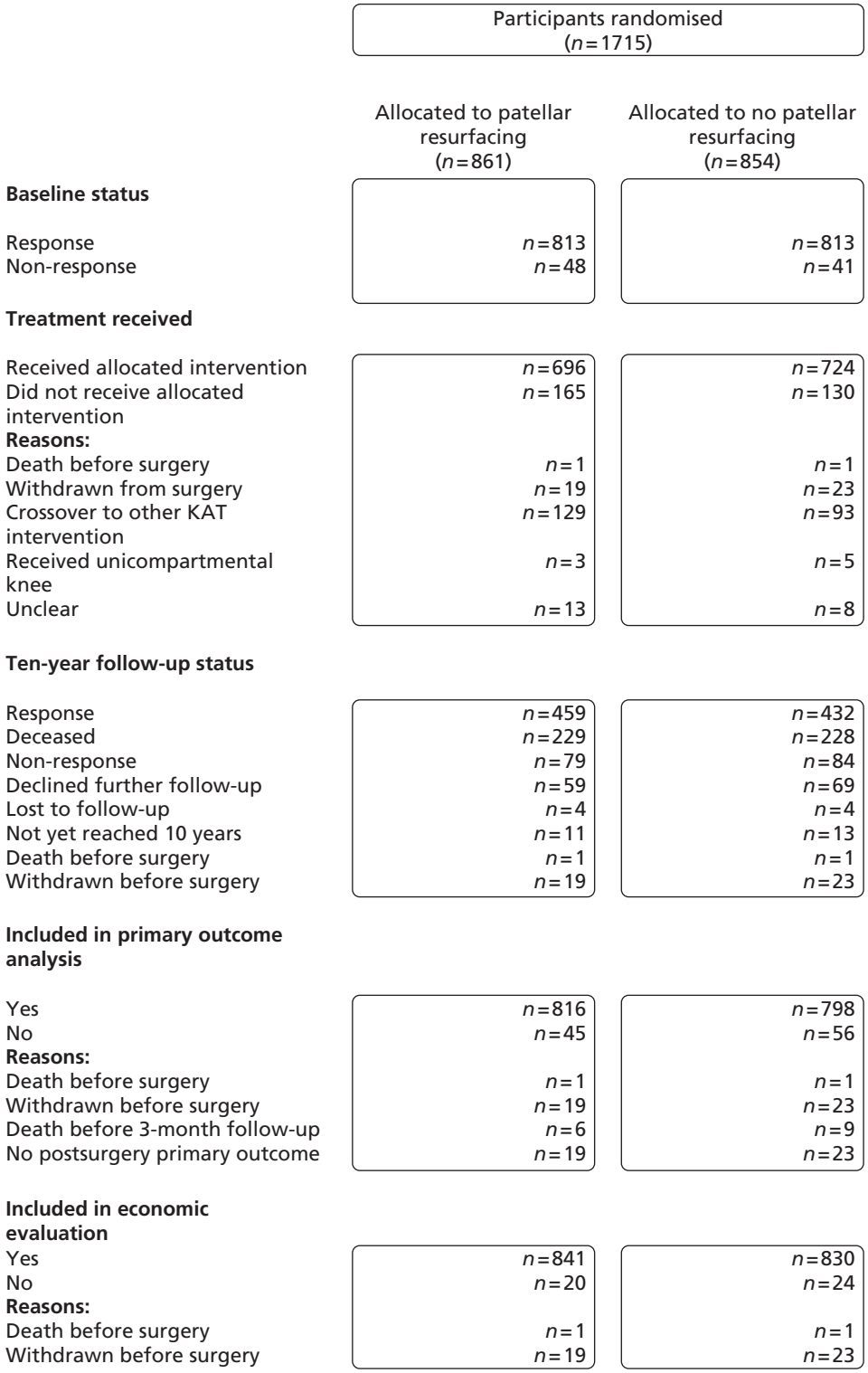

FIGURE 3 CONSORT diagram for patella comparison.

TABLE 4 In-hospital care and short-term complications for patella comparison

Variable	Patellar resurfacing (*n* = 825)		No patellar resurfacing (*n* = 813)	
Any postoperative complications	127	15.4	121	14.9
Knee dislocation	2	0.2	2	0.2
Proven wound infection	10	1.2	9	1.1
Septicaemia	1	0.1	1	0.1
Treated DVT or PE	21	2.5	22	2.7
Confirmed cerebrovascular accident	1	0.1	0	0.0
Confirmed myocardial infarction	6	0.7	2	0.2
Other serious complication	94	11.4	91	11.2
Medical complications	54	6.5	44	5.4
Surgical complications	12	1.5	18	2.2
Fall	0	0.0	2	0.2
Suspicion of infection	7	0.8	9	1.1
Confirmed infection	1	0.1	1	0.1
Skin complications	8	1.0	13	1.6
Stiffness	6	0.7	4	0.5
Suspected thrombolytic complications	6	0.7	1	0.1
Urinary complications	20	2.4	14	1.7
Any additional perioperative knee surgery	14	1.7	19	2.3
Manipulation under anaesthetic	2	0.2	8	1.0
Wound problem	1	0.1	2	0.2
Stiffness	0	0.0	2	0.2
Suspicion of infection	8	1.0	7	0.9
Confirmed infection	0	0.0	0	0.0
Prosthetic complication	1	0.1	0	0.0
Other	2	0.1	0	0.0
	n = *830*		**n = *809***	
Status at discharge				
Alive	826	99.5	807	99.8
Dead	4	0.5	2	0.2
	n = *830*		**n = *809***	
Discharged to home	795	95.8	756	93.4
	n = *834*		**n = *815***	
Days in hospital				
Median, IQR	9	7–11	9	7–11
Mean, SD	10.2	5.7	9.84	4.5

IQR, interquartile range; SD, standard deviation.
Denominator for percentages is the number of responses for that variable. Cell contents are *n* and per cent unless otherwise stated.

Response rates at each follow-up point for patella comparison

Table 5 describes the response rate; the response rate to questionnaires sent was high in both groups over the whole follow-up period, ranging from 84% to 97%. The proportion of participants sent a questionnaire dropped over the life of the trial, as one would expect given a cohort of this nature, owing to death, loss to follow-up and patients declining further follow-up. At 10 years the response rate was approximately 70% of the cohort who were still living.

Outcomes after a median of 10 years post operation

Oxford Knee Score

There was no evidence of a between-group difference in OKS at baseline or any stage thereafter (*Table 6*). The mean OKS in both patellar resurfacing and non-resurfacing groups was 18 preoperatively. It increased to 35 at 1 year and thereafter remained about the same, although it did decrease slightly in the long term (*Figure 4*). The estimated adjusted difference in OKS between the two groups was 0.45 (95% CI –0.66 to 1.56) at 10 years (see *Table 6*). The marginal estimate over the whole 10-year follow-up was 0.61 (95% CI –0.23 to 1.44; $p = 0.153$), a difference in favour of the patellar resurfacing intervention, which reflects slightly, but consistently, higher values in favour of patellar resurfacing over the whole 10-year follow-up (*Figure 5*). Sensitivity analysis imputing the last value before revision gave practically identical results; the marginal estimate was 0.73 (95% CI –0.12 to 1.58; $p = 0.09$).

The distribution of the OKS at 10 years in the two groups is shown in *Figure 6*. The distributions are very similar, and in particular there are few participants with a poor outcome in either group. Question 12 of the OKS enquires about symptoms relating to stair descent. This item showed a similar pattern to the OKS, that is a small but consistent difference in favour of patellar resurfacing over the whole 10-year follow-up (*Figure 7*).

Subgroup analysis

There were two post-hoc subgroup analyses proposed for the primary outcome in this comparison: the shape of the groove in the femoral component (anatomical vs. domed) and age (< 70 vs. ≥ 70 years). The shape of the groove is described as either anatomical or domed, depending on whether it is designed to articulate with an anatomically shaped or domed-shaped patella button.

All prostheses were classified as anatomical or domed. Of the 1614 participants included in the analysis of the primary outcome, OKS, 48 (3%) could not be classified given the information recorded. The subgroup analysis was run three times: first excluding the unknowns, and then again reclassifying these 48 as anatomical, and then domed. The breakdown of shape was the same in each arm of the trial: 29% anatomical, 68% domed and 3% unclassified. *Figure 8* is a plot of the interaction term (or the difference in differences) at each time point for the anatomical shape by patellar resurfacing interaction. The estimates are about zero with 95% CIs fairly wide throughout, reflecting no evidence of a shape effect modification on the primary outcome, where a positive difference would indicate that resurfacing was more favourable if the prostheses were anatomical.

Figure 9 plots the difference in favourable effect for patellar resurfacing for those aged < 70 years, compared with those ≥ 70 years. A positive difference in differences suggests a higher relative benefit for resurfacing in the younger age group. After an early peak favouring patellar resurfacing in the younger subgroup, the difference in differences settles around zero and indicates no evidence for a treatment modification on the primary outcome OKS by age.

EuroQol 5D

There was no evidence of a between-group difference in EQ-5D at baseline or at any stage thereafter (*Table 7*). The mean EQ-5D utility was about 0.40 preoperatively. It increased to about 0.74 at 1 year and thereafter steadily decreased to about 0.66 at 10 years (*Figure 10*). At 10 years, the difference in EQ-5D

TABLE 5 Response rates at each follow-up time point

	Patellar resurfacing group							No patellar resurfacing group						
Time	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive
Month 3	787	91	92	760	97	88	89	784	92	93	759	97	89	90
Year 1	792	92	94	756	95	88	90	786	92	95	744	95	87	90
Year 2	804	93	96	716	89	83	85	776	91	96	709	91	83	87
Year 3	774	90	94	703	91	82	86	755	88	95	684	91	80	86
Year 4	741	86	93	686	93	80	86	725	85	92	675	93	79	86
Year 5	706	82	92	652	92	76	85	690	81	91	635	92	74	84
Year 6	674	78	91	608	90	71	82	665	78	91	586	88	69	80
Year 7	643	75	90	583	91	68	82	629	74	89	563	90	66	80
Year 8	611	71	89	542	89	63	79	592	69	87	523	88	61	77
Year 9	572	66	88	502	88	58	77	556	65	85	482	87	56	74
Year 10	537	62	85	459	85	53	73	515	60	82	432	84	51	69

TABLE 6 Descriptive statistics and estimated treatment effects at each follow-up time point for OKS for patella comparison

	Patellar resurfacing			No patellar resurfacing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	793	18.5	7.4	798	18.1	7.7			
3 months	661	31.2	9.6	679	30.5	9.4	0.78	–0.20 to 1.77	0.12
1 year	635	34.7	9.4	645	34.5	10.2	0.31	–0.69 to 1.30	0.55
2 years	556	35.6	9.8	589	35.2	10.2	0.51	–0.51 to 1.53	0.33
3 years	609	35.5	10.1	602	34.7	10.4	0.83	–0.18 to 1.84	0.11
4 years	610	34.9	10.7	616	34.3	10.6	0.84	–0.17 to 1.84	0.10
5 years	594	35.0	10.6	570	34.6	10.2	0.75	–0.27 to 1.77	0.15
6 years	550	35.1	10.5	534	34.9	10.3	0.28	–0.76 to 1.31	0.60
7 years	530	34.6	11.0	504	34.2	10.5	0.70	–0.35 to 1.74	0.19
8 years	495	34.0	11.0	487	34.0	10.5	0.36	–0.70 to 1.41	0.51
9 years	461	34.2	10.9	431	33.8	10.4	0.79	–0.29 to 1.88	0.15
10 years	418	33.6	11.3	380	33.5	10.8	0.45	–0.66 to 1.56	0.43

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours patellar resurfacing; *n*, the number of responses; SD, standard deviation.

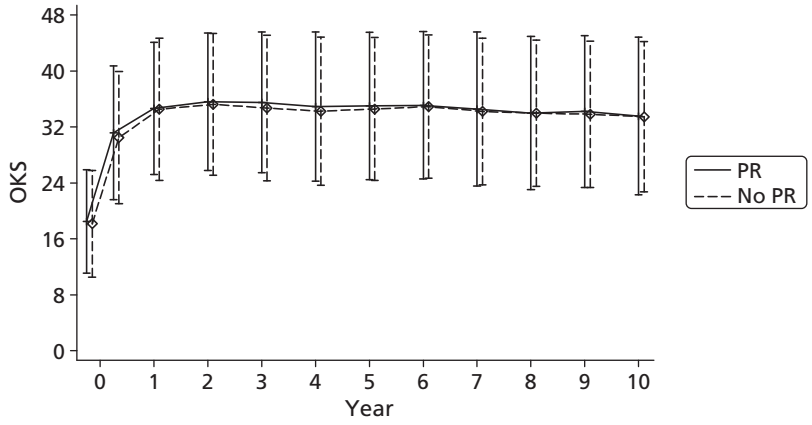

FIGURE 4 Mean (SD) OKS by group at each follow-up time point for patella comparison. PR, patellar resurfacing.

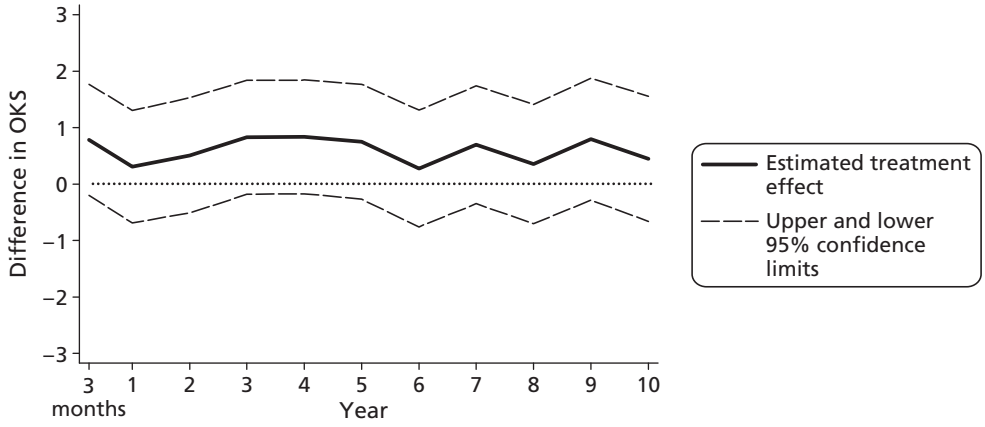

FIGURE 5 Estimated treatment effect on OKS (95% CI) at each follow-up time point for patella comparison. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

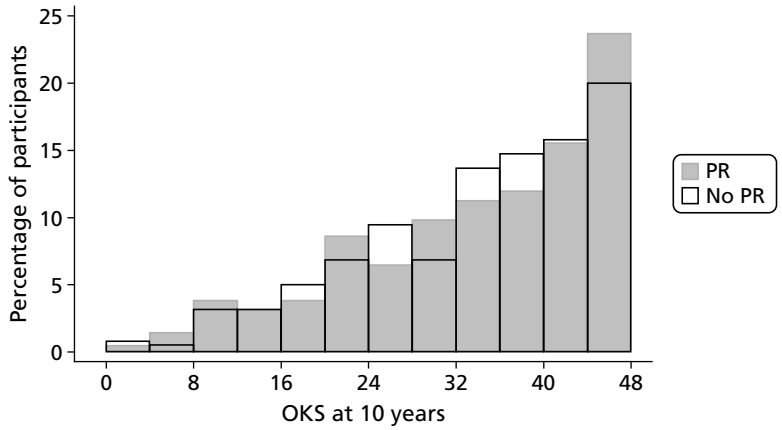

FIGURE 6 Histogram of OKS at 10 years by treatment group for patella comparison. PR, patellar resurfacing.

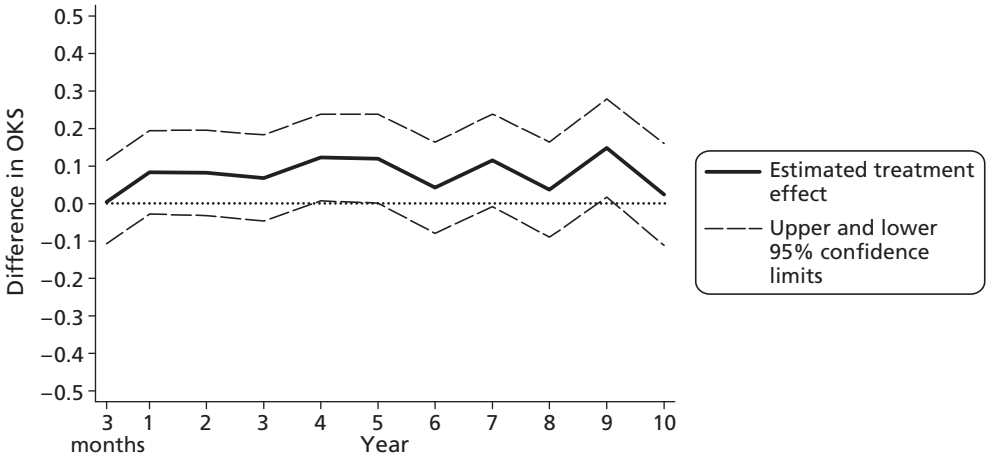

FIGURE 7 Estimated treatment effect on OKS question 12, stairs descent (95% CI), at each follow-up time point for patella comparison. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

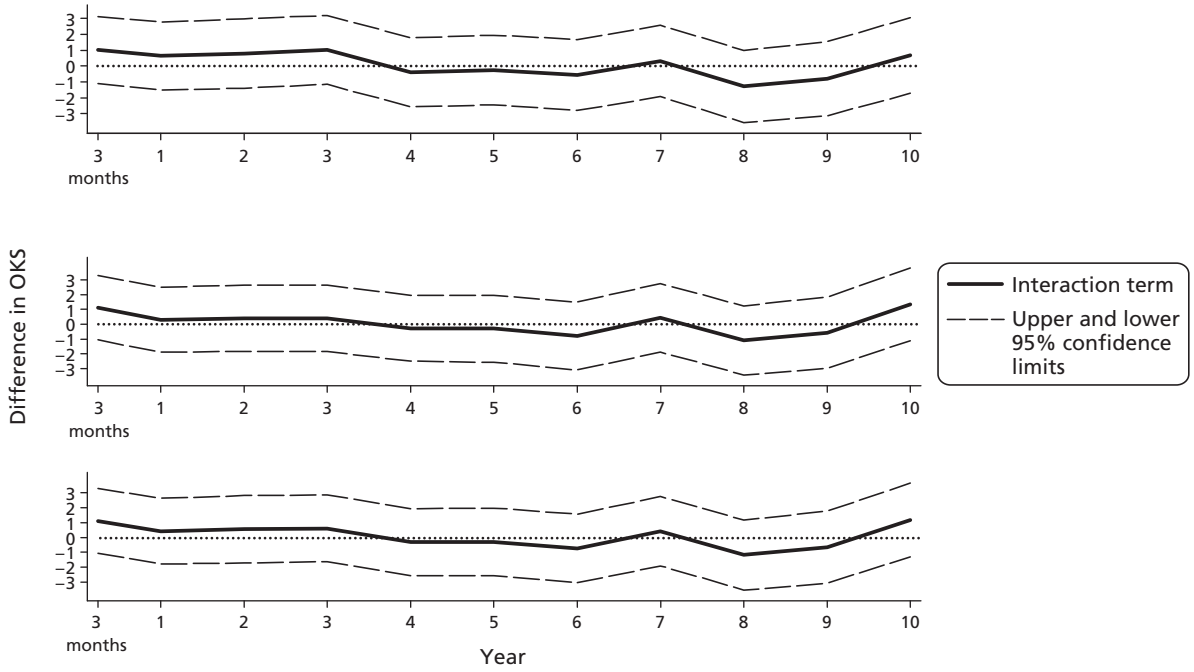

FIGURE 8 Interaction term (solid line) at each follow-up time point for OKS anatomical shape by patellar resurfacing. Dotted lines represent 95% CIs.

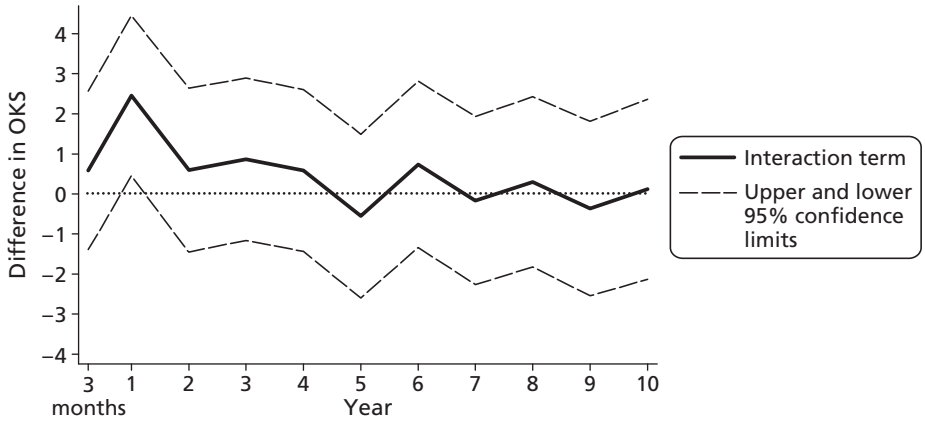

FIGURE 9 Interaction term (solid line) at each follow-up time point for OKS age < 70 years old by patellar resurfacing. Dotted lines represent 95% CIs.

TABLE 7 Descriptive statistics and estimated treatment effects at each follow-up time point for EQ-5D utility for patella comparison

	Patellar resurfacing			No patellar resurfacing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	791	0.404	0.301	807	0.389	0.309			
3 months	737	0.703	0.232	739	0.687	0.240	0.004	–0.021 to 0.029	0.75
1 year	734	0.744	0.231	725	0.732	0.253	0.003	–0.022 to 0.029	0.81
2 years	693	0.743	0.244	689	0.724	0.268	0.014	–0.011 to 0.040	0.28
3 years	679	0.733	0.254	667	0.706	0.278	0.025	–0.001 to 0.051	0.055
4 years	661	0.717	0.266	647	0.688	0.290	0.024	–0.002 to 0.050	0.070
5 years	641	0.718	0.257	611	0.701	0.266	0.016	–0.011 to 0.043	0.24
6 years	589	0.705	0.266	572	0.686	0.279	0.010	–0.017 to 0.037	0.48
7 years	573	0.695	0.284	550	0.677	0.286	0.015	–0.013 to 0.042	0.29
8 years	532	0.669	0.289	512	0.672	0.294	–0.012	–0.040 to 0.016	0.41
9 years	490	0.667	0.296	475	0.659	0.283	0.002	–0.026 to 0.031	0.87
10 years	443	0.665	0.287	424	0.647	0.302	0.012	–0.018 to 0.042	0.42

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours patellar resurfacing; *n*, the number of responses; SD, standard deviation.

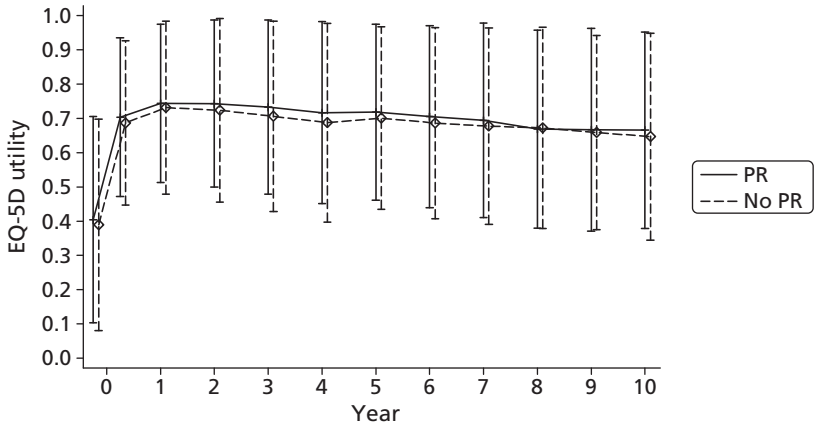

FIGURE 10 Mean (SD) EQ-5D utility by group at each follow-up time point for patella comparison. PR, patellar resurfacing.

was 0.012 (95% CI –0.018 to 0.042) (see *Table 7*). The marginal estimate over the whole 10-year follow-up was 0.011 (95% CI –0.008 to 0.030; $p = 0.27$) in favour of the patellar resurfacing intervention (*Figure 11*).

Short Form 12

There was no evidence of a between-group difference in SF-12 at baseline or at any stage thereafter. SF-12 physical component score (PCS) was 31 for both groups preoperatively (*Table 8*). It increased to 41 at 1 year and thereafter slowly decreased to 37 for both groups at 10 years (*Figure 12*). The marginal estimate over the whole 10-year follow-up was 0.40 (95% CI –0.78 to 1.57; $p = 0.51$) in favour of the patellar resurfacing intervention (*Figure 13*).

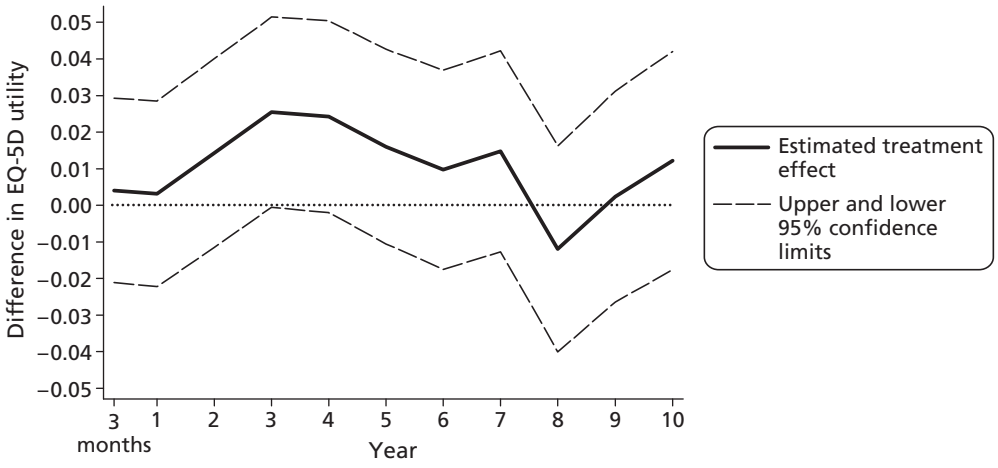

FIGURE 11 Estimated treatment effect on EQ-5D utility (95% CI) at each follow-up time point for patella comparison. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

TABLE 8 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 PCS for patella comparison

	Patellar resurfacing			No patellar resurfacing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	780	31.1	8.0	792	31.3	8.5			
3 months	719	39.4	9.4	708	38.7	9.1	0.55	–0.47 to 1.56	0.29
1 year	725	40.8	10.5	708	40.7	10.4	0.08	–0.94 to 1.09	0.88
2 years	694	40.7	11.0	675	40.8	10.4	0.02	–1.02 to 1.05	0.98
3 years	659	40.8	11.1	651	39.8	10.9	1.00	–0.05 to 2.04	0.06
4 years	652	39.7	11.4	641	39.2	10.9	0.78	–0.26 to 1.83	0.14
5 years	622	39.6	11.0	612	39.4	11.5	0.47	–0.59 to 1.53	0.39
6 years	578	39.1	11.1	554	38.7	11.4	0.52	–0.57 to 1.60	0.35
7 years	559	38.6	11.6	532	38.5	11.5	0.49	–0.61 to 1.59	0.38
8 years	518	37.6	11.2	501	38.1	11.6	–0.33	–1.45 to 0.79	0.56
9 years	478	37.6	11.3	459	37.9	11.4	0.00	–1.14 to 1.15	1.0
10 years	440	37.5	11.5	416	37.3	11.1	0.40	–0.78 to 1.57	0.51

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours patellar resurfacing; *n*, the number of responses; SD, standard deviation.

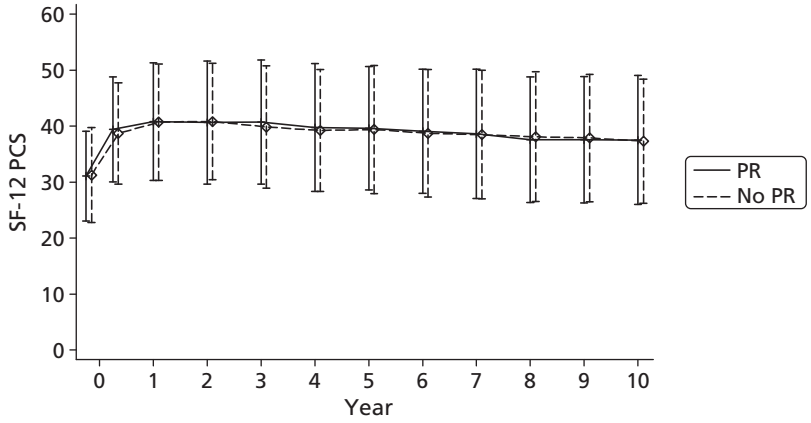

FIGURE 12 Mean (SD) SF-12 PCS by group at each follow-up time point for patella comparison.
PR, patellar resurfacing.

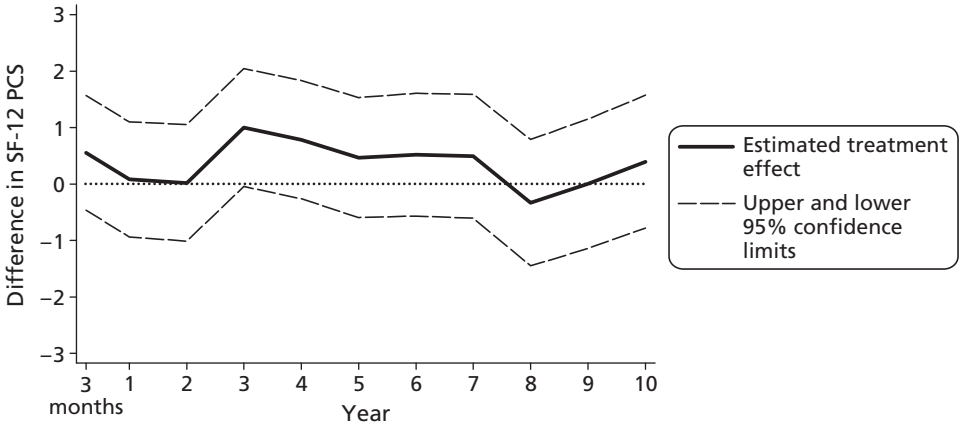

FIGURE 13 Estimated treatment effect on SF-12 PCS (95% CI) at each follow-up time point for patella comparison. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

The mean SF-12 mental component score (MCS) was about 50 for both groups preoperatively. It increased to about 52 at 1 year and then decreased slowly to 49 at 10 years (*Figure 14* and *Table 9*). The marginal estimate over the whole 10-year follow-up was 0.56 (95% CI –0.16 to 1.23; $p = 0.13$) in favour of the patellar resurfacing intervention (*Figure 15*).

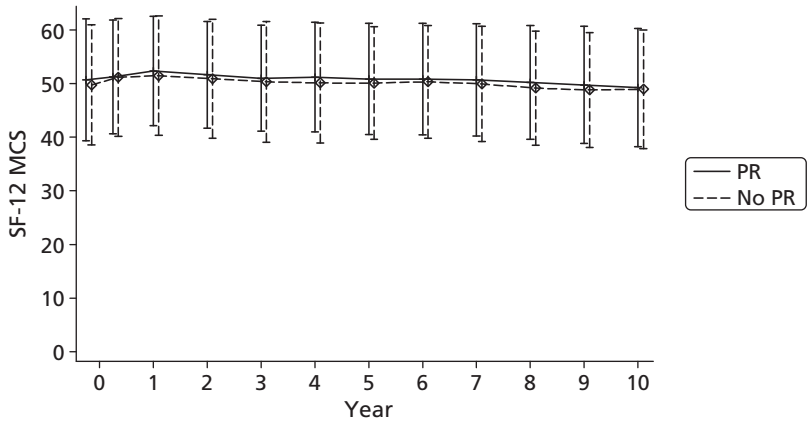

FIGURE 14 Mean (SD) SF-12 MCS by group at each follow-up time point for patella comparison.
PR, patellar resurfacing.

TABLE 9 Descriptive statistics and estimated treatment effects at each follow-up time-point for SF-12 MCS for patella comparison

	Patellar resurfacing			No-patellar resurfacing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	780	50.7	11.4	792	49.7	11.2			
3 months	719	51.2	10.6	708	51.1	11.0	–0.42	–1.41 to 0.56	0.40
1 year	725	52.3	10.2	708	51.5	11.1	0.39	–0.59 to 1.37	0.44
2 years	694	51.6	9.9	675	50.9	11.1	0.20	–0.80 to 1.20	0.70
3 years	659	51.0	9.9	651	50.3	11.3	0.30	–0.71 to 1.31	0.57
4 years	652	51.2	10.2	641	50.1	11.2	0.68	–0.34 to 1.69	0.19
5 years	622	50.8	10.4	612	50.1	10.5	0.69	–0.35 to 1.72	0.19
6 years	578	50.8	10.4	554	50.3	10.5	0.45	–0.61 to 1.51	0.41
7 years	559	50.7	10.5	532	49.9	10.7	0.84	–0.23 to 1.92	0.12
8 years	518	50.2	10.6	501	49.1	10.6	0.91	–0.19 to 2.02	0.10
9 years	478	49.7	10.9	459	48.8	10.7	0.59	–0.55 to 1.72	0.31
10 years	440	49.2	11.0	416	48.9	11.0	–0.04	–1.22 to 1.13	0.94

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours patellar resurfacing; *n*, the number of responses; SD, standard deviation.

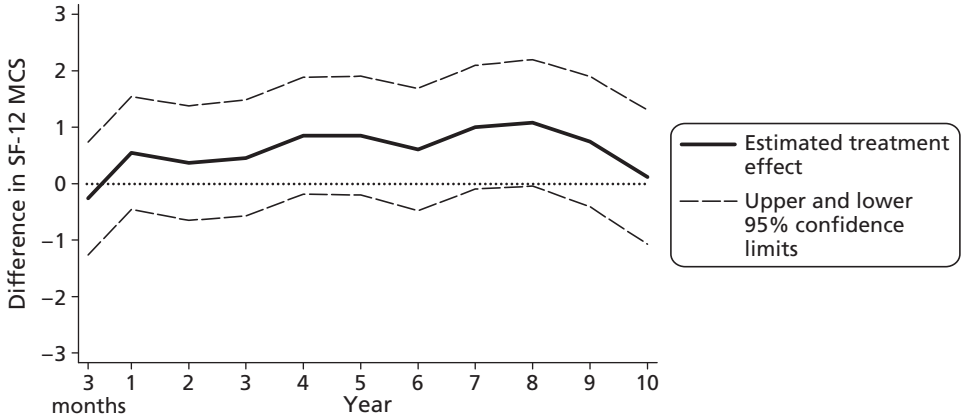

FIGURE 15 Estimated treatment effect on SF-12 MCS (95% CI) at each follow-up time point for patella comparison. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

Clinical outcomes

During the first 10 postoperative years, 15% (122/841) of the resurfaced group and 15% (128/830) of the non-resurfaced group required readmission and/or further intervention (*Table 10*; odds ratio 0.93, 95% CI 0.71 to 1.23, $p = 0.63$); 7% (58/841) of the resurfaced group and 8% (67/830) of the non-resurfaced group required further minor or intermediate operations (odds ratio 0.85, 95% CI 0.53 to 1.32, $p = 0.39$); 2% (15/841) of the resurfaced group and 2% (16/830) of the non-resurfaced group required patellar-related operations (odds ratio 0.93, 95% CI 0.46 to 1.90, $p = 0.85$); and 3% (26/841) of the resurfaced group and 5% (39/830) of the non-resurfaced group required other further major operations (odds ratio 0.65, 95% CI 0.39 to 1.10, $p = 0.11$). The reasons for further surgery included infection, pain, stiffness, loosening and instability. There was no statistically significant difference in the proportion of participants requiring further surgery in the resurfaced or non-resurfaced groups for any of the different levels of secondary intervention. The majority of the readmissions and reoperations were in the first 5 years (81%). Late patellar resurfacing

TABLE 10 Readmissions up to a median of 10 years postoperatively for patella comparison

Readmission type	Patellar resurfacing (*N* = 841)		No patellar resurfacing (*N* = 830)	
	n	%	*n*	%
Total number of procedures requiring readmission	179		209	
No. of participants requiring at least one readmission	122	15	128	15
Minor/intermediate operations				
Total number of operations	72		87	
At least one minor operation	58	7	67	8
Multiple minor operations	13	2	16	2
Number requiring at least one of				
Wound closure			1	< 1
Debridement/exploration/washout	15	2	17	2
MUA	18	2	24	
Arthrolysis and quadriceplasty	1	< 1		
Arthroscopy EUA/biopsy	6	1	11	1
Aspiration	18	2	19	2
Bone removal	2	< 1	1	< 1
Drain abscess	1	< 1		
Cement block exchange			1	< 1
Exchange of polyethylene insert	5	< 1	5	1
Removal screws plates			1	< 1
Patella-related operations				
Any patella-related operation	15	2	16	2
Number requiring at least one of				
Late patellar resurfacing	9	1	16	2
Patella fracture	2	< 1		
Patella revision	2	< 1		
Patella realignment	1	< 1		
Removal of patella button	1	< 1		
Major operations				
Any major operation	26	3	39	5
Multiple major operations	4	< 1	6	1
Number requiring at least one of				
Above-knee amputation			2	< 1
Two-stage revision	9	1	15	2
One-stage revision	19	2	25	3

EUA, examination under anaesthetic; MUA, manipulation under anaesthetic.

was carried out on 1.9% (16/830) of the non-resurfaced group and 1.1% (9/841) of the resurfaced group (odds ratio 0.55, 95% CI 0.24 to 1.26, $p = 0.16$). The reason why some resurfaced group participants had a late resurfacing was that, although they were allocated to resurfacing, they did not have resurfacing at the original operation. For reasons stated previously, 129 of the 861 (15.0%) participants allocated to resurfacing crossed over clinically and did not have the patellar resurfaced at the primary procedure. Of these 129 participants, 9 (7%) had subsequent late resurfacing of the patella. Conversely, 761 of the 854 allocated to the non-resurfaced group did not have a resurfacing at the primary operation; 16 of these 761 participants (2.1%) had late patellar resurfacing. All the 'late' patellar resurfacing procedures took place in the first 5 years. The reasons for these, when recorded, were either 'pain' or 'pain and/or stiffness'. During the second 5 years, there were six patella-related reoperations. They were all in the patella resurfaced group and they were all the result of complications of the patellar resurfacing: two were for patella fracture, two were patella revisions, one was the removal of a patella button and one was patella realignment for patella dislocation. Time-to-event analyses showed that there was no evidence of a difference between the randomised groups on time to any major reoperation or patella-related operation (hazard ratio 0.75; 95% CI 0.50 to 1.14; $p = 0.18$; *Figure 16*); time to any reoperation (hazard ratio 0.87; 95% CI 0.65 to 1.17; $p = 0.35$; *Figure 17*); or time to any reoperation or OKS dropping to below baseline levels beyond 1 year (hazard ratio 0.94; 95% CI 0.78 to 1.12; $p = 0.47$; *Figure 18*).

The OKS for those participants who had late resurfacing is shown in *Figure 19*. Prior to the resurfacing, the OKS was found to deteriorate. In the year before the late resurfacing, the mean OKS was 15.9 (standard

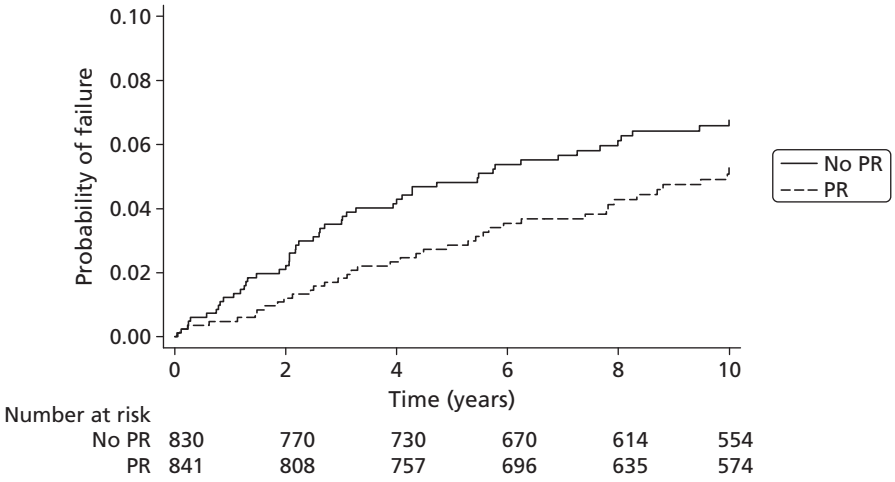

FIGURE 16 Kaplan–Meier failure curves for time to first major reoperation or patella-related operation for patella comparison. PR, patellar resurfacing.

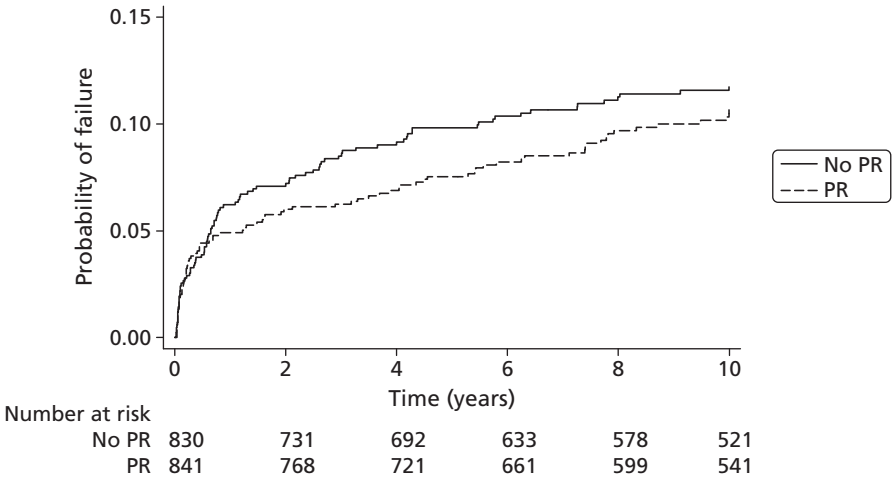

FIGURE 17 Kaplan–Meier failure curves for time to any reoperation for patella comparison. PR, patellar resurfacing.

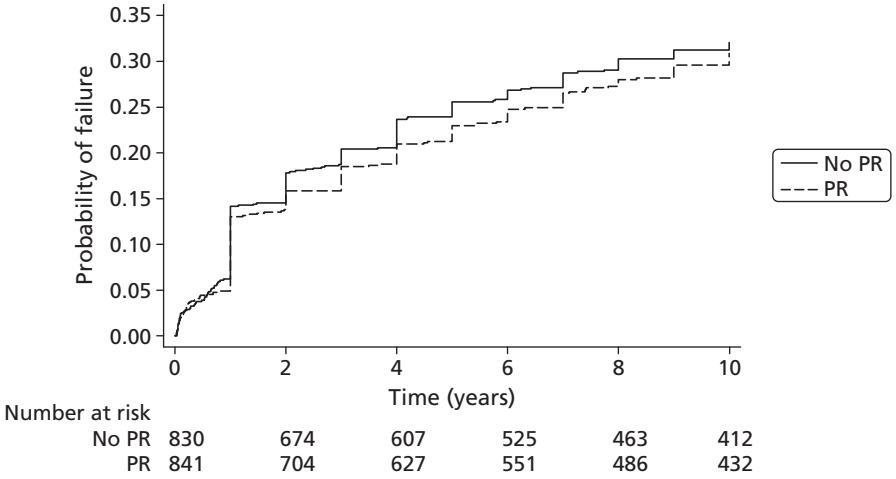

FIGURE 18 Kaplan–Meier failure curves for time to any reoperation or OKS dropping below baseline level at 1 year or later for patella comparison. PR, patellar resurfacing.

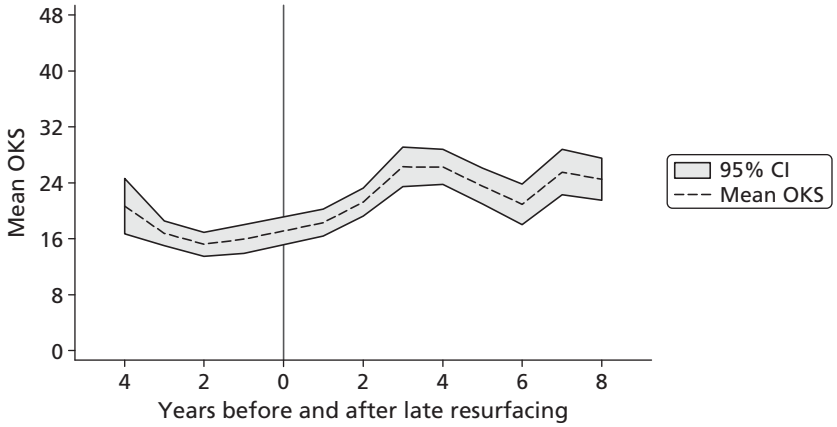

FIGURE 19 Mean (95% CI) OKS for the years pre and post late resurfacing for patella comparison.

deviation 8.9). After the procedure, OKS improved again, averaging 21.3 (standard deviation 8.9) during the second postoperative year. This was higher than before the late resurfacing, but the OKS for these patients remained considerably lower than the mean OKS for the whole trial group.

Cost comparison

The average primary TKR procedure took just over 2 hours (including time in the anaesthetic room and operating theatre, but excluding recovery), with patellar resurfacing non-significantly increasing operation time by an average of 3 minutes ($p = 0.21$; *Table 11*). The mean length of stay was 10 days in both arms, which reflects typical practice at the time when the KAT procedures were conducted, but is substantially longer than today's average of 5.3 days.[82] Peri-/postoperative complications ($p = 0.77$) and further surgery ($p = 0.60$) were equally rare in both groups.

On average, each patella component cost £116 (assuming a 30% discount off list prices). However, deviations from the allocated procedure reduced the incremental cost of patella components with patellar resurfacing versus no resurfacing to £84 per participant, which was, as expected, statistically significant ($p < 0.001$). There was no statistically significant difference in use or cost of tibial ($p = 0.46$) or other components ($p = 0.93$) (see *Table 11*).

The total cost of the inpatient stay and procedure for primary TKR was just over £7000 per participant. Although this appears to be substantially higher than the average cost of Healthcare Resource Groups (HRGs)

TABLE 11 Resource use and costs for patella comparison (all values are per participant and exclude post-randomisation exclusions)

	Allocated to patellar resurfacing ($n = 841$) [mean (SE)]		Allocated to no patellar resurfacing ($n = 830$) [mean (SE)]		Difference (95% CI)	
Resource	Number	Cost (£)	Number	Cost (£)	Number	Cost (£)
Resource use during inpatient stay for primary knee replacement						
Minutes in theatre	124.4 (1.38)	2099 (23)	121.9 (1.43)	2057 (24)	2.48 (–1.43 to 6.39)	42 (–24 to 108)
Days in hospital[a]	10.2 (0.18)	3348 (60)	10.0 (0.16)	3279 (54)	0.21 (–0.27 to 0.69)	69 (–89 to 226)
Total knee components	3.6 (0.02)	1732 (11)	2.9 (0.02)	1640 (11)	0.72 (0.66 to 0.77)[b]	91 (61 to 122)[b]
Patella components	0.8 (0.01)	97 (2)	0.1 (0.01)	13 (1)	0.72 (0.69 to 0.75)[b]	84 (80 to 89)[b]
Tibial components	1.8 (0.01)	784 (6)	1.7 (0.02)	778 (6)	0.00 (–0.04 to 0.05)	6 (–10 to 22)
Other knee components	1.0 (0.00)	851 (7)	1.0 (0.01)	850 (7)	–0.01 (–0.02 to 0.01)	1 (–19 to 20)
Peri-/postoperative complications	0.2 (0.01)	10 (2)	0.2 (0.01)	10 (2)	0.01 (–0.03 to 0.04)	0 (–6 to 6)
Further surgery occurring during hospital stay	0.0 (0.01)	24 (6)	0.0 (0.01)	24 (6)	0.00 (–0.02 to 0.01)	0 (–16 to 16)
Total cost of inpatient stay for primary knee replacement	–	7212 (68)	–	7011 (62)	–	202 (20 to 383)[b]
Resource use over first 10 years after primary knee replacement (excluding initial hospital stay)[c]						
Total hospital readmissions related to study knee	0.21 (0.02)	864 (123)[d]	0.25 (0.02)	1181 (180)[d]	–0.03 (–0.10 to 0.03)	–317 (–748 to 114)[d]
Outpatient consultations related to study knee	3.33 (0.15)	323 (14)[d]	3.32 (0.16)	322 (15)[d]	0.01 (–0.41 to 0.43)	0 (–39 to 40)[d]
Physiotherapy consultations related to study knee	6.60 (0.44)	275 (18)[d]	6.47 (0.43)	270 (17)[d]	0.13 (–1.06 to 1.32)	5 (–43 to 53)[d]
GP consultations related to study knee	3.26 (0.25)	112 (8)[d]	3.08 (0.23)	105 (8)[d]	0.19 (–0.48 to 0.86)	6 (–16 to 29)[d]
Total cost over first 10 years of study (excluding initial hospital stay)	–	1573 (141)[d]	–	1878 (198)[d]	–	–305 (–786 to 176)[d]
Total cost of primary operation and follow-up	–	8785 (161)[d]	–	8889 (211)[d]	–	–104 (–630 to 423)[d]

a Excludes the incremental cost of time spent in high-dependency unit.
b $p < 0.05$.
c Costs and resource-use quantities after discharge were estimated using IPW.
d Discounted at 3.5% per year.

HB21A-C in 2010–11 (£6080),[84] the cost in KAT would have been < £5000 if KAT participants had had similar lengths of stay to today's patients. This would suggest that today's patients have either longer operation times or more expensive brands of knee components than were used in KAT. As a result of the increased cost of patella components and non-significant trends in other cost components, the total cost of the inpatient stay was £202 higher for participants randomised to patellar resurfacing ($p = 0.029$) (see *Table 11*).

However, as discussed previously, participants randomised to no patellar resurfacing were non-significantly more likely to be readmitted for causes related to their knee replacement: for every 100 participants randomised to no patellar resurfacing, there were three additional readmissions ($p = 0.32$). Furthermore, the readmissions experienced by participants randomised to no patellar resurfacing were more costly: an average of £4815 per readmission, versus £4061 per readmission in the patellar resurfacing arm ($p = 0.23$). As a result, readmissions cost an average of £864 per participant for participants allocated to patellar resurfacing, versus £1181 for the no patellar resurfacing arm: suggesting a saving of £317 per participant allocated to patellar resurfacing ($p = 0.15$). As discussed previously, the number of readmissions is highest in the first year after TKR (with 0.115 readmissions per participant in the patellar resurfacing group and 0.127 for no patellar resurfacing) and decreases rapidly thereafter (*Figure 20*). The first year also accounted for the majority of the difference between patellar resurfacing and no resurfacing, although the incidence continued to be slightly higher until year 5, but was negligible thereafter.

The number and cost of ambulatory consultations were similar in the two groups and decreased over time (see *Figure 20*). The average participant had 1.6 orthopaedic outpatient visits, 4.8 physiotherapy consultations and 1.1 GP consultations about their knee during the first year after TKR, which declined to around 0.1 orthopaedic outpatient visits, 0.2 physiotherapy and 0.2 GP consultations per year during years 4–10. Overall, the cost of ambulatory care was £11 higher in the patellar resurfacing group, although no differences were statistically significant (minimum $p = 0.57$; see *Table 11*).

Including readmissions and ambulatory consultations, the total cost of follow-up was £1573 per patient in the patellar resurfacing group and £1878 per participant in the no resurfacing group (see *Table 11*). Readmissions accounted for 55% of the total follow-up cost in the patellar resurfacing group and 63% of that in the no patellar resurfacing group. Although the difference in follow-up cost was not statistically significant ($p = 0.21$), its magnitude more than offsets the added cost of patella components. Overall,

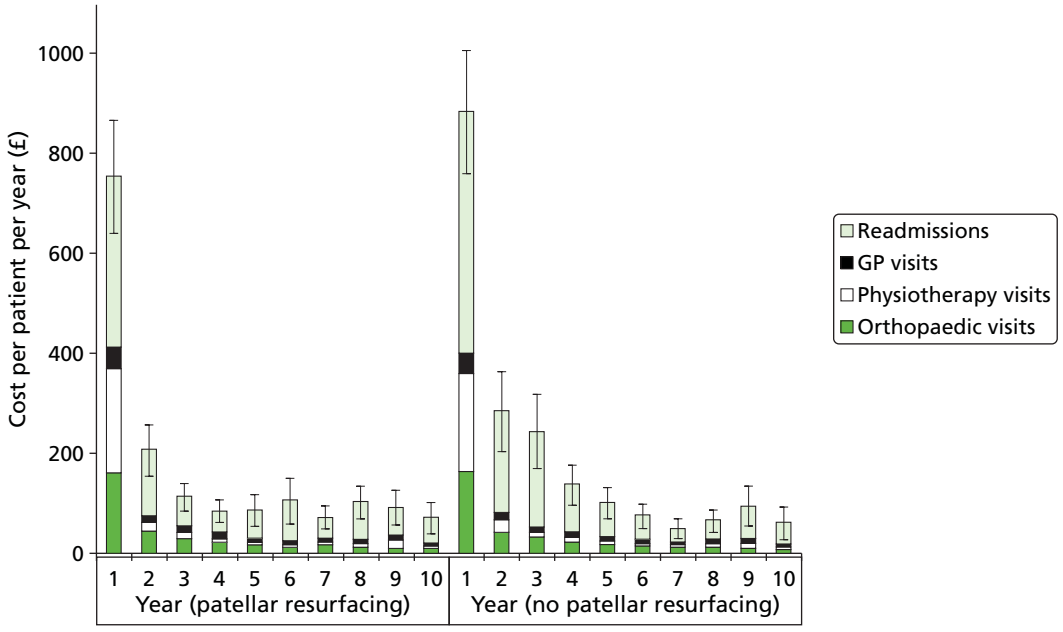

FIGURE 20 Illustration of cost breakdown by year after discharge from hospital for patella comparison. Error bars show SEs around total cost.

the total cost accrued by the patellar resurfacing group within 10 years of TKR was £104 (95% CI –£423 to £630) lower than that in the no patellar resurfacing group ($p = 0.70$).

Within-trial cost-effectiveness results

Base-case analysis

The total cost accrued in each year of the trial generally decreased over time, reflecting mortality, the decreasing probability of readmission and the falling intensity of outpatient follow-up, although some oscillations were observed in later years due to variations in the small number of readmissions each year (*Table 12*, see *Figure 20*). In the first year, participants randomised to patellar resurfacing accrued non-significantly higher costs as a result of the added cost of patella components ($p = 0.67$). However, costs were markedly, but not significantly, lower in the patellar resurfacing group in years 2 ($p = 0.42$), 3 ($p = 0.10$) and 4 ($p = 0.26$) and similar thereafter.

As discussed above, participants had a very poor quality of life at baseline, with a mean baseline utility of around 0.4. Following TKR, utility rose in both groups to around 0.69 at 3 months and 0.74 at 1 year. Quality of life was higher in the patellar resurfacing group at all time points, although differences did not reach statistical significance (all $p > 0.05$).

From EQ-5D utilities, QALYs were calculated by taking the area under the EQ-5D curve, with multiple imputation of missing data and adjustments for mortality, time preference censoring and the small imbalance in baseline EQ-5D utility. This suggested that the average participant experienced around 0.7 QALYs during each of the first 3 years after TKR (see *Table 12*). However, as the QALY metric also allows for mortality (assigning participants a utility of zero after death) and the QALYs in *Table 12* are discounted to allow for the fact that society places a lower value on benefits accrued in the future, the numbers of QALYs observed beyond year 2 decreased substantially more quickly than the mean EQ-5D utility.

The patellar resurfacing group had higher EQ-5D utility (see *Table 7*) and accrued more QALYs (see *Table 12*) than the no resurfacing group in every year. In many cases, the difference in QALYs accrued in a given year was larger than the difference in EQ-5D utility, and QALY differences (unlike those for EQ-5D utility) reached statistical significance in years 3 and 4. The larger QALY differences appear to be partly the result of multiple imputation of missing utility values and partly the result of a non-significant difference in mortality, as mean survival was around 21 days longer for participants randomised to patellar resurfacing ($p = 0.60$). Across the first 10 years after TKR, the average participant randomised to patellar resurfacing accrued 5.30 QALYs: 0.19 more than the no patellar resurfacing group ($p = 0.08$).

At a 10-year time horizon, the patellar resurfacing group, therefore, accrued more QALYs and lower costs than the group allocated to no patellar resurfacing. Patellar resurfacing can, therefore, be said to dominate no patellar resurfacing, being more effective and less costly.

However, differences in neither costs ($p = 0.70$) nor QALYs ($p = 0.08$) reached the conventional level of statistical significance. Plotting incremental costs and incremental QALYs on the cost-effectiveness plane (*Figure 21*) demonstrates that there is a 63% probability that patellar resurfacing dominates no resurfacing, a 34% probability that it is more costly and more effective and only a 4% probability that it is less effective.

Although there is no significant difference in either costs or QALYs individually, the joint distribution of costs and QALYs shows that we can be reasonably confident that patellar resurfacing is either dominant or produces health gains that are large compared with its incremental cost. In most NHS decision-making, treatments are considered cost-effective if they cost no more than a 'ceiling ratio' of around £20,000 per QALY gained.[81] The distribution of costs and QALYs observed here shows that we can be > 95% confident that patellar resurfacing is good value for money if the NHS is willing and able to pay at least £7250 per QALY gained (*Figure 22*), suggesting that patellar resurfacing is very good value for money.

TABLE 12 Base-case cost-effectiveness results for patella comparison

	Allocated to patellar resurfacing ($n = 841$) [mean (SE)]		Allocated to no patellar resurfacing ($n = 830$) [mean (SE)]					
Time point	Total cost (£)	QALYs	Total cost (£)	QALYs	Difference in annual costs (95% CI) (£)	Difference in annual QALYs (95% CI)	Difference in cumulative costs (95% CI) (£)	Difference in cumulative QALYs (95% CI)
Year 1	7967 (113)	0.667 (0.007)	7894 (123)	0.653 (0.007)	73 (–259 to 404)	0.013 (–0.005 to 0.032)	73 (–259 to 404)	0.013 (–0.005 to 0.032)
Year 2	208 (53)	0.715 (0.009)	286 (80)	0.691 (0.009)	–78 (–265 to 110)	0.024 (–0.001 to 0.048)	–2 (–397 to 393)	0.036 (–0.004 to 0.076)
Year 3	114 (28)	0.699 (0.009)	244 (75)	0.656 (0.010)	–130 (–287 to 27)	0.043 (0.016 to 0.070)[a]	–123 (–576 to 330)	0.076 (0.014 to 0.138)[a]
Year 4	86 (22)	0.665 (0.010)	139 (40)	0.630 (0.011)	–52 (–143 to 38)	0.036 (0.006 to 0.065)[a]	–171 (–638 to 296)	0.108 (0.025 to 0.191)[a]
Year 5	88 (31)	0.639 (0.011)	102 (32)	0.610 (0.011)	–14 (–100 to 71)	0.029 (–0.001 to 0.059)	–183 (–660 to 294)	0.133 (0.029 to 0.238)[a]
Year 6	106 (44)	0.605 (0.011)	77 (25)	0.585 (0.012)	29 (–68 to 127)	0.021 (–0.011 to 0.052)	–158 (–646 to 329)	0.150 (0.024 to 0.276)[a]
Year 7	74 (23)	0.569 (0.012)	51 (20)	0.552 (0.012)	23 (–36 to 82)	0.017 (–0.017 to 0.051)	–140 (–634 to 355)	0.164 (0.016 to 0.312)[a]
Year 8	104 (32)	0.535 (0.013)	67 (23)	0.522 (0.013)	37 (–40 to 115)	0.013 (–0.022 to 0.048)	–110 (–611 to 390)	0.174 (0.005 to 0.344)[a]
Year 9	94 (34)	0.502 (0.013)	96 (39)	0.493 (0.013)	–2 (–103 to 98)	0.009 (–0.027 to 0.045)	–112 (–628 to 404)	0.181 (–0.010 to 0.372)
Year 10	74 (31)	0.486 (0.014)	62 (32)	0.477 (0.014)	12 (–75 to 99)	0.008 (–0.030 to 0.046)	–104 (–630 to 423)	0.187 (–0.025 to 0.399)
Total	8785 (161)	5.297 (0.076)	8889 (211)	5.110 (0.080)	–104 (–630 to 423)	0.187 (–0.025 to 0.399)	–104 (–630 to 423)	0.187 (–0.025 to 0.399)

a $p < 0.05$.

Total costs and QALYs accrued in each year of the trial. Costs and QALYs beyond year 1 are discounted at 3.5% per year and include IPW; SEs estimated using bootstrapping. All QALY estimates are adjusted for baseline utility.

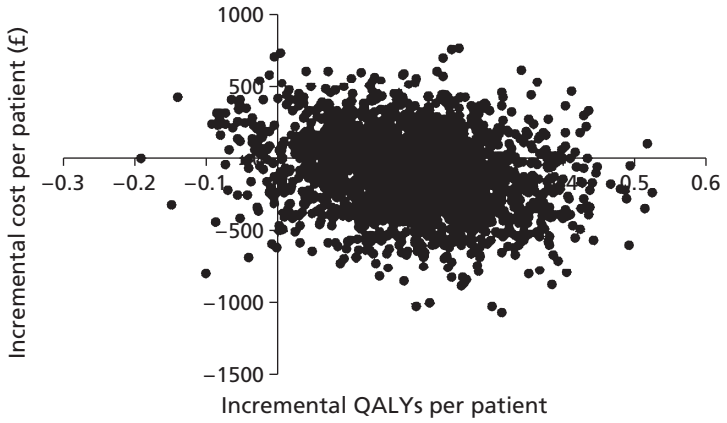

FIGURE 21 Stochastic cost-effectiveness results for patellar resurfacing vs. no resurfacing: scatter graph on cost-effectiveness plane.

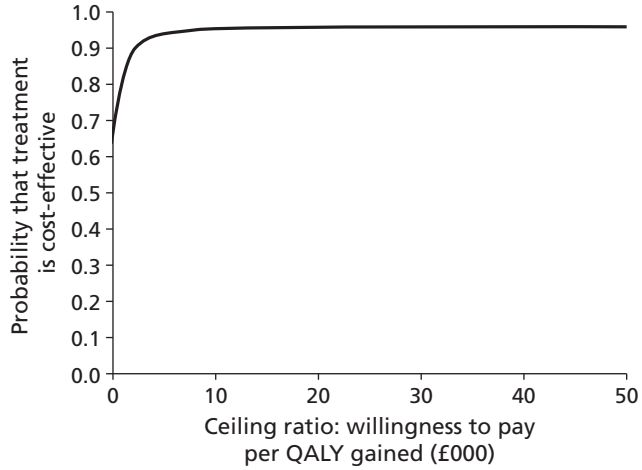

FIGURE 22 Cost-effectiveness acceptability curve for patella comparison.

Sensitivity analysis

However, as with all economic evaluations, our analysis required a number of assumptions and choices among a number of alternative methodologies. We, therefore, conducted sensitivity analyses to assess the impact of using different methods or assumptions.

These analyses demonstrate that the results are extremely robust, with patellar resurfacing dominating no resurfacing and having a > 95% probability of being cost-effective at a ceiling ratio of £20,000 per QALY gained in every analysis except for the complete case analysis (*Table 13*). In particular, the analysis is robust to changes in the time horizon and the discount rates used to adjust for time preference, as the majority of differences in costs and QALYs are in the first few years after primary TKR (which are given higher weight). Changes in costing methodology also have relatively little impact because the conclusion is driven by the comparatively large difference in QALYs and readmissions. It is particularly notable that changing the discount applied to component list prices has no effect on the conclusions and that the 46% reduction in length of stay since KAT operations were completed has little effect on incremental costs, as length of stay is similar in the two groups. Changing the methods used to deal with censoring and imbalance in baseline utility also had minimal impact.

By contrast, the complete case analysis found patellar resurfacing to be substantially more costly and only slightly more effective than no resurfacing, costing £49,160 per QALY gained. As treatments that cost < £20,000 per QALY gained are normally considered cost-effective in NHS decision-making,[81] the complete case analysis would suggest that patellar resurfacing is poor value for money. However, by excluding all

TABLE 13 Results of sensitivity and subgroup analyses for patella comparison

	Allocated to patellar resurfacing (*n* = 841) [mean (SE)]		Allocated to no patellar resurfacing (*n* = 830) [mean (SE)]		Difference (95% CI)			Probability that patellar resurfacing is	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Base-case analysis	8785 (161)	5.297 (0.076)	8889 (211)	5.110 (0.080)	–104 (–630 to 423)	0.187 (–0.025 to 0.399)	Dominant	96%	64%
Sensitivity analyses									
Complete case analysis (*n* = 334, 318, respectively)	8446 (207)	5.565 (0.120)	7767 (168)	5.552 (0.126)	679 (–1204 to 1204)	0.014 (–0.347 to 0.347)	49,160	45%	1%
Per-protocol analysis (*n* = 685, 715, respectively)	8784 (178)	5.389 (0.083)	8925 (227)	5.120 (0.085)	–141 (–708 to 425)	0.269 (0.041 to 0.497)	Dominant	99%	69%
46% reduction in LoS for primary admission	7227 (151)	5.297 (0.076)	7363 (206)	5.110 (0.080)	–136 (–642 to 371)	0.187 (–0.025 to 0.399)	Dominant	96%	70%
Component price discount									
0%	9571 (167)	5.297 (0.076)	9653 (221)	5.110 (0.080)	–83 (–632 to 467)	0.187 (–0.025 to 0.399)	Dominant	96%	61%
50%	8262 (157)	5.297 (0.076)	8379 (205)	5.110 (0.080)	–117 (–630 to 395)	0.187 (–0.025 to 0.399)	Dominant	96%	67%
Cost per bed-day									
£149 (–50%)	6860 (117)	5.297 (0.076)	6919 (156)	5.110 (0.080)	–59 (–447 to 329)	0.187 (–0.025 to 0.399)	Dominant	96%	61%
£448 (+50%)	10,711 (208)	5.297 (0.076)	10,859 (270)	5.110 (0.080)	–148 (–824 to 528)	0.187 (–0.025 to 0.399)	Dominant	96%	66%
Cost per theatre minute									
£7.34 (–50%)	7600 (144)	5.297 (0.076)	7666 (185)	5.110 (0.080)	–66 (–532 to 399)	0.187 (–0.025 to 0.399)	Dominant	96%	60%
£22.00 (+50%)	9971 (178)	5.297 (0.076)	10,111 (239)	5.110 (0.080)	–141 (–733 to 451)	0.187 (–0.025 to 0.399)	Dominant	96%	68%

Analysis	Allocated to patellar resurfacing ($n = 841$) [mean (SE)]		Allocated to no patellar resurfacing ($n = 830$) [mean (SE)]		Difference (95% CI)			Probability that patellar resurfacing is	
	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Discount rate for time preference									
0% costs and QALYs	8915 (173)	6.082 (0.090)	9017 (225)	5.870 (0.095)	–102 (–665 to 460)	0.212 (–0.040 to 0.464)	Dominant	95%	64%
5% costs and QALYs	8739 (157)	5.014 (0.071)	8842 (207)	4.835 (0.075)	–103 (–618 to 412)	0.178 (–0.020 to 0.376)	Dominant	96%	65%
3.5% costs, 0% QALYs	8785 (161)	6.082 (0.090)	8889 (211)	5.870 (0.095)	–104 (–630 to 423)	0.212 (–0.040 to 0.464)	Dominant	95%	64%
No adjustment for baseline utility	8785 (161)	5.318 (0.076)	8889 (211)	5.100 (0.082)	–104 (–630 to 423)	0.218 (–0.001 to 0.438)	Dominant	97%	64%
Within-trial time horizon with no adjustment for censoring	8779 (159)	5.309 (0.078)	8899 (211)	5.108 (0.084)	–120 (–644 to 404)	0.201 (–0.024 to 0.427)	Dominant	96%	67%
8-year time horizon	8660 (153)	4.559 (0.060)	8771 (201)	4.385 (0.065)	–110 (–611 to 390)	0.174 (0.005 to 0.344)[b]	Dominant	98%	67%
9-year time horizon	8731 (157)	4.941 (0.068)	8844 (207)	4.760 (0.073)	–112 (–628 to 404)	0.181 (–0.010 to 0.372)	Dominant	97%	66%
11-year time horizon	8824 (163)	5.621 (0.083)	8958 (215)	5.433 (0.088)	–134 (–669 to 401)	0.188 (–0.045 to 0.421)	Dominant	94%	69%
Dealing with censoring using multiple imputation rather than IPW	8780 (159)	5.291 (0.076)	8888 (211)	5.075 (0.082)	–108 (–632 to 416)	0.217 (–0.003 to 0.436)	Dominant	97%	65%

continued

TABLE 13 Results of sensitivity and subgroup analyses for patella comparison (*continued*)

	Allocated to patellar resurfacing ($n = 841$) [mean (SE)]		Allocated to no patellar resurfacing ($n = 830$) [mean (SE)]		Difference (95% CI)			Probability that patellar resurfacing is	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Subgroup analyses									
Age (years)									
< 70 ($n = 381$, 384)	8843 (245)	5.683 (0.107)	9270 (367)	5.398 (0.115)	–427 (–1288 to 435)	0.285 (–0.016 to 0.585)	Dominant	97%	84%
≥ 70 ($n = 460$, 446)	8733 (217)	4.969 (0.104)	8557 (228)	4.861 (0.109)	176 (–440 to 792)	0.108 (–0.185 to 0.402)	1629	74%	29%
Shape of groove in the femoral component									
Anatomical ($n = 242$, 236)	9442 (341)	5.244 (0.142)	10,170 (504)	4.947 (0.159)	–727 (–1922 to 468)	0.297 (–0.118 to 0.712)	Dominant	94%	88%
Domed ($n = 573$, 566)	8572 (186)	5.335 (0.089)	8233 (195)	5.193 (0.092)	339 (–196 to 873)	0.142 (–0.104 to 0.387)	2388	83%	11%

LoS, length of stay.
a The probability that treatment is cost-effective is based on a £20,000/QALY ceiling ratio.
b $p < 0.05$.

participants who had missing data on any variable collected before the participant was administratively censored (including data from up to 14 questionnaires completed over 10 years), the complete case analysis excludes more than half of the sample, substantially reducing statistical power. Furthermore, complete case analyses are prone to bias, as they do not include all randomised participants and assume that data are missing completely at random.[65] Bias is particularly likely here, as participants cannot have missing data on costs or QALYs after they have died or been administratively censored. Furthermore only participants who receive a patella can have missing data on the cost of a patella and only participants who are readmitted can have missing data on component costs or length of stay during subsequent hospitalisations. Consequently, the results of this analysis should be interpreted with caution.

Subgroup analysis

As surgeons often consider participants' age and their likelihood of out-living their knee prosthesis in decisions around component design, a post-hoc subgroup analysis estimated outcomes for subgroups divided by age (see *Table 13*). Younger participants (< 70 years old at the time of TKR) accrued higher total costs and more QALYs within 10 years of TKR than those aged ≥ 70 years, presumably because of their longer life expectancy. For younger participants, the estimated cost savings and QALY gains from patellar resurfacing were greater than those of the base case, although the finding that patellar resurfacing dominated no resurfacing was the same. By contrast, older participants randomised to patellar resurfacing accrued higher costs than those randomised to no resurfacing and the QALY gains from resurfacing were also lower than in the base case; as a result, patellar resurfacing cost £1629 per QALY gained in participants aged ≥ 70 years, but remained cost-effective.

As discussed above, patella components may be either a domed shape or an anatomical shape, with corresponding changes to the shape of the trochlear groove within the femoral component. It is generally assumed that a non-resurfaced patella would perform better with an anatomical trochlea, rather than one designed for a domed patella button. Subgrouping participants by the shape of the groove within the femoral component suggested that the effectiveness of patellar resurfacing is slightly better among participants with a femoral groove shaped for an anatomical patella than among those with grooves shaped for domed patellas, while patellar resurfacing was also less costly than no resurfacing in the group with anatomical patellas, but more costly in those with domed patellas. However, patellar resurfacing remained very good value for money in both groups. Costs were also higher among participants with anatomical patellofemoral grooves than among those with dome-shaped grooves.

Discussion

In this study, which is the largest RCT of patellar resurfacing, there was no significant difference in clinical outcome between patellar resurfacing or not up to 10 years post operation. We therefore conclude that there is no clinical advantage for patellar resurfacing. However, there are non-significant trends towards increased effectiveness with patellar resurfacing owing to improved outcomes, as well as decreased costs owing to fewer reoperations. Taken together, these findings mean that we can be 96% confident that patellar resurfacing is cost-effective compared with no resurfacing.

The study indicates that up to 10 years post operation, functional status and quality of life are not significantly influenced by patellar resurfacing. The 95% CI of the difference in OKS between patellar resurfacing and no resurfacing was –0.66 to 1.56 (see *Table 6*). A clinically important difference on the OKS scale is thought to be between three and five points, whereas a two-point difference is of possible clinical significance. This study was adequately powered to detect a clinically important difference, even taking into account the participants who did not receive their allocated procedure. Therefore, if there was a difference in OKS too small to be detected by this study, it would also be too small to be of clinical significance. There may, however, be a difference that the OKS is not sensitive enough to identify. If there was, it would probably relate to activities, such as descending stairs, that stress the patellofemoral joint. Question 12 of the OKS enquires about symptoms relating to stair descent. There is no significant

difference between patellar resurfacing and not, even with this question. Our findings that there are no differences in outcome are similar to those from meta-analyses of other RCTs,[85,86] and our estimated CIs rule out a two-point difference on the OKS.

The proportion of participants undergoing patella-related reoperations was similar in the resurfaced (2%) and non-resurfaced (2%) groups. This contradicts the meta-analyses of previous RCTs, which tended to show an increased patella-related reoperation rate in the non-resurfaced group.[85] There were, however, different patterns of patella-related reoperations in the two groups. Late patellar resurfacing, which tended to be carried out in the first 5 years, was more commonly carried out in the non-resurfaced group (2%) than in the resurfaced group (1%). In contrast, operations for complications related to patellar resurfacing which were carried out in the second 5 years were carried out only in the resurfaced group (1%). This observation, in part, explains the difference between our conclusion and those of the meta-analyses. The follow-up of the studies in the meta-analyses tended to be shorter than that of KAT. During the first 5 years of our study, there was a non-significant trend towards an increased rate of patella-related reoperation, as in the meta-analyses. This, however, disappeared in the 10-year analysis.

In large-scale, multicentre, pragmatic surgical RCTs such as KAT non-adherence to allocated procedure is inevitable. Analysis of reoperation rates was by intention to treat to avoid selection bias that per-protocol or as-treated analyses are prone to. On an intention-to-treat basis, there was no evidence of a difference between the two groups in the rate of patella-related reoperations. It is useful in this instance, however, to consider the procedure received, as clearly late resurfacing is possible only if the patella is not resurfaced in the first place. There were 853 confirmed participants who did not receive a patella-resurfacing index operation (see *Figure 3*) and, of these, 25 (3%) had a late resurfacing. In those that received patellar resurfacing, the incidence of patella-related reoperation was 6/789 (0.8%), which all occurred after 5 years.

There are two further reasons for the difference in the conclusions of our study and the meta-analyses. First, the authors did not abstract the correct data from the KAT 2-year report (which was included in the meta-analysis) and, furthermore, the remaining included studies in the meta-analyses tended to be small, single-centre studies. We would argue that evidence from KAT is more relevant, as it offers a pragmatic assessment of the treatment policy and would reflect what would happen in practice if there were a national guideline recommending patellar resurfacing. It is also important to consider the evidence according to the operation received. There was a very high incidence (7%) of late patellar resurfacing in the small (16%) subgroup of participants who were randomised to patellar resurfacing but did not have a resurfacing at the initial operation. The incidence of late resurfacing in this subgroup is three times higher than that in the other participants who did not have resurfacing. There are various possible reasons for this observation: perhaps these participants or their surgeons may have been aware that they had not had their allocated patellar resurfacing and, therefore, may have been more likely to request or be advised to have patellar resurfacing if they had a degree of residual anterior pain, as they were more likely to be suspicious that the failure to resurface the patella was the cause of the ongoing pain. Alternatively, participants with very severe damage to the patella may not have had resurfacing because of technical difficulties, but, because of the severe damage, if they had ongoing pain, a surgeon might have felt a late resurfacing would help.

Traditionally, patellar resurfacing has been done with a dome-shaped replacement. To match this, the cross-section of the trochlea has been circular. This cross-sectional shape is very different from the cross-sectional shape of the normal patella, and is possibly a cause of poor results following knee replacement without resurfacing. To improve the results of knee replacement without resurfacing, knee replacements with an anatomically shaped trochlea were introduced. These designs can be used with an anatomically shaped patella button. It was expected that the shape of the trochlea would influence the results of the study, with non-resurfaced patellas performing better with trochleas designed to work with anatomical, rather than domed, patellas. The study, however, found that the shape of the trochlea had no

influence on the relative merits of patellar resurfacing or not. It therefore does not seem to matter whether a knee replacement is designed to have an anatomical or a dome-shaped patella.

There has been some debate as to the merits of late resurfacing.[87–89] This study provides evidence to suggest that participants who undergo this procedure have a slowly reducing functional score in the years prior to late resurfacing and that after surgery their functional scores do improve by about five OKS points (from approximately 16 to 21). However, after their late resurfacing, their scores were nearer the mean preoperative score (18) than the mean postoperative score (35) of the other participants in the trial. It is, therefore, not clear whether participants are actually receiving some real but small benefit from the late resurfacing or whether the small improvement in score occurring after the late resurfacing and the drop in score preceding this is a manifestation of random variations in score. Furthermore, it is clear that participants who have late resurfacing do have a problem with their knee but that this problem is, largely at least, not related to their lack of resurfacing, and that exploration of the knee and resurfacing does not solve it. Evidence from KAT does not support the use of late resurfacing. If, despite this, patients are offered late resurfacing, they should be advised that this procedure is likely to, at best, provide marginal benefit.

The occurrence of late resurfacing is usually considered to be a manifestation of some patients who have not initially had resurfacing having a very poor outcome and, therefore, an argument for resurfacing. We found that there was no difference in the distribution of postoperative scores in the resurfaced and non-resurfaced groups; in particular, there was not a higher incidence of participants with very poor outcomes in the non-resurfaced group (see *Figure 6*). We therefore have to conclude that the likely reason why late resurfacing is carried out is not because there are worse results with no resurfacing, but rather because, if a participant has problems after TKR and there is a simple operation such as a late resurfacing that might help and that can be done, then a surgeon will do it. This may also be part of the explanation why there is a trend towards more readmissions, minor/intermediate and major reoperations and higher postoperative costs in the non-resurfaced group. For a patient with a poor outcome from a TKR, a surgeon may be more likely to explore a knee to resurface the patella, if this has not already been done, and once the knee is exposed a surgeon may be more likely to find a problem and attempt to rectify it. Furthermore, if there are more operations, there are more likely to be complications of the operations and more ambulatory consultations will be needed. Therefore, if a surgeon is to pursue a policy of not resurfacing the patella, he or she should also have a policy not to reoperate on the knee unless a definite problem, other than a non-resurfaced patella, is identified. In other words, when assessing a patient who is having trouble following knee replacement, he or she should ignore whether or not the patella has been resurfaced. If late patellar resurfacing were not undertaken, the health gains and cost-savings associated with conducting patellar resurfacing during primary TKR would be substantially smaller or potentially non-existent.

In the second 5 years, the only patella-related reoperations were in the resurfaced group. These were all related to complications of the patellar resurfacing, which occurred only in the second 5 years. There were two patellar resurfacing revisions, two reoperations for patella fracture, one realignment and one removal of button. Operations for patella complications tend to be more major undertakings than late resurfacings and have more complications. In addition, as is the case with late patellar resurfacing, they tend not to have a good outcome. As late resurfacing tended to occur in the first 5 years and complications with the resurfacing occurred in the second 5 years, there is a concern that with time the incidence of complications with resurfacing will continue to increase, such that in the long-term there will be more patella-related reoperations in the resurfaced group than in the non-resurfaced.

The economic evaluation suggested that the cost of the primary inpatient stay was about £200 higher ($p = 0.03$) for the resurfaced group than for the non-resurfaced group. This was partly because the implants were about £100 cheaper ($p < 0.001$) with no resurfacing and partly because other costs were lower. Therefore, as far as the hospital is concerned, not resurfacing the patella results in an appreciable cost saving. However, KAT provides strong evidence that this is a false economy, as over 10 years we can be 96% confident that patellar resurfacing is good value for money at a £20,000/QALY ceiling ratio, saving £100 and gaining 0.2 QALYs per participant treated. For every 100 participants who undergo

patellar resurfacing, we would expect to avoid three knee-related readmissions; the savings associated with avoiding these readmissions more than offsets the additional costs of patella components. These results were robust to changes in assumptions and methods, with no sensitivity analysis, other than a complete case analysis, which has inherent biases,[65] changing the conclusion that patellar resurfacing dominates no resurfacing. In particular, the finding that varying the cost of bed-days, theatre time and discounts from component list prices does not change the conclusions suggests that the conclusions would apply to a wide range of hospitals across the UK. Furthermore, the finding that the conclusions would remain the same if the length of stay were reduced to the level seen in 2010–11 suggests that the findings from participants randomised in 1999–2003 are likely to still be valid today. However, as discussed above, the cost-effectiveness of patellar resurfacing may be less favourable if it were compared with a policy of avoiding all resurfacing (whether early or late). As late patellar resurfacing may affect readmissions and ambulatory consultations and quality of life for some time either side of the resurfacing procedure, it is difficult to evaluate this scenario without modelling work.

A subgroup analysis indicated that patellar resurfacing was more cost-effective in participants < 70 years old at the time of operation, although it remained good value for money in both groups. A second subgroup analysis found no appreciable difference in cost-effectiveness depending on whether the femoral component was designed for an anatomical or domed patella replacement.

Conclusions

In conclusion, at 10 years there is no clear clinical benefit to resurfacing the patella. It provides no functional advantage and results in a similar reoperation rate to that observed in patients who have not had patellar resurfacing, and, in particular, it is not associated with a lower rate of patella-related reoperations. These findings are different from those of previous studies, which have tended to show a higher patella-related reoperation rate with not resurfacing, primarily as resurfacing at the initial operation prevents late resurfacing. The difference appears to be because our study has a longer follow-up and is pragmatic in design. Therefore, our conclusions are likely to be more relevant to recommendations about general clinical practice. Furthermore, we have found that the outcome of patellar resurfacing is not influenced by whether the femoral component is patella friendly or not, and that late patellar resurfacing has little, if any, benefit.

The health economic analysis did, however, strongly suggest that resurfacing the patella is cost-effective, because it is associated with lower costs and better outcomes over the 10-year period. Although the differences in costs and QALYs were not statistically significant when considered individually, when taken together they are significant and are indicative of a real advantage for resurfacing. Secondary analysis indicates that patellar resurfacing is more cost-effective in participants aged < 70 than in older patients, although it remains good value for money in both age groups. The health economic analysis therefore provides evidence to support the routine use of resurfacing.

There are two caveats. First, we have found that the number of reoperations for patella complications increases with time. There is, therefore, a concern that in the resurfaced group in the long term the incidence of reoperation will increase more in the resurfaced than in the non-resurfaced group. Further follow-up is required to see if this happens. Second, if surgeons who do not resurface the patella also had a policy to ignore the patella and not to do late resurfacing in participants with a poor outcome, the QALY gains and cost savings associated with patellar resurfacing would decrease.

Chapter 4 Mobile bearing versus fixed bearing

Description of the groups at trial entry

Of the 2352 participants recruited, 539 were randomised within the comparison of mobile versus fixed bearings. The two randomised groups were well matched at baseline (*Table 14*). In both groups, the mean age was 69 years. In the mobile bearing group, 39% were male and in the fixed group 41%. In both groups, the mean BMI was approximately 30 kg/m^2 and 93% of both groups had osteoarthritis. Participants were also well matched on ASA grade and previous knee surgery.

Surgical management

Of the 116 surgeons in 34 centres in the UK who participated in KAT, 24 (21%) recruited participants to the mobile versus fixed bearings comparison. Of the 539 randomised in this comparison, 469 (87%) received the allocated procedure (*Figure 23*); 22 were subsequently withdrawn and received no surgery; 4 received a unicompartmental replacement; and for 2 the procedure received was unknown. Of the 263 participants allocated to fixed bearings, 10 (4%) received the mobile bearing intervention, and in the mobile bearing group 32/276 (12%) received the fixed bearing intervention. The main reasons reported for crossover to the other allocation were communication errors relating to allocation, clinical decision after randomisation and components not being available for the allocated procedure.

In-hospital care and short-term complications

Postoperative complications were reported in 11.3% (61) of the 539 participants; however, specific problems, such as wound infection, septicaemia, DVT or PE, cerebrovascular accident and myocardial infarction, were rare (*Table 15*). Overall, 2.0% (11) of 539 participants had additional knee surgery. Two participants had dislocations, one in each group. There were two deaths, one in each group: one from respiratory arrest and the other from DVT and PE. The median length of stay was 8 days in each group and most participants were discharged to their own home. There were no differences between the randomised groups with regard to any of the above factors.

Response rates at each follow-up point

Table 16 describes the response rate; the response rate to questionnaires sent was high in both groups over the whole follow-up period, ranging from 80% to 98%. The proportion of participants sent a questionnaire dropped over the life of the trial, as one would expect given a cohort of this nature, owing to death, loss to follow-up and participants declining further follow-up. At 10 years, the response rate was approximately 55% of the cohort who were still living.

Outcomes after a median of 10 years post operation

Oxford Knee Score

There was no evidence of a between-group difference in OKS at baseline or at any stage thereafter (*Table 17*). The mean OKS in both mobile bearing and fixed bearing groups was approximately 17 at baseline. It increased to approximately 33 at 1 year and thereafter remained about the same, although it did decrease slightly in the long term (*Figure 24*). The difference in OKS between the two groups was small, 0.28 (95% CI –1.86 to 2.43) at 10 years (see *Table 17*). The marginal estimate over the whole 10-year follow-up was 0.29 (95% CI –1.17 to 1.75; $p = 0.70$) in favour of the mobile bearing intervention (*Figure 25*). Sensitivity analysis imputing the last value before revision gave practically identical results; the marginal estimate was 0.34 (95% CI –0.16 to 1.85; $p = 0.65$).

TABLE 14 Description of groups at trial entry for mobile vs. fixed bearing

Characteristic	Mobile bearing (*n* = 276)		Fixed bearing (*n* = 263)	
Age (years) (mean, SD)	69	8	69	9
Female	169	61.0	155	58.9
BMI (kg/m^2) (mean, SD)	29.5	5.3	30.3	6.0
ASA				
Completely fit and healthy	36	13.0	43	16.3
Some illness but has no effect on normal activity	155	56.2	149	56.7
Symptomatic illness present but minimal restriction	63	22.8	52	19.8
Symptomatic illness causing severe restriction	1	0.4	3	1.1
Missing	21	7.6	16	6.1
Primary type of knee arthritis				
Osteoarthritis	243	88.0	234	89.0
Rheumatoid	18	6.5	15	5.7
Both	0	–	1	0.4
Missing	15	5.4		4.9
Extent of knee arthritis affecting mobility				
One knee	65	23.5	64	24.3
Both knees	99	35.7	96	36.5
General	113	40.8	103	39.2
	n = *264*		**n = *244***	
Other conditions affecting mobility	48	18.2	50	20.5
Medical	19	7.2	23	9.4
Locomotor/musculoskeletal	38	14.4	32	13.1
	n = *264*		**n = *248***	
Previous knee surgery	95	36.0	93	37.5
Ipsilateral osteotomy	5	1.9	5	2.0
Ipsilateral patellectomy	1	0.4	0	0.0
Contralateral previous knee replacement	25	9.5	27	10.9
Other previous knee surgery	67	25.4	65	26.2
Arthroscopy	58	22.0	58	23.4
Other related surgery	12	4.5	7	2.8

SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

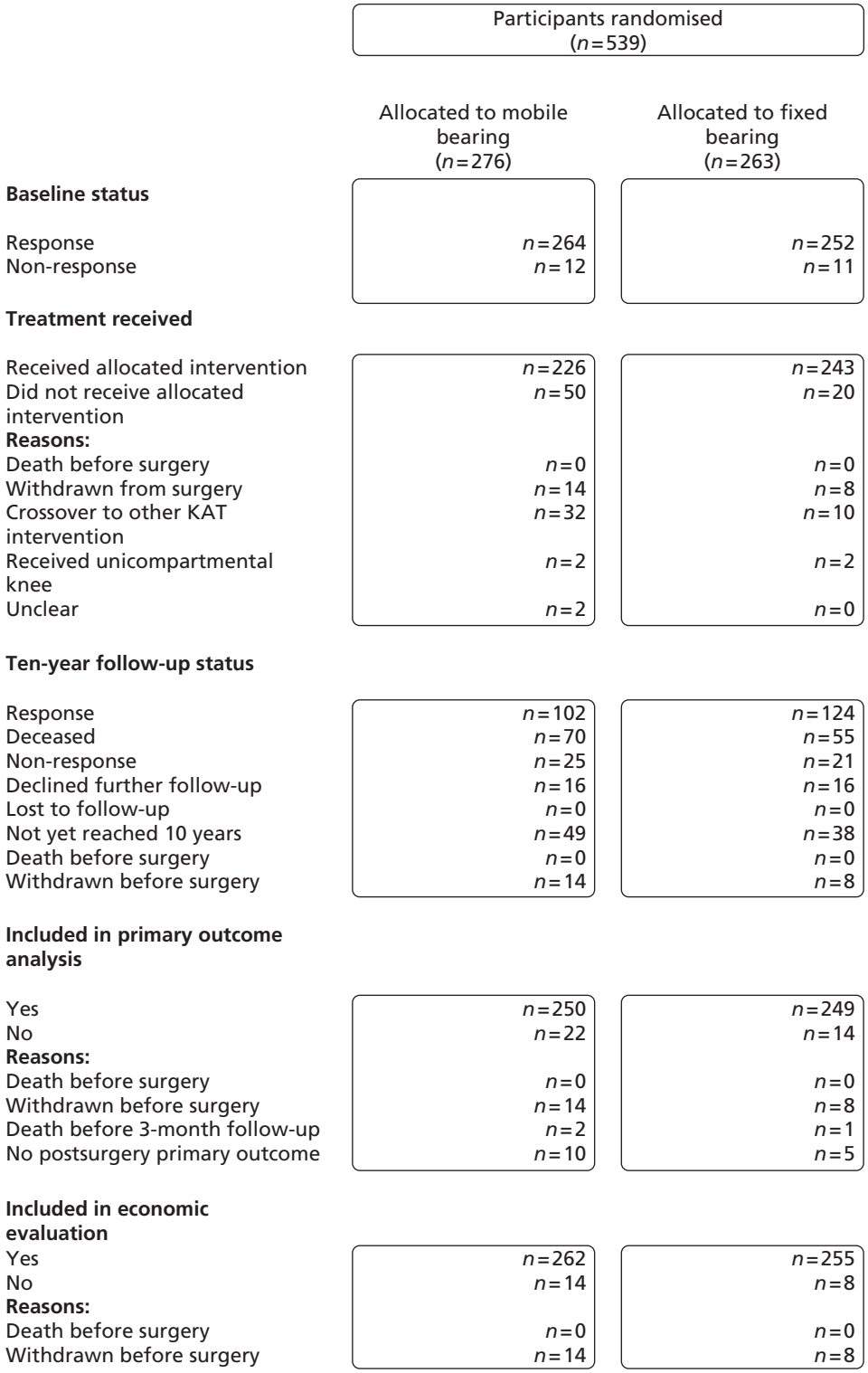

FIGURE 23 CONSORT diagram for mobile vs. fixed bearing.

TABLE 15 In-hospital care and short-term complications for mobile vs. fixed bearing

Variable	Mobile bearing (*n* = 259)		Fixed bearing (*n* = 249)	
Any postoperative complications	34	13.1	27	10.8
Knee dislocation	1	0.4	1	0.4
Proven wound infection	2	0.8	3	1.2
Septicaemia	0	0.0	1	0.4
Treated DVT or PE	3	1.2	6	2.4
Confirmed cerebrovascular accident	0	0.0	0	0.0
Confirmed myocardial infarction	1	0.4	1	0.4
Other serious complication	27	10.4	19	7.6
Medical complications	10	3.9	8	3.2
Surgical complications	6	2.3	6	2.4
Fall	0	0.0	1	0.4
Suspicion of infection	2	0.8	1	0.4
Confirmed infection	0	0.0	0	0.0
Skin complications	2	0.8	1	0.4
Stiffness	2	0.8	1	0.4
Suspected thrombolytic complications	1	0.4	0	0.0
Urinary complications	4	1.5	5	2.0
Any further perioperative knee surgery	5	1.9	6	2.4
Manipulation under anaesthetic	2	0.8	3	1.2
Wound problem	2	0.8	1	0.4
Stiffness	0	0.0	0	0.0
Musculoskeletal ligamentous (including imbalance)	0	0.0	0	0.0
Patella complication	0	0.0	0	0.0
Suspicion of infection	1	0.4	1	0.4
Confirmed infection	0	0.0	0	0.0
Prosthetic complication	0	0.0	0	0.0
	n = *258*		**n = *250***	
Status at discharge				
Alive	257	99.6	249	99.6
Dead	1	0.4	1	0.4
Discharged to home	246	95.3	243	97.2
	n = *256*		**n = *247***	
Days in hospital				
Median (IQR)	8	7–11	8	7–11
Mean (SD)	9.76	6.5	9.94	4.9

IQR, interquartile range; SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

TABLE 16 Response rates at each follow-up time point for mobile vs. fixed bearing

	Mobile bearing							Fixed bearing						
Time	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive
Month 3	241	87	88	226	94	82	82	234	89	89	230	98	87	88
Year 1	250	91	93	231	92	84	86	246	94	96	233	95	89	91
Year 2	244	88	93	217	89	79	83	240	91	95	214	89	81	85
Year 3	238	86	92	216	91	78	83	233	89	94	215	92	82	86
Year 4	223	81	89	204	91	74	81	225	86	93	207	92	79	86
Year 5	220	80	89	202	92	73	82	214	81	91	196	92	75	83
Year 6	213	77	88	191	90	69	79	205	78	90	189	92	72	83
Year 7	202	73	87	182	90	66	78	201	76	90	182	91	69	81
Year 8	193	70	87	164	85	59	74	191	73	88	172	90	65	79
Year 9	182	66	85	154	85	56	72	184	70	87	165	90	63	78
Year 10	127	46	62	102	80	37	50	145	55	70	124	86	47	60

TABLE 17 Descriptive statistics and estimated treatment effects at each follow-up time point for OKS for mobile vs. fixed bearing

	Mobile bearing			Fixed bearing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	257	17.2	7.6	243	16.5	7.4			
3 months	193	30.4	9.8	196	29.4	9.6	0.38	–1.41 to 2.18	0.68
1 year	187	33.4	10.5	200	32.6	10.7	0.66	–1.14 to 2.46	0.47
2 years	185	33.6	10.5	176	32.8	10.4	–0.13	–1.96 to 1.70	0.89
3 years	192	34.3	10.1	191	32.7	11.2	0.76	–1.05 to 2.57	0.41
4 years	173	33.4	10.3	192	32.4	11.1	0.59	–1.24 to 2.42	0.53
5 years	169	33.2	10.7	181	33.6	10.0	–0.41	–2.26 to 1.43	0.66
6 years	169	33.3	10.0	165	32.6	10.7	0.51	–1.36 to 2.38	0.59
7 years	156	32.3	10.5	165	33.2	10.2	–1.17	–3.05 to 0.72	0.23
8 years	147	32.5	11.0	160	31.4	10.8	0.68	–1.23 to 2.58	0.49
9 years	135	32.0	11.1	156	31.2	11.0	0.95	–0.98 to 2.88	0.33
10 years	86	31.1	11.4	114	31.2	11.2	0.28	–1.86 to 2.43	0.78

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours mobile bearings; *n*, the number of responses; SD, standard deviation.

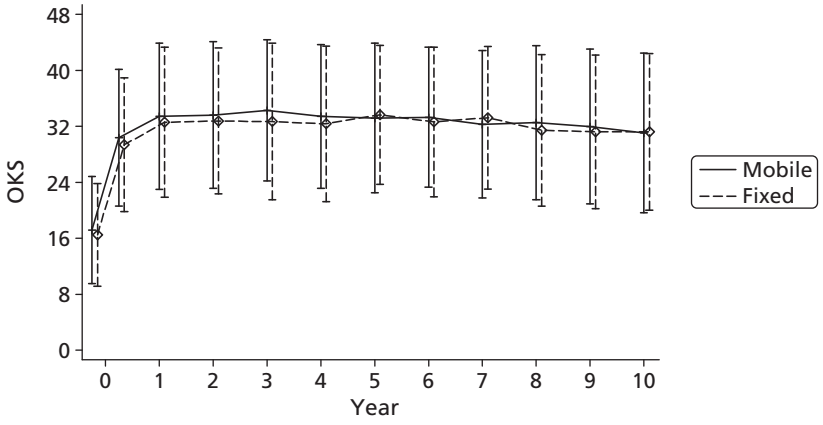

FIGURE 24 Mean (SD) OKS by group at each follow-up time point for mobile vs. fixed bearing.

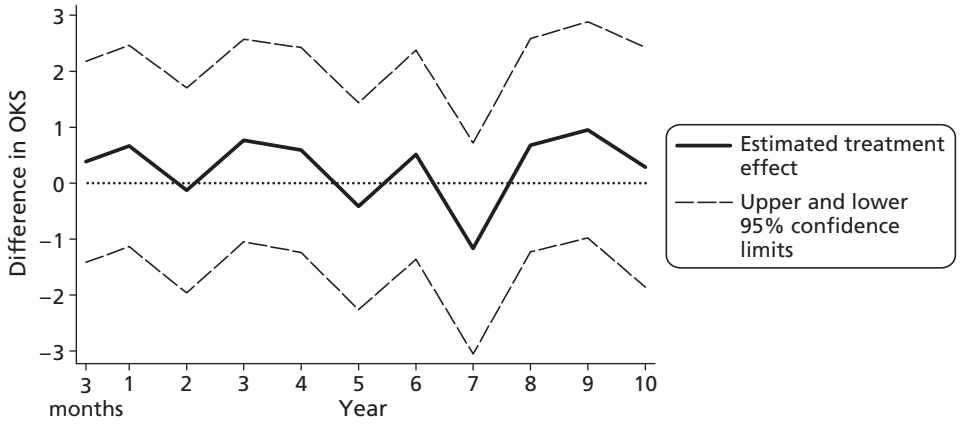

FIGURE 25 Estimated treatment effect on OKS (95% CI) at each follow-up time point for mobile vs. fixed bearing. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours mobile bearing.

Figure 26 explores the potential for interaction in those allocated to two interventions by plotting difference in OKS between mobile and fixed bearings among those allocated to patellar resurfacing compared with those allocated to no patellar resurfacing. A positive difference in differences suggests a higher relative benefit for mobile bearings in the patellar resurfacing group. The graph indicates that there may be a potential interaction, suggesting patellar resurfacing when using a mobile bearing may be beneficial. However, there is considerable uncertainty around these estimates as a result of the reduced sample size in the partial factorial aspect of the trial.

EuroQol 5D

There was no evidence of a between-group difference in EQ-5D at baseline or at any stage thereafter (*Table 18*). The mean EQ-5D utility was approximately 0.32 at baseline. It increased to approximately 0.70 at 1 year and thereafter steadily decreased to about 0.67 at 10 years (*Figure 27*). At 10 years the difference in EQ-5D was 0.041 (95% CI –0.021 to 0.104) (see *Table 18*). The marginal estimate over the

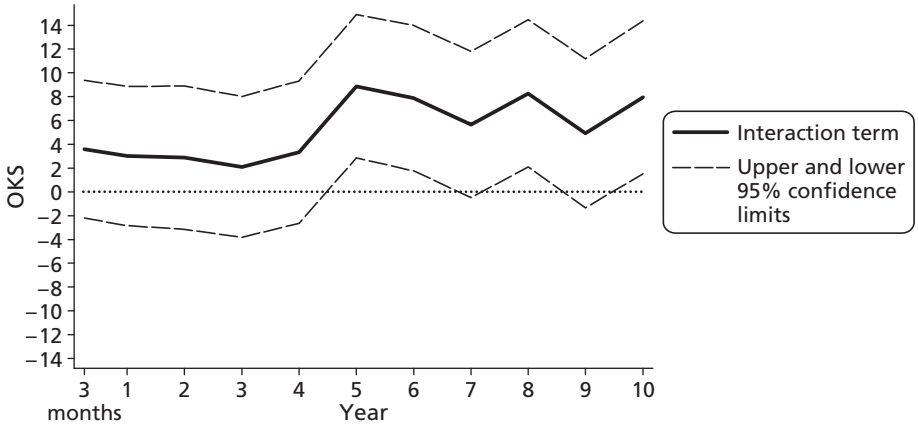

FIGURE 26 Interaction term (solid line) at each follow-up time point for OKS for patellar resurfacing by mobile bearing. Dotted lines represent 95% CIs.

TABLE 18 Descriptive statistics and estimated treatment effects at each follow-up time point for EQ-5D utility for mobile vs. fixed bearing

	Mobile bearing			Fixed bearing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	253	0.320	0.316	241	0.336	0.309			
3 months	225	0.664	0.274	223	0.664	0.240	0.012	–0.038 to 0.062	0.63
1 year	221	0.716	0.286	227	0.689	0.290	0.035	–0.015 to 0.085	0.17
2 years	211	0.710	0.285	209	0.675	0.267	0.036	–0.015 to 0.086	0.17
3 years	206	0.710	0.263	204	0.658	0.313	0.030	–0.021 to 0.081	0.26
4 years	195	0.681	0.304	192	0.657	0.300	0.009	–0.043 to 0.061	0.73
5 years	194	0.680	0.290	187	0.692	0.267	–0.024	–0.076 to 0.029	0.37
6 years	184	0.668	0.289	177	0.672	0.297	–0.003	–0.056 to 0.050	0.92
7 years	175	0.669	0.293	172	0.638	0.302	0.020	–0.034 to 0.073	0.47
8 years	162	0.662	0.310	169	0.641	0.299	0.010	–0.045 to 0.064	0.72
9 years	150	0.639	0.292	160	0.615	0.325	0.038	–0.018 to 0.093	0.18
10 years	98	0.653	0.302	120	0.604	0.310	0.041	–0.021 to 0.104	0.19

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours mobile bearings; *n*, the number of responses; SD, standard deviation.

whole 10-year follow-up was 0.018 (95% CI –0.020 to 0.056; $p = 0.36$) in favour of the mobile bearing intervention (*Figure 28*).

Short Form 12

There was no evidence of a between-group difference in SF-12 measured either at baseline or at any stage thereafter. Mean SF-12 PCS was approximately 31 for both groups at baseline (*Table 19*). It increased to approximately 39 at 1 year and thereafter slowly decreased to approximately 36 for both groups at 10 years (*Figure 29*). The difference in score at 10 years was –0.15 (95% CI –2.37 to 2.07) (see *Table 19*). The marginal estimate over the whole 10-year follow-up was 0.19 (95% CI –1.26 to 1.64; $p = 0.79$) (*Figure 30*).

The mean SF-12 MCS was 48 for both groups preoperatively (*Table 20*). It increased to about 50 at 1 year and then decreased slowly to 48 at 10 years (*Figure 31*). The difference in score at 10 years was –0.91 (95 %CI –3.31 to 1.48). The marginal estimate over the whole 10-year follow-up was –0.18 (95% CI –1.41 to 1.26; $p = 0.91$) (*Figure 32*).

Clinical outcomes

During the first 10 postoperative years, 16% (41/262) of the mobile bearing group and 18% (45/255) of the fixed bearing group required readmission and/or further intervention (odds ratio 0.84; 95% CI 0.52 to 1.34; $p = 0.47$; *Table 21*); 8% (22/262) of the mobile bearing group and 6% (16/255) of the fixed bearing group required further minor or intermediate operations (odds ratio 1.36; 95% CI 0.69 to 2.68; $p = 0.37$);

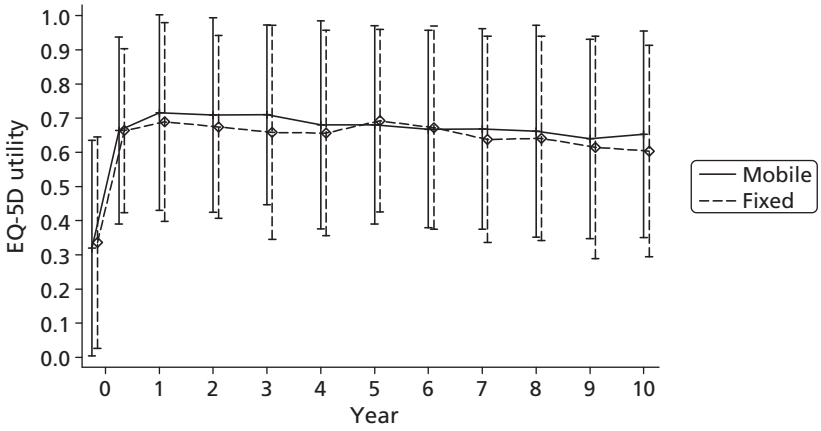

FIGURE 27 Mean (SD) EQ-5D utility by group at each follow-up time point for mobile vs. fixed bearing.

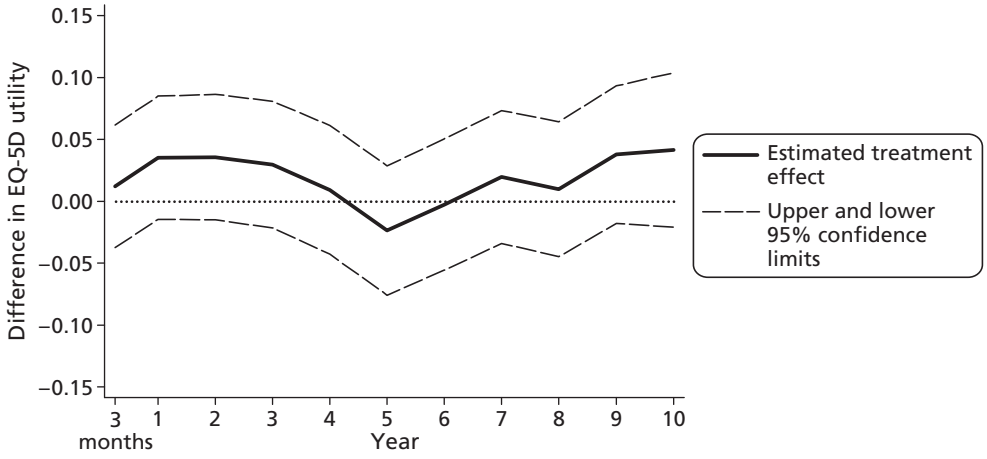

FIGURE 28 Estimated treatment effect on EQ-5D utility (95% CI) at each follow-up time point for mobile vs. fixed bearing. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours mobile bearings.

TABLE 19 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 PCS for mobile vs. fixed bearing

	Mobile bearing			Fixed bearing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	251	31.0	8.1	237	30.4	7.9			
3 months	213	38.5	9.5	215	38.1	9.7	–0.20	–2.02 to 1.63	0.83
1 year	218	40.4	10.6	225	38.7	10.8	1.08	–0.73 to 2.89	0.24
2 years	212	40.4	11.4	200	38.7	10.6	1.01	–0.84 to 2.86	0.29
3 years	208	39.1	11.0	203	37.9	10.8	0.36	–1.49 to 2.21	0.70
4 years	194	38.5	11.1	198	38.5	11.7	–0.32	–2.19 to 1.56	0.74
5 years	190	38.2	12.1	189	38.6	10.9	–0.80	–2.69 to 1.09	0.41
6 years	182	37.9	11.6	179	37.4	11.4	0.21	–1.70 to 2.13	0.83
7 years	171	38.4	11.2	171	37.1	11.5	0.41	–1.53 to 2.35	0.68
8 years	155	38.1	11.4	162	37.2	11.4	0.29	–1.69 to 2.28	0.77
9 years	149	36.5	11.3	162	35.8	11.3	–0.12	–2.11 to 1.87	0.91
10 years	97	36.6	11.8	118	35.9	11.4	–0.15	–2.37 to 2.07	0.89

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours mobile bearings; *n*, the number of responses; SD, standard deviation.

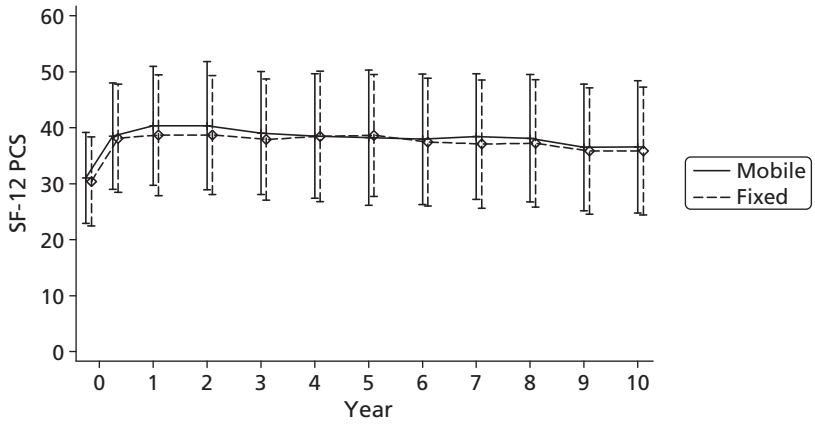

FIGURE 29 Mean (SD) SF-12 PCS by group at each follow-up time point for mobile vs. fixed bearing.

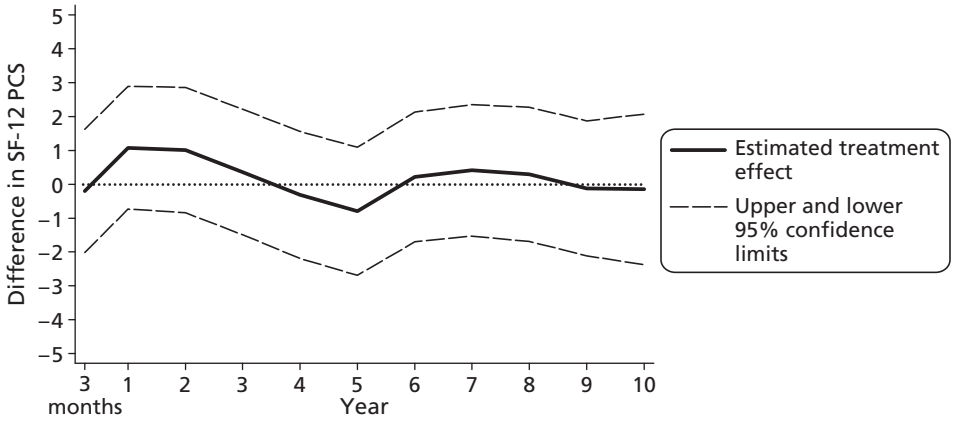

FIGURE 30 Estimated treatment effect on SF-12 PCS (95% CI) at each follow-up time point for mobile vs. fixed bearing. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

TABLE 20 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 MCS for mobile vs. fixed bearing

	Mobile bearing			Fixed bearing					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	251	48.1	12.0	237	48.6	11.9			
3 months	213	48.2	11.8	215	49.5	11.0	–0.81	–2.68 to 1.06	0.40
1 year	218	50.6	11.2	225	50.1	12.1	0.14	–1.72 to 1.99	0.89
2 years	212	49.8	10.8	200	50.8	11.3	–0.59	–2.49 to 1.32	0.55
3 years	208	49.8	10.5	203	48.3	11.7	1.21	–0.69 to 3.12	0.21
4 years	194	49.7	10.9	198	49.5	11.5	0.18	–1.76 to 2.12	0.85
5 years	190	49.5	10.2	189	50.1	10.8	–0.46	–2.42 to 1.50	0.65
6 years	182	49.0	10.8	179	49.0	11.3	0.09	–1.90 to 2.08	0.93
7 years	171	49.0	11.0	171	49.4	10.3	–0.74	–2.77 to 1.28	0.47
8 years	155	48.2	12.2	162	48.9	10.9	–0.73	–2.81 to 1.35	0.49
9 years	149	49.7	10.8	162	48.1	11.2	1.53	–0.56 to 3.63	0.15
10 years	97	47.5	11.4	118	48.9	10.5	–0.91	–3.31 to 1.48	0.45

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours mobile bearings; *n*, the number of responses; SD, standard deviation.

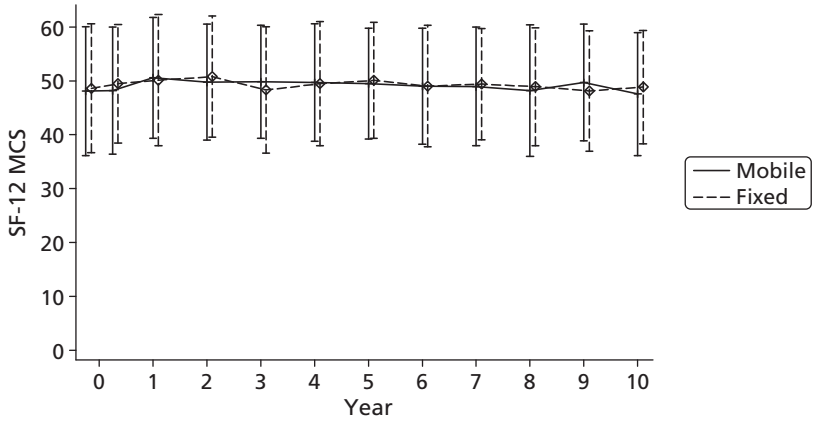

FIGURE 31 Mean (SD) SF-12 MCS by group at each follow-up time point for mobile vs. fixed bearing.

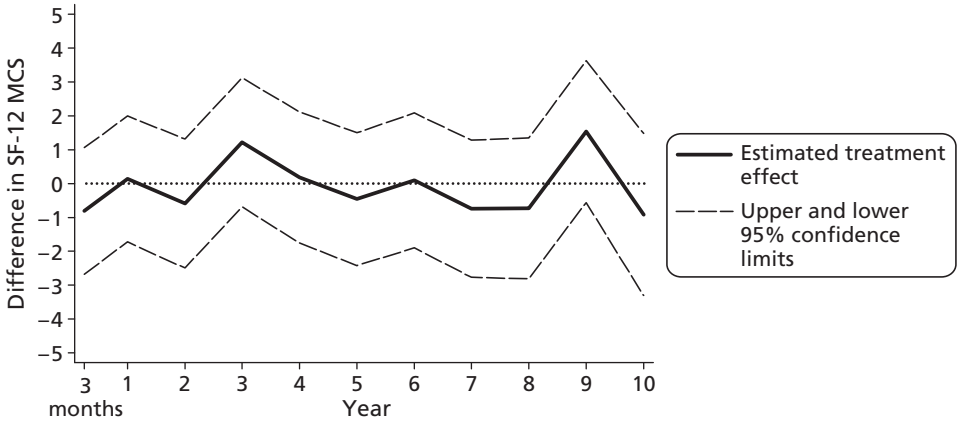

FIGURE 32 Estimated treatment effect on SF-12 MCS (95% CI) at each follow-up time point for mobile vs. fixed bearing. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours patellar resurfacing.

TABLE 21 Readmissions up to a median of 10 years postoperatively for mobile vs. fixed bearing

	Mobile bearing (*N* = 262)		Fixed bearing (*N* = 255)	
Readmission type	***n***	**%**	***n***	**%**
Total readmissions	57		63	
No. of participants requiring at least one readmission	41	16	45	18
Minor/intermediate operations				
Total number operations	26		15	
Participants requiring				
At least one minor operation	22	8	16	6
Multiple minor operations	3	1	3	1
Number requiring at least one of				
Debridement/exploration/washout	4	2	1	< 1
Manipulation under anaesthetic	7	3	6	2
Arthroscopy EUA/biopsy	10	4	7	3
Late patellar resurfacing	2	1	4	2
Patella revision	1	< 1		
Operations for instability				
Total number of operations	6			
Any operation for instability	5	2		
Multiple operations for instability	1	< 1		
Number requiring at least one of				
Open relocation or exchange of bearing	3	1		
Revision for instability	2	1		
Revision for dislocation	1	< 1		
Major operations				
Total number operations	11		9	
Any major operation	9	3	8	3
Multiple major operations	2	1	1	< 1
Number requiring at least one of				
Two-stage revision	2	1	3	1
Revision pain/loosening	7	3	6	2

EUA, examination under anaesthetic.

and 3% (9/262) of the mobile bearing group and 3% (8/255) of the fixed bearing group required other further major operations (odds ratio 1.07; 95% CI 0.36 to 3.25; $p = 1.00$). There were six reoperations for bearing dislocation or instability in the mobile bearing group in five participants (2%) compared with none in the fixed bearing group ($p = 0.062$). Time-to-event analyses showed that there was no evidence of a difference between the randomised groups on time to any major reoperation or reoperation for instability (hazard ratio 1.47; 95% CI 0.60 to 3.61; $p = 0.39$; *Figure 33*); time to any reoperation (hazard ratio 1.39; 95% CI 0.81 to 2.37; $p = 0.23$; *Figure 34*); or time to any reoperation or OKS dropping to below baseline levels beyond 1 year (hazard ratio 0.93; 95% CI 0.67 to 1.29; $p = 0.66$; *Figure 35*).

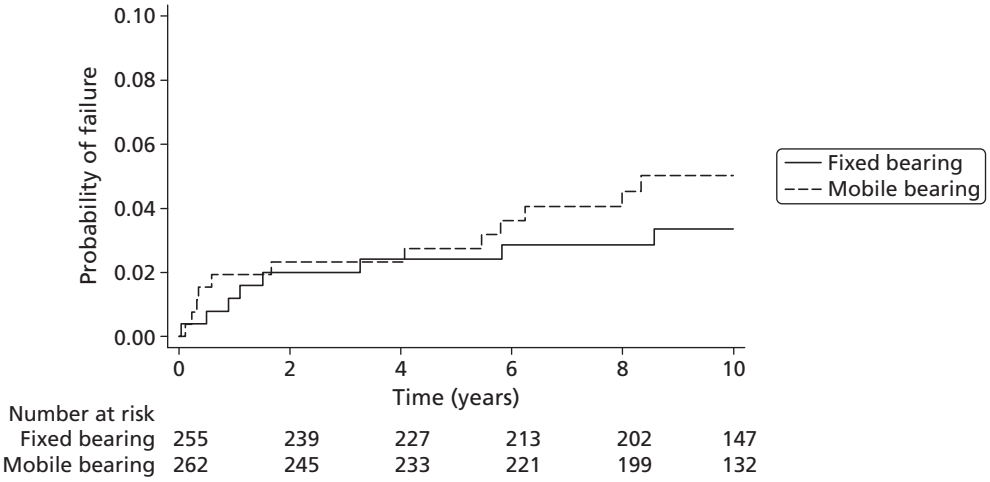

FIGURE 33 Kaplan–Meier failure curves for time to first major reoperation for mobile vs. fixed bearing.

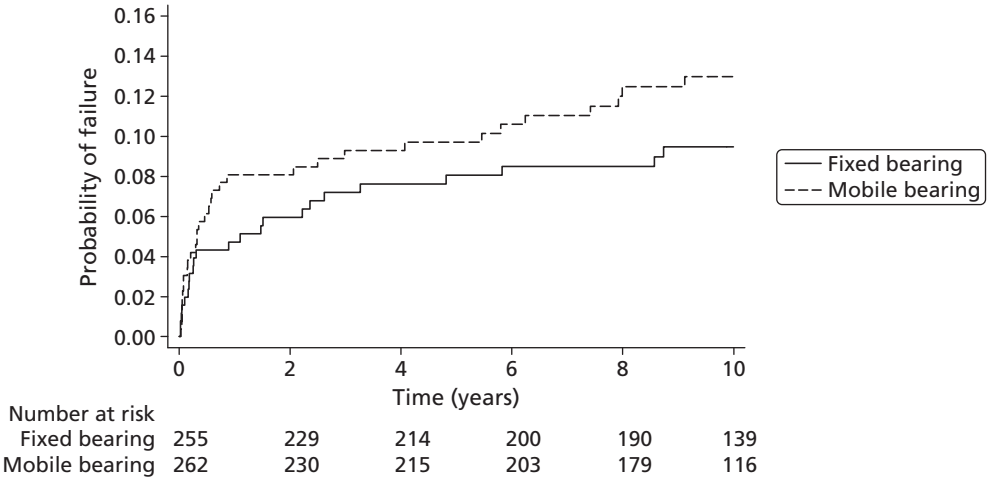

FIGURE 34 Kaplan–Meier failure curves for time to any reoperation for mobile vs. fixed bearing.

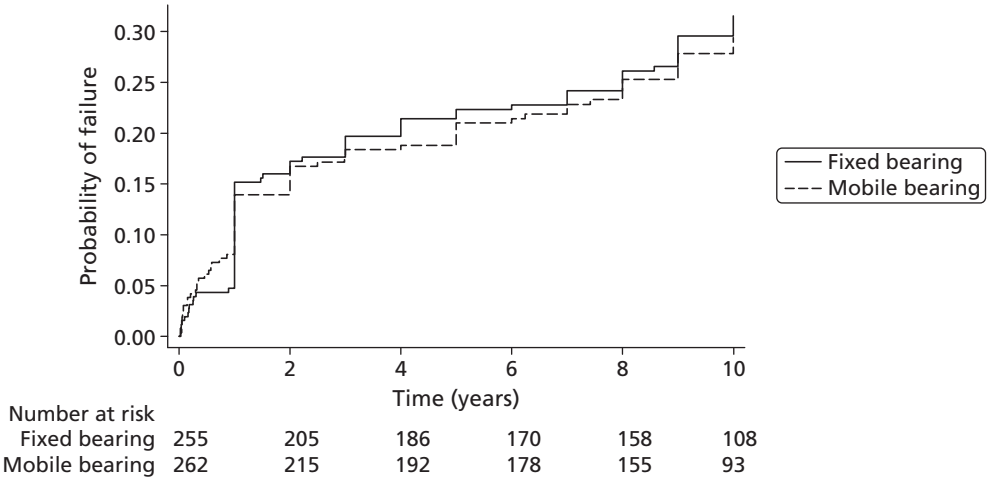

FIGURE 35 Kaplan–Meier failure curves for time to any reoperation or OKS dropping below baseline score for mobile vs. fixed bearing.

Cost comparison

The participants randomised to mobile bearings had a similar mean operation time ($p = 0.87$) and length of hospital stay ($p = 0.79$) to those in the fixed bearing group, which were comparable to those seen among participants randomised in the patellar resurfacing comparison (*Table 22*). There were also no significant differences in the cost or incidence of complications (minimum $p = 0.64$) or further surgery (minimum $p = 0.88$) during the primary hospital stay.

However, mobile bearings significantly increased the cost of tibial and femoral knee components. Participants assigned to fixed bearings used significantly fewer tibial components ($p < 0.001$) than those in the mobile bearing group, as all mobile bearings require a separate bearing, while fixed bearings may be all-polyethylene monoblocks. Additionally, participants assigned to mobile bearings tended to have more expensive tibial trays (mean £712/tray for mobile vs. £682/tray for fixed bearings) and inserts (mean £255/insert for mobile vs. £196/insert for fixed bearings). As a result, the total cost of tibial components was £126 (95% CI £94 to £158; $p < 0.001$) higher for participants randomised to mobile rather than fixed bearings. Mobile bearings were also associated with more costly femoral components, increasing the cost of femoral and other components by £155 (95% CI £119 to £191; $p < 0.001$) per participant. The total cost of the primary hospital stay was therefore £239 higher for participants in the mobile bearing group than for those in the fixed bearing group, although between-participant variability in non-component costs meant that this difference was not statistically significant ($p = 0.20$) (see *Table 22*).

However, the increased cost of components during the primary hospital stay was partially offset by non-significant reductions in the cost of readmissions and ambulatory consultations during the 10 years after TKR. Overall, participants randomised to fixed bearings had 1.4 more GP ($p = 0.71$), physiotherapy ($p = 0.51$) and orthopaedic consultations ($p = 0.30$) over the first 10 years after TKR and had follow-up costs that were £154 higher than those of participants randomised to mobile bearings ($p = 0.74$). The difference in the number of orthopaedic outpatient, physiotherapy and GP consultations was highest in year 1, whereas the difference in the cost of readmissions was greatest in years 2–4 (*Figure 36*). The total cost in each year of the trial fell dramatically after the first year, but oscillated in later years owing to chance variations in the number of readmissions per year within the comparatively small sample. Costs were particularly high in year 6, when there were three readmissions in the mobile bearing arm and two in the fixed bearing arm. Total costs were £207 higher in the mobile bearing group in year 1, between £65 and £111 lower during years 2–4 and higher again in most subsequent years (see *Table 23*). Total costs (including the primary hospital stay and 10 years' outpatient follow-up) were therefore £85 (95% CI –£911 to £1081) higher in the group randomised to mobile bearings ($p = 0.87$).

Within-trial cost-effectiveness results

Base-case analysis

Following the quality-of-life trends described above, the mobile bearing arm accrued non-significantly more QALYs during the first 4 years after TKR (minimum $p = 0.14$). However, the mobile bearing arm accrued fewer QALYs in most subsequent years (minimum $p = 0.59$; *Table 23*), despite life expectancy being 9.29 years in the two groups ($p = 0.98$). Over the 10-year time horizon, the larger quality of life increases observed in earlier years outweighed the quality of life decreases seen in later years and the mobile bearing group therefore accrued 0.051 (95% CI –0.333 to 0.435) more QALYs than the fixed bearing group ($p = 0.79$).

Mobile bearings were therefore associated with non-significantly higher costs (mean difference £85; $p = 0.87$) and marginally more QALYs (mean difference 0.051; $p = 0.79$) over the 10-year time horizon. The ICER for mobile bearings is therefore £1666 per QALY gained compared with fixed bearings, although there is substantial uncertainty around this point estimate. In NHS decision-making, treatments that increase health and NHS costs are generally considered to be good value for money if they have an ICER

TABLE 22 Resource use and costs for mobile vs. fixed bearing. All values are per participant and exclude postrandomisation exclusions

	Allocated to mobile bearing ($n = 262$) [mean (SE)]		Allocated to fixed bearing ($n = 255$) [mean (SE)]		Difference (95% CI)	
Resource	Number	Cost (£)	Number	Cost (£)	Number	Cost (£)
Resource use during inpatient stay for primary knee replacement						
Minutes in theatre	121.4 (2.26)	2048 (38)	120.8 (2.37)	2038 (40)	0.55 (–5.84 to 6.95)	9 (–99 to 117)
Days in hospital[a]	9.8 (0.40)	3211 (133)	9.9 (0.31)	3255 (102)	–0.14 (–1.13 to 0.86)	–45 (–373 to 283)
Total knee components	3.5 (0.03)	1979 (24)	3.3 (0.05)	1702 (17)	0.19 (0.07 to 0.30)[b]	277 (221 to 334)[b]
Patella components	0.5 (0.03)	49 (4)	0.5 (0.03)	52 (4)	–0.03 (–0.12 to 0.06)	–3 (–14 to 7)
Tibial components	1.9 (0.01)	952 (12)	1.7 (0.03)	826 (12)	0.21 (0.14 to 0.27)[b]	126 (94 to 158)[b]
Other knee components	1.0 (0.01)	979 (17)	1.0 (0.01)	824 (6)	0.01 (–0.02 to 0.04)	155 (119 to 191)[b]
Peri-/postoperative complications	0.1 (0.02)	3 (2)	0.1 (0.02)	5 (3)	0.01 (–0.04 to 0.07)	–1 (–8 to 5)
Further surgery occurring during hospital stay	0.0 (0.01)	23 (9)	0.0 (0.01)	25 (10)	0.00 (–0.03 to 0.03)	–2 (–29 to 25)
Total cost of inpatient stay for primary knee replacement	–	7263 (145)	–	7024 (114)	–	239 (–125 to 602)
Resource use over first 10 years after primary knee replacement (excluding initial hospital stay)[c]						
Total hospital readmissions related to study knee	0.22 (0.04)	1010 (243)[d]	0.23 (0.03)	1,080 (£344)[d]	–0.01 (–0.11 to 0.09)	–70 (–892 to 751)[d]
Outpatient consultations related to study knee	3.53 (0.29)	340 (26)[d]	3.95 (0.29)	381 (27)[d]	–0.42 (–1.22 to 0.37)	–41 (–114 to 32)[d]
Physiotherapy consultations related to study knee	6.32 (0.63)	262 (26)[d]	6.97 (0.75)	295 (32)[d]	–0.65 (–2.58 to 1.28)	–32 (–113 to 48)[d]
GP consultations related to study knee	3.61 (0.56)	122 (18)[d]	3.89 (0.52)	132 (17)[d]	–0.28 (–1.77 to 1.21)	–10 (–59 to 39)[d]
Total cost over first 10 years of study (excluding initial hospital stay)	–	1735 (265)[d]	–	1889 (377)[d]	–	–154 (–1055 to 748)[d]
Total cost of primary operation and follow-up	–	8998 (310)[d]	–	8913 (405)[d]	–	85 (–911 to 1081)[d]

a Excludes the incremental cost of time spent in high-dependency unit.
b $p < 0.05$.
c Costs and resource-use quantities after discharge were estimated using IPW.
d Discounted at 3.5% per year.

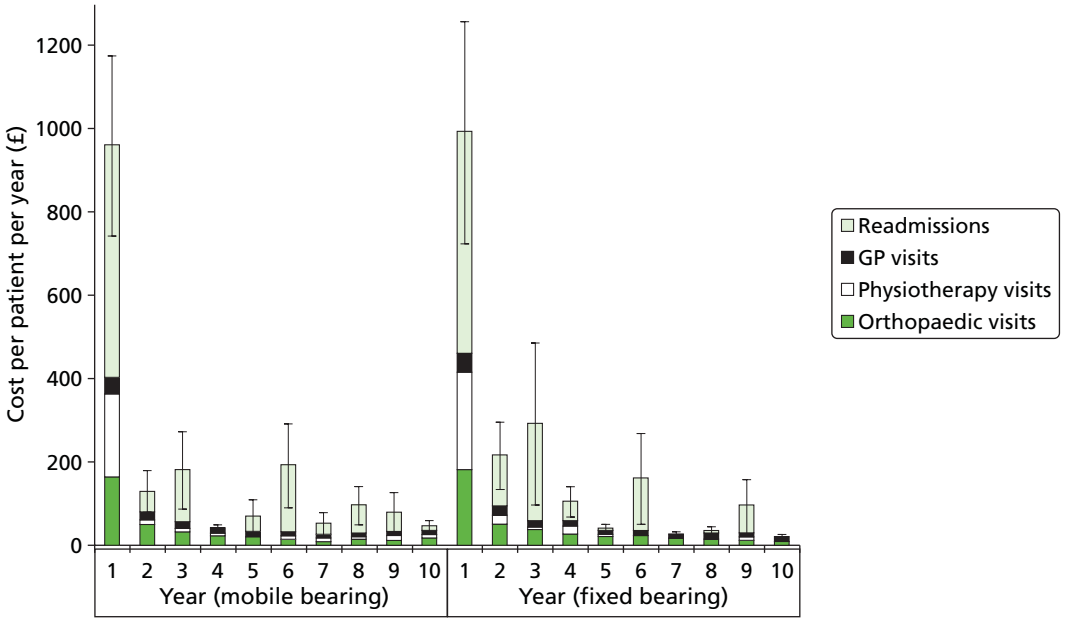

FIGURE 36 Illustration of cost breakdown by year after discharge from hospital for mobile vs. fixed bearing. Error bars show SEs around total cost.

below £20,000 per QALY gained,[81] making mobile bearings highly cost-effective based on their ICER point estimate, although there remains substantial uncertainty around this figure.

However, there was substantial uncertainty around both incremental costs and incremental QALYs, with a joint distribution spread across the four quadrants of the cost-effectiveness plane (*Figure 37*). There was a 32% probability that mobile bearings were more costly and more effective, a 29% probability that mobile bearings dominated fixed bearings (being less costly and more effective), a 27% probability that mobile bearings were dominated and a 13% probability that they were less costly and less effective (south-west quadrant). In particular, the uncertainty meant that the cost-effectiveness acceptability curve was very flat, with the probability of mobile bearings being cost-effective varying between 42% and 60% (*Figure 38*). At a £20,000/QALY ceiling ratio, the probability of mobile bearings being cost-effective was 59%.

Sensitivity analyses

Sensitivity analyses suggested that the base-case conclusions were sensitive to the methods used to deal with missing data and protocol violations (*Table 24*). The complete case analysis, based on 96 and 97 participants (excludes all participants with missing data on any resource-use variable or quality-of-life measurement prior to death or administrative censoring), found mobile bearings to be substantially more costly and marginally less effective than fixed bearings. The per-protocol analysis also found mobile bearings to be dominated by fixed bearings (being more costly and less effective).

However, all other sensitivity analyses were consistent with the base-case finding that participants randomised to mobile bearings accrued marginally higher QALYs than those randomised to fixed bearings and that there is a 51–65% probability that mobile bearings are cost-effective at a £20,000/QALY ceiling ratio, although two analyses (increasing the discount of component prices and increasing the cost per bed-day) found mobile bearings to dominate fixed bearings. Time horizon had a marked effect on both incremental costs and incremental QALYs because of the tendency for participants assigned to mobile bearing to accrue fewer QALYs and higher costs in years 5–11. At an 8-year time horizon, the estimated incremental QALYs were greater than those in the base-case analysis, whereas both lower incremental costs and lower incremental QALYs were observed at an 11-year time horizon. This may suggest that a longer follow-up could reverse the direction of differences in both costs and QALYs, making mobile bearings less costly and less effective than fixed bearings.

TABLE 23 Base-case cost-effectiveness results for mobile vs. fixed bearing

Time point	Allocated to mobile bearing ($n = 262$) [mean (SE)]		Allocated to fixed bearing ($n = 255$) [mean (SE)]		Difference in annual costs (95% CI) (£)	Difference in annual QALYs (95% CI)	Difference in cumulative costs (95% CI) (£)	Difference in cumulative QALYs (95% CI)
	Total cost (£)	QALYs	Total cost (£)	QALYs				
Year 1	8224 (217)	0.627 (0.015)	8018 (267)	0.613 (0.014)	207 (–465 to 878)	0.014 (–0.023 to 0.051)	207 (–465 to 878)	0.014 (–0.023 to 0.051)
Year 2	129 (51)	0.678 (0.018)	219 (80)	0.642 (0.018)	–89 (–278 to 99)	0.036 (–0.012 to 0.084)	120 (–594 to 835)	0.049 (–0.031 to 0.129)
Year 3	183 (92)	0.656 (0.019)	294 (195)	0.624 (0.018)	–111 (–535 to 312)	0.032 (–0.018 to 0.082)	16 (–900 to 933)	0.078 (–0.043 to 0.199)
Year 4	43 (9)	0.622 (0.020)	107 (37)	0.608 (0.020)	–65 (–139 to 10)	0.014 (–0.040 to 0.068)	–42 (–975 to 891)	0.091 (–0.071 to 0.253)
Year 5	72 (39)	0.594 (0.021)	41 (10)	0.609 (0.020)	30 (–48 to 108)	–0.015 (–0.071 to 0.040)	–16 (–955 to 924)	0.078 (–0.124 to 0.279)
Year 6	193 (100)	0.573 (0.021)	162 (109)	0.585 (0.021)	31 (–257 to 319)	–0.013 (–0.069 to 0.044)	11 (–963 to 985)	0.067 (–0.172 to 0.307)
Year 7	54 (29)	0.550 (0.021)	28 (6)	0.543 (0.022)	26 (–31 to 84)	0.006 (–0.052 to 0.065)	32 (–945 to 1010)	0.072 (–0.205 to 0.349)
Year 8	97 (45)	0.509 (0.023)	36 (11)	0.520 (0.021)	61 (–30 to 152)	–0.011 (–0.071 to 0.049)	80 (–904 to 1064)	0.063 (–0.250 to 0.377)
Year 9	79 (49)	0.477 (0.023)	96 (64)	0.488 (0.023)	–17 (–176 to 142)	–0.011 (–0.074 to 0.052)	67 (–927 to 1062)	0.055 (–0.293 to 0.403)
Year 10	46 (16)	0.467 (0.027)	22 (7)	0.472 (0.026)	24 (–11 to 59)	–0.005 (–0.077 to 0.067)	85 (–911 to 1081)	0.051 (–0.333 to 0.435)
Total	8998 (310)	5.007 (0.143)	8913 (405)	4.956 (0.141)	85 (–911 to 1081)	0.051 (–0.333 to 0.435)	85 (–911 to 1081)	0.051 (–0.333 to 0.435)

a $p < 0.05$.

Total costs and QALYs accrued in each year of the trial. Costs and QALYs beyond year 1 are discounted at 3.5% per year and include IPW; SEs estimated using bootstrapping. All QALY estimates are adjusted for baseline utility.

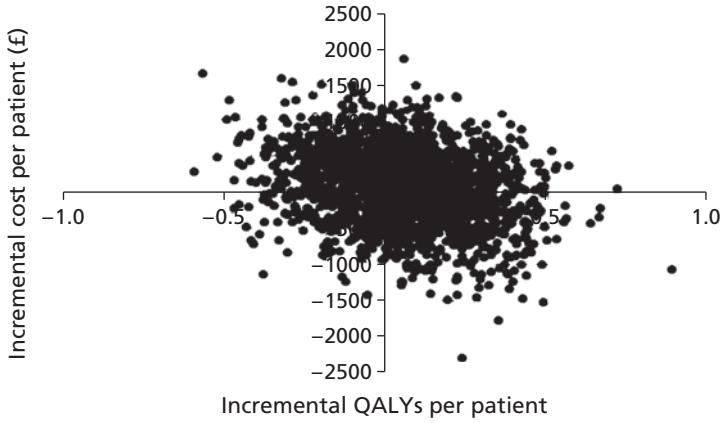

FIGURE 37 Stochastic cost-effectiveness results for mobile vs. fixed bearing: scatter graph on cost-effectiveness plane.

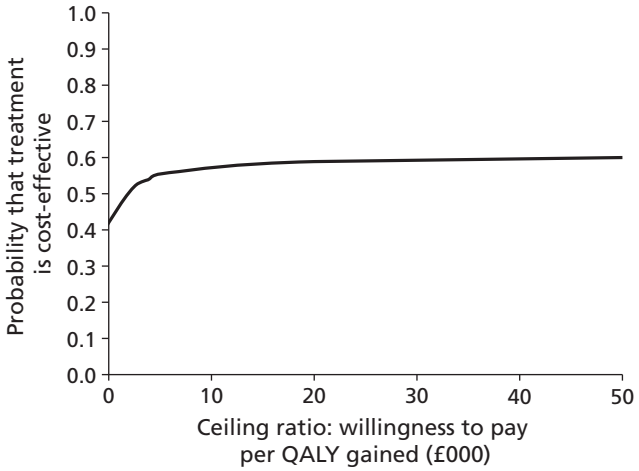

FIGURE 38 Cost-effectiveness acceptability curve for mobile vs. fixed bearing.

Subgroup analyses

Subgroup analyses suggested that both the costs and benefits of mobile bearings differ with age (see *Table 24*). In particular, both the incremental costs and incremental health benefits of mobile bearings were markedly larger for participants aged < 70 years; although the cost-effectiveness ratio for this group was similar to that of the total population, the probability that mobile bearings were cost-effective compared with fixed bearings rose to 86%, compared with 59% in the base-case analysis, despite the smaller sample size. By contrast, mobile bearings were less costly but produced a smaller QALY gain than fixed bearings in older participants, saving £618 per QALY lost, which would not be considered good value for money.

Potential for interactions between mobile bearings and patellar resurfacing

Analysing the subset of 240 participants randomised to both the mobile bearing and patellar resurfacing comparisons as a factorial trial, it was found that there were interactions that had a marked effect on estimated incremental costs and QALYs. In particular, non-significant qualitative interactions between the two treatment allocation factors were observed for costs ($p = 0.12$), QALYs ($p = 0.08$) and net monetary benefits ($p = 0.06$), which means that the incremental effect of mobile bearings changes sign depending on whether participants were allocated to patellar resurfacing or no resurfacing. [Net monetary benefits are a linear measure of cost-effectiveness that facilitates statistical analysis and comparison of multiple groups. The total net monetary benefit was calculated by multiplying the total number of QALYs accrued in each treatment arm by the £20,000/QALY ceiling ratio and subtracting total costs.] In particular,

TABLE 24 Results of sensitivity and subgroup analyses for mobile vs. fixed bearing

	Allocated to mobile bearing ($n = 262$) [mean (SE)]		Allocated to fixed bearing ($n = 255$) [mean (SE)]		Difference (95% CI)			Probability that mobile bearings are	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/QALY (£)	Cost-effective[a]	Less costly
Base-case analysis	8998 (310)	5.007 (0.143)	8913 (405)	4.956 (0.141)	85 (–911 to 1081)	0.051 (–0.333 to 0.435)	1666	59%	42%
Sensitivity analyses									
Complete case analysis ($n = 96$, 97, respectively)	8217 (297)	5.398 (0.247)	7809 (239)	5.430 (0.207)	408 (–341 to 1157)	–0.032 (–0.655 to 0.591)	Dominated	44%	14%
Per-protocol analysis ($n = 220$, 238, respectively)	9233 (359)	5.025 (0.164)	8897 (427)	5.029 (0.142)	336 (–759 to 1430)	–0.004 (–0.421 to 0.413)	Dominated	46%	26%
46% reduction in LoS for primary admission	7504 (285)	5.007 (0.143)	7398 (393)	4.956 (0.141)	106 (–844 to 1056)	0.051 (–0.333 to 0.435)	2073	59%	40%
Component price discount									
0%	9907 (326)	5.007 (0.143)	9681 (415)	4.956 (0.141)	226 (–806 to 1258)	0.051 (–0.333 to 0.435)	4421	57%	32%
50%	8393 (299)	5.007 (0.143)	8401 (398)	4.956 (0.141)	–9 (–982 to 964)	0.051 (–0.333 to 0.435)	Dominant	60%	50%
Cost per bed-day									
£149 (–50%)	7123 (227)	5.007 (0.143)	6916 (270)	4.956 (0.141)	208 (–483 to 898)	0.051 (–0.333 to 0.435)	4066	58%	27%
£448 (+50%)	10,873 (398)	5.007 (0.143)	10,911 (544)	4.956 (0.141)	–37 (–1355 to 1280)	0.051 (–0.333 to 0.435)	Dominant	60%	51%
Cost per theatre minute									
£7.34 (–50%)	7805 (274)	5.007 (0.143)	7762 (373)	4.956 (0.141)	43 (–862 to 948)	0.051 (–0.333 to 0.435)	837	60%	45%
£22.00 (+50%)	10191 (347)	5.007 (0.143)	10,064 (438)	4.956 (0.141)	127 (–966 to 1221)	0.051 (–0.333 to 0.435)	2495	58%	39%

Analysis	Allocated to mobile bearing ($n = 262$) [mean (SE)]		Allocated to fixed bearing ($n = 255$) [mean (SE)]		Difference (95% CI)			Probability that mobile bearings are	
	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/QALY (£)	Cost-effective[a]	Less costly
Discount rate for time preference									
0% costs and QALYs	9121 (326)	5.752 (0.168)	9024 (423)	5.706 (0.167)	97 (–947 to 1142)	0.046 (–0.407 to 0.500)	2097	57%	42%
5% costs and QALYs	8954 (304)	4.738 (0.134)	8872 (398)	4.686 (0.132)	81 (–898 to 1060)	0.052 (–0.307 to 0.412)	1549	60%	42%
3.5% costs, 0% QALYs	8998 (310)	5.752 (0.168)	8913 (405)	5.706 (0.167)	85 (–911 to 1081)	0.046 (–0.407 to 0.500)	1830	57%	42%
No adjustment for baseline utility	8998 (310)	5.017 (0.146)	8913 (405)	4.955 (0.147)	85 (–911 to 1081)	0.062 (–0.345 to 0.470)	1363	60%	42%
Within-trial time horizon with no adjustment for censoring	8986 (309)	4.892 (0.145)	8929 (406)	4.870 (0.147)	57 (–940 to 1054)	0.022 (–0.384 to 0.427)	2622	53%	44%
8-year time horizon	8904 (303)	4.302 (0.118)	8824 (402)	4.239 (0.114)	80 (–904 to 1064)	0.063 (–0.250 to 0.377)	1267	65%	42%
9-year time horizon	8964 (309)	4.664 (0.131)	8897 (405)	4.609 (0.127)	67 (–927 to 1062)	0.055 (–0.293 to 0.403)	1232	61%	43%
11-year time horizon	9041 (312)	5.300 (0.160)	9037 (417)	5.287 (0.155)	4 (–1015 to 1024)	0.012 (–0.414 to 0.439)	359	51%	49%
Dealing with censoring using multiple imputation rather than IPW	8988 (309)	4.995 (0.147)	8927 (408)	4.935 (0.146)	60 (–940 to 1060)	0.060 (–0.347 to 0.467)	1008	60%	44%

continued

TABLE 24 Results of sensitivity and subgroup analyses for mobile vs. fixed bearing (*continued*)

	Allocated to mobile bearing ($n = 262$) [mean (SE)]		Allocated to fixed bearing ($n = 255$) [mean (SE)]		Difference (95% CI)			Probability that mobile bearings are	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/QALY (£)	Cost-effective[a]	Less costly
Subgroup analyses									
Age (years)									
< 70 ($n = 130$, 122)	8964 (439)	5.428 (0.197)	8649 (325)	5.112 (0.209)	315 (–749 to 1379)	0.317 (–0.212 to 0.845)	995	86%	28%
≥ 70 ($n = 132$, 133)	9032 (434)	4.597 (0.208)	9159 (732)	4.803 (0.188)	–127 (–1787 to 1533)	–0.206 (–0.746 to 0.334)	618 SW	24%	54%
Randomised to more than one comparison									
Randomised to resurfacing ($n = 47$, 51)	9068 (466)	5.559 (0.264)	9169 (1165)	4.959 (0.289)	–101 (–2540 to 2338)	0.600 (–0.158 to 1.357)	Dominant	93%	51%
Randomised to no resurfacing ($n = 52$, 43)	11,100 (1147)	4.732 (0.311)	8481 (464)	5.029 (0.294)	2620 (195 to 5044)	–0.298 (–1.139 to 0.544)	Dominated	17%	99%

LoS, length of stay.
a Probability that treatment is cost-effective is based on a £20,000/QALY ceiling ratio.
Cost-effectiveness ratios marked with 'SW' are in the south-west quadrant, in which treatments with high ratios are considered good value for money.

participants randomised to both mobile bearing and no patellar resurfacing accrued substantially higher costs and substantially fewer QALYs than those allocated to the other three combinations of treatment allocation. As a result of the interactions for QALYs and costs, mobile bearings dominated fixed bearings in participants who were also randomised to patellar resurfacing and had a 93% chance of being cost-effective at the £20,000/QALY ceiling ratio, but were dominated by fixed bearings, with a 17% chance of being cost-effective in participants randomised to no resurfacing.

As there is evidence that the incremental costs and benefits of mobile bearings may depend on whether or not participants are also randomised to patellar resurfacing, it is useful to also examine whether making a joint decision about these two aspects of TKR (rather than independent decisions) would change the conclusions. Treating the four combinations of treatment allocation as mutually exclusive strategies for TKR suggests that fixed bearings without patellar resurfacing dominate fixed bearings with patellar resurfacing, and mobile bearings without resurfacing are less costly and more effective than both of these alternatives. However, the strategy with highest clinical effectiveness and cost-effectiveness comprises mobile bearing with patellar resurfacing, which costs £1109 per QALY gained compared with fixed bearing and no patellar resurfacing. Taking account of interactions and evaluating the cost-effectiveness of mobile bearings and patellar resurfacing simultaneously is, therefore, consistent with the conclusion of the base-case analysis that both mobile bearings and patellar resurfacing are expected to be cost-effective.

Discussion

The mobile bearing component of KAT indicates that at 10 years post operation functional status, quality of life, and reoperation and revision rates are not significantly improved or made worse by the use of a mobile bearing prosthesis. In addition, there is substantial uncertainty around the cost-effectiveness of mobile bearings. This study therefore confirms the findings of previous RCTs and systematic reviews, showing that there is no real benefit conferred by using mobile bearings in TKR.[24–29]

There was no significant difference between the mobile and fixed bearing designs for any participant-reported outcome measure at any postoperative stage, which indicates that, at least up to 10 years, there is no difference in function or quality of life between the two designs. Furthermore, the estimated CIs rule out the prespecified MCID on the primary outcome. The readmission rate was the same for the two groups. There was also no statistically significant difference in the rate of minor, intermediate or major reoperations.

The main intended benefit of mobile bearings is improved function and reduced wear and loosening. These theoretical advantages would manifest as differences in participant-reported outcomes and incidence of reoperation for aseptic loosening. As there are no differences in these outcome measures at 10 years, these advantages are unconfirmed and remain theoretical. However, wear is a long-term problem for which differences may appear after 10 years, so the follow-up should be continued. The theoretical disadvantage of a mobile bearing (namely bearing instability) would manifest as reoperations for instability or dislocation. There were six reoperations in five participants (2%) related to instability or dislocation of the bearing in the mobile bearing group and none in the fixed bearing group ($p = 0.062$). This is, therefore, a real disadvantage of the mobile bearing. As the study has not demonstrated a definite clinical advantage of mobile bearings, it provides a good reason not to use a mobile bearing.

The economic evaluation suggested that mobile bearings increased the cost of knee components by £277 per participant, which was partly offset by reductions in readmissions and ambulatory consultations in the first 4 years after primary TKR. Over the 10-year time horizon, mobile bearings cost an additional £85 (95% CI –£911 to £1081) per participant treated. Although the mobile bearing group had a better quality of life in the first few years after knee replacement, this trend was reversed in subsequent years, giving an overall QALY difference of just 0.051 between mobile and fixed bearings. Based on mean costs and benefits, we would expect mobile bearings to be good value for money, costing £1666 per QALY gained

compared with fixed bearings. However, as the QALY difference observed is extremely small and there is substantial uncertainty around both costs and QALYs, we can be only 59% confident about this conclusion. Sensitivity analyses demonstrated that this finding is sensitive to the methods used to deal with missing data, protocol violations and time horizon, but not costing methodology. In the subgroup of patients under the age of 70 years, the cost of the mobile bearings relative to the fixed (£315; 95% CI –£749 to £1379) as well as the QALYs gained (0.317; 95% CI –0.212 to 0.845) increased, and as a result the chance of mobile bearings being cost-effective at a £20,000/QALY ceiling ratio increased to 86%.

Although mobile bearings were found to have greater expected net benefits than fixed bearings, which could justify their adoption based on current information, more information is likely to be necessary to confirm this conclusion: particularly given the very small QALY gain and the substantial uncertainty around both incremental QALYs and incremental costs. In particular, the mobile bearing group tended to accrue fewer QALYs and greater costs in years 5–11, which suggests that longer follow-up may reverse the trends observed, potentially making mobile bearings less costly and less effective over a longer time horizon. Further follow-up is therefore needed to assess the long-term costs and benefits of mobile bearings.

There was some evidence that patellar resurfacing affects the incremental costs and benefits of mobile bearings, although the interactions observed in the subset of participants randomised to both comparisons were not statistically significant. If the patella is resurfaced, then a mobile bearing appears to be more cost-effective than a fixed bearing. However, the numbers are small, the clinical explanation for an interaction of this type is unclear and this analysis was one of several secondary or subgroup analyses. Findings should therefore be interpreted cautiously and further study is needed to determine why the interaction occurs before recommendations based on these interactions can be made.

Conclusion

The study has shown no definitive advantage or disadvantage for mobile or fixed bearings in terms of postoperative functional status, quality of life, reoperation and revision rates or cost-effectiveness. We therefore cannot make any strong conclusions about whether surgeons should or should not use mobile bearings.

We did, however, identify two disadvantages of mobile bearings that would discourage surgeons from using mobile bearings. First, there was an incidence of 2% of bearing instability in the mobile bearing group and none in the fixed bearing group. Second, there was a cost saving for the hospital associated with the use of fixed bearings.

Further follow-up of the patients would be useful: first, to determine whether the theoretical advantage of decreased wear and the observed trend towards lower QALYs beyond year 5 with mobile bearings in the long term is real; second, to determine whether the trend towards mobile bearings having a greater cost-effectiveness in patients < 70 years becomes significant or if it disappears; and, third, to monitor the potential interactions between patellar resurfacing and mobile bearings.

Chapter 5 All-polyethylene versus metal-backed tibial components

Description of the groups at trial entry

Of the 2352 participants in the trial, 409 were randomised within the comparison of metal-backed versus all-polyethylene tibial components. The two randomised groups were well matched at baseline (*Table 25*). In both groups the mean age was similar. In the metal-backed group, 49% were male compared with 46% in the all polyethylene group. In both groups, the mean BMI was about 29 kg/m^2, and 95% of both groups had osteoarthritis. Participants were also well matched on the ASA classification and previous knee surgery.

Surgical management

Of the 116 surgeons in 34 centres in the UK that participated in KAT, 17 (15%) recruited participants to the metal-backed versus all polyethylene comparison. Of the 409 randomised in this comparison, 365 (89%) received the allocated procedure; seven participants were withdrawn before surgery; two received a unicompartmental knee replacement; and in three cases it was unclear what surgery was received (*Figure 39*). The remainder, for various reasons, either received a metal-backed tibia when they were allocated an all-polyethylene tibia (15%, 31 of 207) or, conversely, received an all-polyethylene tibia when allocated a metal-backed tibia (< 1.0%, 1 of 202). The most common reasons for non-compliance were logistical constraints, such as prostheses being unavailable at the time of operation or clinical decision.

In-hospital care and short-term complications

Information on intra- and postoperative complications was returned for 398 (99%) operations. Intraoperative complications were observed in only a small percentage of the participants (2.8%; 11 of 398), and the operative procedure caused problems in few participants (1.8%; 7 of 398). Overall, there were no differences between the randomised groups in these respects. Postoperative complications were reported in 16% (65) of the 398 participants for whom information was available; however, specific problems, such as wound infection, septicaemia, DVT or PE, cerebrovascular accident and myocardial infarction, were rare. Overall, 1.3% (5) of the 398 participants had additional knee surgery. One participant died from a brain stem infarction in the intermediate postoperative period. Overall, 96% (382) of the 398 participants were discharged directly to their home. The median length of hospital stay was 10 days (*Table 26*). There were no differences between the randomised groups with regard to any of the above factors.

Response rates at each follow-up point

Table 27 describes the response rate; the response rate to questionnaires sent was high in both groups over the whole follow-up period, ranging from 82% to 97%. The proportion of participants sent a questionnaire dropped over the life of the trial, as one would expect given a cohort of this nature, owing to death, loss to follow-up and patients declining further follow-up. At 10 years, the response rate was approximately 60% of the cohort that were still living.

TABLE 25 Description of groups at trial entry for all-polyethylene vs. metal-backed components

Characteristic	All polyethylene (*n* = 207)		Metal-backed (*n* = 202)	
Age (years) (mean, SD)	70	8	69	9
Female	111	53.6	103	51.0
BMI (kg/m^2) (mean, SD)	28.7	4.6	28.7	4.6
ASA				
Completely fit and healthy	27	13.0	22	10.9
Some illness but has no effect on normal activity	127	61.4	127	62.9
Symptomatic illness present but minimal restriction	46	22.2	46	22.8
Symptomatic illness causing severe restriction	1	0.5	1	0.5
Missing	6	2.9	6	3.0
Primary type of knee arthritis				
Osteoarthritis	193	93.2	189	95.0
Rheumatoid	9	4.3	10	5.0
Both	1	0.5	1	0.5
Missing	4	1.9	2	1.0
Extent of knee arthritis affecting mobility				
One knee	46	22.2	49	24.3
Both knees	80	38.6	80	75
General	81	39.1	78	38.6
	n = *199*		**n = *203***	
Other conditions affecting mobility	23	11.3	22	11.1
Medical	8	3.9	12	6.0
Locomotor/musculoskeletal	16	7.9	14	7.0
Previous knee surgery	73	36.0	76	38.2
Ipsilateral osteotomy	1	0.5	1	0.5
Ipsilateral patellectomy	0	0.0	1	0.5
Contralateral previous knee replacement	27	13.3	33	16.6
Other previous knee surgery	48	23.6	44	22.1
Arthroscopy	42	20.7	34	17.1
Other related surgery	8	3.9	12	6.0

SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

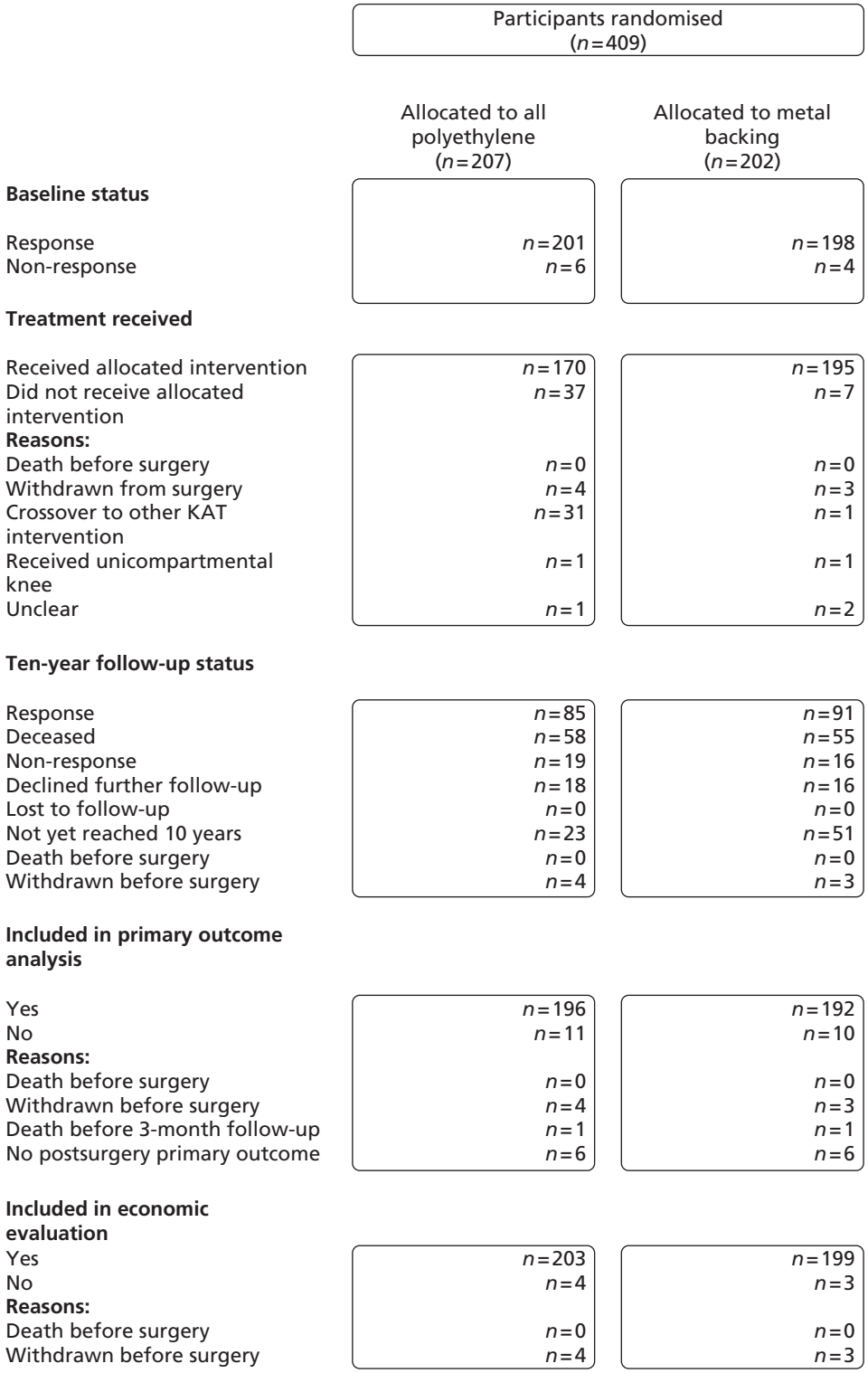

FIGURE 39 CONSORT diagram for all-polyethylene vs. metal-backed tibial components.

TABLE 26 In-hospital care and short-term complications for all-polyethylene vs. metal-backed tibial components

Variable	All polyethylene (*n* = 202)		Metal-backed (*n* = 197)	
Any postoperative complications	35	17.8	30	14.9
Knee dislocation	0	0.0	0	0.0
Proven wound infection	1	0.5	1	0.5
Septicaemia	0	0.0	0	0.0
Treated DVT or PE	5	2.5	3	1.5
Confirmed cerebrovascular accident	0	0.0	0	0.0
Confirmed myocardial infarction	1	0.5	1	0.5
Other serious complication	28	13.9	27	13.7
Medical complications	14	6.9	16	8.1
Surgical complications	0	0.0	3	1.5
Fall	0	0.0	1	0.5
Suspicion of infection	8	4.0	4	2.0
Confirmed infection	0	0.0	0	0.0
Skin complications	2	1.0	2	1.0
Stiffness	2	1.0	1	0.5
Suspected thrombolytic complications	3	1.5	2	1.0
Urinary complications	3	1.5	2	1.0
	n = *201*		**n = *196***	
Any further knee surgery before hospital discharge	4	2.0	1	0.5
Manipulation under anaesthetic	2	1.0	0	0.0
Wound problem	0	0.0	0	0.0
Stiffness	0	0.0	0	0.0
Musculoskeletal ligamentous (including imbalance)	0	0.0	0	0.0
Patella complication	0	0.0	0	0.0
Suspicion of infection	2	1.0	1	0.5
Confirmed infection	0	0.0	0	0.0
Dislocation	0	0.0	0	0.0
Prosthetic complication	0	0.0	0	0.0
Unknown	0	0.0	0	0.0
Status at discharge				
Alive	201	99.5	196	100.0
Dead	1	0.5	0	0.0
Discharged to home	192	95.0	190	96.9
Days in hospital				
Median (IQR)	9	8 to 12	8	7 to 11
Mean (SD)	10.38	4.7	9.7	4.7

IQR, interquartile range; SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

TABLE 27 Response rates at each follow-up time point for all-polyethylene vs. metal-backed tibial components

	All polyethylene							Metal-backed						
Time	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive	No. sent	% of randomised	% of alive	No. responses	% of sent	% of randomised	% of alive
Month 3	197	95	96	189	96	91	92	192	95	96	187	97	93	93
Year 1	195	94	96	185	95	89	91	190	94	97	181	95	90	93
Year 2	193	93	96	176	91	85	88	190	94	98	171	90	85	89
Year 3	187	90	94	172	92	83	87	182	90	96	167	92	83	88
Year 4	180	87	93	165	92	80	85	174	86	94	166	95	82	89
Year 5	167	81	90	156	93	75	84	169	84	94	156	92	77	87
Year 6	160	77	89	149	93	72	83	163	81	94	149	91	74	86
Year 7	154	74	89	142	92	69	82	153	76	92	140	92	69	84
Year 8	140	68	86	127	91	61	78	147	73	90	133	90	66	82
Year 9	133	64	85	115	86	56	74	136	67	88	121	89	60	79
Year 10	104	50	70	85	82	41	57	107	53	73	91	85	45	62

Outcomes after a median of 10 years post operation

Oxford Knee Score

There was no evidence of a between-group difference in OKS at baseline or at any stage thereafter (*Table 28*). The mean OKS in both groups was about 17.5 preoperatively. It increased to about 33 at 1 year and thereafter remained about the same. The difference in OKS between the two groups was small and was –1.19 (95% CI –3.48 to 1.11; $p = 0.311$) at 10 years (*Figure 40*, see *Table 28*). The marginal estimate over the whole 10-year follow-up was –1.36 (95% CI –2.98 to 0.26; $p = 0.10$) in favour of the metal-backed intervention (*Figure 41*). Sensitivity analysis imputing the last value before revision gave practically identical results; the marginal estimate was –1.41 (95% CI –3.06 to 0.25; $p = 0.10$).

Figure 42 explores the potential for interaction in those allocated to two interventions by plotting the difference in effect for all-polyethylene components for those allocated to patellar resurfacing compared

TABLE 28 Descriptive statistics and estimated treatment effects at each follow-up time point for OKS for all-polyethylene vs. metal-backed tibial components

	All polyethylene			Metal-backed					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	195	17.3	7.7	198	17.9	7.8			
3 months	165	29.3	9.4	162	31.0	9.9	–1.95	–3.88 to –0.01	0.048
1 year	154	32.7	9.8	157	34.7	10.2	–1.55	–3.51 to 0.41	0.120
2 years	150	33.3	10.5	142	35.4	10.7	–1.21	–3.19 to 0.78	0.233
3 years	150	33.8	10.0	150	34.7	10.4	–0.80	–2.78 to 1.18	0.427
4 years	153	33.5	10.3	149	34.7	10.3	–1.65	–3.63 to 0.32	0.101
5 years	139	33.7	10.7	145	34.5	9.8	–1.37	–3.37 to 0.63	0.180
6 years	136	33.6	10.5	135	34.0	10.2	–0.94	–2.96 to 1.08	0.364
7 years	131	33.6	10.7	131	33.9	9.7	–1.13	–3.16 to 0.91	0.278
8 years	114	32.9	10.4	122	33.5	9.9	–1.52	–3.60 to 0.57	0.154
9 years	104	32.0	11.7	110	33.0	9.4	–1.55	–3.68 to 0.58	0.154
10 years	79	32.1	10.3	81	32.5	10.1	–1.19	–3.48 to 1.11	0.311

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours all-polyethylene components; *n*, the number of responses; SD, standard deviation.

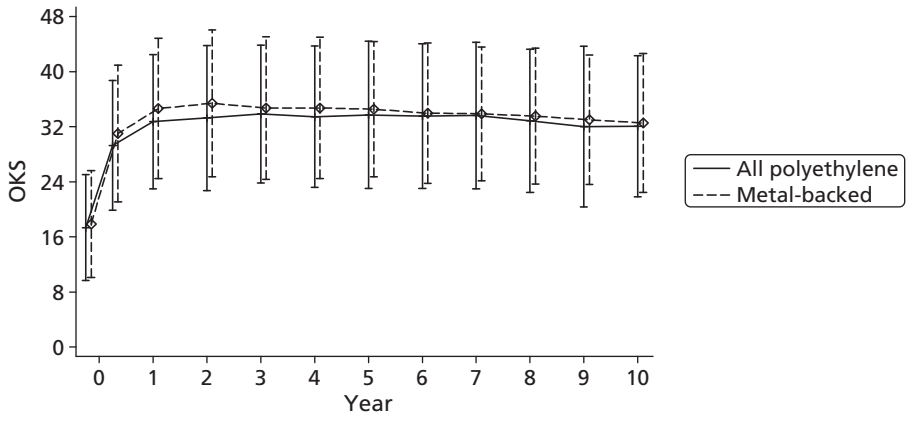

FIGURE 40 Mean (SD) OKS by group at each follow-up time point for all-polyethylene vs. metal-backed tibial components.

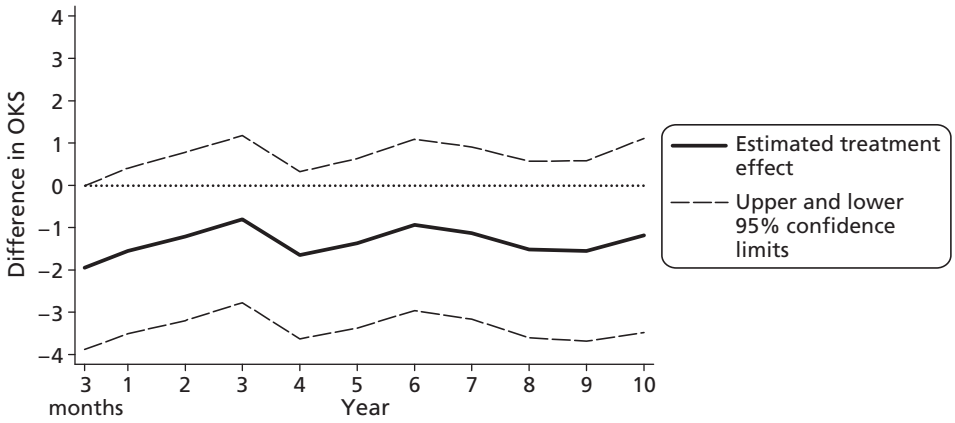

FIGURE 41 Estimated treatment effect on OKS (95% CI) at each follow-up time point for all-polyethylene vs. metal-backed tibial components. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours all-polyethylene components.

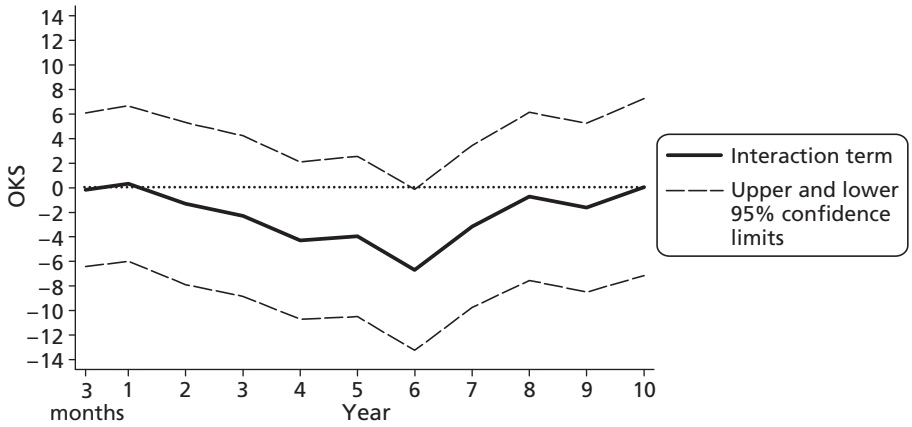

FIGURE 42 Interaction term (solid line) at each follow-up time-point for OKS for patellar resurfacing by all-polyethylene backing. Dotted lines represent 95% CIs.

with those allocated to no patellar resurfacing. A positive difference in differences suggests higher relative benefit for all-polyethylene backing in the patellar resurfacing group. The graph indicates that there may be a potential interaction, suggesting that not resurfacing the patella, if using all polyethylene components, might be beneficial. However, there is considerable uncertainty around these estimates owing to the reduced sample size in the partial factorial aspect of the trial and estimating CIs around interaction terms.

EuroQol 5D

There was a trend towards the metal-backed group having better EQ-5D scores than the all polyethylene group (*Figure 43*). In 3 years (years 4, 5 and 9), the *p*-value was < 0.05 (*Table 29*, *Figure 44*). The marginal estimate over the whole 10-year follow-up was –0.042 (95% CI –0.081 to –0.003; $p = 0.033$) in favour of the metal-backed intervention (see *Figure 44*).

Short Form 12

There was a trend towards the metal-backed group having a significantly better SF-12 PCS than the all polyethylene group (*Figure 45*). In 3 years (3, 4 and 9) the *p*-value was < 0.05 (*Table 30*, *Figure 46*). The marginal estimate over the whole 10-year follow-up was –1.63 (95% CI –3.19 to –0.069; $p = 0.041$) in favour of the metal-backed intervention.

The SF-12 MCS was similar between the two groups at most time points (*Table 31*, *Figure 47*). The marginal estimate over the whole 10-year follow-up was –0.22 (95% CI –1.73 to 1.29; $p = 0.77$), a minimal difference between groups (*Figure 48*).

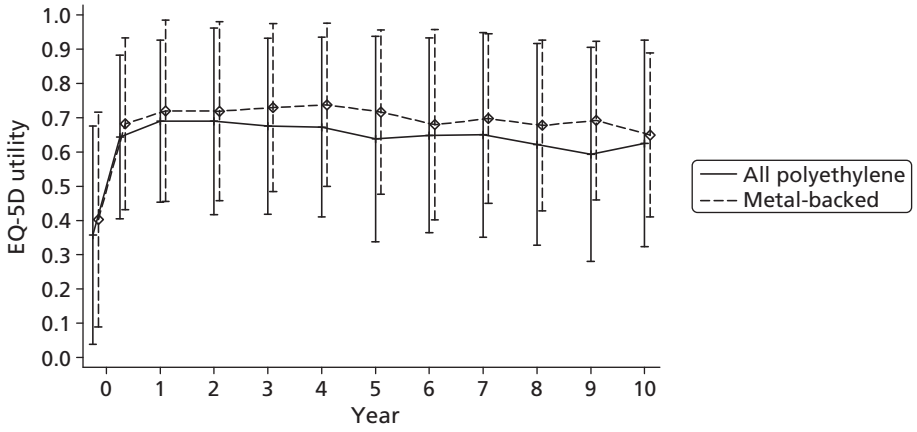

FIGURE 43 Mean (SD) EQ-5D utility by group at each follow-up time point for all-polyethylene vs. metal-backed tibial components.

TABLE 29 Descriptive statistics and estimated treatment effects at each follow-up time point for EQ-5D utility for all-polyethylene vs. metal-backed tibial components

	All polyethylene			Metal-backed					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	196	0.357	0.319	196	0.402	0.314			
3 months	179	0.644	0.239	182	0.682	0.251	–0.029	–0.080 to 0.022	0.27
1 year	178	0.690	0.237	176	0.720	0.265	–0.019	–0.071 to 0.032	0.47
2 years	174	0.690	0.272	163	0.719	0.262	–0.011	–0.063 to 0.041	0.68
3 years	163	0.675	0.257	165	0.730	0.246	–0.048	–0.101 to 0.005	0.074
4 years	159	0.673	0.262	163	0.738	0.238	–0.061	–0.114 to –0.008	0.024
5 years	153	0.638	0.300	149	0.717	0.240	–0.066	–0.120 to –0.012	0.017
6 years	146	0.648	0.284	145	0.680	0.278	–0.033	–0.087 to 0.022	0.24
7 years	139	0.650	0.299	135	0.697	0.248	–0.054	–0.109 to 0.002	0.059
8 years	122	0.622	0.295	130	0.678	0.249	–0.049	–0.106 to 0.008	0.093
9 years	113	0.593	0.313	116	0.692	0.232	–0.093	–0.152 to –0.034	0.002
10 years	83	0.625	0.302	88	0.650	0.239	–0.014	–0.079 to 0.050	0.661

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours all-polyethylene components; *n*, the number of responses; SD, standard deviation.

Clinical outcomes

There were 21/203 (10%) and 28/199 (14%) participants who were readmitted over the 10-year follow-up period (*Table 32*) (odds ratio 0.72; 95% CI 0.39 to 1.31; $p = 0.30$). The reoperation rate for minor and intermediate operations was very similar between the two groups (odds ratio 0.85; 95% CI 0.37 to 1.91; $p = 0.81$), and the majority of these reoperations took place within the first 5 years. Major reoperations were slightly more common in the all polyethylene group, but were rare overall (odds ratio 2.32; 95% CI 0.52 to 14.16; $p = 0.35$). The majority of the major operations took place in the first 5 years. Time-to-failure analysis of time until the first major reoperation estimated the hazard ratio as 2.30 (95% CI 0.60 to 8.90; $p = 0.23$; *Figure 49*), reflecting the higher number of reoperations in the all polyethylene group, but the CI is wide owing to the low number of reoperations. For time to any reoperation, the estimated hazard ratio was 0.85 (95% CI 0.44 to 1.68; $p = 0.65$; *Figure 50*). Broadening

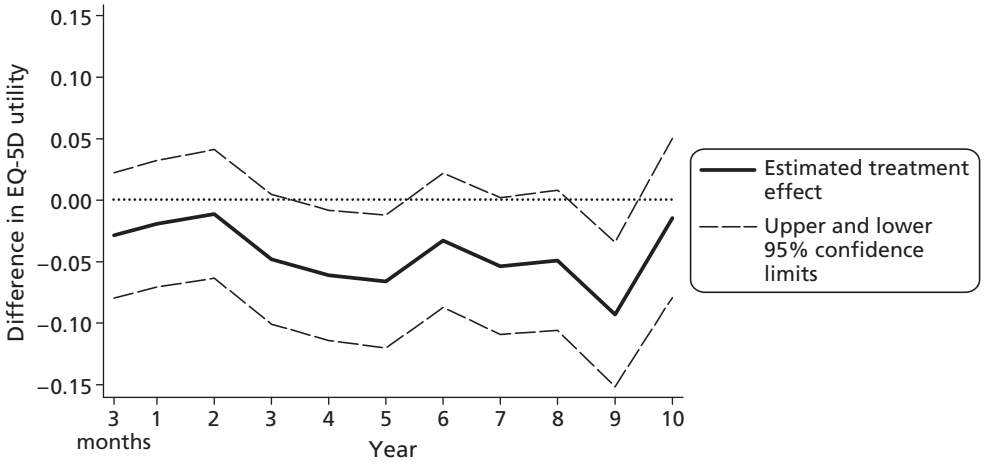

FIGURE 44 Estimated treatment effect on EQ-5D utility (95% CI) at each follow-up time point for all-polyethylene vs. metal-backed tibial components. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours all-polyethylene components.

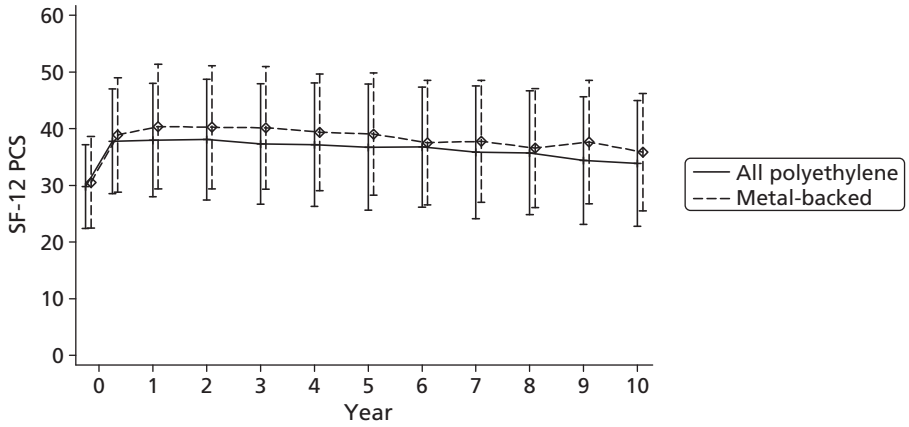

FIGURE 45 Mean (SD) SF-12 PCS by group at each follow-up time point for all-polyethylene vs. metal-backed tibial components.

TABLE 30 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 PCS for all-polyethylene vs. metal-backed tibial components

	All polyethylene			Metal-backed					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	195	29.8	7.4	195	30.5	8.1			
3 months	180	37.8	9.2	178	38.9	10.1	–0.79	–2.79 to 1.20	0.44
1 year	172	38.0	10.0	176	40.4	11.0	–1.81	–3.82 to 0.21	0.079
2 years	167	38.1	10.7	156	40.3	10.9	–1.63	–3.70 to 0.43	0.12
3 years	165	37.3	10.6	157	40.2	10.8	–2.68	–4.74 to –0.61	0.011
4 years	157	37.2	10.9	158	39.4	10.3	–2.11	–4.19 to –0.03	0.047
5 years	149	36.7	11.1	148	39.1	10.8	–1.93	–4.05 to 0.18	0.073
6 years	141	36.8	10.6	143	37.5	11.0	–0.28	–2.42 to 1.86	0.80
7 years	136	35.8	11.7	134	37.8	10.8	–2.02	–4.19 to 0.15	0.068
8 years	121	35.8	11.0	130	36.6	10.5	–0.45	–2.67 to 1.77	0.69
9 years	114	34.4	11.3	114	37.6	10.9	–2.78	–5.06 to –0.50	0.017
10 years	83	33.9	11.1	86	35.9	10.4	–1.46	–3.96 to 1.05	0.26

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours all-polyethylene components; *n*, the number of responses; SD, standard deviation.

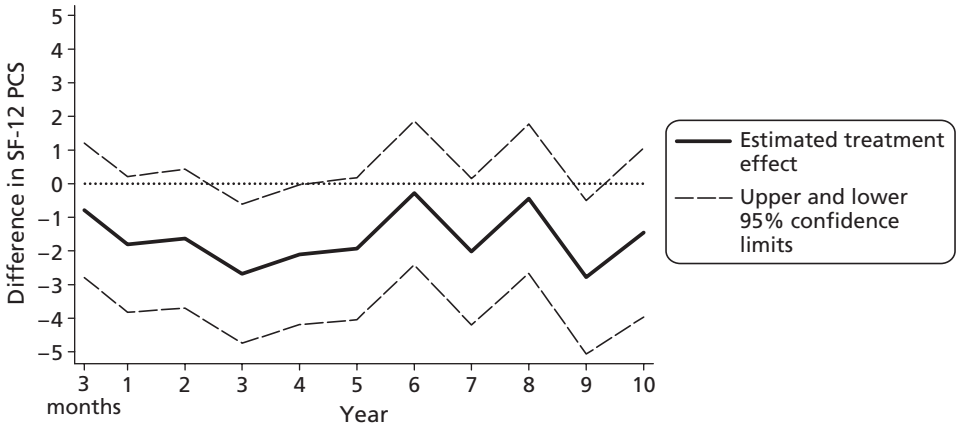

FIGURE 46 Estimated treatment effect on SF-12 PCS (95% CI) at each follow-up time point for all-polyethylene vs. metal-backed tibial components. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours all-polyethylene components.

TABLE 31 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 MCS for all-polyethylene vs. metal-backed tibial components

	All polyethylene			Metal-backed					
Time point	*n*	Mean	SD	*n*	Mean	SD	Diff.	95% CI	*p*-value
Baseline	195	49.5	12.2	195	49.1	12.6			
3 months	180	50.0	11.7	178	50.7	11.2	–1.14	–3.21 to 0.92	0.278
1 year	172	51.4	10.5	176	51.2	11.6	0.20	–1.89 to 2.29	0.853
2 years	167	51.0	10.2	156	51.4	10.2	–0.45	–2.59 to 1.70	0.683
3 years	165	50.4	10.2	157	50.1	10.3	0.12	–2.02 to 2.27	0.909
4 years	157	50.8	11.3	158	49.7	11.3	0.72	–1.44 to 2.88	0.515
5 years	149	49.1	11.4	148	49.4	11.9	–0.46	–2.66 to 1.75	0.685
6 years	141	49.2	11.7	143	50.4	10.8	–2.05	–4.28 to 0.19	0.073
7 years	136	50.5	11.5	134	49.7	11.0	0.04	–2.24 to 2.32	0.972
8 years	121	47.8	11.7	130	48.9	11.3	–1.46	–3.80 to 0.87	0.219
9 years	114	50.3	10.9	114	47.5	11.2	2.40	–0.01 to 4.81	0.051
10 years	83	49.9	12.0	86	48.1	10.7	0.24	–2.44 to 2.92	0.862

Diff., the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon – a positive difference favours all-polyethylene components; *n*, the number of responses; SD, standard deviation.

the definition of failure, to include any participant with an OKS after 1 year dropping below the baseline reported OKS, resulted in a hazard ratio of 1.45 (95% CI 0.99 to 2.18; $p = 0.056$; *Figure 51*); participants in the all polyethylene group were more likely to fail by this definition.

Cost comparison

The subset of participants for whom surgeons were in equipoise about whether to give an all-polyethylene or metal-backed tibial component tended to have a shorter operation time than those randomised in either of the other two comparisons (105 minutes for all polyethylene and 109 minutes for metal-backed, vs. 120 minutes for other comparisons; *Table 33*). On average, operation time was 4.5 minutes shorter for

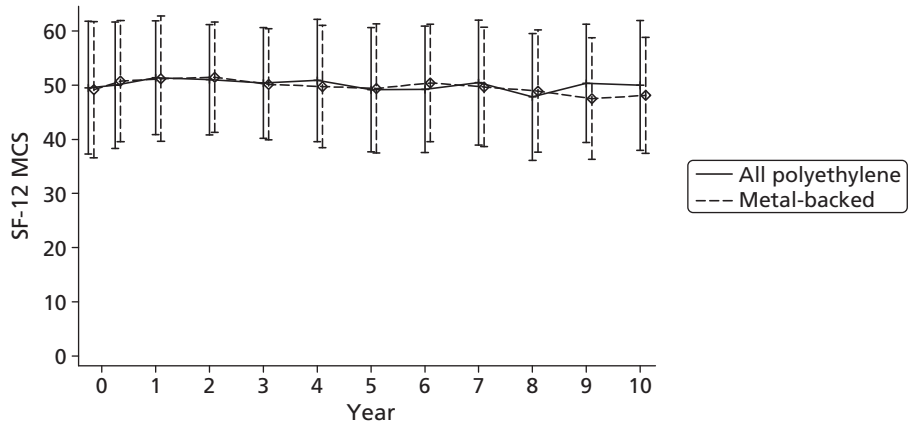

FIGURE 47 Mean (SD) SF-12 MCS by group at each follow-up time point for all-polyethylene vs. metal-backed tibial components.

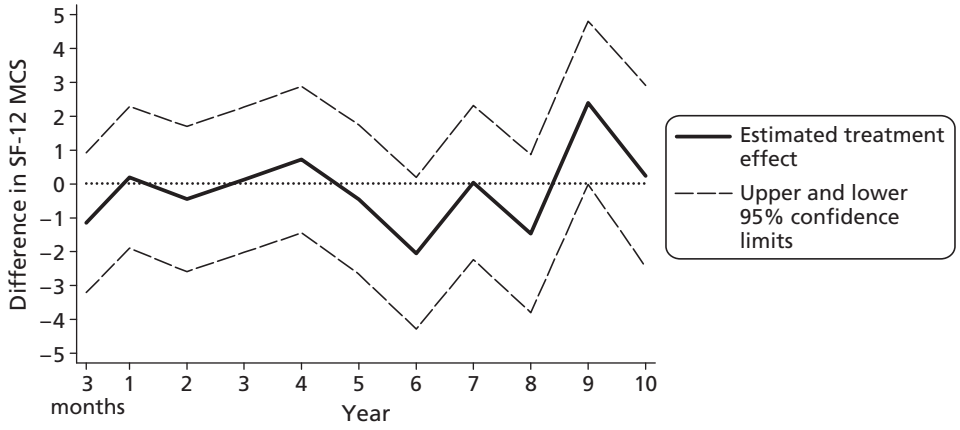

FIGURE 48 Estimated treatment effect on SF-12 MCS (95% CI) at each follow-up time point for all-polyethylene vs. metal-backed tibial components. Treatment effect is the estimated difference between treatments at that time point adjusted for minimisation covariates and surgeon; a positive difference favours all-polyethylene components.

participants randomised to receive all-polyethylene tibial components than for those in the metal-backed group ($p = 0.14$).

Conversely, the average participant randomised to all-polyethylene tibias tended to stay 0.7 days longer in hospital ($p = 0.16$). The cost of postoperative complications was similar in the two groups, although the cost of further surgery to the knee during the hospital stay was more than twice as high in the group randomised to all-polyethylene tibias.

All-polyethylene tibial components were 42% less expensive than metal-backed tibial components, equating to a saving of £362 per participant ($p < 0.001$). This is primarily because for the all-polyethylene tibias a single monoblock polyethylene component was required, whereas for the metal-backed tibias a polyethylene bearing was required in addition to a metallic tibial component. However, there was no significant difference in the number or cost of patellas, femoral components or other components used between the randomised groups (all $p > 0.05$).

Although the non-significant increase in length of stay partially offset the savings from using cheaper tibial components and reducing operation time, the overall cost of the inpatient stay was £208 (95% CI –£131 to £546) lower for the all polyethylene group than for those randomised to metal-backed tibial components ($p = 0.23$).

TABLE 32 Readmissions up to a median of 10 years post operation for all-polyethylene vs. metal-backed tibial components

Readmission type	All polyethylene (*N* = 203)		Metal-backed (*N* = 199)	
	n	%	*n*	%
Total readmissions	33		34	
No. of participants requiring at least one readmission	21	10	28	14
Minor/intermediate operations				
Total number operations	20		19	
Participants requiring				
At least one minor operation	14	7	16	8
Multiple minor operations	4	2	2	1
Number requiring at least one of				
Debridement/exploration/washout	1	< 1	1	< 1
MUA	5	2	8	4
Arthroscopy EUA/biopsy	6	3	7	3
Drain abscess	1	< 1		
Exchange poly	2	1	1	< 1
Removal of patella button	1	< 1		
Late patellar resurfacing	1	< 1		
Patella revision			1	< 1
Major operations				
Total number of operations	7		3	
Participants requiring at least one major operation	7	3	3	1
Number requiring at least one of				
Above-knee amputation	1	< 1	1	< 1
Revision for aseptic loosening	2	1	2	1
Revision for instability	1	< 1		
Revision for pain	2	1		
Revision for malalignment	1	< 1		

EUA, examination under anaesthetic; MUA, manipulation under anaesthetic.

However, the all polyethylene group tended to have higher levels of knee-related resource use during the 10 years after discharge from hospital. Although the number of readmissions was approximately the same in each group ($p = 0.94$), those participants in the all polyethylene group who were readmitted tended to have slightly more costly procedures (mean cost of readmission £4744, vs. £4292 in the metal-backed group; $p = 0.79$). This is likely to reflect the higher number of one-stage revisions in the all polyethylene group (see *Table 32*). As a result, the average cost of readmissions per participant was slightly higher in the all polyethylene group ($p = 0.87$). This trend was most pronounced in year 2, although the cost of readmissions was higher in the metal-backed group in year 1 and highly variable in subsequent years (see *Figure 52*). All-polyethylene components were also associated with a 17% increase in orthopaedic outpatient consultations ($p = 0.18$) and a 33% increase in physiotherapy consultations ($p = 0.08$). The trend towards higher numbers of physiotherapy and outpatient visits in the all polyethylene group was observed in every year except years 5 and 9 (see *Figure 52*).

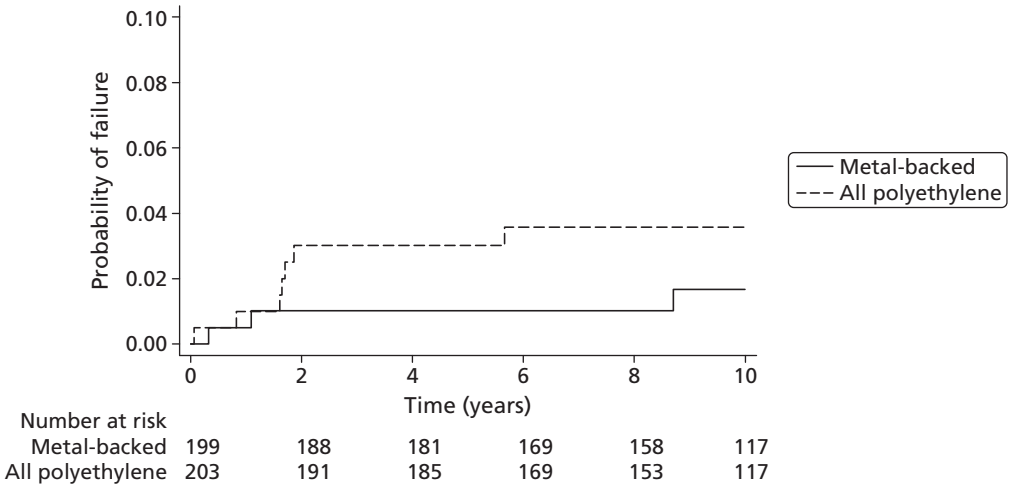

FIGURE 49 Kaplan–Meier failure curves for time to first major reoperation for all-polyethylene vs. metal-backed tibial components.

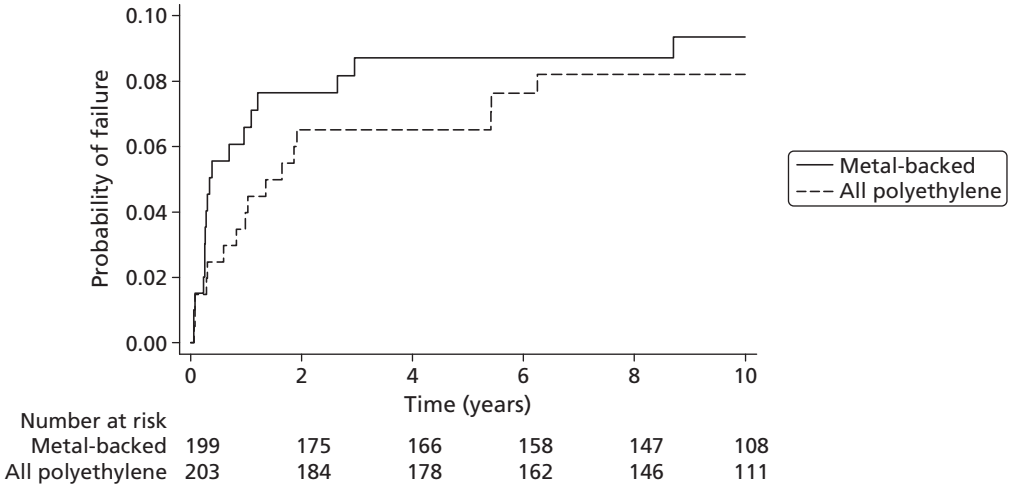

FIGURE 50 Kaplan–Meier failure curves for time to any reoperation for all-polyethylene vs. metal-backed tibial components.

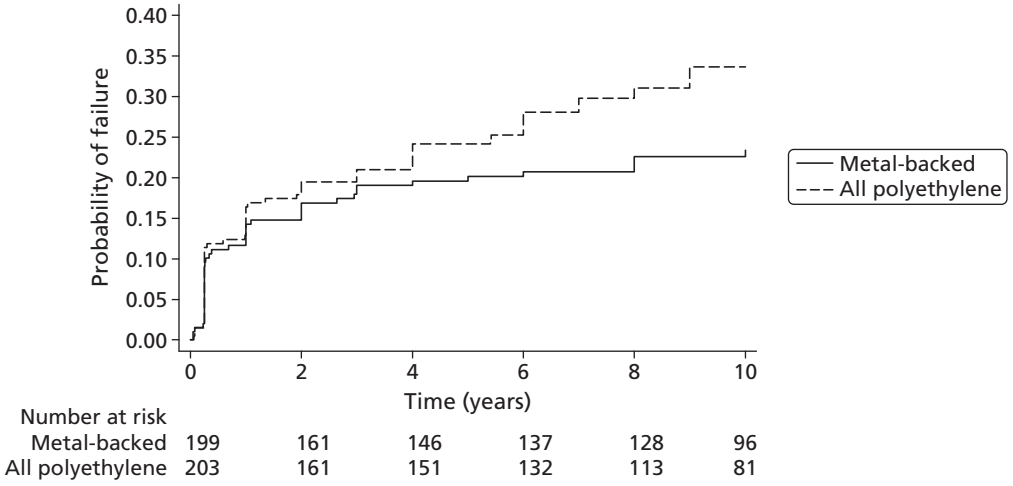

FIGURE 51 Kaplan–Meier failure curves for time to any reoperation or OKS dropping below baseline level at 1 year or later for all-polyethylene vs. metal-backed tibial components.

The increased cost of readmissions and ambulatory follow-up offset nearly all of the savings from all-polyethylene components that were observed in the primary hospital stay. As a result, the total cost over the 10-year time horizon was almost identical in the two groups (£8225 for all polyethylene vs. £8235 for metal-backed; $p = 0.98$).

Within-trial cost-effectiveness results

Base-case analysis

As was the case for the mobile bearing comparison, total cost in years 3–12 was primarily driven by readmissions and was low in the years in which no participants were admitted (*Figure 52*). Nonetheless, incremental cost was higher in the all polyethylene group in all years other than year 1 (in which costs were driven by the cost of the primary TKR procedure) and years 5 and 9 (in which the metal-backed group had more readmissions and more outpatient consultations; *Table 34*).

However, QALYs showed a consistent trend over the first 10 years after primary TKR, being consistently (but not statistically significantly) lower in the all polyethylene group than in those randomised to metal-backed tibial components at every time point (minimum $p = 0.06$). The difference in QALYs tended to increase over time, suggesting that the long-term benefits of metal-backed components may be greater than is observed with a 10-year time horizon. This trend appears to be a result of increasing differences in quality of life, as life expectancy was actually around 36 days longer in the all polyethylene group ($p = 0.66$).

Over the 10-year time horizon, the incremental cost of all-polyethylene tibial components compared with metal-backed components was –£10 (95% CI –£872 to £851; $p = 0.98$), whereas the incremental QALY gain was –0.293 (95% CI –0.706 to 0.119; $p = 0.16$). The evidence from KAT therefore suggests that all-polyethylene tibial components are less costly and less effective than metal-backed components, with the point estimate lying in the 'south-west' quadrant of the cost-effectiveness plane (*Figure 53*). In principle, treatments that are cost-saving and less effective than their comparators could increase the amount of health generated by NHS treatments, by freeing up resources that can be invested in other treatments that generate greater health gains than those lost by using the less effective treatment. Based on the £20,000 ceiling ratio typically used in NHS decision-making and assuming that the NHS has symmetrical preferences for losses and gains, treatments that are less effective and less costly would be considered good value for money if they saved at least £20,000 per QALY lost.

The base-case KAT results suggest that the NHS would save £10 and lose 0.293 QALYs for every participant treated with all-polyethylene tibial components rather than metal-backed components, which equates to an ICER of just £35 per QALY lost. This is substantially below the £20,000/QALY threshold, suggesting that all-polyethylene components are poor value for money and should not be used in place of metal-backed components, which cost just £35 per QALY gained compared with all polyethylene.

However, there is a modest amount of uncertainty around both incremental costs and incremental QALYs (see *Figure 53*). In particular, there is an 8% chance that all-polyethylene tibial components are more effective than metal-backed components and a 47% chance that they are more costly.

Taking account of the joint density of incremental costs and QALYs demonstrates that there is a 91% probability that metal-backed tibial components are good value for money compared with all-polyethylene components at a £20,000/QALY ceiling ratio (*Figure 54*).

TABLE 33 Resource use and costs for all-polyethylene vs. metal-backed tibial components

Resource	Allocated to all polyethylene (*n* = 203) [mean (SE)]		Allocated to metal-backed (*n* = 199) [mean (SE)]		Difference (95% CI)	
	Number	Cost (£)	Number	Cost (£)	Number	Cost (£)
Resource use during inpatient stay for primary knee replacement						
Minutes in theatre	104.5 (1.94)	1763 (33)	109.1 (2.46)	1840 (41)	–4.54 (–10.64 to 1.56)	–77 (–180 to 26)
Days in hospital[a]	10.4 (0.33)	3433 (108)	9.8 (0.35)	3213 (114)	0.67 (–0.26 to 1.60)	220 (–87 to 527)
Total knee components	2.7 (0.04)	1439 (17)	3.5 (0.04)	1805 (13)	–0.85 (–0.96 to –0.74)[b]	–366 (–408 to –323)[b]
Patella components	0.5 (0.03)	73 (6)	0.5 (0.04)	77 (6)	–0.01 (–0.11 to 0.09)	–3 (–20 to 13)
Tibial components	1.2 (0.03)	505 (11)	2.0 (0.01)	866 (7)	–0.83 (–0.88 to –0.78)[b]	–362 (–388 to –336)[b]
Other knee components	1.0 (0.00)	861 (9)	1.0 (0.01)	862 (8)	0.00 (–0.02 to 0.01)	0 (–24 to 23)
Peri/postoperative complications	0.2 (0.03)	8 (3)	0.2 (0.03)	9 (4)	0.02 (–0.05 to 0.10)	–1 (–11 to 9)
Further surgery occurring during hospital stay	0.0 (0.01)	24 (14)	0.0 (0.01)	9 (7)	0.01 (–0.01 to 0.04)	15 (–15 to 45)
Total cost of inpatient stay for primary knee replacement	–	6667 (122)	–	6875 (125)	–	–208 (–546 to 131)
Resource use over first 10 years after primary knee replacement (excluding initial hospital stay)[c]						
Total hospital readmissions related to study knee	0.16 (0.04)	771 (278)[d]	0.17 (0.03)	713 (218)[d]	0.00 (–0.11 to 0.10)	58 (–634 to 750)[d]
Outpatient consultations related to study knee	3.68 (0.28)	353 (26)[d]	3.14 (0.28)	303 (26)[d]	0.54 (–0.23 to 1.32)	50 (–23 to 123)[d]
Physiotherapy consultations related to study knee	8.10 (0.94)	338 (38)[d]	6.08 (0.71)	255 (29)[d]	2.01 (–0.25 to 4.27)	83 (–9 to 175)[d]
GP consultations related to study knee	2.81 (0.45)	95 (15)[d]	2.58 (0.43)	89 (15)[d]	0.23 (–1.00 to 1.46)	7 (–35 to 48)[d]
Total cost over first 10 years of study (excluding initial hospital stay)	–	1558 (306)[d]	–	1360 (241)[d]	–	198 (–566 to 961)[d]
Total cost of primary operation and follow-up	–	8225 (344)[d]	–	8235 (272)[d]	–	–10 (–872 to 851)[d]

a Excludes the incremental cost of time spent in high-dependency unit.
b $p < 0.05$.
c Costs and resource-use quantities after discharge were estimated using IPW.
d Discounted at 3.5% per year.
All values are per participant and exclude postrandomisation exclusions.

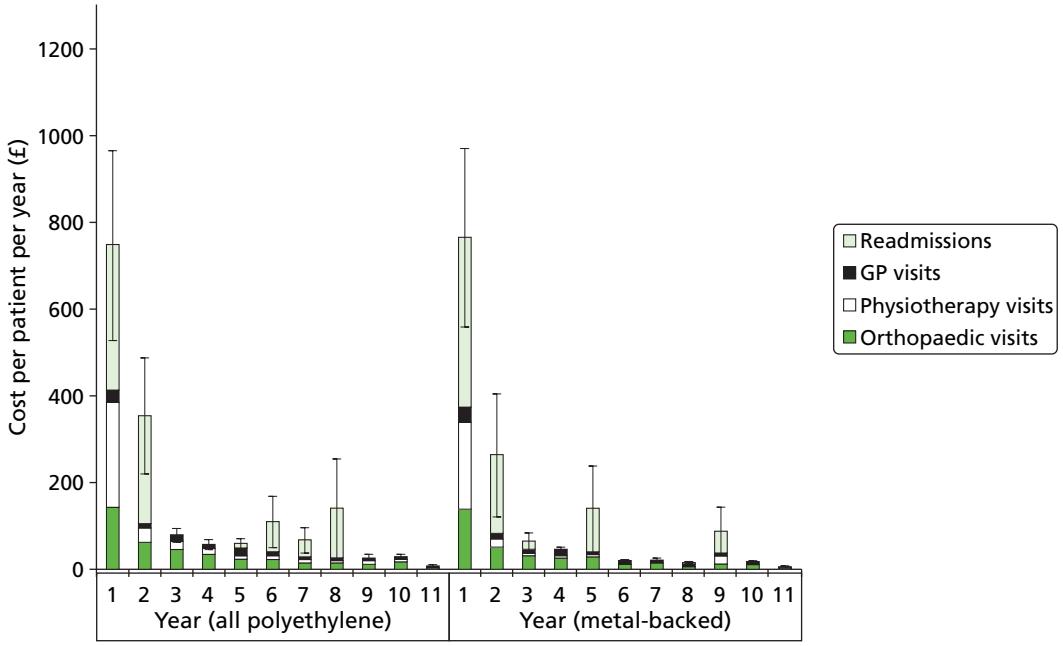

FIGURE 52 Illustration of cost breakdown by year after discharge from hospital for all-polyethylene vs. metal-backed tibial components. Error bars show SEs around total cost.

Sensitivity analyses

Sensitivity analyses suggested that the all polyethylene group accrued higher costs than the metal-backed group in four scenarios (*Table 35*). First, as expected, increasing the discount on knee components, such that hospitals pay only 50% (not 70%) of the list price, reduces costs in the metal-backed group more than in the all polyethylene group. Second, increasing the cost per bed-day to £448/day (50% higher than the national average excess bed-day cost in England and Wales) increases the cost in the all polyethylene group more than in the metal-backed group because of the longer primary hospital stay and additional readmissions. Third, if future costs and benefits are not discounted to current values, costs increase proportionately more in the all polyethylene group, as the additional costs accrued beyond year 1 are given greater weight. Fourth, reducing the time horizon and excluding costs accrued in years 9 and 10 changes the conclusions owing to the readmission and outpatient/physiotherapy consultations that occurred in the all metal-backed group in year 9. In other analyses, the magnitude of the cost savings varied from £1 to £156.

As the imbalance in baseline utility was larger in this comparison than in those with greater participant numbers, adjusting for baseline utility had the greatest effect on QALYs. However, no sensitivity analyses changed the conclusion that the all polyethylene group accrued non-significantly fewer QALYs than the metal-backed group, although the incremental QALYs varied between –0.145 and –0.370. Similarly, the point estimates in all analyses confirmed the base-case finding that all polyethylene is poor value for money, being dominated by metal-backed components or having a low cost-effectiveness ratio in the south-west quadrant in all analyses. The probability that all-polyethylene tibial components represent good value for money varied between 5% and 12%, but never reached conventional levels of statistical significance.

Subgroup analyses

Examining how incremental costs and benefits vary with age is of particular relevance for this comparison, as all-polyethylene components are often given on cost grounds to older participants who are not expected to outlive their knee prostheses. However, the results appear to suggest that this practice is unjustified. Although in both arms participants aged ≥ 70 years had higher costs than younger participants, the increase in costs with age was substantially larger for participants randomised to all

TABLE 34 Base-case cost-effectiveness results for all-polyethylene vs. metal-backed tibial components

Time point	Allocated to all polyethylene (*n* = 203) [mean (SE)]		Allocated to metal-backed (*n* = 199) [mean (SE)]		Difference in annual costs (95% CI) (£)	Difference in annual QALYs (95% CI)	Difference in cumulative costs (95% CI) (£)	Difference in cumulative QALYs (95% CI)
	Total cost (£)	QALYs	Total cost (£)	QALYs				
Year 1	7414 (219)	0.623 (0.015)	7639 (206)	0.637 (0.016)	–225 (–816 to 365)	–0.015 (–0.054 to 0.024)	–225 (–816 to 365)	–0.015 (–0.054 to 0.024)
Year 2	354 (135)	0.669 (0.018)	262 (141)	0.672 (0.020)	92 (–297 to 480)	–0.003 (–0.055 to 0.049)	–137 (–841 to 568)	–0.018 (–0.102 to 0.067)
Year 3	78 (14)	0.648 (0.019)	65 (20)	0.667 (0.020)	13 (–36 to 61)	–0.018 (–0.073 to 0.036)	–125 (–837 to 587)	–0.035 (–0.164 to 0.095)
Year 4	56 (11)	0.626 (0.020)	42 (9)	0.666 (0.021)	14 (–13 to 42)	–0.040 (–0.097 to 0.016)	–112 (–830 to 606)	–0.071 (–0.244 to 0.102)
Year 5	57 (15)	0.589 (0.022)	139 (99)	0.646 (0.021)	–81 (–278 to 116)	–0.056 (–0.116 to 0.003)	–183 (–930 to 565)	–0.120 (–0.336 to 0.095)
Year 6	108 (61)	0.552 (0.023)	19 (5)	0.598 (0.022)	89 (–30 to 209)	–0.046 (–0.109 to 0.017)	–107 (–872 to 657)	–0.159 (–0.417 to 0.099)
Year 7	67 (30)	0.537 (0.024)	21 (5)	0.570 (0.023)	47 (–12 to 106)	–0.033 (–0.098 to 0.031)	–69 (–845 to 706)	–0.186 (–0.485 to 0.112)
Year 8	141 (116)	0.508 (0.025)	15 (5)	0.545 (0.024)	126 (–102 to 355)	–0.037 (–0.103 to 0.030)	30 (–825 to 885)	–0.215 (–0.553 to 0.123)
Year 9	24 (8)	0.460 (0.026)	88 (56)	0.525 (0.024)	–63 (–173 to 47)	–0.065 (–0.134 to 0.004)	–18 (–878 to 842)	–0.265 (–0.640 to 0.111)
Year 10	27 (8)	0.441 (0.029)	16 (5)	0.481 (0.027)	11 (–8 to 29)	–0.039 (–0.116 to 0.038)	–10 (–872 to 851)	–0.293 (–0.706 to 0.119)
Total	8225 (344)	4.926 (0.152)	8235 (272)	5.219 (0.151)	–10 (–872 to 851)	–0.293 (–0.706 to 0.119)	–10 (–872 to 851)	–0.293 (–0.706 to 0.119)

Total costs and QALYs accrued in each year of the trial. Costs and QALYs beyond year 1 are discounted at 3.5% per year and include IPW; SEs estimated using bootstrapping. All QALY estimates are adjusted for baseline utility.

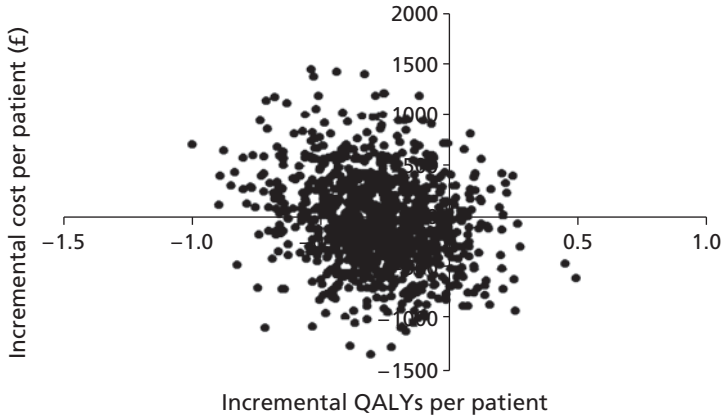

FIGURE 53 Stochastic cost-effectiveness results for all-polyethylene vs. metal-backed tibial components: scatter graph on cost-effectiveness plane.

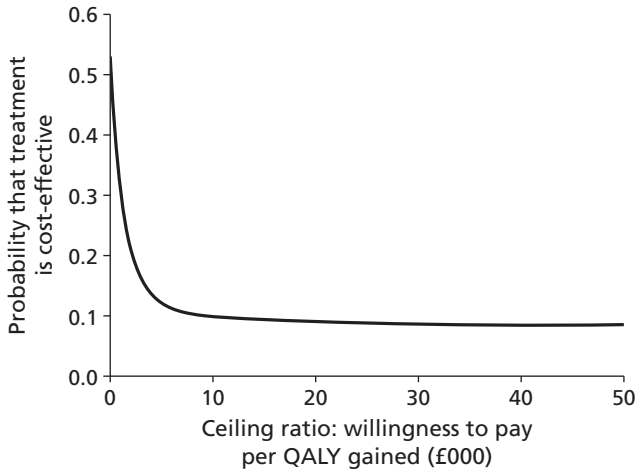

FIGURE 54 Cost-effectiveness acceptability curve for all-polyethylene vs. metal-backed tibial components.

polyethylene (see *Table 35*). As a result, the all polyethylene arm had non-significantly higher costs than the metal-backed arm in the older age group, and all-polyethylene components were therefore dominated by metal-backed components. This analysis, therefore, suggests that all-polyethylene tibial components are poor value for both age groups and may be more costly and particularly ineffective in older participants.

Potential for interactions between metal backing and patellar resurfacing

We also examined whether there is evidence of an interaction between metal backing and patellar resurfacing in the subgroup of 145 participants who were also randomised in the patella comparison. Analysing the data for these participants as a factorial trial suggests that there are qualitative interactions between metal backing and patellar resurfacing for costs ($p = 0.577$), QALYs ($p = 0.047$) and net monetary benefit ($p = 0.060$) that change the conclusions of the analysis, although the interaction for costs could easily be explained by chance. These qualitative interactions mean that both costs and QALYs are substantially higher in the group randomised to all-polyethylene tibial components and no patellar resurfacing and the group randomised to metal-backed tibial components and patellar resurfacing (see *Table 35*) than in the other two groups. As a result, all-polyethylene components appear to be poor value for money in the patellar resurfacing group (saving £429 per QALY lost), but good value for money in those participants randomised to no patellar resurfacing (costing £512 per QALY gained). However, the results of this sensitivity analysis should be interpreted with great caution, as it is based on a small number of participants and the large non-significant interactions observed could easily have arisen by chance.

TABLE 35 Results of sensitivity and subgroup analyses for all-polyethylene vs. metal-backed tibial components comparison

	Allocated to all polyethylene (*n* = 203) [mean (SE)]		Allocated to metal-backed (*n* = 199) [mean (SE)]		Difference (95% CI)			Probability that all polyethylene is	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Base-case analysis	8225 (£344)	4.926 (0.152)	8235 (272)	5.219 (0.151)	–10 (–872 to 851)	–0.293 (–0.706 to 0.119)	35 SW	9%	53%
Sensitivity analyses									
Complete case analysis (*n* = 56, 85, respectively)	7496 (306)	5.304 (0.247)	7755 (251)	5.449 (0.235)	–259 (–1029 to 511)	–0.145 (–0.797 to 0.506)	1779 SW	35%	25%
Per-protocol analysis (*n* = 170, 186, respectively)	8262 (402)	4.955 (0.163)	8272 (288)	5.192 (0.159)	–10 (–976 to 957)	–0.237 (–0.671 to 0.198)	40 SW	15%	47%
46% reduction in LoS for primary admission	6627 (325)	4.926 (0.152)	6740 (253)	5.219 (0.151)	–113 (–921 to 695)	–0.293 (–0.706 to 0.119)	385 SW	9%	62%
Component price discount									
0%	8864 (352)	4.926 (0.152)	9020 (275)	5.219 (0.151)	–156 (–1033 to 722)	–0.293 (–0.706 to 0.119)	531 SW	10%	65%
50%	7799 (339)	4.926 (0.152)	7712 (271)	5.219 (0.151)	87 (–765 to 938)	–0.293 (–0.706 to 0.119)	Dominated	9%	44%
Cost per bed-day									
£149 (–50%)	6254 (230)	4.926 (0.152)	6350 (169)	5.219 (0.151)	–96 (–657 to 465)	–0.293 (–0.706 to 0.119)	328 SW	9%	65%
£448 (+50%)	10,196 (462)	4.926 (0.152)	10,121 (381)	5.219 (0.151)	76 (–1102 to 1253)	–0.293 (–0.706 to 0.119)	Dominated	9%	47%
Cost per theatre minute									
£7.34 (–50%)	7231 (317)	4.926 (0.152)	7250 (260)	5.219 (0.151)	–20 (–825 to 786)	–0.293 (–0.706 to 0.119)	67 SW	9%	54%
£22.00 (+50%)	9219 (372)	4.926 (0.152)	9220 (286)	5.219 (0.151)	–1 (–924 to 922)	–0.293 (–0.706 to 0.119)	3 SW	9%	52%

continued

TABLE 35 Results of sensitivity and subgroup analyses for all-polyethylene vs. metal-backed tibial components comparison (*continued*)

	Allocated to all polyethylene ($n = 203$) [mean (SE)]		Allocated to metal-backed ($n = 199$) [mean (SE)]		Difference (95% CI)			Probability that all polyethylene is	
Analysis	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Discount rate for time preference									
0% costs and QALYs	8328 (370)	5.653 (0.180)	8306 (283)	6.006 (0.178)	22 (–894 to 938)	–0.353 (–0.841 to 0.134)	Dominated	9%	50%
5% costs and QALYs	8187 (335)	4.663 (0.142)	8209 (268)	4.935 (0.142)	–22 (–865 to 821)	–0.272 (–0.657 to 0.114)	81 SW	9%	54%
3.5% costs, 0% QALYs	8225 (344)	5.653 (0.180)	8235 (272)	6.006 (0.178)	–10 (–872 to 851)	–0.353 (–0.841 to 0.134)	29 SW	9%	53%
No adjustment for baseline utility	8225 (344)	4.895 (0.154)	8235 (272)	5.265 (0.155)	–10 (–872 to 851)	–0.370 (–0.802 to 0.063)	28 SW	5%	53%
Within-trial time horizon with no adjustment for censoring	8219 (343)	4.848 (0.154)	8228 (271)	5.205 (0.156)	–10 (–870 to 851)	–0.356 (–0.790 to 0.077)	27 SW	6%	53%
8-year time horizon	8187 (343)	4.252 (0.123)	8157 (269)	4.467 (0.126)	30 (–825 to 885)	–0.215 (–0.553 to 0.123)	Dominated	12%	49%
9-year time horizon	8205 (343)	4.602 (0.137)	8223 (271)	4.866 (0.139)	–18 (–878 to 842)	–0.265 (–0.640 to 0.111)	68 SW	10%	53%
11-year time horizon	8231 (344)	5.233 (0.167)	8240 (272)	5.543 (0.165)	–9 (–871 to 853)	–0.310 (–0.761 to 0.141)	29 SW	10%	53%
Dealing with censoring using multiple imputation rather than IPW	8229 (345)	4.884 (0.153)	8235 (272)	5.256 (0.155)	–5 (–869 to 859)	–0.372 (–0.803 to 0.059)	14 SW	95%	48%

Analysis	Allocated to all polyethylene ($n = 203$) [mean (SE)]		Allocated to metal-backed ($n = 199$) [mean (SE)]		Difference (95% CI)			Probability that all polyethylene is	
	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Total cost (£)	Total QALYs	Cost/ QALY (£)	Cost-effective[a]	Less costly
Subgroup analyses									
Age (years)									
< 70 ($n = 92, 88$)	7732 (337)	5.203 (0.220)	7924 (293)	5.239 (0.214)	–192 (–1071 to 687)	–0.036 (–0.627 to 0.555)	5327 SW	46%	32%
≥ 70 ($n = 111, 111$)	8632 (557)	4.691 (0.291)	8484 (425)	5.193 (0.217)	148 (–1230 to 1526)	–0.503 (–1.073 to 0.067)	Dominated	5%	56%
Randomised to more than one comparison									
Randomised to resurfacing ($n = 36, 34$)	7833 (567)	5.046 (0.330)	8036 (411)	5.518 (0.337)	–202 (–1575 to 1170)	–0.472 (–1.397 to 0.453)	429 SW	16%	37%
Randomised to no resurfacing ($n = 38, 37$)	8085 (409)	5.569 (0.248)	7782 (384)	4.976 (0.311)	303 (–798 to 1404)	0.593 (–0.175 to 1.360)	512	94%	71%

LoS, length of stay.
a Probability that treatment is cost-effective is based on a £20,000/QALY ceiling ratio.
Cost-effectiveness ratios marked with 'SW' are in the south-west quadrant, in which treatments with high ratios are considered good value for money.

Discussion

In this study we found improved outcome scores for metal-backed compared with all-polyethylene tibial components and found metal backing to be cost-effective. The patterns of results for OKS, SF-12 and EQ-5D were similar, all favouring metal backing and being statistically significant for SF-12 and EQ-5D. There was, however, no difference in complication, reoperation or revision rates. These findings are different from those of previous RCTs and meta-analyses of the RCTs,[32,34] in which no difference in outcome was found. However, KAT is much larger than most previous RCTs and primarily assessed patient-reported outcome measures. Previous studies, which did not include a formal assessment of costs and cost-effectiveness, have concluded that all-polyethylene implants are more cost-effective, as the implant costs less and as the outcome is the same.[33,34] These studies, therefore, recommended that all-polyethylene implants should be used, particularly in the elderly. However, 10-year data from KAT, which is the only RCT with a full economic evaluation, does not support this conclusion and suggests that metal-backed implants should be used – and particularly in the elderly.

Surgeons tend to prefer metal-backed tibial components because of their modularity, which makes the surgery easier. In addition, the modularity should theoretically improve the functional outcome, as, after cementing, the surgeon can select the appropriate thickness of polyethylene to achieve optimal ligament tension, and the appropriate constraint to achieve optimal stability. The study does show a functional benefit from the metal-backed tibial components, although the marginal estimate of the benefit of the metal-backed component over the whole trial period was statistically significant only for EQ-5D and SF-12 PCSs and not for OKS. It is surprising that the difference was significant for the generic scores rather than the knee-specific score. Further investigation of this is required.

All-polyethylene tibial components should have fewer problems with wear and osteolysis than metal-backed tibial components. This is because they have thicker polyethylene, which decreases articular surface wear, and, as there is no modular junction, they can have no backside wear. The loading at the bone–cement interface and within the cancellous bone will be different with the two component designs. It is debatable which type of loading is best and, therefore, which will be associated with the lowest loosening rate. It is therefore possible that there will be a difference in the revision rate between the two designs, even though previous studies have not shown one.[90,91] If there is a difference, it will be most marked in the long term. At 10 years there is a slightly, but not significantly, higher revision rate for the all-polyethylene tibial component. Longer follow-up is required to determine if this difference in revision rates increases.

The economic evaluation indicates that we can be 91% confident that all-polyethylene tibial components are poor value for money. Although all-polyethylene components are cheaper than metal-backed components initially, the cost savings are offset by non-significant increases in the primary hospital stay and the cost of readmissions, outpatient consultations and physiotherapy, such that estimated total costs over the 10-year time horizon were just £10 lower in the all polyethylene group ($p = 0.98$). Participants randomised to all-polyethylene tibial components also had a lower quality of life at all time points and accrued 0.293 fewer QALYs than those randomised to metal-backed components ($p = 0.16$). As the potential savings were insufficient to warrant the observed reduction in health, all-polyethylene components are expected to be poor value for money, with metal backing costing just £35 per QALY gained compared with all-polyethylene. Our analysis assumes that decision-makers have symmetrical preferences and that their willingness to accept QALY losses to realise savings is equal to their willingness to pay for QALY gains. If decision-makers were averse to QALY losses and used a higher ceiling ratio than £20,000 per QALY lost in the south-west quadrant, the probability that all-polyethylene tibial components are poor value for money would be $> 91\%$. Furthermore, subgroup analyses suggested that all-polyethylene components are particularly ineffective and may increase total costs in participants aged ≥ 70 years, suggesting that the use of all-polyethylene components as a less costly option in older participants is inappropriate. Sensitivity analyses suggested that the conclusions are robust to changes in the methods and assumptions used in the analysis.

There was some (non-significant) evidence of an interaction between patellar resurfacing and metal backing. In particular, subgroup analyses suggested that patients randomised to all polyethylene and no resurfacing and metal backing with resurfacing accrued more QALYs than the other two combinations. However, these observed interactions could be explained by chance and we are not aware of a good clinical explanation for why they occur. Further investigation into the potential for clinical, kinematic or statistical interactions between patellar resurfacing and metal backing is warranted.

Conclusion

In this large 10-year pragmatic RCT, we have found that the functional results with a metal-backed tibial component are better than with an all-polyethylene tibia. Although the complication, reoperation rates and revision rates are similar, there is a concern that in the longer term there may be an increased revision rate with the all-polyethylene tibia. The metal-backed tibia was also cost-effective compared with the all-polyethylene tibia, with secondary analyses suggesting that metal backing is better (rather than worse) value for money in participants aged $\geq$ 70 years. This study provides an evidence base supporting the routine use of metal-backed tibias in all patients. The study does not support the previous general recommendation that all-polyethylene tibias should be used to save money in the elderly;[33,34] indeed, it suggests that it not only is more costly in the elderly but also generates fewer QALYs.

Chapter 6 Unicompartmental versus total knee replacement

Description of the groups at trial entry

Of the 2374 participants randomised, 34 were recruited to the comparison assessing unicompartmental knee replacement versus TKR.

Description of data available for those recruited

A description of the group of participants recruited to this comparison is in *Table 36*.

Outcomes after a median of 10 years post operation

Oxford Knee Score

Table 37 and *Figure 55* describe OKS over the 10-year follow-up period by allocated group.

EuroQol 5D

Table 38 and *Figure 56* describe EQ-5D over the 10-year follow-up period by allocated group.

Short Form 12

Table 39 and *Figure 57* describe the SF-12 PCS over the 10-year follow-up period by allocated group.

Table 40 and *Figure 58* describe SF-12 MCS over the 10-year follow-up period by allocated group.

Discussion

Recruitment to this arm of the trial was very slow and was therefore terminated early. Prior to stopping, 34 patients had been recruited. As there has been only one other randomised trial of unicompartmental knee replacement versus TKR, it was felt that the clinical scores should be described.[92] No difference was found, as would be expected with small numbers. Complications, reoperations and revisions were not analysed, as it was felt the numbers were too small for this analysis to be of any value. The data from KAT has therefore not contributed significantly to the debate about whether unicompartmental knee replacement should or should not routinely be used. The experience gained from KAT has, however, been very useful in the planning of another randomised study of unicompartmental knee replacement and TKR – TOPKAT (Total Or Partial Knee Arthroplasty Trial).[93]

During the planning and application for funding stages of KAT, unicompartmental replacements were implanted through the standard approach used for TKR and many surgeons had equipoise about the two types of replacement. We should, therefore, have been able to recruit, using the standard KAT methodology, an appropriate number of patients for the trial. However, prior to starting the recruitment, a new, minimally invasive technique for implanting unicompartmental replacement was introduced. This has many advantages over the standard approach, including a faster recovery, lower morbidity and improved function. As a result, many surgeons who would have recruited to the trial instead learnt the minimally invasive technique. In addition, some surgeons lost their equipoise. As a result, the recruitment rate was very much lower than predicted. The new trial, TOPKAT, was therefore designed differently from KAT in that it has two options. Surgeons with equipoise are able to randomise in a standard fashion, whereas surgeons who do not have equipoise can use an expertise-based randomisation. As most

TABLE 36 Description of groups at trial entry for unicompartmental knee replacement vs. TKR

Characteristic	Unicompartmental (*n* = 18)		TKR (*n* = 16)	
Age (years) (mean, SD)	66	7	67	8
Female	10	56	9	56
BMI (kg/m^2) (mean, SD)	29.8	3.7	28.7	5.0
ASA				
Completely fit and healthy	2	11	3	19
Some illness but has no affect on normal activity	13	72	8	5
Symptomatic illness present but minimal restriction	2	11	2	13
Symptomatic illness causing severe restriction	0		0	
Missing	1	6	3	19
Primary type of knee arthritis				
Osteoarthritis	18	100	15	94
Rheumatoid			1	6
Extent of knee arthritis affecting mobility				
One knee	2	11	3	16
Both knees	10	56	6	38
General	6	33	7	44
	n = *18*		**n = *16***	
Other conditions affecting mobility	1	6	2	13
Locomotor/musculoskeletal	1	6	2	13
	n = *18*		**n = *16***	
Previous knee surgery	7	39	4	25
Ipsilateral osteotomy			1	6
Ipsilateral patellectomy				
Contralateral previous knee replacement	4	22	2	13
Other previous knee surgery	3	17	2	13
Arthroscopy	2	11	1	6
Other related surgery	1	6		

SD, standard deviation.
Cell contents are *n* and per cent unless otherwise stated.

TABLE 37 Descriptive statistics and estimated treatment effects at each follow-up time point for OKS for unicompartmental knee replacement vs. TKR

	Unicompartmental			TKR		
Time point	*n*	Mean	SD	*n*	Mean	SD
Baseline	18	21.7	8.0	15	18.1	7.5
3 months	13	30.7	10.1	12	32.8	8.1
1 year	13	34.1	12.8	13	33.8	9.8
2 years	12	38.3	7.3	13	35.2	10.7
3 years	17	37.5	7.5	14	33.4	10.5
4 years	14	36.6	9.3	14	33.9	9.9
5 years	14	36.0	11.0	15	36.9	10.5
6 years	14	35.1	10.9	15	36.9	10.3
7 years	13	35.0	8.3	14	33.8	9.6
8 years	14	34.2	8.9	12	34.9	10.6
9 years	14	32.0	9.3	11	35.7	8.3
10 years	13	31.2	9.7	10	34.1	11.3

n, the number of responses; SD, standard deviation.

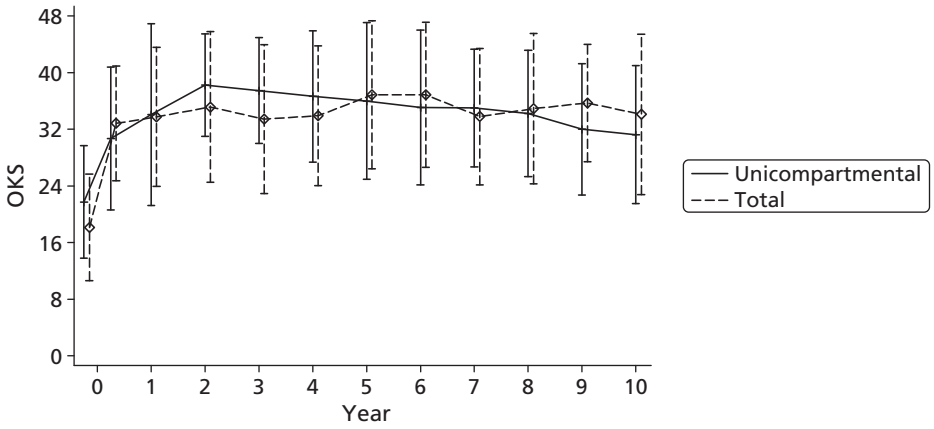

FIGURE 55 Mean (SD) OKS by group at each follow-up time point for unicompartmental knee replacement vs. TKR.

TABLE 38 Descriptive statistics and estimated treatment effects at each follow-up time point for EQ-5D for unicompartmental knee replacement vs. TKR

	Unicompartmental			TKR		
Time point	*n*	Mean	SD	*n*	Mean	SD
Baseline	18	0.447	0.312	15	0.428	0.300
3 months	16	0.686	0.193	14	0.732	0.124
1 year	16	0.717	0.282	15	0.698	0.206
2 years	15	0.820	0.120	16	0.741	0.242
3 years	17	0.803	0.147	15	0.769	0.158
4 years	16	0.775	0.149	14	0.694	0.218
5 years	14	0.835	0.166	15	0.741	0.180
6 years	14	0.715	0.272	15	0.757	0.193
7 years	15	0.728	0.206	15	0.690	0.177
8 years	15	0.724	0.250	14	0.701	0.272
9 years	15	0.690	0.087	11	0.697	0.207
10 years	13	0.649	0.110	10	0.685	0.259

n, the number of responses; SD, standard deviation.

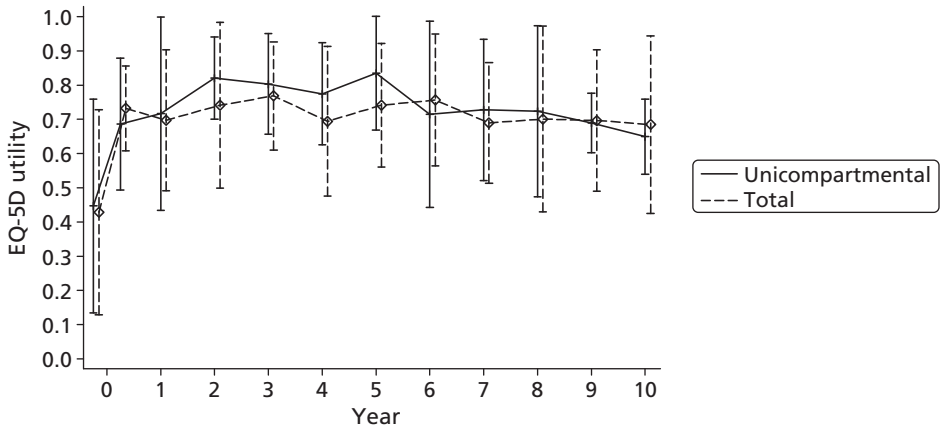

FIGURE 56 Mean (SD) EQ-5D utility by group at each follow-up time point for unicompartmental knee replacement vs. TKR.

TABLE 39 Descriptive statistics and estimated treatment effects at each follow-up time point for SF-12 PCS for unicompartmental knee replacement vs. TKR

	Unicompartmental			TKR		
Time point	*n*	Mean	SD	*n*	Mean	SD
Baseline	16	34.5	8.5	15	31.0	7.4
3 months	15	40.4	7.2	14	37.2	9.4
1 year	15	43.7	11.1	15	40.8	8.9
2 years	15	43.2	5.5	15	41.9	10.2
3 years	17	41.6	9.1	15	41.3	11.4
4 years	15	41.0	8.9	14	40.5	10.8
5 years	15	42.5	11.4	15	43.7	10.4
6 years	15	41.5	11.8	14	42.6	10.2
7 years	14	41.6	9.7	15	39.5	9.1
8 years	14	40.9	9.1	13	40.8	10.1
9 years	15	35.9	8.1	11	37.2	10.3
10 years	12	35.5	8.7	10	39.6	9.9

n, the number of responses; SD, standard deviation.

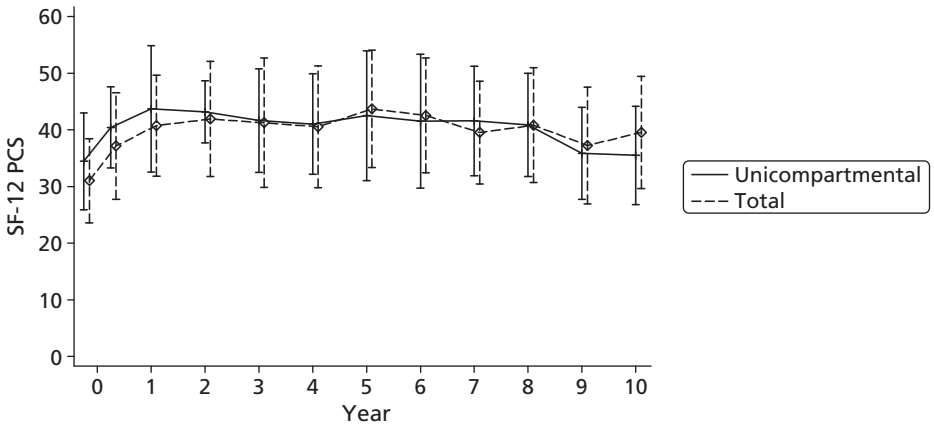

FIGURE 57 Mean (SD) SF-12 PCS by group at each follow-up time point for unicompartmental knee replacement vs. TKR.

TABLE 40 Descriptive statistics and estimated treatment effects at each follow-up time point for the SF-12 MCS for unicompartmental knee replacement vs. TKR

	Unicompartmental			TKR		
Time point	*n*	Mean	SD	*n*	Mean	SD
Baseline	16	49.4	11.9	15	48.7	9.9
3 months	15	50.0	10.5	14	54.1	10.2
1 year	15	51.1	8.7	15	53.1	10.1
2 years	15	52.6	7.7	15	51.1	10.9
3 years	17	51.7	10.7	15	52.3	9.9
4 years	15	52.3	10.8	14	48.4	11.1
5 years	15	47.6	9.8	15	46.4	10.1
6 years	15	48.5	8.5	14	48.9	9.9
7 years	14	47.6	10.4	15	49.1	9.5
8 years	14	47.6	9.4	13	51.4	11.5
9 years	15	48.0	10.9	11	51.8	11.7
10 years	12	46.3	6.1	10	48.9	8.2

n, the number of responses; SD, standard deviation.

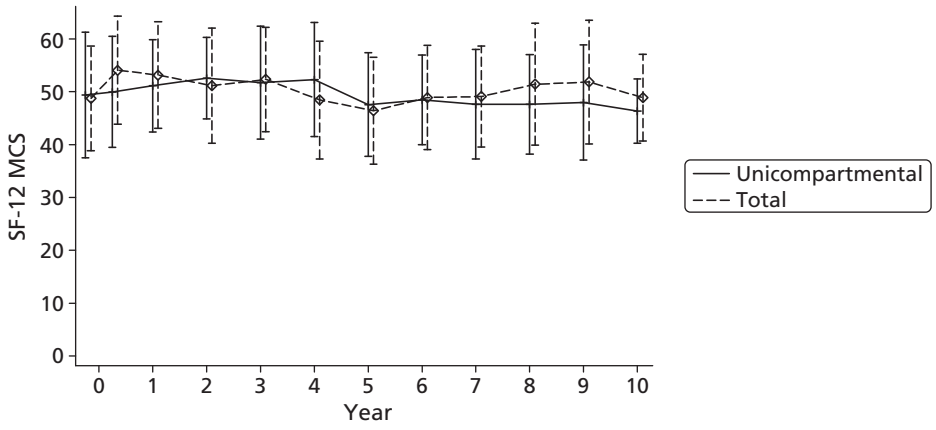

FIGURE 58 Mean (SD) SF-12 MCS by group at each follow-up time point for unicompartmental knee replacement vs. TKR.

surgeons have now learnt the minimally invasive technique, many more are now willing to be involved in the standard randomisation arm. In the expertise-based option of the trial, patients who are appropriate for the study are randomised and then either have a unicompartmental replacement implanted by a surgeon who believes in unicompartmental replacement or a total replacement implanted by a surgeon who believes in total replacement. The TOPKAT study, which has been funded by the NIHR HTA board, finished its recruitment in September 2013 (HTA project reference number 08/14/08).

Chapter 7 Implications for practice and for future research

Patellar resurfacing versus no patellar resurfacing

Currently there is great variability in the use of resurfacing both in the NHS and world-wide. This is primarily because some surgeons believe in resurfacing and some do not. In addition, a small proportion of surgeons resurface the patella in some patients and not others. With some designs of knee replacement, the trochlea is anatomically shaped. This design is considered patella-friendly and to perform well without patella replacement. Previous studies have not clearly demonstrated whether or not it is preferable to resurface the patella, or whether this depends on the design of the knee replacement, the state of the patella or other patient factors.

In this pragmatic study, which is substantially larger than previous RCTs, we found no significant difference in clinical outcome, in terms of pain and function (assessed by OKS, EQ-5D or SF-12), complications, readmission or reoperations between patients with and without patellar resurfacing (*Table 41*). There was also no significant difference in the incidence of patella-related reoperations. However, as there was a non-significant trend towards improved quality of life (0.187 QALYs per patient treated) and decreased costs (£104 per patient treated) associated with resurfacing, patellar resurfacing was cost-effective. The KAT results indicate a 96% probability that patellar resurfacing is cost-effective at a £20,000/QALY ceiling ratio. Sensitivity analyses indicated that this conclusion was generally robust. Subgroup analyses also suggested patellar resurfacing is more cost-effective in patients aged < 70 years, although it remains good value for money in patients aged ≥ 70 years. The study, therefore, provides an evidence base supporting routine resurfacing of the patella in all patients.

We did not find evidence that the outcome of patellar resurfacing is influenced by whether the femoral component had a trochlea designed to fit an anatomical patella button or a domed patella button; the trial findings therefore apply whether or not the femoral component is considered to be patella-friendly. We also found that late patellar resurfacing had little or no benefit, suggesting that, if a patient has not had patellar resurfacing, late resurfacing should be avoided if possible.

Further research is needed: with increasing follow-up, there was an increasing number of reoperations for complications of resurfacing and a decreasing number of late patellar resurfacing procedures. Some of the complications resulting from resurfacing, such as patella fracture, require complex reconstructions and may be associated with poor outcomes. The operations for patella complications are undertaken in patients who have had resurfacing, whereas the late resurfacings are undertaken in patients who have not had resurfacing. Therefore, there is a concern that after 10 years the rate of complications and reoperations in the resurfaced patella group will increase more than in the non-resurfaced group. If there is a substantial increase in the reoperation rate in the resurfaced group, particularly if it is associated with a worsening clinical outcome resulting from resurfacing complications, our conclusion that the patella should routinely be resurfaced would change. Follow-up to 15 and 20 years is required.

Late patellar resurfacing, overall, had little effect on outcome. However, this does not necessarily mean that no patients improved after late resurfacing. Further research is required to understand the factors associated with a good or poor outcome after late resurfacing. If guidelines that advised against late resurfacing of the patella were made and adhered to, the benefit of resurfacing might disappear. We found some evidence of an interaction between patellar resurfacing and mobile bearings and all-polyethylene tibias. This needs to be explored in more depth to determine if this is a real effect, or just chance.

TABLE 41 Summary of findings from each chapter

Outcome	Patellar resurfacing vs. no resurfacing	Mobile vs. fixed bearings	All-polyethylene vs. metal-backed tibial components
Functional (OKS)	Small but consistent difference in favour of patellar resurfacing; 95% CI suggests MCID unlikely; treatment effect not modified by patella shape	Similar between groups	Consistent benefit favouring metal-backed, not statistically significant
Quality of life (EQ-5D utility, SF-12 PCS and MCS)	Similar between groups	Similar between groups	Similar pattern to OKS but statistically significant differences found
Reoperation	Similar between groups	Similar in both groups; however, five participants required reoperation for instability or dislocation in the mobile bearing group	Similar between groups
Incremental QALYs (95% CI)	0.187 (–0.025 to 0.399; $p = 0.08$)	0.051 (–0.333 to 0.435; $p = 0.79$)	–0.293 (–0.706 to 0.119; $p = 0.16$)
Incremental costs (95% CI) (£)	–104 (95% CI –630 to 423; $p = 0.70$)	85 (–911 to 1081; $p = 0.87$)	–10 (–872 to 851; $p = 0.98$)
Base-case cost-effectiveness result	Patellar resurfacing dominates no resurfacing, with a 96% probability of being cost-effective	Mobile bearings cost £1666 per QALY gained vs. fixed bearing, with a 59% probability of being cost-effective	All polyethylene saves £35 per QALY lost vs. metal-backed, with a 9% probability of being cost-effective
Sensitivity analysis results	Complete case finds resurfacing not cost-effective	Complete case and per-protocol analyses find mobile bearings dominated	Conclusions robust to changes in methods other than assumptions about interactions
Subgroup analysis results	Cost-effective in both age subgroups. Probability of being cost-effective: 97% in participants < 70 years, 74% in participants ≥ 70 years	Cost-effective in participants < 70 years (86% probability), but not ≥ 70 years (24% probability)	All polyethylene is poor use of resources in age subgroups. Probability of being cost-effective: 46% in participants < 70 years, 5% in participants ≥ 70 years

Mobile bearing versus fixed bearing

Mobile bearings were introduced to minimise wear. They achieve this by having larger areas of contact and thus lower contact stresses. However, their advantage of decreased wear may be nullified by them having more articulating surfaces. Improved wear should result in a decrease in long-term failure rate. Mobile bearings can also be used to alter the kinematics of the knee replacement. Improved kinematics should result in an improved functional outcome. The main theoretical disadvantage is instability and dislocation of the mobile bearing. In addition, mobile-bearing devices tend to be more expensive than fixed-bearing devices. Previous studies have shown no clear advantage or disadvantage of mobile bearings.

We found no definite advantage or disadvantage of mobile bearings in terms of postoperative functional status, quality of life, reoperation and revision rates, or cost-effectiveness (see *Table 41*). We did, however, identify two disadvantages of mobile bearings that could encourage surgeons to use fixed-bearing devices. First, there was a 2% incidence of instability or bearing dislocation in the mobile bearing group and none in the fixed bearing group. Second, although there was no significant difference in overall costs in the long term, there was a short-term saving for the hospital, as fixed bearings are appreciably cheaper than mobile bearings.

Further follow-up of the cohort would allow assessment of the long-term benefits, risks and costs of mobile bearings. The main theoretical advantage of mobile bearings is decreased wear. Wear can cause failure of knee replacement either mechanically, if the bearing is worn through, or through loosening and osteolysis. Both modes of failure require revision surgery. Failure due to wear tends to occur in the second decade after knee replacement. Therefore, if decreased wear were a real as well as a theoretical advantage of mobile bearings, it would probably be seen in the second decade. Follow-up of the patients in KAT at least to 15 years would clarify this.

Within the health economic analysis, trends were observed which, if they persist in the long term, will have important implications. The current evidence suggests that patients treated with mobile bearings are expected to have marginally higher QALYs which are sufficient to justify the small increased cost. There is, however, substantial uncertainty around this finding. In particular, there is some evidence that the benefits of mobile bearings are short lived, with the group assigned to mobile bearings tending to have higher costs and accrue fewer QALYs from the fourth year after TKR onwards. In the secondary analyses of the subgroup of patients < 70 years, the findings were somewhat stronger than those in the cohort as a whole. In particular, there was an estimated 86% probability that mobile bearings were cost-effective at a £20,000/QALY ceiling ratio. If mobile-bearing knee replacements are cost-effective, they are likely to be most cost-effective in the young active patients, as theoretically they should provide better function and longevity. It may be, therefore, in the long term that mobile bearings are cost-effective in patients aged < 70 years, whereas in patients aged ≥ 70 years fixed bearings may dominate, generating more QALYs and being less expensive. Again, longer term follow-up would help to determine if this is the case.

All polyethylene versus metal-backed

Currently metal-backed tibial components are used for most knee replacements. Previous randomised trials and meta-analyses of these trials found no difference in clinical outcome between the two types of tibial component. As all-polyethylene components are substantially cheaper than metal-backed components, the general recommendation within the orthopaedics community is that, in the elderly, all-polyethylene devices should be used so as to save money.[33,34] There have, however, not been any formal economic analyses to support this recommendation.

We found that the functional results with a metal-backed tibia were better than those with an all-polyethylene tibia (see *Table 41*). This difference was statistically significant when the function was assessed with the EQ-5D and SF-12, but not with the OKS. The complication and reoperation rates were similar. There was a non-significant trend towards a higher major reoperation rate with the all-polyethylene tibia. The economic analysis indicated that the initial cost saving, resulting from the all-polyethylene tibia being cheaper, was offset by higher subsequent costs such that overall the costs of the two types of tibia were similar. However, as metal-backed components were found to be more effective, there was a 91% probability that metal backing is cost-effective compared with all-polyethylene components, costing £35 per QALY gained. Previous recommendations suggested that metal-backed tibias would be less cost-effective than the all-polyethylene tibias in older people; however, we found the opposite: metal-backed tibial components were more cost-effective in patients ≥ 70 years than in younger patients, but were cost-effective in both age groups. This suggests that routinely using the metal-backed tibia in all patients would be good value for money. Hence, we believe that the previous recommendation that all-polyethylene tibias should be used to save money in the elderly is incorrect. Although initially they save money for the hospital, overall they will cost the health service more and are less effective.

Further follow-up would provide very useful clarification. Theoretically, one would expect differences in the revision rates of all-polyethylene and metal-backed tibias in the long term. All-polyethylene designs are likely to have fewer problems due to wear, as they tend to have thicker polyethylene and as there is no possibility of backside wear between the polyethylene and the metal backing. In addition, the transmission of load to the proximal tibia is different, so there may be a difference in loosening rates. Up to 10 years we found a non-significantly higher incidence of major reoperations in the all-polyethylene group. As the incidence of revision tends to increase with time, longer follow-up would clarify whether or not this is a real difference. There was also some conflicting evidence about the functional advantages of the metal-backed tibia. Although the patterns of results were similar, the OKS did not demonstrate a significant advantage, whereas the EQ-5D and SF-12 did. Further follow-up would clarify this.

Unicompartmental versus total knee replacement

The question of whether unicompartmental knee replacements should be widely used or not remains a topical and controversial issue. Potentially, they could offer appreciable advantages compared with TKRs. Unfortunately, because of inadequate recruitment, we were not able to address this subject. The experience gained from KAT has, however, been very useful, as it provided the necessary background information for planning of another study, TOPKAT, to address this issue. TOPKAT finished recruitment in September 2013.

General implications for clinical practice from the trial as a whole

Taken together, the results of the randomisations provide evidence to support routine resurfacing of the patella and the use of metal-backed tibial components, and suggest mobile bearings should be used with caution and probably only in younger patients.

In each of the randomisations, some differences among the various arms were observed. For the functional outcome scores, the differences tended to be relatively small. For reoperations and revisions, although the relative differences were large, the absolute differences were small because the overall reoperation and revision rates were low. For the health economic outcomes, the differences were clearer. Surgeons should be aware of this when selecting implants and should adopt more expensive devices only when there is evidence to support this.

If failure is defined as a reoperation or OKS being less than it was preoperatively, then at 10 years the cumulative failure rate is about 30%. This is a relatively large figure and patients should be warned about this preoperatively. Further work is also needed to improve implant design and techniques. However, it does not necessarily mean that 30% of patients end up with a poor result. This is partly because with time the OKS may improve, and also because patients usually have a satisfactory outcome from reoperations or revision surgery. At 10 years about 90% of patients have a better OKS than they did preoperatively.

Comparing the KAT population with data from the national Patient Reported Outcome Measures (PROMs) data set, which covers around 85% of participants undergoing TKR in England in 2010–11, suggests that KAT participants are typical of those undergoing TKR this decade. KAT participants had a mean baseline OKS of 18.0 (cf. 19.0 in PROMs) and a baseline EQ-5D of 0.38 (cf. 0.41 in PROMs).[91] Postoperative scores seen in KAT at 12 months were also similar to those observed in the national PROMs data set at 6 months (OKS 34.1 vs. 33.8 in PROMs; EQ-5D 0.73 vs. 0.70 in PROMs).[91]

The length of stay observed for KAT procedures (mean 10 days; standard deviation 5 days) is typical of that observed across England and Wales in 2000–3.[94] However, the average length of stay has fallen substantially in the past 10 years, such that the mean hospital stay for primary knee replacement is now 5.3 days.[82] As a result of their longer length of stay, the average total cost of the inpatient stay for primary TKR estimated in KAT (mean £7070; standard deviation £1873) is substantially higher than the current national average in England and Wales (£6080, based on HRGs HB21A-C in 2010–11).[84] However, if the length of stay among KAT participants had been the same as that seen in recent years, the mean estimated cost of KAT primary admissions would have been reduced to £5526 (standard deviation £1212): £554 lower than the current national average. The reason for this difference is unclear. Differences in costing methodology could be one explanation. In particular, our analysis used Scottish data on operating theatre costs, because of a lack of available data on the cost of operating theatre time in England, and based the cost of the inpatient stay on the cost per excess bed-day to avoid double counting. However, the difference may also reflect changes in resource use over time, such as the higher cost of knee replacement components now than in KAT, a greater usage of regional anaesthesia, or more physiotherapy and other rehabilitation resources so as to achieve an early discharge.

Whereas the clinical results are likely to be applicable world-wide, the findings of economic evaluations are generally more sensitive to changes in relative prices and clinical practice and are specific to a UK setting. There may also be variations in clinical practice and procurement polices within the UK that could affect cost-effectiveness. In particular, the discounts that hospitals receive off component list prices and the loan charges incurred for instruments vary between hospitals, with low-volume centres typically incurring higher costs. There are also substantial variations in component price among manufacturers, which may increase variations among hospitals or surgeons who predominantly use components by one or two manufacturers. Other variations in hospital care, such as variations in recovery room use, were also observed. The indications and rates of revision surgery are also likely to vary among centres, although such variations cannot easily be identified within a sample of this size. Other unit costs will also vary geographically: particularly between Scotland and England and between London and provincial towns. However, given that the economic results were primarily driven by the magnitude and direction of quality of life differences and were insensitive to even substantial changes in the cost of components and hospital care, the findings from KAT are likely to have wider relevance than other evaluations in which costs comprise the major driver. Variation between centres also has equity implications. At present, a shortage of data on the relative merits of different prostheses leads to marked variation among surgeons in the types of prostheses used.

At present, surgeons also take account of several patient characteristics when deciding on the most appropriate type of prosthesis, such as disease severity, deformity, diagnosis, age and activity. In particular, more costly component designs, such as metal-backed components and mobile bearings, are predominantly given to younger participants, who are more active and more likely to outlive their prostheses. In KAT, secondary subgroup analyses suggested that patellar resurfacing, mobile bearings and all-polyethylene tibial components were less cost-effective in participants aged ≥ 70 years than in younger participants. However, patellar resurfacing and metal backing were nonetheless cost-effective for both age groups, suggesting that allocation by age is not appropriate. However, subgroup analyses did suggest that mobile bearings were dominated by fixed bearings in older participants, but dominant in younger participants, suggesting that age and activity may be an important consideration for this aspect of component design, although further research is needed.

The results also have implications for hospital and commissioning budgets. Although economic results suggest that patellar resurfacing and metal backing are cost-effective from an NHS perspective, both aspects of prosthesis design increase costs during participants' primary hospital stay, which are offset by reductions in subsequent care and improvements in quality of life.

General research implications from the trial as a whole

The trial used a partial factorial design, which has been used in only a handful of trials to date, including the Women's Health Initiative[92] and the UK prospective diabetes study.[95] This study design enabled us to address three distinct research questions in the same study, increasing our effective sample size by recruiting some participants to two comparisons and avoiding the need to incur the fixed costs of trial administration and analysis for each comparison. These benefits are of particular relevance to orthopaedics, for which long follow-up time is essential and component designs raise a series of inter-related research questions.

The partial factorial design also enabled an exploratory assessment of interactions between patellar resurfacing and the other aspects of component design. Although the trial was extremely underpowered for this analysis, this sensitivity analysis suggested substantial qualitative interactions among the comparisons that could change the conclusions of the metal backing and patellar resurfacing comparisons. Although the results of these sensitivity analyses could be explained by chance and should be interpreted with caution, they nonetheless highlight an important area for future research. Although it may not be feasible to conduct a fully factorial trial adequately powered to detect interactions, preliminary work to explore the potential interaction between patellar resurfacing and metal backing or mobile bearings may be warranted.

The partial factorial study design also introduces challenges for the trial-based economic evaluation. KAT data are being used in ongoing research to explore the appropriate methodology for economic evaluation of factorial design trials,[96] which could help improve the quality of subsequent research. Orthopaedic research also raises additional challenges for trial-based economic evaluation: particularly in relation to valuing joint prostheses and operating theatre time and dealing with data collected over a 10-year trial period.

Limitations

The study was designed about 15 years ago. Therefore, the questions that were considered to be important then may not be relevant today. However, the questions are, in fact, still important particularly as there are limited funds available for health care. The prostheses used in the study are no longer commonly used today. However, as the questions were generic and as there have only been small changes in prosthetic design, this makes no difference to the conclusions. Similarly, clinical practice has not changed substantially, except that larger numbers of knee replacements are implanted and the inpatient stay is shorter, so this should not affect the conclusions. Traditional randomised trials in orthopaedics have had tight inclusion and exclusion criteria and have included surgeon-based outcome measures as well as radiographs. KAT is very different as it is pragmatic in nature and is therefore better at guiding health policy. A great strength of KAT is the detailed health economic analysis; however, the resource-use data collection focused on the main drivers and excluded non-knee-related costs, pain medication and mobility aids. In addition, we did not have accurate data on the discounts that hospitals receive. We therefore assumed that there was a flat rate of discount across all components, which may not be the case in practice. The partial factorial design of the study means that we cannot easily allow for interactions among treatment factors or have the power to accurately estimate or exclude such interactions.

Analysis of the non-randomised data

The comprehensive range of data on clinical characteristics, quality of life and resource use that have been collected for KAT could be used to address additional research questions related to knee replacement.

The trial data were used as an observational data set to explore how the cost-effectiveness of TKR varies with baseline characteristics and to assess the evidence base underpinning the eligibility criteria for TKR that had recently been introduced by a number of primary care trusts.[97] This research demonstrated that, although the costs and benefits of TKR vary with OKS, TKR is highly cost-effective for participants of grades 1–2 who had baseline OKS < 40 and for ASA grade 3 participants with OKS < 35. The study also showed that the cost-effectiveness of TKR was independent of BMI and of disease in other joints. This study was published in *BMJ Open* and presented at a number of national and international meetings. EQ-5D and OKS data from KAT were also used alongside data from the national PROMs programme to develop a mapping algorithm that can be used to estimate EQ-5D responses and utilities from patients' responses to the OKS questionnaire,[98] thereby facilitating future research assessing cost-effectiveness on older data sets that include OKS but not EQ-5D. KAT data were also used to explore the potential clustering effects of surgeon and/or centre in surgical trials and contributed to a database of intracluster correlation coefficients to aid in the design of future randomised surgical trials.[99] There is also a collaboration between KAT and COAST (another study funded by NIHR) in which KAT data are being used to develop a predictive model of knee replacement outcome.

Further research

The three main priorities for further research are:

1. Continue follow-up of KAT patients up to a minimum of 15 years.
2. Additional detailed analysis of the 10-year KAT data set.
3. Further RCTs in joint replacement based on the experience gained from KAT. A good example of this is TOPKAT, a study designed to determine whether total or partial knee replacement is better.

The analysis of the median 10-year follow-up data from KAT patients has gone a long way towards providing a substantially firmer evidence base to guide answers to the questions addressed by the randomisations within KAT. However, further follow-up to a minimum of 15 years and analysis of these data should result in stronger conclusions, which should provide the basis for more detailed, stronger and complete recommendations. There are two reasons for this. First, differences among the arms of the various randomisations may appear or become more marked in the second decade post knee replacement, and, second, the power of the study will increase with longer follow-up, which will allow more detailed subgroup analysis. Failure due to many causes, such as component loosening, polyethylene wear and osteolysis, tends to occur more frequently in the second decade than the first. Therefore, any design features, such as patellar resurfacing, mobile bearings and metal backing of the tibia, that influence these failure mechanisms are likely to have a greater effect on revision rates in the second decade than the first. In the longer term, outcome scores following knee replacement tend to drop. Therefore, functional differences among different designs of knee replacement may become more marked in the second decade. With time there will be more reoperations and revisions, which will increase the power of the study. For the standard analysis of the outcome scores, increased observations over time will not increase power, although the power of the marginal benefit calculation may increase with longer follow-up. Similarly, as costs and QALYs accumulate over time, the power of the health economic analysis may also increase if the follow-up is increased to 15 and 20 years.

Ongoing follow-up is particularly important for the patellar resurfacing randomisation, as we have found that with increasing follow-up there were an increasing number of reoperations for complications of resurfacing and a decreasing number of late patellar resurfacing procedures. We are therefore concerned that after 15 years there may be an increasing number of problems with resurfacing the patella that may change our findings, suggesting that the patella should not be resurfaced routinely. With the mobile bearing randomisation, we found that after up to 10 years there was no definite difference between the two arms. However, the main advantage of the mobile bearing, which is decreased wear, is most likely to manifest in the second decade. Long-term follow-up could also explore the trend towards lower QALYs

with mobile bearings beyond year 5 and explore the trend towards mobile bearings having a better cost-effectiveness in younger people than in older people. Follow-up to 15 and 20 years should clarify these issues. In the metal-backed versus all polyethylene randomisation, the 10-year results suggest a clear health economic advantage for the metal-backed tibia. There was, however, no clear clinical difference. Up to 10 years, we found a non-significantly higher incidence of major reoperations in the all polyethylene group. As the incidence of revision tends to increase with time, longer follow-up will clarify whether or not this is a real difference. There was also some conflicting evidence about the functional advantages of the metal-backed tibia. The OKS did not demonstrate a significant advantage, whereas the EQ-5D and SF-12 did, although the patterns of results were very similar. Further follow-up would also clarify this.

We believe the median 10-year KAT data set is the best data set for knee replacement that exists. It contains detailed data on patient demographics, surgical findings and management and implant characteristics for a very large number of patients. It also contains data from annual follow-up about clinical scores, complications, reoperations, costs and resource use. Further observational analysis of the data set, which should ideally be extended to a minimum of 10 years, could be undertaken to describe the natural history of knee replacement and to answer many of the key outstanding questions relating to TKR. For example, KAT data could be used to identify patient, centre, surgical and implant factors associated with a poor outcome, in terms of clinical score or reoperation rate, which would help surgeons improve the results of knee replacements. It could be used to determine the optimum way to follow-up knee replacement patients. It could be used to develop a detailed long-term health economic model of knee replacement and thus to improve the cost-effectiveness of knee replacement. It could be used to explore important observations made in the study such as that, when failure is defined as reoperation or a worse OKS than pre operation, the cumulative failure rate at 10 years is about 30% and that the various outcome measures discriminate differently among knee replacement designs.

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David W Murray (Professor, orthopaedics) was chief investigator for the trial, contributed to the design of the trial, led on the clinical aspects of the trial, contributed to the overall conduct of the trial, contributed to the preparation of the report and is guarantor for the study.

Graeme S MacLennan (Senior Statistician, statistics) contributed to the overall conduct of the trial, led on the statistical aspects of the trial, conducted the statistical analysis of the data and contributed to the preparation of the report.

Suzanne Breeman (Trial Manager, Health Service Research, trial management) was responsible for the day-to-day management of the trial, monitored data collection and contributed to the preparation of the report.

Helen A Dakin (Senior Researcher, health economics) contributed to the overall conduct of the trial, conducted the economic analysis, prepared economic results for publication and contributed to the preparation of the report.

Linda Johnston (Clinical Audit and Research Manager, orthopaedic and trauma surgery) contributed to the overall conduct of the trial, contributed to the recruitment and follow-up of patients, and contributed to the preparation of the report.

Marion K Campbell (Director, HSR triallist, statistics) contributed to the overall conduct of the trial, advised on methodological aspects of the trial and contributed to the preparation of the report.

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Appendix 1 Trial protocol

kat

Knee Arthroplasty Trial

PROTOCOL

VERSION 6 – March 2009

SUMMARY

AIMS

This study addresses questions about four developments in knee replacement surgery:

- Is a metal backing plate for the tibial component of the total knee replacement better than a single high density polyethylene component?
- Is it better to resurface the patella as part of a knee replacement or not?
- Does a polyethylene moving component (bearing) between the tibia and femur have a better outcome than standard designs without a moving bearing?
- Is it better to replace a single component of the knee or to replace the whole knee joint?

The assessment of outcome for each of the comparisons is based on:

- Patient-assessed function and health status
- Reoperation rates
- The 'worth' of any additional cost to the NHS

BRIEF OUTLINE OF THE STUDY

Surgeon participants

Surgeons may opt to take part in any (or all) of the comparisons for which they have no clear preference for one of the options.

Patient eligibility

Any patient who requires a knee replacement, and who the surgeon feels would be eligible for the trial.

Information and randomisation

Individual patients will be entered into no more than two possible permutations of the study. Prior to admission to hospital, patients will be sent information about the study, inviting them to take part, and describing the possible options for their operation. If they agree to take part, they will be randomised around the time they are admitted to hospital for their operation. Randomisation will be carried out by the central Trial Office.

Data collection

During their hospital admission, standard information will be collected on the patient's operation and recovery, including short-term complications and data relating to their hospital stay.

Three months and annually after their operation, patients will be sent postal questionnaires asking about their general health, their knee function, and their use of the health service, including any re-admissions and revision surgery. Follow-up will continue for up to eleven years after their operation, to ensure that the long-term performance of the knee operation is properly assessed.

Practical arrangements in clinical centres

The trial is designed to limit the extra work for collaborating surgeons to tasks which only they can do. They will take the lead in the study locally, but resources will be available to provide support. The clinical co-ordinating centres are in Dundee (Department of Orthopaedics and Trauma Surgery) and Oxford (Nuffield Orthopaedics Centre). Full-time co-ordinating nurses will be based in Dundee and Oxford to provide support for nurses in collaborating centres. The Trial Office within the Health Services Research Unit in Aberdeen will carry out telephone randomisation, patient postal follow-up, data management, processing and analysis.

Authorship

Publications generated from the study will be attributed to the KAT Trial Group, which will consist of all those who have wholeheartedly contributed to the trial.

Figure 1: Summary of patient progress in the study

Stages in the study	Actions required by:		
	Surgeon	**Study Nurse**	**Aberdeen Trial Office**
Patient deemed eligible ↓	Eligibility determined by surgeon		
Patient sent information ↓		Study nurse and Trial office liaise to send information to patient	
Patient agrees to take part, completes initial questionnaire ↓		Nurse consents patient, collects patient information	
Randomisation ↓		Nurse phones Trial Office	Randomisation by Trial Office
Operation and postoperative hospital stay ↓	Minimal operative details collected by surgeon.	Postoperative information collected by nurse	
Follow-up at 3 months ↓			Postal follow-up by Trial Office
Follow-up at 1 year ↓			Postal follow-up by Trial Office
Follow-up annually			Postal follow-up by Trial Office

CONTENTS

Appendices (to protocol)

This protocol describes a major UK-wide randomised trial to measure the clinical and cost effectiveness of different types of knee replacement. The trial is designed to be as simple as possible for participants and collaborating orthopaedic surgeons. Funds have been provided by the NHS R&D Health Technology Assessment Programme and include resources for both local co-ordination in trial centres and long-term follow-up.

1. OUTLINE OF THE TRIAL

The trial is evaluating four aspects of knee replacements:

A. Metal backing of the tibial component compared with a single high density polyethylene component.

B. Patellar resurfacing compared with no resurfacing.

C. A polyethylene mobile bearing component between the tibia and femur compared with a fixed bearing arthroplasty.

D. Uni-compartmental arthroplasty compared with total knee replacement.

Individual patients can participate in a maximum of two comparisons and then only if the surgeon responsible for care is substantially uncertain about these particular aspects.

2. SURGEON ELIGIBILITY

Any consultant orthopaedic surgeon may take part provided he or she:

a. Undertakes knee replacements routinely.

b. is prepared to allow the choice between the specific options in at least one of the four comparisons to be decided by random allocation. (This recognises that surgeons will vary in the comparisons for which they will accept random allocation; during the trial collaborating surgeons will choose which (or all) of the four comparisons they will recruit to - see below.)

3. PATIENT ELIGIBILITY

A patient under the care of a collaborating surgeon will be eligible if:

a. A decision has been made to have primary knee replacement surgery.

b. The surgeon has no clear preference for a specific option in at least one of the comparisons. (A patient is therefore not eligible for a trial comparison if the surgeon considers that a particular type of operation is clearly indicated; an example is those patients requiring a highly constrained knee replacement to replace function of the collateral ligaments.)

It is recognised that eligibility will depend on patients' differing functional requirements which are influenced by their age. Although there will not be formal age differentiation in the trial as some people are chronologically older than their function and vice versa, the results of fixed bearing knees in terms of patient satisfaction and longevity of implant (Knutson, 1992) would strongly support the view that until better established the mobile bearing arthroplasty should be reserved for younger patients. It is amongst these patients that the undoubtedly

higher technical demands of the operation which increase the risk can be matched by aspirations to increased benefit. It is therefore expected that surgeons will be more prepared to randomise younger patients to this comparison.

4. TRIAL RECRUITMENT

Potential participants will be sent information about the trial comparisons in which the surgeon responsible for care has agreed to participate. When a formal approach is made to the patient this will be to take part in one or two of comparisons, but not more than two. Exact arrangements for recruitment will depend on local admission procedures but will be based on the following:

Fully informing potential participants about the trial

Information about the trial will be given in two stages. A letter of invitation together with information about the parts of the trial in which the surgeon has agreed to participate will be sent to potential participants at home (Appendices A and B). Information will also be sent to their general practitioners in case they are consulted (Appendix C). More detailed information concentrating on the options for which the patient is eligible will be given to potential participants during discussion with a surgeon or research nurse at a pre-assessment clinic or when admitted before surgery.

Consent to participate in the trial

All eligible patients who agree to participate will sign a trial consent form (Appendix D). On this, they will confirm that they have been given the information they require and that the study has been explained to them. They will also confirm that they understand that they will be sent a questionnaire from the Trial Office each year.

Formal trial entry and random allocation

Participants will be formally entered into the trial by telephoning an automated service within the Trials Office in Aberdeen. At this phone call, basic descriptive information is given first (hospital; surgeon; patient's name; sex and date of birth) followed by information on the American Knee Society Grade (unilateral, bilateral, generalised arthritis) and the comparison(s) (i.e. A, B, C, or D - see Sections 1 and 5) to which the participant will be recruited. Once these details have all been supplied, the random allocation will be given in return. The allocation will be stratified by the surgeon, with minimisation according to the patient's age, sex, American Knee Society Grade, and whether or not in another randomised comparison. After this phone call the participant is considered irrevocably in the trial for the purposes of the research, irrespective of what happens subsequently. Recruitment will be on the day before surgery (or sooner) to allow theatre staff to prepare appropriate equipment and prostheses. Patients in the fourth comparison (uni-compartmental compared with total) will not be eligible for any of the other comparisons. Each patient can only be entered into the trial once. In the event of a patient being admitted for bilateral knee replacements, the knee indicated by the patient to be the most painful is the knee that should be considered for randomisation.

5. THE FOUR COMPARISONS BEING MADE

The trial comparisons are outlined in Section 1.

In comparison A, the prosthesis used would be the same in every aspect of design other than the tibial component which would be metal backed or not depending on the trial allocation. This option is generally available amongst systems of knee replacement.

Comparison B is straightforward clinically in that surgeons can opt to replace the patella or not irrespective of the design of the prosthesis used.

In respect of comparison C, there may be more variation in the choice between fixed bearing and mobile bearing prostheses. Essentially, the surgeon will choose the metal backed cruciate retaining or substituting design that he or she uses routinely. This will be compared with a mobile bearing design, which preferably but not essentially should be similar in design and make to the surgeon's usual choice of fixed bearing prosthesis.

Comparison D is somewhat different to the other three comparisons. In this, surgeons will use their normal fixed bearing knee or their normal uni-compartmental knee.

CLINICAL MANAGEMENT IN THE TRIAL

The surgeon performing the operation will be expected to follow the trial allocation. However, if in the opinion of the surgeon, a clear indication arises for a different operative approach, this should be used and the reason specified.

All other factors will be kept similar if possible, and the surgeon will therefore usually use one manufacturer's range of total knee replacement (see section 5 above).

All other aspects of care, such as deep vein thrombosis prophylaxis, antibiotic prophylaxis, post-operative length of stay and post-operative rehabilitation, are left to the discretion of the surgeon responsible for care.

6. OUTCOME ASSESSMENT

Participation does not require any special tests or extra hospital visits (over and above standard care).

Most data describing outcomes will be collected directly from participants through postal questionnaires. The same questionnaire will be completed at three months and then annually (Appendix E). It will include:

- The Oxford Knee Score (a twelve-item instrument measuring patients' perceptions of pain and function).
- The SF-12 (an abbreviated form of the SF-36, explaining more than 90% of the variance of the SF36).
- The EQ-5D (to derive quality-adjusted life years, QALYs).
- Questions about any further hospital admissions and surgery.

Clinical data will be collected in a standardised way from casenotes to describe operative complications, and any further surgery, especially for revision.

Participants in England and Wales will be flagged at the Office for National Statistics for notification of death registration (and possible later tracing if contact has been lost during follow-up). Participants in Scotland will be followed up through the NHS Central Register (including notification of death registration)(for consent form and participant letters see appendix D).

Follow-up is planned for at least ten years.

7. FLEXIBILITY OF THE DESIGN TO SUIT ALL COLLABORATING SURGEONS

Individual patients can be recruited to either one or two of the comparisons. The study design is therefore a partial factorial randomised controlled trial.

Individual surgeons will choose to which of the comparisons they will recruit patients. It is unlikely that any surgeon will recruit to all four comparisons. The local trial will therefore be limited to those comparisons that a collaborating surgeon has decided to contribute to. The trial will be described to colleagues and potential participants in these terms.

A good example of the whole process may be:

Mr Jones agrees to collaborate in the trial but only feels happy using total condylar knee replacements. He prefers cruciate substituting designs but is ambivalent about metal backing and is uncertain about patellar replacement. He therefore contracts to follow the trial allocation for metal or non-metal backing prosthesis plus or minus a patella i.e. two randomised comparisons. Information given to Mr Jones' patients will be related to these two comparisons only. Mr Jones will decide whether a particular patient is eligible for one, the other, or both these comparisons, and will then seek informed consent accordingly.

8. ARRANGEMENTS IN CLINICAL CENTRES

The role of collaborating surgeons

The trial is designed to limit the extra work for collaborating surgeons to tasks which only they can do. Study nurses will facilitate the trial locally (see below), and the central organisation will take responsibility for data management and patient follow-up.

Collaborating surgeons will:

a. establish the trial locally (for example by getting agreement from clinical colleagues, facilitating local research ethics committee approval, identifying and appointing a local study nurse, liaising with the local R&D manager, and ensuring that all clinical staff involved in the care of patients having knee replacement surgery are informed about the trial).
b. take responsibility for clinical aspects of the trial locally.
c. notify the Trial Office of any unexpected clinical event which might be related to trial participation.
d. provide support and supervision for all aspects of the work of the local study nurse.
e. represent the centre at KAT collaborators meetings.

The role of study nurses

Each clinical centre will have a part-time study nurse, physiotherapist or other equivalent form of staff, whose number of sessions of employment will depend on the number of patients being recruited in a centre. Their responsibilities will be to:

a. Keep local staff informed about the trial and its progress.
b. Keep regular contact with the local surgeon(s).
c. Maintain regular contact with one of the co-ordinating nurses (see below).
d. Identify all those having knee replacement surgery in advance of their admission, and keep a log of whether or not they were recruited to the trial (with reasons for non-participation).
e. Arrange for the initial letter of invitation and information leaflet to be sent to potential participants and to their GPs.
f. Assist the surgeon (for example at a pre-assessment clinic) to give additional information and seek consent to trial entry.
g. Ensure that arrangements are in place for formal trial entry and random allocation, once a participant is admitted for surgery.
h. Arrange for the GP to be informed about recruitment.
i. Ensure that the initial data form describing the index hospital admission is completed promptly and sent to the Trial Office.
j. Collect data describing complications and subsequent admissions to hospital.
k. Facilitate later follow-up, by for example helping with local tracing.
l. Assist in the conduct of satellite studies, if applicable.
m. Provide support for participants in other ways if there are difficulties.
n. Represent the centre at study nurse meetings.

9. CLINICAL CO-ORDINATION

The clinical co-ordinating centres are in Dundee (Department of Orthopaedics and Trauma Surgery) and Oxford (Nuffield Orthopaedics Centre). At the start of the trial, representatives from these centres will visit all surgeons expressing an interest in collaborating, aiming to get a commitment from collaborating surgeons to recruit to specified comparisons.

Full-time co-ordinating nurses will be based in Dundee and Oxford. They will:

a. Support the study nurses in collaborating centres.
b. At the start, help to appoint and train study nurses.
c. Act as a first point of enquiry about any clinical aspect of the trial.

d. Help the Trial Office to ensure complete data collection (through study nurses) during the initial hospital stay, and following any later hospital admission.
e. Act as an intermediary between the Trial Office in Aberdeen and study nurses, and have weekly contact with the Trial Office.
f. Help the Trial Office in connection with any difficulties with later patient follow-up.
g. Act as local study nurses in Dundee and Oxford.

10. DATA CO-ORDINATION

Telephone randomisation and data collection, processing and analysis will be the responsibility of the Trial Office within the Health Services Research Unit in Aberdeen. Staff there will:

a. Facilitate the sending of information to patients and GPs from study nurses.
b. Provide an automated telephone randomisation service for formal trial entry.
c. Monitor collection of in-hospital data and process them, and seek missing or uncertain data.
d. Post our personalised follow-up forms to all participants (at three months and then annually), maximising response by reminders and phone calls, and process returned forms.
e. Ensure the confidentiality and security of all trial forms and data.
f. Conduct extensive data checking and cleaning.
g. Perform interim and main analyses.

12. STATISTICAL AND ECONOMIC CONSIDERATIONS

Sample sizes sought in the four randomised comparisons

The sample sizes sought for the four comparisons have been based on a number of considerations. They have drawn on the relationship between changes in the OKS and other well known outcome instruments, and what previous research has suggested is plausible. They have also taken account of clinical issues, such as the size of differences that seem likely judged on current experience, the possibility of adverse effects, and cost differences.

The table describes the statistical power to detect differences of 1.5, 3.0 and 4.5 in the mean OKS for three sample sizes (700, 350, and 175 in each group), firstly with an alpha error of $2P<0.01$ and secondly for an alpha error of $2P<0.05$. These calculations assume a standard deviation for the OKS of 10 points.

Table 1 **Statistical power to identify differences of 1.5, 3.0 and 4.5 in mean OKS for three sample sizes, at two levels of statistical significance.**

Mean difference in OKS		1.5		3.0		4.5	
		2P<0.01	2P<0.05	2P<0.01	2P<0.05	2P<0.01	2P<0.05
Number in	700	60	80	>99	>99	>99	>99
each randomised	350	<50	50	91	97	99	>99
group	175	<50	<50	60	80	94	98

Although the OKS is the principal outcome, possible differential effects on revision rates have also been considered where appropriate. Although these are presented here as simple rate differences, these analyses will in fact be able to identify smaller differences with the same statistical power as that indicated. There are two reasons. First, these analyses will be based on the time to revision using prosthesis 'survival curves' rather than a simple dichotomous variable. Second, survival curves will also be generated for a composite outcome which includes patients whose knee prostheses are judged (by falling below a predefined threshold on the Oxford score) to have failed, in addition to those who actually had revision (thus increasing the number of 'events', and hence statistical power).

(i) Metal backing of tibial component

The concern in this comparison is that loosening of non-metal backed tibial components may lead to severe symptoms in the long-term. The aim therefore is for a sample size which is large enough to identify a difference equivalent to a typical category change in the American Knee Society Score (that is, a difference of about 3.0 in the OKS). This will require a minimum of 175 per group to have reasonable power (80%) with an alpha error of 2P<0.05 (see Table). A comparison with 235 in each group, for example, would have 90% power to identify this difference.

(ii) Patellar resurfacing

Based on preliminary results of follow-up of a small randomised trial - currently unpublished - comparing patellar resurfacing with no resurfacing, the effect of resurfacing, if it exists, is likely to be relatively small and near a difference in the mean OKS of 1.5. The table shows that a trial with 700 in each group would have 80% power to identify this difference (2P<0.05) A trial of this size (about 1500 people) would also have reasonable

power to identify differences in revision rates over prolonged follow-up - more than 90% power to detect a halving from 10% to 5%, for example.

(iii) Uni-compartmental arthroplasty

A non-randomised comparison of two cohorts characterised by management with either a uni-compartmental prosthesis or total knee replacement showed a difference in the mean OKS scores of 3.4, whereas follow-up of similar but smaller randomised cohorts suggested a smaller difference of 1.6, albeit with a wide confidence interval. The aim is therefore for a trial with at least 175 participants in each group, so that there is a good chance of identifying a difference in the mean OKS of 3.0. There may be higher revision rates after uni-compartmental arthroplasty. A trial of this size would have 90% power to identify an increase from 5% to 15% in this respect.

(iv) Mobile versus fixed bearing arthroplasty

The substantially greater costs of mobile bearing prostheses can only be justified if there are clear benefits. The aim is to identify benefits equivalent to an increase in the OKS of 3.0 or greater. A trial with 350 in each group (see Table) has over 90% power to identify this at the 1% level of significance and 97% power to show a significant difference at the 5% level. There are concerns about possible short-term failures, such as dislocation or related mechanical problems, associated with the mobile bearing arthroplasty. If 1% such complications are expected in the fixed bearing group, a trial with 350 in each group has about 90% power to identify an increase to 5%.

Other details of the analysis plan

All analyses will be based on 'intention to treat' and no participant with data will be excluded. The principal comparisons will be between:

a. All those allocated a metal backed tibial component compared with all those allocated a single component.
b. All those allocated patellar resurfacing compared with all those allocated no resurfacing.
c. All those allocated mobile bearing compared with all those allocated fixed bearing.
d. All those allocated uni-compartmental arthroplasty compared with all those allocated total knee replacement.

These main analyses will measure the 'main effects' of the alternative approaches. The partial factorial design will, however, provide an opportunity to assess whether there is any

interaction between patellar resurfacing and the other comparisons (that is, whether a combination has any greater or lesser effect than would be expected from the main effects).

Differences between the groups in revision rates might bias comparisons of the Oxford scores. For this reason these analyses will be run in two ways: firstly on the actual scores at a particular time, irrespective of further surgery (aiming to compare the clinical policies actually used, including repeat surgery); and second, after imputing a score for those who had revision surgery (aiming to compare the initial surgery used in the trial). Although patient survival will be a measure of outcome and described in trial reports, most analyses will be based on the assumption that the alternative prostheses do not have differential effects on mortality. Analyses of the Oxford score will principally be based on survivors but possible effects of excluding those who died will be explored using imputed scores based on the data available. In respect of the revision analyses, participants will be assumed to be at risk only when alive, using a multi-decrement life table approach. It is difficult to predict the proportion of participants who will die or be lost to follow-up, but allowance has been made by aiming to recruit at least 1500, 750 and 400 as applicable.

Additional analyses, stratified by surgeon, will explore any effects of make of prosthesis, surgical experience ('the learning curve') and rehabilitation policy.

Timing and frequency of analyses and reporting

Two principal analyses are planned - at six years and then at twelve years.

By six years, participants will have had a median of four years follow-up (assuming it takes six months to initiate the trial, two years to recruit all patients, and six months to complete and report analyses). By this stage, data on early complications, which are likely to be mainly medical, will be available. There will be some early failures, for example due to infection. Outright device failure will be uncommon, but differences in functional scoring could be apparent.

By twelve years, follow-up will have been for a median of ten years. A substantially larger number of device failures and subsequent revisions will have occurred by then.

Confidential interim analyses will be performed at other times as requested by the Data Monitoring Committee, which is expected to meet at least annually (see below).

Economic evaluation

The type of economic analysis performed for each comparison will depend on the findings. If there are no differences in outcome for a particular comparison, cost minimisation analysis will be used. If differences emerge, cost-effectiveness analyses from a societal perspective will be performed. The primary measure of effectiveness will be pain and function as assessed by the Oxford Knee Score. Information on utilities will also be available for analysis because trial patients will also complete EQ-5D for which population-weighted values are available.

Costs of alternative forms of knee-replacement surgery may be considered as either short term or long term. In the short term, differences in costs of alternatives will arise from differences in surgical procedure, technology, forms of care during hospital stay, length of hospital stay and short-term complications (wound infection, deep vein thrombosis, pulmonary embolism). In the long term, major differences in costs of the surgical alternatives will arise in relation to differences in longer term outcomes, particularly recurrence of pain and physical dysfunction requiring further primary, community and hospital care, and, in some cases, need to revise surgery.

Three data gathering components will be used to address these major sources of variation in costs (i) early (ii) medium to long term and (iii) modelling.

(i) Early data collection

Cost generating events in the short term will be recorded by means of a patient-specific checklist administered by research nurses at the participating hospitals, using theatre records and hospital notes. This will cover time in theatre and on ward, surgical procedure(s), diagnostic and investigative procedures and tests, and duration and intensity of rehabilitation.

(ii) Medium to long-term data collection

Following initial hospitalisation, information on health care resources used will be recorded using questions integrated into the main follow-up questionnaire administered to all patients annually. This will estimate annual numbers of knee-related primary care consultations, out-patient visits, and use of other health care services. Full information on all subsequent in-patient admissions for investigative procedures or revision surgery will be recorded using the research nurse system described elsewhere in this protocol.

(iii) Modelling

Primary economic analysis will use the resource volumes and rates of revision surgery recorded during the follow-up period. However, in order to extend the economic analysis beyond the follow-up period, some modelling will be performed, using trial data on observed revision rates, resource use and risk factors to set parameter values. Uncertainty surrounding the model results will be formally reported.

Unit costs for all cost generating resource events recorded above will be obtained from participating centres and from national data sets.

13. TRIAL COMMITTEES

The Steering Committee

The trial is overseen by a Steering Committee made up of the principal grant holders, David Murray (Oxford), Ray Fitzpatrick (Oxford) and Adrian Grant (Aberdeen), together with Richard Morris (London), Alasdair Gray (Oxford), Nick Fiddian (Bournemouth), Rami Abboud (Dundee), Marion Campbell (Aberdeen) and a representative from each participating centre. Meetings will be chaired by David Murray. The Steering Committee will take responsibility for any major decisions, such as the need to close recruitment early to one or more parts of the study or to change the protocol for any reason.

The Project Management Group

The trial is co-ordinated by its Project Management Group. This consists of the principal grant holders, David Murray (Oxford), Ray Fitzpatrick (Oxford) and Adrian Grant (Aberdeen), together with Richard Morris (London), Alasdair Gray (Oxford), Nick Fiddian (Bournemouth), Rami Abboud (Dundee), Marion Campbell (Aberdeen) and those employed to work on the trial in the co-ordinating centres. Observers may be invited to attend at the discretion of the Project Management Group. This group will meet at four monthly intervals initially with the meetings being chaired by David Murray.

The Data Monitoring Committee

A data monitoring committee will be established, independent of the trial organisers. The committee will consist of three members (one of whom will act as chairman): an orthopaedic surgeon who is not involved in the trial; a clinician with experience of trials; and a statistician with experience of monitoring accumulating trial data.

During the period of recruitment to the trial, interim analyses will be supplied, in strict confidence, to the data monitoring committee, together with any other analyses that the committee may request. This may include analyses of data from other comparable trials. In the light of these interim analyses, the data monitoring committee will advise the Steering Committee if, in its view, one or more of the randomised comparisons in the trial has provided both (a) proof beyond reasonable doubt that for all or some types of patients one particular type of prosthesis is clearly indicated or contraindicated[1], and (b) evidence that might reasonably be expected to influence materially the care of people who require knee replacement by clinicians who know the results of this and comparable trials. The Steering Committee can then decide whether or not to modify intake to the trial or to report results early. Unless this happens, however, the steering committee, project management group, clinical collaborators, and trial staff (except those who supply the confidential analyses) will remain ignorant of the interim results considered by the committee.

The frequency of interim analyses will depend on the judgement of the chairman of the committee, in consultation with the Steering Committee.

14. FINANCE

The trial is supported by a grant from the Health Technology Assessment Programme of the NHS Executive Research and Development Programme with supplementary funding from the major manufacturers of knee prostheses in the UK.

15. SATELLITE STUDIES

The funds provided by the NHS R&D HTA Programme are to conduct the main trial as described in this protocol. Nevertheless, it is recognised that the value of the KAT trial will be enhanced by smaller ancillary studies of specific aspects. Plans for such studies should, however, be discussed and agreed in advance with the Project Management Group.

16. PUBLICATION

The success of the trial depends entirely on the wholehearted collaboration of a large number of doctors and nurses. For this reason, chief credit for the trial will be given, not to

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Note:

[1] Appropriate criteria for proof beyond reasonable doubt cannot be specified precisely. A difference of at least three standard deviations in the interim analysis of a major endpoint may be needed to justify halting, or modifying, such a study prematurely. If this criteria were to be adopted, it would have the practical advantage that the exact number of interim analyses would be of little importance, and so no fixed schedule is proposed (Peto R et al *Br J Cancer* 1976; **34:** 584-612).

the committees or central organisers, but to all those who have wholeheartedly collaborated in the trial. The trial's publication policy is described in detail in Appendix G. The results of the trial will be reported first to trial collaborators. The main report will be drafted by the Trial Management Group, and the final version will be agreed by the Steering Committee before submission for publication, on behalf of the Collaboration.

To safeguard the integrity of the main trial, reports of any satellite studies will not be submitted for publication without prior discussion with the Project Management Group.

Once the main report has been published, a lay summary will be sent to participants who have indicated they would like to receive one.

Protocol Appendix A

PATIENT LETTER GIVING GENERAL INFORMATION ABOUT THE STUDY PRIOR TO HOSPITAL ADMISSION

(To be printed on study headed paper with the address of the relevant Study nurse)

Dear {Patient}[1]

STUDY OF KNEE REPLACEMENT

I am writing on behalf of {Participating Consultant Orthopaedic Surgeon}. I understand you are due to have a knee replacement in the near future. This letter is to tell you about a national study comparing various types of knee replacement in regular use in the NHS. We are always trying to improve the care we give, and this study will help us do so by allowing us to find out which knee replacement designs should be used in the future.

Depending on the problem with your knee, you may be asked to join the study when you come to the hospital. You will be given full details then. This letter is just to let you know about the study.

The study is about these questions:

* Should the tibial component of an artificial knee be metal backed? [2]
  It is not clear whether it is best to make one of the components of the knee out of plastic or out of a combination of metal and plastic. For people involved in this part of the study one of the two designs of knee replacements will be used. The choice will be made randomly.

* Should the knee cap be resurfaced? [2]
  We are not certain whether or not it is best to replace the surface of the knee cap at the time of knee replacement. For people in this part of the study the choice whether to replace your knee cap or not would be made randomly.

* Should a knee replacement have a mobile bearing?[2]
  Many new designs of knee replacement have a plastic bearing that is free to move. It is not clear whether this is an advantage or not. For people in this part of the study either a standard knee replacement or one with a mobile bearing will be implanted and the choice would be made randomly.

* Unicompartmental or total knee replacement?[2]
  If the disease in the knee is confined to one portion then it is possible just to replace the damaged portion (unicompartmental knee replacement) or to replace the whole knee (total knee replacement). It is not clear whether a unicompartmental knee replacement or total knee replacement is better in these circumstances. For people in this part of the study the decision as to whether to use a unicompartmental or total knee replacement will be made randomly.

Your surgeon in discussion with you will decide what is best for you and will only ask you to join the study if (s)he thinks this is appropriate. If you then agree to take part in the study, we will ask you to fill in a short questionnaire before your operation. We will write to

[1] *Letters will be individually addressed.*

[2] *Patients will be given information about only the parts of the study which may be of relevance to them.*

you three months and then each year after the operation to find out how well you feel your knee replacement is functioning.

We shall discuss the study with you at the clinic when we see you before your operation. If you have any questions about the study we will be pleased to answer them then.

Yours sincerely

Study Nurse[3]
Researcher to <<Participating Consultant Orthopaedic Surgeon>>

[3]The relevant study centre nurse will sign the letter

Protocol Appendix B

kat

Knee Arthroplasty Trial

PATIENT INFORMATION LEAFLETS

kat

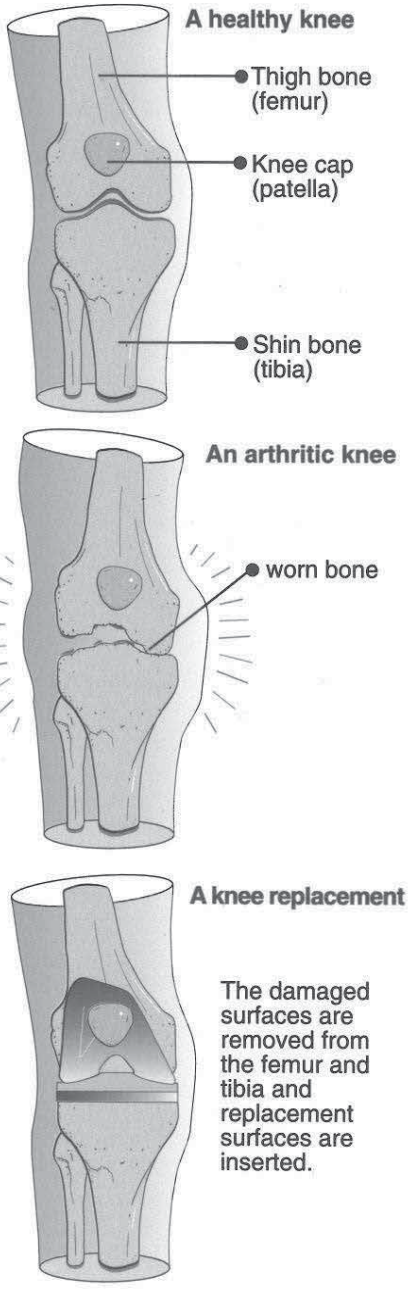
Knee Arthroplasty Trial

Background Information

Knee replacement is an extremely successful treatment for arthritis and other knee problems (detailed in the diagrams opposite). There are, however, many different types of knee replacement available and it is not clear which are best, or whether some are more appropriate for some conditions than others. To answer some of these questions we are undertaking a large study involving many hospitals and about 1500 people having their knees replaced. The study is funded by the National Health Service and we hope that you can take part.

There are four main questions being asked in the study. Depending upon the extent and type of the disease in your knee, your surgeon may invite you to take part in one or two parts of the study.

The parts you may be invited to join are described on separate leaflets attached to this one.



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Knee Arthroplasty Trial

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Knee Arthroplasty Trial
A

Should the part that replaces the top of the shin bone (tibia) have a metal back?

Your knee replacement consists of at least two parts.

1. The part that is used to resurface the thigh bone is made of metal and has a rounded surface.

2. The part that is used to replace the bottom end of the shin bone may be made completely of plastic or be partly metal and partly plastic (with the metal between the bone and plastic shown opposite).

The metal is supposed to spread the load more evenly on the bone and therefore should be less likely to loosen. However, because of the metal back, the plastic is thinner and more likely to wear out. It is therefore not clear whether the metal back is an advantage. If you agree to be involved in this part of the study then the choice of whether this part will be metal backed or not will be made randomly. This means that you would have an equal chance of having a metal or non metal backed component and the decision would be taken by the study office. By comparing the results of knee replacements with metal backs with those made totally of plastic we will be able to determine whether or not metal backed components should be used.

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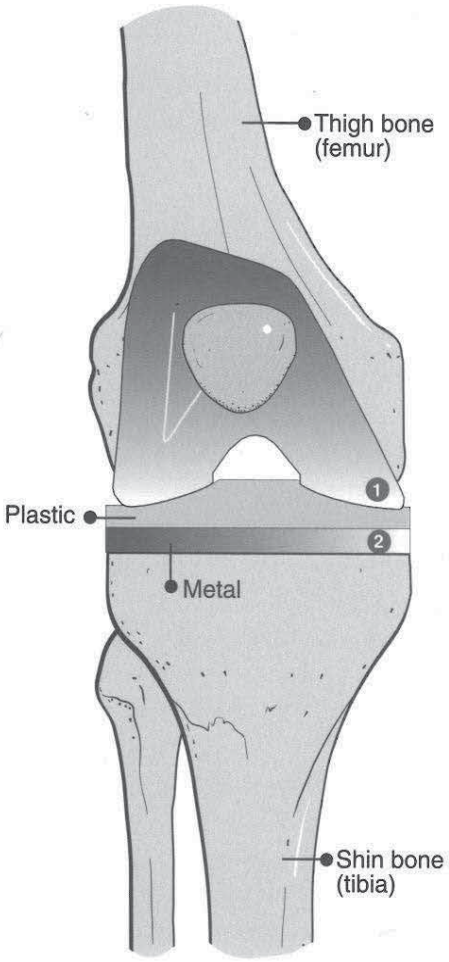
A metal backed total knee replacement



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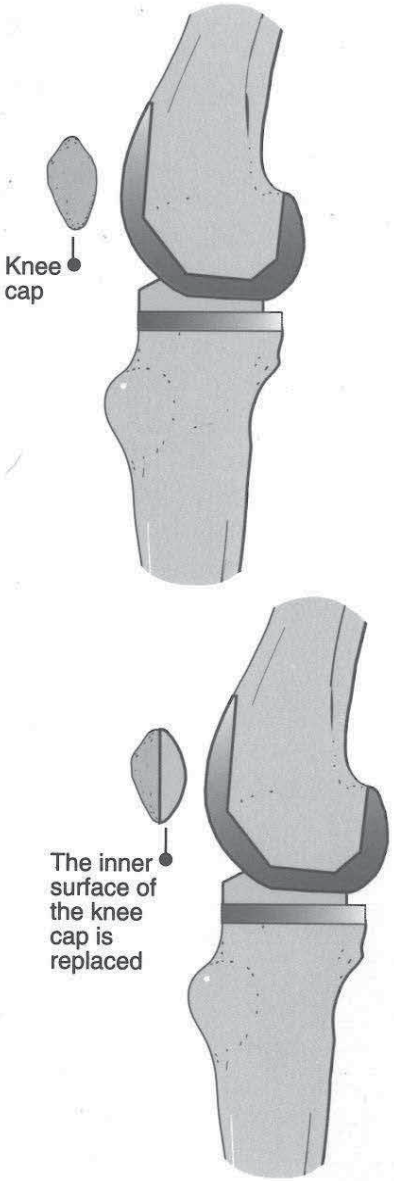
Knee Arthroplasty Trial

B

Should the inner surface of the knee cap be resurfaced?

When performing a total knee replacement some surgeons routinely replace the inner surface of the knee cap whilst others virtually never do. It is not clear whether it is better to do this or not. After knee replacement a small proportion of patients have pain in the front of their knee. It is possible that the chance of having this pain is slightly lower if the inner surface of the knee cap is replaced. However, there may then be problems, for example, the new knee cap may wear out. If you agree to be involved in this part of the study then the choice as to whether or not the inner surface of your knee cap will be replaced will be made randomly. This means that you would have an equal chance of having the inner surface of your knee cap replaced or not replaced and the decision would be taken by the study office.
The results of knee replacement in patients who have had the inner surface of knee caps replaced will be compared with those who have not. This study will provide information as to whether it is necessary to replace the inner surface of the knee cap at the time of knee replacement.



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Knee Arthroplasty Trial

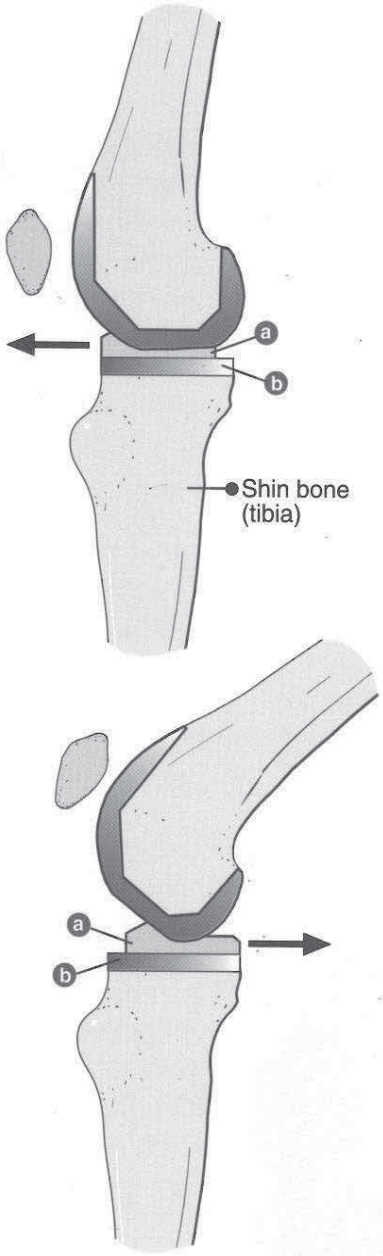
Should the knee replacement have a 'mobile bearing'?

Recently many manufacturers have introduced knee replacements with mobile bearings. In these, the plastic part on the shin bone (tibia) ⓐ is free to move on the flat surface of metal ⓑ of the tibial component. This has two advantages in theory.

1. It should allow a more normal movement of the knee, shown by the black arrow on each diagram.
2. It should reduce wear.

However, there are a number of possible disadvantages of this type of knee. For example, it is more difficult to implant and there is a chance that the bearing may dislocate and come out of joint.

If you agree to be involved in this part of the study then the choice of implanting your knee with either a mobile or non-mobile bearing will be made randomly. This means that you would have an equal chance of having a mobile or a non-mobile bearing and the decision would be taken by the study office. By comparing the results of the mobile and non-mobile bearing knee replacements we will find out the benefits and any problems of mobile bearings.



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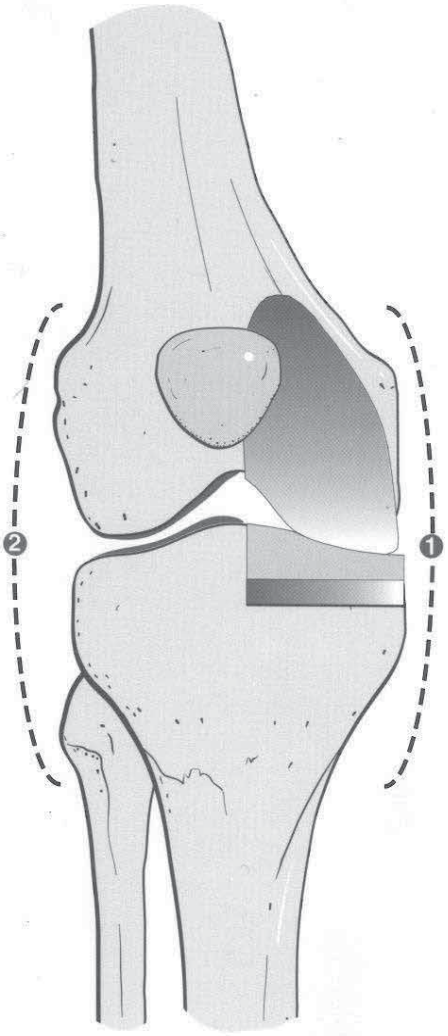
A unicompartmental knee replacement?

The joint between the thigh bone and the shin bone consists of two compartments:

❶ Inside ('medial')

❷ Outside ('lateral')

In about a quarter of knees, the disease is mainly in the inside compartment. In this situation it is possible to replace only the damaged compartment and retain the healthy compartment (unicompartmental knee replacement). The alternative is to replace all the structures of the knee (total knee replacement) which is described in the background information. It is not clear under these circumstances whether a unicompartmental knee replacement or a total knee replacement is better. If you agree to be involved in this part of the study then the choice as to whether a unicompartmental knee or total knee replacement is used will be made randomly. This means that you would have an equal chance of having a unicompartmental or total knee replacement and the decision would be taken by the study office. By comparing the results of unicompartmental knees with total replacements we will be able to determine in which situation it is best to use a unicompartmental rather than a total knee replacement.



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Knee Arthroplasty Trial

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Knee Arthroplasty Trial

What will happen if you join the study?

- You will be asked to fill in questionnaires about your knee before your knee replacement surgery, at three months after your operation and yearly for up to ten years, to find out if you have been having any problems.
- The details of your operation will be collected from your surgeon.
- A member of the research team will visit you before you leave hospital to ask you whether you have had any problems with your knee after your operation.

The study does not involve any additional tests or hospital visits.

We want to reassure you that:

- Your involvement in the study is entirely voluntary.
- You are free to withdraw at any time and this would not affect your current or future medical treatment.
- If your surgeon decides that you should have a particular type of knee replacement he or she will follow that judgement regardless of the study.
- Your treatment will be provided within the NHS and your care is covered by the usual NHS indemnity arrangements.
- All information collected for the study will be treated as confidential and used only for the purpose of the study. Individuals will not be identified in any reports of the findings.
- We will inform your GP that you are taking part.
- We will write to tell you the results of the study.

Finally

- You may keep this information sheet and will be given a copy of your consent form.
- If you have any questions or worries your surgeon and others helping with the study will discuss them with you in detail when you are seen before your operation.

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Knee Arthroplasty Trial

Where can you seek advice?

If you would like free, independent advice about taking part in this study, you can contact any of the following **Community Health Council** Offices.

Protocol Appendix C

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Knee Arthroplasty Trial

INFORMATION SHEET & LETTERS FOR GENERAL PRACTITIONERS

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Knee Arthroplasty Trial

Further Information for General Practitioners

BACKGROUND

There is no doubt about the value of knee replacement surgery, with 20,000 knee replacements performed annually in the UK, at an estimated cost of £70 million. However, a wide variety of prostheses are currently being used, and uncertainty exists as to which are the best options, particularly for younger and fitter patients whose potential benefit is greatest.

In particular, controversy still exists as to whether to mount the tibial bearing on a metal baseplate or not, the benefit of patellar re-surfacing, and whether an element of axial rotation of the tibial bearing is in the long term beneficial. The role of less expensive hemiarthroplasty designs particularly in the younger age group also awaits proper scrutiny. Unless there is an unexpected radical breakthrough in biomaterials research, there is a consensus that, for available materials, knee replacement design is unlikely to change in broad terms in the foreseeable future, and certainly not in the next decade.

The planned study is therefore timely and will provide information which is important for clinicians, patients and policy makers about the most appropriate forms of surgery.

AIMS

This study addresses questions about four developments in knee replacement surgery:

- Is a metal backing plate for the tibial component of the total knee replacement better than a single high density polyethylene component?
- Is it better to resurface the patella as part of a knee replacement or not?
- Does a polythylene moving component (bearing) between the tibia and femur have a better outcome than standard designs without a moving bearing?
- Is it better to replace a single component of the knee or to replace the whole knee joint?

The assessment of outcome for each of the comparisons is based on:

- Patient-assessed function and health status
- Reoperation rates
- The 'worth' of any additional cost to the NHS

BRIEF OUTLINE OF THE STUDY

Surgeons may opt to take part in any (or all) of the comparisons for which they have no clear preference for one of the options. Individual patients will be entered into no more than two possible permutations, however. Prior to admission to hospital, patients are sent information about the study, inviting them to take part, and describing the possible options for their operation. If they agree to take part, they will be randomised around the time they are admitted to hospital for their operation. During their hospital admission, standard information will be collected on their operation and recovery, including short-term complications and data relating to their hospital stay.

Three months and annually after their operation, participants will be sent postal questionnaires asking about their general health, their knee function, and their use of the health service, including any re-admissions and revision surgery. Follow-up will continue for up to eleven years after their operation, to ensure that the long-term performance of the knee operation is properly assessed.

KAT Co-ordinating Office, Health Services Research Unit (FLEA), University of Aberdeen, Polwarth Building, Foresterhill, ABERDEEN AB25 2ZD Tel: [redacted] Email: KAT@abdn.ac.uk
This study is funded by NHS Research & Development Health Technology Assessment Programme

LETTER LETTING GPS KNOW THAT A PATIENT HAS BEEN APPROACHED[1]

Dear

KNEE ARTHROPLASTY TRIAL

The NHS R&D Programme is evaluating developments in knee replacement surgery in a large national trial (The knee arthroplasty trial or KAT, for short).

Your patient, (patient name, DOB), is being considered for recruitment to the KAT study. Recently s/he has been sent information about the study, describing the trial options for which s/he is likely to be eligible.

We enclose a brief outline of the study for your information. We realise that s/he may make an appointment to discuss whether or not to take part in the trial and we hope this information will be useful then.

Involvement of your patient in the trial would not mean any significant work for you. All data for the study will be collected from hospital case notes and by patient completed questionnaire.

Yours sincerely

KAT Study Nurse

[1] On Kat headed paper with relevant study nurse address

LETTER LETTING GPS KNOW THAT A PATIENT HAS BEEN RECRUITED TO THE TRIAL[1] (GP previously notified of approach)

Dear

KNEE ARTHROPLASTY TRIAL

You may remember that we wrote to you recently describing the KAT Study. Your patient, (patients name, DOB,) has agreed to join the study.

When s/he has had the operation, you will receive discharge information as usual from your patient's orthopaedic surgeon.

We will carry out follow-up by sending postal questionnaires direct to (patient's name) at three months post-operatively and annually for up to ten years. We would be grateful if you would help us by sticking the label provided on (patient's name)'s notes, contacting telephone number [redacted]: if the patient changes address, is too ill to complete questionnaires, or dies. Other than that, we should not need to obtain any other information from you.

If you require any further details about the study, please do not hesitate to contact me.

Yours sincerely

KAT Study Nurse

Encl

[1] On Kat headed paper with relevant study nurse address

ALTERNATIVE LETTER LETTING GPS KNOW THAT A PATIENT HAS BEEN RECRUITED TO THE TRIAL[1] (GP not previously notified of approach)

Dear

KNEE ARTHROPLASTY TRIAL

The NHS R&D Programme is evaluating developments in knee replacement surgery in a large national trial (The knee arthroplasty trial or KAT, for short).

Your patient, (patient's name, DOB,) after being sent information about the study and meeting with myself has agreed to take part.

I enclose a brief outline of the study for your information. I have advised (patient's name) to contact myself if s/he has any further questions.

When s/he has had the operation, you will receive discharge information as usual from your patient's orthopaedic surgeon.

We will carry out follow-up by sending postal questionnaires direct to (patient's name) at three months post-operatively and annually for up to ten years. We would be grateful if you would help us by sticking the label provided on (patient's name)'s notes, contacting telephone number [redacted]: if the patient changes address, is too ill to complete questionnaires, or dies. Other than that, we should not need to obtain any other information from you.

Yours sincerely

KAT Study Nurse

Encl

[1] On Kat headed paper with relevant study nurse address

Protocol Appendix D

kat

Knee Arthroplasty Trial

CONSENT FORMS AND LETTERS

kat

Knee Arthroplasty Trial

CONSENT FORM

I have:

- Discussed the study with: _____
- Been given the Information Sheet about the study
- Received satisfactory answers to questions
- Been given enough information about the study

I understand that:

- I am free to withdraw from the study at any time without having to give a reason
- If I withdraw, this will not affect my care
- My family doctor will be notified that I am taking part in the study
- My family doctor and the person I have nominated as my best contact may be approached for additional information
- I will be sent questionnaires three months and each year after my operation
- Information from my hospital notes and NHS information to do with my knee replacement may be collected

I agree to take part in the study

Please sign here: _____

Your name in block capitals: _____

Date: _____

I confirm that I have explained to the person named above, the nature and purpose of the study and the procedures involved.

Signature of investigator: _____

Date: _____

Study Centre No _____ Patient Study No _____

(For use by co-ordinating centre in Aberdeen)

KAT Co-ordinating Office, Health Services Research Unit (FLea), University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen AB25 2ZD [redacted] E mail: KAT@abdn.ac.uk

kat

Knee Arthroplasty Trial

CONSENT FORM

to obtain information from the NHS Central Register

Study Number: «StudyNo»

Participant Name: «Patient»

I have received your letter regarding the collection of information relevant to the KAT Trial.

I understand that I can refuse to agree this request without giving an explanation.

I agree to information relevant to the KAT trial being obtained from the NHS Central Register.

Signature of Participant

Date

Please sign and return this form to:
The KAT Trial Office, Health Services Research Unit, University of Aberdeen, Foresterhill, Aberdeen, ABS5 2ZD, Tel: [redacted]

ISRCTN45837371

LETTER TO SCOTTISH PARTICIPANTS REQUESTING CONSENT TO OBTAIN INFORMATION FROM THE NHS CENTRAL REGISTER[1]

Dear {Participant name}

Knee Arthroplasty Trial (known as the KAT Trial)

Thank you for agreeing to take part in the KAT trial. We greatly appreciate your interest and help with this trial and would very much like to continue to keep in touch with you.

We have been given permission by the Multi-Centre Research Ethics Committee to contact you to ask whether you are happy for us to collect relevant information about your health and hospital admissions since joining the study from routinely collected hospital data. This information would be obtained through the national NHS Central Register and would involve you doing absolutely nothing. We just need to get your agreement to do this. It is very important and useful to collect this information. This will help us to find out how best to help people with knee replacements like the one you received. All the information we collect is treated with the strictest confidence.

We therefore enclose a form and, if you are happy for us to collect this information, could you please sign and return the white copy to us in the reply-paid envelope (no stamp is required). Please keep the blue copy for yourself.

We greatly appreciate your interest and help with the study and very much hope you will consider our request favourably. It really will help to make sure the results of the study are as accurate as possible. If you have any queries about this please do not hesitate to contact us.

Once again, many thanks for your help.

Yours sincerely,

KAT Trial Co-ordinator

[1] On Kat headed paper with Trial Office address

LETTER TO SCOTTISH PARTICIPANTS WITHDRAWN DUE TO ILL HEALTH REQUESTING CONSENT TO OBTAIN INFORMATION FROM THE NHS CENTRAL REGISTER[1]

Dear {Participant name}

Knee Arthroplasty Trial (known as the KAT Trial)

Some time ago you joined the KAT Trial, which aims to find out how best to help people with knee replacements like the one you received. We enclose an information leaflet to remind you about the study. After joining the Study you unfortunately had to withdraw.

We have been given permission by the Multi-Centre Research Ethics Committee to contact you to ask whether you are happy for us to collect relevant information about your health and hospital admissions from routinely collected hospital data. This information would be obtained through the national NHS Central Register and would involve you doing absolutely nothing. We just need to get your agreement to do this. It is very important and useful to collect this information. This will help us to find out how best to help people with knee replacements like the one you received. All the information we collect is treated with the strictest confidence.

We therefore enclose a form and, if you are happy for us to collect this information, could you please sign and return the white copy to us in the reply-paid envelope (no stamp is required). Please keep the blue copy for yourself.

We greatly appreciate your interest and help with the study and very much hope you will consider our request favourably. It really will help to make sure the results of the study are as accurate as possible. If you have any queries about this please do not hesitate to contact us.

Once again, many thanks for your help.

Yours sincerely,

KAT Trial Co-ordinator

[1] On Kat headed paper with Trial Office address

FOLLOW-UP LETTER TO SCOTTISH PARTICIPANTS REQUESTING CONSENT TO OBTAIN INFORMATION FROM THE NHS CENTRAL REGISTER[1]

Dear {Participant name}

Knee Arthroplasty Trial (known as the KAT Trial)

Thank you for agreeing to take part in the KAT trial. We greatly appreciate your interest and help with this trial and would very much like to keep in touch with you.

Last month we wrote to you to ask whether you would be happy for us to collect relevant information about your health and hospital admissions since joining the study. This information would be obtained through the national NHS Central Register and would involve you doing absolutely nothing. We just need to get your agreement to do this. It is very important and useful to collect this information. This will help us to find out how best to help people with knee replacements like the one you received. All the information we collect is treated with the strictest confidence.

To date, we have not received a reply to our previous request. We therefore enclose another agreement form and, if you are happy for us to collect this information, could you please sign and return the white copy to us in the reply-paid envelope (no stamp is required). Please keep the blue copy for yourself.

We greatly appreciate your interest and help with the study and very much hope you will consider our request favourably. It really will help to make sure the results of the study are as accurate as possible. If you have any queries about this please do not hesitate to contact us.

Once again, many thanks for your help.

Yours sincerely,

KAT Trial Co-ordinator

[1] On Kat headed paper with Trial Office address

Protocol Appendix E

kat

Knee Arthroplasty Trial

PARTICIPANT QUESTIONNAIRES & LETTERS

kat

Knee Arthroplasty Trial

Study Centre No

Patient Study No

CONFIDENTIAL

KAT STUDY

PARTICIPANT ENTRY QUESTIONNAIRE

Thank you in advance for completing this questionnaire.

We are going to ask you a few questions about your general health followed by some specific questions about your knee.

This study is funded by the NHS Research and Development Health Technology Assessment Programme

RIGHT

YOUR HEALTH TODAY

1. **By placing a cross (X) in one box in each group below, please indicate which statement best describes your own health state today. Do not X more than one box in each group.**

Mobility

- I have no problems in walking about ☐
- I have some problems in walking about ☐
- I am confined to bed ☐

Self-Care

- I have no problems with self care ☐
- I have some problems washing and dressing myself ☐
- I am unable to wash myself ☐

Usual activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities ☐
- I have some problems with performing my usual activities ☐
- I am unable to perform my usual activities ☐

Pain / Discomfort

- I have no pain or discomfort ☐
- I have moderate pain or discomfort ☐
- I have extreme pain or discomfort ☐

Anxiety / Depression

- I am not anxious or depressed ☐
- I am moderately anxious or depressed ☐
- I am extremely anxious or depressed ☐

YOUR GENERAL HEALTH

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities.

If you are unsure about how to answer any questions please give the best answer you can and make any of your own comments if you like. Do not spend too much time in answering as your immediate response is likely to be the most accurate.

2. In general, would you say your health is: *(Please X one box)*

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much? *(Please X one box on each line)*

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐

4. During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health?</u> *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Were you limited in the **kind** of work or other activities	☐	☐	☐	☐	☐

Study Centre No ☐☐

Patient Study No ☐☐☐☐☐

5. **During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?** *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Didn't do work or other activities as **carefully** as usual	☐	☐	☐	☐	☐

6. **During the <u>past 4 weeks</u> how much did <u>pain</u> interfere with your normal work (including work both outside the home and housework)?** *(Please X one box)*

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

7. **These questions are about how you feel and how things have been with you during the <u>past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling.** *(Please X one box on each line)*

   How much time during the <u>past 4 weeks</u>:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Have you felt calm and peaceful?	☐	☐	☐	☐	☐
Did you have a lot of energy?	☐	☐	☐	☐	☐
Have you felt downhearted and low?	☐	☐	☐	☐	☐

8. **During the <u>past 4 weeks</u>, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc)?** *(Please X one box)*

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

HEALTH PROBLEMS CAUSED BY YOUR KNEE

The following questions ask about problems which may have been caused by your right knee during the **past 4 weeks**. (Please X one box for each question.)

9. During the past 4 weeks how would you describe the pain you have from your right knee?

None	Very mild	Mild	Moderate	Severe
☐	☐	☐	☐	☐

10. During the past 4 weeks have you had any trouble with washing and drying yourself (all over) because of your right knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

11. During the past 4 weeks have you had any trouble getting in and out of a car or using public transport because of your right knee? (whichever you tend to use).

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

12. During the past 4 weeks for how long have you been able to walk before the pain from your right knee becomes severe? (with or without a stick).

No pain at all, or no pain for more than 30 mins	16 to 30 mins	5 to 15 mins	Around the house only	Not at all - pain severe on walking
☐	☐	☐	☐	☐

13. During the past 4 weeks after a meal (sat at a table), how painful has it been for you to stand up from a chair because of your right knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
☐	☐	☐	☐	☐

14. During the past 4 weeks have you been limping when walking, because of your right knee?

Rarely/ never	Sometimes or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

15. During the past 4 weeks could you kneel down and get up again afterwards? (thinking of your right knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

16. During the past 4 weeks have you been troubled by pain from your right knee in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
☐	☐	☐	☐	☐

17. During the past 4 weeks how much has pain from your right knee interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
☐	☐	☐	☐	☐

18. During the past 4 weeks have you felt that your right knee might suddenly 'give way' or let you down?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

19. During the <u>past 4 weeks</u> could you do the household shopping <u>on your own</u>? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

20. During the <u>past 4 weeks</u> could you walk down one flight of stairs? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

Thank you again!

kat

Knee Arthroplasty Trial

Study Centre No

Patient Study No

CONFIDENTIAL

KAT STUDY

PARTICIPANT THREE MONTH QUESTIONNAIRE

We are going to ask you a few questions about your general health followed by some specific questions about your knee. We would also like to know if you have needed to consult any medical services over the past three months.

Even though you may have had both knees replaced, when answering the following questions, please think only of your right knee (not both knees).

This study is funded by the NHS Research and Development Health Technology Assessment Programme

RIGHT

YOUR HEALTH TODAY

1. By placing a cross (X) in one box in each group below, please indicate which statement best describes your own health state today. Do not X more than one box in each group.

Mobility

I have no problems in walking about ☐
I have some problems in walking about ☐
I am confined to bed ☐

Self-Care

I have no problems with self care ☐
I have some problems washing and dressing myself ☐
I am unable to wash myself ☐

Usual activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐
I have some problems with performing my usual activities ☐
I am unable to perform my usual activities ☐

Pain / Discomfort

I have no pain or discomfort ☐
I have moderate pain or discomfort ☐
I have extreme pain or discomfort ☐

Anxiety / Depression

I am not anxious or depressed ☐
I am moderately anxious or depressed ☐
I am extremely anxious or depressed ☐

YOUR GENERAL HEALTH

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities.

If you are unsure about how to answer any questions please give the best answer you can and make any of your own comments if you like. Do not spend too much time in answering as your immediate response is likely to be the most accurate.

2. In general, would you say your health is *(Please X one box)*

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much? *(Please X one box on each line)*

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐

4. During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health?</u> *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Were you limited in the **kind** of work or other activities	☐	☐	☐	☐	☐

Study Centre No ☐☐

Patient Study No ☐☐☐☐☐

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Didn't do work or other activities as **carefully** as usual	☐	☐	☐	☐	☐

6. During the past 4 weeks how much did pain interfere with your normal work (including work both outside the home and housework)? *(Please X one box)*

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

7. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please indicate the one answer that comes closest to the way you have been feeling. *(Please X one box on each line)*

How much time during the past 4 weeks:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Have you felt calm and peaceful?	☐	☐	☐	☐	☐
Did you have a lot of energy?	☐	☐	☐	☐	☐
Have you felt downhearted and low?	☐	☐	☐	☐	☐

8. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc)? *(Please X one box)*

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

HEALTH PROBLEMS CAUSED BY YOUR KNEE

The following questions ask about problems which may have been caused by your right knee during the **past 4 weeks**. *(Please X one box for each question.)*

9. During the past 4 weeks how would you describe the pain you have from your right knee?

None	Very mild	Mild	Moderate	Severe
☐	☐	☐	☐	☐

10. During the past 4 weeks have you had any trouble with washing and drying yourself (all over) because of your right knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

11. During the past 4 weeks have you had any trouble getting in and out of a car or using public transport because of your right knee? (whichever you tend to use).

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
☐	☐	☐	☐	☐

12. During the past 4 weeks for how long have you been able to walk before the pain from your right knee becomes severe? (with or without a stick).

No pain at all, or no pain for more than 30 mins	16 to 30 mins	5 to 15 mins	Around the house only	Not at all - pain severe on walking
☐	☐	☐	☐	☐

13. During the past 4 weeks after a meal (sat at a table), how painful has it been for you to stand up from a chair because of your right knee?

Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
☐	☐	☐	☐	☐

14. During the past 4 weeks have you been limping when walking, because of your right knee?

Rarely/ never	Sometimes or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

15. During the past 4 weeks could you kneel down and get up again afterwards? (thinking of your right knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

16. During the past 4 weeks have you been troubled by pain from your right knee in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
☐	☐	☐	☐	☐

17. During the past 4 weeks how much has pain from your right knee interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
☐	☐	☐	☐	☐

18. During the past 4 weeks have you felt that your right knee might suddenly "give way" or let you down?

Rarely/ never	Sometimes, or just at first	Often, not just at first	Most of the time	All of the time
☐	☐	☐	☐	☐

19. During the past 4 weeks could you do the household shopping on your own? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

20. During the past 4 weeks could you walk down a flight of stairs? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

CONSULTATION WITH MEDICAL SERVICES

We would like to know about any medical problems that you have had with your right knee.

21. Since leaving hospital, have you been back to the hospital outpatients to see an orthopaedic surgeon for any reason relating to your right knee?

No ☐ If **No**, go to question 22

Yes ☐ If **Yes**, how many times?

(e.g. 0 1) ☐☐ Number of times

22. Since leaving hospital, have you visited a physiotherapist for any reason relating to your right knee?

No ☐ If **No**, go to question 23

Yes ☐ If **Yes**, how many times? ☐☐ Number of times

23. Since leaving hospital, have you been to see your General Practitioner for any reason relating to your right knee?

No ☐ If **No**, go to question 24

Yes ☐ If **Yes**, how many times? ☐☐ Number of times

24. Since your operation have you been admitted into any hospital <u>for any reason</u>?

No ☐ *If **No**, go to final section*

Yes ☐ *If **Yes**, please give (rough) date, hospital and reason, if possible*

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Hospital ☐

Reason ☐

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Hospital ☐

Reason ☐

FINAL SECTION

Thank you for completing this questionnaire. It really will help us to find out how we can best help people who have knee operations like yours.

We would like to contact you again in about nine months time. If your circumstances are likely to change, please let us know below:

House Name

House Number

Street Name

District

Town/City

County

Postcode

Telephone No *(including code)*

Once you have completed this questionnaire please return it in the pre-paid envelope provided to the following address:

KAT Co-ordinating Office, Health Services Research Unit (FLea),
University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen AB25 2ZQ

kat

Knee Arthroplasty Trial

Study Centre No	Year	Patient Study No

CONFIDENTIAL

KAT STUDY

PARTICIPANT ANNUAL FORM

We are going to ask you a few questions about your general health followed by some specific questions about your knee. We would also like to know if you have needed to consult any medical services over the past year.

Even though you may have had both knees replaced, when answering the following questions, please think only of your right knee (not both knees).

This study is funded by the NHS Research and Development Health Technology Assessment Programme

RIGHT

YOUR HEALTH TODAY

1. **By placing a cross (X) in one box in each group below, please indicate which statement best describes your own health state today. Do not X more than one box in each group.**

Mobility

- I have no problems in walking about ☐
- I have some problems in walking about ☐
- I am confined to bed ☐

Self-Care

- I have no problems with self care ☐
- I have some problems washing and dressing myself ☐
- I am unable to wash myself ☐

Usual activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities ☐
- I have some problems with performing my usual activities ☐
- I am unable to perform my usual activities ☐

Pain / Discomfort

- I have no pain or discomfort ☐
- I have moderate pain or discomfort ☐
- I have extreme pain or discomfort ☐

Anxiety / Depression

- I am not anxious or depressed ☐
- I am moderately anxious or depressed ☐
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YOUR GENERAL HEALTH

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities.

If you are unsure about how to answer any questions please give the best answer you can and make any of your own comments if you like. Do not spend too much time in answering as your immediate response is likely to be the most accurate.

2. In general, would you say your health is *(Please X one box)*

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much? *(Please X one box on each line)*

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
Climbing **several** flights of stairs	☐	☐	☐

4. During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health?</u> *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Were you limited in the **kind** of work or other activities	☐	☐	☐	☐	☐

Study Centre No	Year	Patient Study No
☐☐	☐☐	☐☐☐☐☐

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? *(Please X one box on each line)*

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like	☐	☐	☐	☐	☐
Didn't do work or other activities as **carefully** as usual	☐	☐	☐	☐	☐

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	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Have you felt calm and peaceful?	☐	☐	☐	☐	☐
Did you have a lot of energy?	☐	☐	☐	☐	☐
Have you felt downhearted and low?	☐	☐	☐	☐	☐

8. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc)? *(Please X one box)*

All of the time	Most of the time	Some of the time	A little of the time	None of the time
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HEALTH PROBLEMS CAUSED BY YOUR KNEE

The following questions ask about problems which may have been caused by your right knee during the **past 4 weeks**. *(Please X one box for each question.)*

9. During the past 4 weeks how would you describe the pain you have from your right knee?

None	Very mild	Mild	Moderate	Severe
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10. During the past 4 weeks have you had any trouble with washing and drying yourself (all over) because of your right knee?

No trouble at all	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
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11. During the past 4 weeks have you had any trouble getting in and out of a car or using public transport because of your right knee? (whichever you tend to use).

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12. During the past 4 weeks for how long have you been able to walk before the pain from your right knee becomes severe? (with or without a stick).

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16. During the past 4 weeks have you been troubled by pain from your right knee in bed at night?

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17. During the past 4 weeks how much has pain from your right knee interfered with your usual work (including housework)?

Not at all	A little bit	Moderately	Greatly	Totally
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18. During the past 4 weeks have you felt that your right knee might suddenly "give way" or let you down?

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19. During the past 4 weeks could you do the household shopping on your own? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
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20. During the past 4 weeks could you walk down a flight of stairs? (thinking of your knee)

Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
☐	☐	☐	☐	☐

CONSULTATION WITH MEDICAL SERVICES

We would like to know about any medical problems that you have had with your right knee.

21. In the last year, have you been back to the hospital outpatients to see an orthopaedic surgeon for any reason relating to your right knee?

No ☐ If **No**, go to question 22

Yes ☐ If **Yes**, how many times?

(e.g. 0 1) ☐☐ Number of times

22. In the last year, have you visited a physiotherapist for any reason relating to your right knee?

No ☐ If **No**, go to question 23

Yes ☐ If **Yes**, how many times? ☐☐ Number of times

23. In the last year, have you been to see your General Practitioner for any reason relating to your right knee?

No ☐ If **No**, go to question 24

Yes ☐ If **Yes**, how many times? ☐☐ Number of times

24. In the last year, have you been admitted into any hospital <u>for any reason</u>?

No ☐ *If **No**, go to final section*

Yes ☐ *If **Yes**, please give (rough) date, hospital and reason, if possible*

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Hospital ☐

Reason ☐

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Hospital ☐

Reason ☐

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Hospital ☐

Reason ☐

FINAL SECTION

Thank you for completing this questionnaire. It really will help us to find out how we can best help people who have knee operations like yours.

We would like to contact you again in about a years time. If your circumstances or those of your best contact are likely to change, please let us know by filling in the enclosed sheet.

Once you have completed all parts of this questionnaire please return it in the pre-paid envelope provided to the following address:

KAT Co-ordinating Office, Health Services Research Unit,
University of Aberdeen, Polwarth Building, Foresterhill, Aberdeen AB25 2ZQ

3 MONTH FOLLOW-UP LETTER TO PARTICIPANT[1]

Dear {Participant name}

Thank you for agreeing to take part in the KAT study.

It is now three months since you had your {left/right} knee replacement. We would therefore like to ask you about how your knee replacement is functioning and the medical services you have used since the operation. We have enclosed a questionnaire which we would be delighted if you could complete and return in the pre paid envelope.

We shall contact you again in nine months time (which will be a year following your operation) and then annually after this time, with further questions about your knee replacement.

If you have any questions about this study please do not hesitate to contact us.

We wish you good health and look forward to receiving your questionnaire.

Yours sincerely,

KAT Trial Co-ordinator

Encl

[1] On Kat headed paper with Trial Office address

ONE YEAR FOLLOW-UP LETTER TO PARTICIPANT[1]

Dear {Participant name}

Thank you for your continued participation in the KAT study.

It is now a year since you had your {left/right} knee replacement. We would therefore like to ask you about how your knee replacement is functioning and the medical services you have used since your operation. We have enclosed the annual questionnaire which we would be delighted if you could complete and return in the pre paid envelope.

We shall contact you again in a year with further questions about your knee replacement.

If you have any questions about this study please do not hesitate to contact us.

We wish you good health and look forward to receiving your questionnaire.

Yours sincerely,

KAT Trial Co-ordinator

[1] On Kat headed paper with Trial Office address

YEAR TWO - TEN FOLLOW-UP LETTER TO PARTICIPANT[1]

Dear «Title» «Surname»

Thank you for your continued participation in the KAT study.

It is now a year since we last contacted you about your «IndexDesc» knee replacement. We would therefore like to ask you about how your knee replacement is functioning and the medical services you have used in the past year. We have enclosed the annual questionnaire which we would be delighted if you could complete and return in the pre paid envelope.

We shall contact you again in a year with further questions about your knee replacement.

If you have any questions about this study please do not hesitate to contact us.

We wish you good health and look forward to receiving your questionnaire.

Yours sincerely,

KAT Trial Co-ordinator

Encl

[1] On Kat headed paper with Trial Office address

3 MONTH FOLLOW-UP REMINDER LETTER TO PARTICIPANT[1]

Dear {Participant name}

Thank you for agreeing to take part in the KAT study. Your help is very important in finding out how best to help people with knee replacements like the one you received. We greatly appreciate your interest and help with this trial and would very much like to keep in touch with you.

We recently sent you a questionnaire asking about how your {left/right} knee replacement is functioning and the medical services you have used since your operation. To date, we do not appear to have received your questionnaire. We are really interested in your views and we would be most grateful if you could spare a few minutes of your time to complete the questionnaire and return it to us in the pre paid envelope (I have enclosed another copy of the questionnaire). Please be assured that the information you give will be treated with the strictest confidence. If you have any worries or questions, please do not hesitate to contact me at the Kat Office in Aberdeen [redacted]. If you do not wish to complete the questionnaire, please return it blank in the pre paid envelope.

We wish you good health and look forward to hearing from you. Thank you once again for your help.

Yours sincerely,

KAT Trial Co-ordinator

Encl

[1] On Kat headed paper with Trial Office address

ANNUAL FOLLOW-UP REMINDER LETTER TO PARTICIPANT[1]

Dear {Participant name}

Thank you for agreeing to take part in the KAT study. Your help is very important in finding out how best to help people with knee replacements like the one you received. We greatly appreciate your interest and help with this trial and would very much like to keep in touch with you.

We recently sent you a questionnaire asking about how your {left/right} knee replacement is functioning and the medical services you have used in the last year. To date, we do not appear to have received your questionnaire. We are really interested in your views and we would be most grateful if you could spare a few minutes of your time to complete the questionnaire and return it to us in the pre paid envelope (I have enclosed another copy of the questionnaire). Please be assured that the information you give will be treated with the strictest confidence. If you have any worries or questions, please do not hesitate to contact me at the Kat Office in Aberdeen [redacted]. If you do not wish to complete the questionnaire, please return it blank in the pre paid envelope.

We wish you good health and look forward to hearing from you. Thank you once again for your help.

Yours sincerely,

KAT Trial Co-ordinator

Encl

[1] On Kat headed paper with Trial Office address

Protocol Appendix F

kat

Knee Arthroplasty Trial

SURGEON FORM, PARTICIPANT DETAILS AND HOSPITAL CARE FORM

Study Centre No

kat

Knee Arthroplasty Trial

Patient Study No

Patient Name

Date of birth Day Month Year

Date of operation Day Month Year

Confirmation of treatment allocated by randomisation (mark each line with a cross X)

A:	**Metal backed**	☐	**Non-metal backed**	☐	**Not randomised** ☐
B:	**Patellar Resurfacing**	☐	**No patellar resurfacing**	☐	**Not randomised** ☐
C:	**Mobile bearing**	☐	**Fixed bearing**	☐	**Not randomised** ☐
D:	**Uni-compartmental arthroplasty**	☐	**Total knee replacement**	☐	**Not randomised** ☐

Please attach stickers for all components used for the operation or fill in the appropriate information:

CAT. NO. _____

Component _____

CAT. NO. _____

Component _____

CAT. NO. _____

Component _____

CAT. NO. _____

Component _____

RIGHT KNEE

PTO FOR SURGEON'S FORM

kat
Knee Arthroplasty Trial

SURGEON'S FORM

Please complete straight after the operation by marking boxes with a cross (X) or giving details as requested

Pre-operative

The study knee is the right knee

Fixed flexion deformity No ☐ Yes ☐ → How many degrees? ☐☐ °

Valgus/Varus deformity No ☐ Yes ☐ → Varus ☐ Valgus ☐

Was the deformity? Mild ☐ Moderate ☐ Severe ☐

Was it correctable? No ☐ Yes ☐

Intra-operative

Patella

Normal ☐ Partial loss of cartilage ☐ Full thickness cartilage loss ☐ Less than 5mm bone loss ☐ More than 5mm bone loss ☐

Anterior cruciate ligament Intact ☐ Damaged ☐ Absent ☐

Posterior cruciate ligament Intact ☐ Recessed or damaged ☐ Divided ☐

Lateral retinacular release No ☐ Yes ☐

Was cement used for:

Tibia No ☐ Yes ☐ **Femur** No ☐ Yes ☐ **Patella** No ☐ Yes ☐

Intra-operative complications? No ☐ Yes ☐

If 'yes', Patella fracture ☐ Other ☐

If other, please specify

Was the consultant's usual surgical technique followed? No ☐ Yes ☐

If 'no', please give details

Did the patient receive the allocated procedure? No ☐ Yes ☐

If 'no', please give details

At end of operation

Fixed flexion deformity No ☐ Yes ☐ → How many degrees? ☐☐ °

Name of surgeon performing operation

Grade of operator

Consultant ☐ Associate specialist/staff grade ☐ SPR ☐ SHO ☐

Grade of senior surgeon present

Consultant ☐ Associate specialist/staff grade ☐ SPR ☐

RIGHT KNEE **PTO FOR THEATRE FORM**

kat

Knee Arthroplasty Trial

Study Centre No

Patient Study No

CONFIDENTIAL

KAT STUDY

PARTICIPANT DETAILS FORM

For completion by local KAT researcher

This study is funded by the NHS Research and Development Health Technology Assessment Programme.

PERSONAL INFORMATION
Please check faxed patient information and write amendments below, if necessary.

Title *(Mr, Mrs etc)* **Surname**

First Names

Date of Birth Day Month Year

House Name

House Number

Street Name

District

Town/City

County

Postcode

Telephone No *(including code)*

Place of Birth *(including county)*

Marital Status Single Married Divorced Widowed

Sex Male Female

Maiden name if female and ever married

NHS Number

Hospital Number *(if known)*

CHI Number *(Scotland only)*

GENERAL PRACTITIONER
Check faxed details and amend if necessary.
Surname

First Name(s) *(if known)*

House Name

House Number

Street Name

District

Town/City

County

Postcode

Telephone No
(including code)

'BEST CONTACT' *(friend or family member)*
Title *(Mr, Mrs etc)* **Surname**

First Names

House Name

House Number

Street Name

District

Town/City

County

Postcode

Telephone No
(including code)

Relationship to participant

DESCRIPTIVE INFORMATION ABOUT THE PARTICIPANT

1. Weight ☐☐☐ **kgs**

2. Height ☐☐☐ **cms**

3. Type of knee arthritis? Osteoarthritis ☐ (Cross X one box)

Rheumatoid ☐

4. Is the arthritis in? Single knee ☐

Both knees ☐

General ☐

5. Are there any other conditions which are affecting the participant's mobility? No ☐

Yes ☐

If **Yes**, please specify _____

6. Has the participant had any previous knee surgery? No ☐

Yes ☐

If **Yes**, was it

Ipsilateral osteotomy ☐

Ipsilateral patellectomy ☐

Contralateral previous knee replacement ☐

Other ☐

If Other, please specify _____

Please send this completed form, together with the participant entry questionnaire, the surgeon's form, and the hospital care form, to the KAT co-ordinating office, when the participant leaves hospital. Prepaid envelopes are provided.

kat

Knee Arthroplasty Trial

Study Centre No

Patient Study No

CONFIDENTIAL

KAT STUDY

PARTICIPANT HOSPITAL CARE FORM

For completion by KAT researcher at hospital discharge. Please send completed form, together with the participant details form, participant entry questionnaire and the surgeon's form in a prepaid envelope provided to:

KAT Co-ordinating Office
Health Services Research Unit (FLea)
University of Aberdeen
Polwarth Building
Foresterhill
Aberdeen AB25 2ZQ

This study is funded by the NHS Research and Development Health Technology Assessment Programme.

INFORMATION TO BE COLLECTED FROM THE PATIENT'S THEATRE NOTES

1. Please specify the grade of the anaesthetist present at operation.

Consultant ☐ Associate specialist/staff grade ☐ SPR ☐ SHO ☐

2. What type of anaesthetic was used?

General ☐
Regional ☐
Both ☐

3. Please specify time of: (Use 24-hour clock)

entrance to anaesthetic room ☐☐ hrs ☐☐ mins
leaving operating room ☐☐ hrs ☐☐ mins
leaving recovery room ☐☐ hrs ☐☐ mins

If date of leaving recovery room is different from entrance to anaesthetic room
Please specify: Day ☐☐ Month ☐☐

4. What was the patient's A.S.A. Grade?

1 Completely fit and healthy ☐
2 Some illness but this has no effect on normal daily activity, that is an asymptomatic condition such as hypertension ☐
3 Symptomatic illness present, but minimal restriction on life eg mild diabetes mellitus ☐
4 Symptomatic illness causing severe restriction eg severe chronic bronchitis, unstable diabetes ☐
5 Moribund ☐

HOSPITAL CARE

5. Date of Admission Day ☐☐ Month ☐☐ Year ☐☐☐☐

6. Date of Discharge Day ☐☐ Month ☐☐ Year ☐☐☐☐

Discharged home ☐
Transferred to a rehabilitation unit ☐ Name: ☐
Died ☐
Other ☐

If other, please specify ☐

7. Did the patient have any postoperative complications? No

Yes ☐

If **Yes**, what? ☐

Knee dislocation

A wound infection confirmed by a microbiology report ☐

Septicaemia confirmed by blood culture ☐

DVT confirmed by a radiology report ☐

PE confirmed by radiology report ☐

Confirmed cerebal vascular accident ☐

Confirmed Myocardial Infarction ☐

Other ☐

If Other, please specify ☐

☐

8. Did the patient require any further knee surgery? No

Yes ☐

If **Yes**, what? ☐

Manipulation under anaesthesia

Other ☐

If Other, please specify ☐

☐

Why?

Knee stiffness

Dislocation ☐

Wound infection ☐

Other ☐

If Other, please specify ☐

☐

AUTHORSHIP POLICY

1. Principles of Authorship

The following principles of authorship have been derived from editorial publications from leading journals (see references) and are in accordance with the rules of the International Committee of Medical Journal Editors.

Group authorship

Group authorship will be appropriate for some publications, such as main reports. This will apply when the intellectual work underpinning a publication 'has been carried out by a group, and no one person can be identified as having substantially greater responsibility for its contents than others'.[1] In such cases the authorship will be presented by the collective title - The KAT Trial Group - and the article should carry a footnote of the names of the people (and their institutions) represented by the corporate title. In some situations one or more authors may take responsibility for drafting the paper but all group members qualify as members; in this case, this should be recognised using the byline 'Jane Doe *and* the Trial Group'.[2] Group authorship may also be appropriate for publications where one or more authors take responsibility for a group, in which case the other group members are not authors but may be listed in the acknowledgement (the byline would read 'Jane Doe *for* the Trial Group'). [2]

Individual authorship

Other papers, such as describing satellite studies, will have individual authorship. In order to qualify for authorship an individual must fulfil the following criteria[1]:

a. Each author should have participated sufficiently in the work represented by the article to take public responsibility for the content.

b. Participation must include three steps:

- conception or design of the work represented by the article OR analysis and interpretation of the data OR both; AND
- drafting the article or revising it for critically important content; AND
- final approval of the version to be published.

Participation solely in the collection of data is insufficient by itself and those persons who have contributed intellectually to the article but those contributors do not justify authorship may be acknowledged and their contribution described.[1]

Determining authorship

Tentative decisions on authorship should be made as soon as possible.[1] These should be justified to, and agreed by, the Project Management Group. Any difficulties or disagreements will be resolved by the Steering Committee.

2. Authorship for Publication Arising from the KAT Trial Group

Operationalising authorship rules

We envisage two types of report (including conference presentations) arising from the KAT trial and its associated projects:

a. *Reports of work arising from the main KAT trial* - If all grant-holders and research staff fulfil authorship rules, group authorship should be used under the collective title of 'The KAT Trial Group'; if one or more individuals have made a significant contribution above and beyond other group members but where all group members fulfil authorship rules, authorship will be attributed to 'Jane Doe and the KAT Trial Group'.

b. *Reports of satellite studies and subsidiary projects* - Authorship should be guided by the authorship rules outlined in Section 1 above. Grant-holders and research staff not directly associated with the specific project should only be included as authors if they fulfil the authorship rules. Grant-holders and research staff who have made a contribution to the project but do not fulfil authorship rules should be recognised in the Acknowledgement section. The role of the KAT Trial Group in the development and support of the project should be recognised in the Acknowledgement section. The lead researcher should be responsible for ratifying authorship with the Project Management Group.

For reports which specifically arise from the KAT trial but where all members do not fulfil authorship rules (for example, specialist sub-study publications), authorship should be attributed to 'Jane Doe for the KAT Trial Group'. If individual members of the group are dissatisfied by a decision, they can appeal to the Management Group for reconciliation. If this cannot be achieved, the matter should be referred to the Steering Group.

Quality assurance

Ensuring quality assurance is essential to the good name of the trial group. For reports of individual projects, internal peer review among members of the Project Management Group is a requirement prior to submission of papers. All reports of work arising from the KAT

trial including conference abstracts should be peer reviewed by the Project Management Group.

The internal peer review for reports of work arising from the KAT project is mandatory and submission may be delayed or vetoed if there are serious concerns about the scientific quality of the report. The Project Management Group will be responsible for decisions about submission following internal peer review. If individual members of the group are dissatisfied by decisions, the matter may be referred to the Steering Group.

The Project Management Group undertake to respond to submission of articles for peer review at the Project Management Group Meeting following submission (assuming the report is submitted to the trial secretariat in Aberdeen at least two weeks prior to the meeting).

REFERENCES

1. Huth EJ (1986). Guidelines on authorship of medical papers. *Annals of Internal Medicine*, ***104***, *269-274.*
2. Glass RM (1992). New information for authors and readers. Group authorship, acknowledgements and rejected manuscripts. *Journal of the American Medical Association*, ***268***, *99.*

Protocol Appendix H

kat

Knee Arthroplasty Trial

DUMMY TABLES

VERSION: 12 October 1999

Table 0 (all) Reasons for non-recruitment into the whole trial

	N	(%)
Total number of knee replacements by participating surgeons		
Not recruited		
(a) Surgeon participating but chose not to randomise		
(b) Patient unwilling to participate/accept randomisation		
(c) Missed patient		
(d) Other		

Table 0A Reasons for non-recruitment into comparison A

	N	(%)
Total number of knee replacements by participating surgeons		
Not recruited		
(a) Surgeon participating in metal backed vs. non metal backed prosthesis comparison, but chose not to randomise		
(b) Patient declined		
(c) Missed patient		
(d) Other		

Note: There will be similar Table O's for the other three comparisons (B-D).

Table 1 Number recruited by participating surgeons

	Comparison A		Comparison B		Comparison C		Comparison D	
	MB	NMB	*PRS*	NPRS	MBC	FBC	UC	TKR
Total number of patients recruited								
Number recruited by each surgeon – n (%) [1]								
Surgeon A								
Surgeon B								
Surgeon C								
etc.								

[1] Surgeons will not be named

Comparison A:
MB = Metal backed
NMB = Non-metal backed

Comparison B:
PRS = Patellar resurfacing
NPRS = No patellar resurfacing

Comparison C:
MBC = Mobile bearing component
FBC = Fixed bearing component

Comparison D:
UC = Uni-compartmental arthroplasty
TKR = Total knee replacement

Table 2A Description of groups at trial entry - comparison A

	Randomised to: Metal backed	Non-metal backed
Total number of patients recruited		
*Age – mean (sd)		
* Sex – n (%)		
Male		
Female		
Weight (kg) – mean (sd)		
Height (cm) – mean (sd)		
ASA – n (%)		
1		
2		
3		
4		
Primary type of knee arthritis - n (%)		
Osteoarthritis		
Rheumatoid		
* Extent of arthritis affecting mobility - n (%)		
One knee		
Both knees		
General		
Other medical condition affecting mobility – n (%)		
Yes		
No		
Other previous knee surgery - n (%)		
Ipsilateral Osteotomy		
Ipsilateral Patelectomy		
Contralateral Previous knee replacement		
Deprivation score of area of residence – n (%)		
Deprived (1-2)		
Middle (3-5)		
Affluent (6-7)		
* In another randomised comparison - n (%)		

***Allocation minimised by these factors.**
Allocation stratified by surgeon.

Table 2A continued Status of knee at start of operation – comparison A

	Metal backed N =	Non-metal backed N =
Status of surface of patella – n (%)		
Normal cartilage		
Partial cartilage loss		
Full cartilage loss		
< 5mm bony erosion		
> 5mm bony erosion		
Fixed flexion deformity – n (%)		
Yes		
No		
If yes, degrees – mean (sd)		
Valgus – n (%)		
Varus – n (%)		
Deformity – n (%)		
Mild		
Moderate		
Severe		
Correctable – n (%)		
Yes		
No		
State of Anterior cruciate – n (%)		
Intact		
Damaged		
Absent		

Note: Similar Table 2 for the other three comparisons (B-D).

Table 2A continued Description of groups at trial entry – comparison A

	Randomised to:	
	Metal backed	Non-metal backed
Number returning baseline questionnaires		
Oxford Knee Score – mean (sd)		
SF12 score – mean (sd)		
Physical Functioning		
Mental Health		
EQ – 5D – mean (sd)		

Note: There will be a similar Table 2 for the other three comparisons (B-D).

Table 3A Actual management and operative details – comparison A

		Randomised to:	
		Metal backed	Non-metal backed
		N =	N =
Metal backed – n (%)			
Modular			
Fixed			
Non metal backed – n (%)			
Patellar resurfaced – n (%)			
Domed			
Anatomic			
Cement used for – n (%)			
Tibia	**Yes**		
	No		
Femur	**Yes**		
	No		
Patella	**Yes**		
	No		
Number having no knee replacement surgery – n (%) [1]			
Number having other knee replacement surgery (e.g. mobile bearing) – n (%) [2]			

[1,2] **A few of those formally recruited to this comparison will end up having no knee surgery (operation cancelled and patient later judged unfit, for example), or having another type of knee surgery (because the surgeon later decides this is indicated). They need to be shown here, followed up and analysed in the group to which they were originally allocated.**

Table 3B Actual management and operative details – comparison B

	Randomised to:	
	Patellar resurfacing N =	No patellar resurfacing N =
Patellar resurfacing – n (%)		
Domed		
Anatomic		
No patellar resurfacing – n (%)		
Metal backed – n (%)		
Modular		
Fixed		
Non metal backed – n (%)		
Mobile bearing – n (%)		
Fixed bearing– n (%)		
Cement used for – n (%)		
Tibia Yes		
No		
Femur Yes		
No		
Patella Yes		
No		
Number having no knee replacement surgery – n (%) [1]		
Number having uni-compartmental surgery – n (%) [2]		

[1,2] See note under comparison A

Table 3C Actual management and operative details – comparison C

	Randomised to: Mobile bearing N =	Fixed bearing N =
Mobile bearing – n (%)		
Fixed bearing – n (%)		
Metal backed		
Non metal backed		
Patellar resurfaced – n (%)		
Domed		
Anatomic		
Cement used for – n (%)		
Tibia Yes		
No		
Femur Yes		
No		
Patella Yes		
No		
Number having no knee replacement surgery – n (%) [1]		
Number having uni-compartmental surgery – n (%) [2]		
Mobile		
Fixed		

[1,2] See note under comparison A.

Table 3D Actual management and operative details – comparison D

	Randomised to: Uni-compartmental N =	Total knee replacement N =
Uni-compartmental – n (%)		
Mobile		
Fixed		
Total knee replacement – n (%)		
Metal backed – n (%)		
Modular		
Fixed		
Non metal backed – n (%)		
Patellar resurfaced – n (%)		
Domed		
Anatomic		
Mobile bearing – n (%)		
Cement used for – n (%)		
Tibia Yes		
No		
Femur Yes		
No		
Patella Yes		
No		
Number having no knee replacement surgery – n (%) [1]		

[1] **See note under comparison A.**

Table 3A continued Actual management and operative details – comparison A

	Metal backed N =	Non-metal backed N =
Lateral patella retinacular release – n (%)		
Yes		
No		
Fixed Flexion Deformity – n (%)		
Yes		
No		
If yes, degrees – mean (sd)		
PCL at end of operation – n (%)		
Intact		
Recessed/damaged		
Divided		
Intra-operative complications – n (%)		
Patella fracture		
Other		
Usual surgical technique followed – n (%)		
Yes		
No		
If no, why?		

Note: This part of Table 3 is common to all four comparisons.

Table 3A continued Actual management and operative details – comparison A

	Metal backed N =	Non-metal backed N =
Operation time – mean (sd)		
Type of anaesthetic used – n (%)		
General		
Regional		
Both		
Grade of surgeon performing operation – n (%)		
Consultant		
Associate specialist/staff grade		
SPR		
SHO		
Grade of senior surgeon present at operation – n (%)		
Consultant		
Associate specialist/staff grade		
SPR		
Grade of anaesthetist – n (%)		
Consultant		
Associate specialist/staff grade		
SPR		
SHO		

Note: This part of Table 3 is common to all four comparisons.

Table 4A In-hospital care and short term complications – comparison A

	Metal backed N =	Non-metal backed N =
Post-operative Complications – n (%)		
Knee dislocation		
Proven wound infection [1]		
Septicaemia [2]		
DVT (Treated)		
Treated pulmonary embolism		
Cerebal vascular		
Myocardial infarction [3]		
Further knee surgery – n (%)		
Manipulation under anaesthetic		
Other		
Reasons for further knee surgery		
Knee stiffness		
Dislocation		
Wound infection		
Other		
Status at discharge – n (%)		
Alive		
Dead		
Destination if discharged – n (%)		
Home		
Rehabilitation unit		
Other		
Length of stay in hospital (days) – mean (sd)		

[1] Purulent discharge plus positive bacteriology or need for further surgery

[2] Clinical evidence of systemic infection plus positive blood culture

[3] Confirmation from senior physician

Note: Similar Table 4 for the other three comparisons (B-D).

Table 5A Follow-up at 3 months (and then annually, with primary analyses at 5 and 10 years) – comparison A

	Metal backed N =	Non-metal backed N =
Number due for follow-up		
Number with follow-up information		
Oxford Knee Score – mean (sd)		
SF12 score – mean (sd)		
Physical Functioning		
Mental Health		
EQ – 5D – mean (sd)		
Change from baseline - mean (sd)		
Oxford Knee Score		
SF12 score		
Physical Functioning		
Mental Health		
EQ – 5D		

Note: Similar Table 5 for the other three comparisons (B-D).

Table 5A continued Follow-up at 3 months (and then annually, with primary analyses at 5 and 10 years) – comparison A

	Metal backed N =	Non-metal backed N =
Readmitted to hospital – n (%)		
Number of times		
1		
> 1		
Reasons for readmission		
Related to operated knee		
Possibly related to index surgery (e.g. DVT, PE)		
Other		
Further knee surgery – n (%)		
Yes		
No		
Number of visits to GP – mean (sd)		
Number of outpatient visits to orthopaedic surgeon – mean (sd)		
Number of visits to physiotherapist – mean (sd)		

Note: Similar Table 5 for the other three comparisons (B-D).

LIST OF ABBREVIATIONS

CEAC	Cost-effectiveness acceptability curve
CI	Confidence interval
CUA	Cost Utility Analysis
CUA	Cost-utility analysis
DVT	Deep vein thrombosis
EO	Expert Opinion
EQ-5D	EuroQol – 5 Dimensions (questionnaire)
GP	General Practitioner
HCF	Health Care Form
HCHS	Hospital and community health services [inflation index]
HES	Hospital Episode Statistics
HTA	Health Technology Assessment
ICE	Imputation using Chained Equations
ICER	Incremental cost-effectiveness ratio
IPW	Inverse probability weighting
ISD	Information Services Division
KAT	Knee Arthroplasty Trial
NHS	National Health Service
NIHR	National Institute of Health Research
OKS	Oxford Knee Score
OLS	Ordinary least squares
PAF	Patient Annual Form
PE	Pulmonary embolism
QALY	Quality Adjusted Life Year
SD	Standard deviation
SE	Standard error
SF	Surgeon's Form
SF-12	Short Form – 12 (questions)
TKR	Total knee replacement

Appendix 2 Readmission form

Kat
Knee Arthroplasty Trial

THE KAT STUDY

HOSPITAL RE-ADMISSION FORM

Patient Study No | | | | | |

The re-admission is related to:

Knee replacement ☐ **Surgery in general** ☐ **Not related** ☐ **Other** ☐

First name | | | | | | | | | | | **Surname** | | | | | | | | | |

Hospital |

Date of Admission **Day** / **Month** / **Year**

Date of Discharge **Day** / **Month** / **Year**

Discharged home ☐

Transferred to a rehabilitation unit ☐ Name of unit

Died ☐

Other ☐

If Other, please specify

Reason for Readmission *(Please cross as appropriate)*

Surgical ☐ **Medical** ☐ **Other** ☐

Please give details below

Please continue over the page.

This study is funded by the NHS Research and Development Health Technology Assessment Programme.

PTO

Did the patient require any further knee surgery? **NO** ☐ **YES** ☐

If Yes, what?

Manipulation under anaesthesia	☐	Washout	☐
Debridement	☐	Aspiration	☐
1st stage revision	☐	2nd stage revision	☐
Revision	☐	1st patella resurfacing	☐
Above knee amputation	☐	Other	☐

If Other, please specify (Eg excision arthroplasty, arthrodesis or internal fixation of fractures)

If revision procedure or 2nd stage revision procedure please specify which component

Patella revision ☐ **Tibial revision** ☐ **Femur revision** ☐

What was the reason for revision?

Infection ☐
Loosening ☐
Pain ☐
Mechanical failure/fracture ☐
Dislocation ☐
Other ☐

If Other, please specify

Please attach stickers for all components used for the operation or fill in the appropriate information and attach a photocopy of the participant's operation notes!

Cat No .....
Component .....

Cat No .....
Component .....

Cat No .....
Component .....

Cat No .....
Component .....

Appendix 3 Multiple imputation models: methods for missing data for analyses of costs and cost-effectiveness

TABLE 42 Variables imputed using mean imputation or conditional mean imputation prior to multiple imputations

Variable	% (*n*) non-zero cases that are missing	Description	Mean imputation function used	Variable amalgamated into
nounitstransfused	22 (7/32)	Number of units of blood products transfused after end of primary knee replacement surgery but before discharge	Missing number of units for patients who were transfused was assumed to equal 2.32 (mean number of units used by patients who were transfused during their primary admission)	N/A
unitstransfusedadm'j'	20 (1/5)	Number of units of blood transfused during the *j*th readmission	Missing number of units for patients who were transfused was assumed to equal 2.32 (mean number of units used by patients who were transfused during their primary admission)	Total cost readmission'j'
patellaprice'j'	13 (9/67)	Price of patellar components used in the *j*th readmission	Missing patella list prices for patients who used patella were assumed to equal £163.36 (mean cost of patellas used in revision surgery)	Total cost readmission'j'
tibialinsertprice'j'	19 (19/100)	Price of tibial tray components used in the *j*th readmission	Missing insert list prices for patients who used a tibial insert were assumed to equal £411.84 (mean cost of inserts used in revision surgery)	Total cost readmission'j'
tibialtrayprice'j'	14 (12/83)	Price of tibial insert components used in the *j*th readmission	Missing tray list prices for patients who used a tibial tray were assumed to equal £1025.10 (mean cost of trays used in revision surgery)	Total cost readmission'j'

continued

TABLE 42 Variables imputed using mean imputation or conditional mean imputation prior to multiple imputations (*continued*)

Variable	% (*n*) non-zero cases that are missing	Description	Mean imputation function used	Variable amalgamated into
femurprice'j'	10 (8/81)	Price of femoral components used in the *j*th readmission	Missing femoral list prices for patients who used a femoral component were assumed to equal £2151.55 (mean cost of femurs used in revision surgery)	Total cost readmission'j'
otherprice'j'	7 (13/180)	Price of each other component (e.g. augments and blocks) used in the *j*th readmission	Missing list prices of other components for patients who used an other component were assumed to equal £561.26 per component (mean cost of other components used in revision surgery)	Total cost readmission'j'
LOS'j' for washout	11 (2/19)	Length of stay for patients' *j*th readmission if that readmission is for washout only	Length of stay was assumed to be 9 days (mean length of stay for the 17 cases with known length of stay)	Total cost readmission'j'
LOS'j' for 2nd stage of two-state revision	7 (2/29)	Length of stay for patients' *j*th readmission if that readmission is for the second stage of a two-stay revision	Length of stay was assumed to be 13.3 days (mean length of stay for the 27 cases with known length of stay)	Total cost readmission'j'
Diedduringyear1or2	0 (0)[a]	Dummy equal to 1 if the patient died during one of these 2 years; 0 otherwise. Most missing data represent patients who were still alive when the database was closed on 8 June. Some data were missing at earlier time points because some Scottish patients declined consent for death monitoring in 2006	Remaining life expectancy at last observation was estimated for each patient administratively censored before year 10 based on their sex, country and age at last observation, based on ONS life tables.[36] For multiple imputation, administratively censored patients were assumed to have died in year y or y + 1 if their remaining life expectancy plus the year when they were last observed was ≤ y + 1, but > y – 1	None IPW was used in place of imputed survival indicators in base-case costs and QALY calculations. However, complete data on survival were needed to run multiple imputation of other values, in order to condition EQ-5D and ambulatory consultation numbers
Diedduringyear2or3	0 (0)[a]			
Diedduringyear3or4	0 (0)[a]			
Diedduringyear4or5	0 (10)[a]			
Diedduringyear5or6	1 (20)[a]			
Diedduringyear6or7	1 (29)[a]			
Diedduringyear7or8	2 (34)[a]			
Diedduringyear8or9	2 (35)[a]			
Diedduringyear9or10	8 (182)[a]			
Diedduringyear10or11	44 (984)[a]			
Diedduringyear11or12	66 (1485)[a]			

a Equals the number patients for whom vital status is not shown at this time point across all 2252 patients.

TABLE 43 Methods for multiple imputation for each variable

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
Age	Age at time of operation (years)	N/A	0 (0)	N/A	N/A	N/A
Sex	1 = male; 0 = female	56 (1271)	0 (0)	N/A	N/A	Covariate
bl_New OKS	New OKS (0–48)	0 (1)	5 (121)	Regress, match	Full model	Covariate: strong predictor of EQ-5D utility
BMI	Body mass index (kg/m^2)	N/A	5 (105)	Regress, match	Full model	Covariate
Obese	1 = BMI ≥ 30; 0 = BMI < 30	58 (1244)	5 (105)	Passively imputed from BMI ≥ 30	N/A	Covariate
Disease type	0 = rheumatoid with/ without osteoarthritis; 1 = osteoarthritis	5 (108)	2 (42)	Logit	Full model	Covariate
Disease place	1 = one knee; 2 = both knees; 3 = general	N/A	2 (42)	Mlogit	Full model	Covariate
ASA grade	ASA grade (1, 2, 3, 4 or 5)	N/A	5 (111)	Ologit	Full model	Covariate
Timing of operation	Year of operation plus month/12	N/A	0 (0)	N/A	N/A	Covariate; strong predictor of length of stay
Treatment1 [metal-backed]	Dummy • = 1 if randomised to that treatment • = 0 if randomised to comparator or not included in that comparison	91 (2053)	0 (0)	N/A	N/A	Treatment indicator
Treatment2 [non-metal-backed]		91 (2049)	0 (0)	N/A	N/A	Treatment indicator
Treatment3 [patella resurface]		63 (1411)	0 (0)	N/A	N/A	Treatment indicator
Treatment4 [no patella]		63 (1422)	0 (0)	N/A	N/A	Treatment indicator
Treatment5 [mobile bear]		88 (1990)	0 (0)	N/A	N/A	Treatment indicator

continued

TABLE 43 Methods for multiple imputation for each variable (*continued*)

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
Treatment6 [fixed bearing]		89 (1997)	0 (0)	N/A	N/A	Treatment indicator
Total LOS	Total length of stay for primary TKR admission (days)	N/A	2 (37)	Regress, match	Full model	Cost component
Op time	Length of operation	N/A	3 (76)	Regress, match	Full model	Cost component
Any post op comp	Dummy • 1 = more than one postoperative complication occurred during primary hospital stay • 0 = no postoperative complications recorded	84 (1874)	1 (23)	Logit	Full model, omitting transfused and cost of CCU and CT or US and recoding ASA as numerical not three dummies	Conditioning variable ASA recoded as numerical variable as ASA grade 4 perfectly predicted complications. Transfused and cost of CCU and CT or US omitted as these comprise postoperative complications and therefore perfectly predict the presence of complications Auglogit was used to predict this variable in some imputation runs owing to perfect prediction
Transfused	Dummy equal to 1 if the patient was transfused during his or her primary hospital stay, excluding transfusions conducted during the primary TKR procedure	99 (2196)	1 (24)	Logit, conditional on any post op comp = 1	Age at operation sex bl_new oks bmi obese i.disease place as a grade timing of operation no readmissions by yr5 op time total los cost of further surgery cost of CCU and CT or US eq5d_bl eq5d_3m eq5d_1y-eq5d_11y treatment1-treatment6 died during year 1 or 2- died during year 11 or 12	Cost component Most variables dropped owing to collinearity or perfect prediction, leaving only those expected to have most effect on blood use Disease type dropped owing to perfect prediction: owing to small numbers, no patients with rheumatoid arthritis were transfused. ASA was recoded as a numerical variable as ASA grade 2 perfectly predicted

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
Cost of CCU and CT or US	Cost of time in CCU or of CT or US conducted in the primary hospital stay	96 (2145)	1 (24)	Ologit, conditional on any post op comp = 1	Full model excluding any post op comp	Cost component
Cost of further surgery	Cost of further surgery conducted during patients' primary hospital stay	97 (2164)	1 (24)	Ologit	Full model	Cost component Auglogit was used to predict this variable in some imputation runs owing to perfect prediction
Used patella	1 = used patella in primary TKR	52 (1158)	0 (7)	Logit	Full model excluding patella price	Conditioning variable
Used tibial insert	1 = used tibial insert in primary TKR	26 (585)	1 (28)	Logit	Full model excluding tibial insert price	Conditioning variable
Used other	1 = used other component(s) in primary TKR	98 (2171)	1 (29)	Logit	Full model excluding other price	Conditioning variable
Patella price	Price of patellar component used in the primary TKR (0 if not used)	53 (1158)	2 (56)	Regress, match, conditional on used patella = 1	Full model	Cost component
Tibial tray price	Price of tibial tray used in the primary TKR	N/A	7 (147)	Regress, match	Full model	Cost component
Tibial insert price	Price of tibial insert used in the primary TKR (0 if not used)	27 (585)	4 (83)	Regress, match, conditional on used tibial insert = 1	Full model	Cost component
Femur price	Price of femoral component used in the primary TKR	N/A	4 (89)	Regress, match	Full model	Cost component

continued

TABLE 43 Methods for multiple imputation for each variable (*continued*)

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
Other price	Price of other components used in the primary TKR other than the four listed above (0 if not used)	98 (2171)	2 (45)	Regress, match, conditional on used other = 1	Age at operation sex bl_newoks bmi obese disease type i.disease place i.asagrade timing of operation no readmissions treatment1 treatment2 treatment3 treatment4 treatment5 treatment6 patella price femur price tibia price tray tibia2priceinsert used patella used tibia insert op time total los died during year 1 or 2- died during year 11 or 12	Cost component Full model could not be estimated as only 52 patients were known to have used other components in their primary readmission. Omitted indicators of complications or further surgery, EQ-5D utility and resource use after hospital discharge
No readmissions		86 (1928)	0 (0)	N/A	N/A	Indicator of postoperative knee problems
TOTAL Cost Admission 1	Total cost of first readmission[b]	86 (1928)	0 after mean imputation	N/A	N/A	Cost component
TOTAL Cost Admission 2	Total cost of second readmission[b]	96 (2151)		N/A	N/A	Cost component
TOTAL Cost Admission 3,4,5,6	Total cost of third and subsequent readmissions combined[b]	98 (2215)		N/A	N/A	Cost component
Died during year 1 or 2	Equal to 1 if the patient died in that 2-year period and 0 otherwise	96 (2163)	0 after mean imputation	N/A	N/A	Capture impact of proximity to death on resource use and quality of life Used to ensure that imputation models of quality of life and resource-use data were based only on patients who were alive at the start of that year
Died during year 2 or 3		97 (2180)				
Died during year 3 or 4		96 (2158)				
Died during year 4 or 5		95 (2129)				

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
Died during year 5 or 6		94 (2112)				
Died during year 6 or 7		94 (2111)				
Died during year 7 or 8		94 (2107)				
Died during year 8 or 9		93 (2094)				
Died during year 9 or 10		93 (2102)				
Died during year 10 or 11		96 (2152)				
Died during year 11 or 12		98 (2202)				
No ortho visits_1y	No. of orthopaedic outpatient consultations for knee per year	19 (373)	11 (257)	Regress, match. Year 1 is conditional on being discharged alive from hospital; subsequent years are conditional on being alive at the end of previous year	Full model	Cost component
No ortho visits_2y		72 (1402)	14 (313)			
No ortho visits_3y		82 (1588)	14 (312)			
No ortho visits_4y		86 (1669)	14 (322)			
No ortho visits_5y		88 (1656)	16 (362)			
No ortho visits_6y		90 (1677)	17 (388)			
No ortho visits_7y		92 (1706)	18 (397)			
No ortho visits_8y		93 (1699)	19 (430)			
No ortho visits_9y		94 (1678)	21 (469)			
No ortho visits_10y		95 (1553)	27 (611)			
No ortho visits_11y		96 (982)	54 (1226)			

continued

TABLE 43 Methods for multiple imputation for each variable (*continued*)

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
No physio visits_1y	No. of physiotherapy consultations for knee per year	34 (661)	12 (280)	Regress, match. Year 1 is conditional on being discharged alive from hospital; subsequent years are conditional on being alive at the end of previous year	Full model	Cost component
No physio visits_2y		93 (1804)	14 (316)			
No physio visits_3y		96 (1859)	14 (318)			
No physio visits_4y		96 (1867)	14 (317)			
No physio visits_5y		97 (1844)	16 (351)			
No physio visits_6y		97 (1815)	17 (390)			
No physio visits_7y		98 (1815)	17 (394)			
No physio visits_8y		98 (1785)	19 (433)			
No physio visits_9y		98 (1745)	21 (467)			
No physio visits_10y		98 (1606)	27 (616)			
No physio visits_11y		99 (1013)	55 (1229)			
No GP visits_1y	No. of GP consultations for knee per year	58 (1149)	12 (272)	Regress, match. Year 1 is conditional on being discharged alive from hospital; subsequent years are conditional on being alive at the end of previous year	Full model	Cost component
No GP visits_2y		88 (1697)	14 (316)			
No GP visits_3y		90 (1733)	14 (326)			
No GP visits_4y		90 (1734)	15 (332)			
No GP visits_5y		92 (1748)	16 (354)			
No GP visits_6y		93 (1716)	18 (401)			
No GP visits_7y		93 (1727)	18 (402)			
No GP visits_8y		94 (1715)	19 (426)			
No GP visits_9y		95 (1681)	21 (475)			
No GP visits_10y		95 (1555)	27 (614)			
No GP visits_11y		96 (988)	54 (1226)			

Variable	Coding	% (*n*) zero[a]	% (*n*) missing	Imputation function	Explanatory variables used as predictors	Rationale
eq5d_BL	EQ-5D utility at baseline, 3 months or year *y*	0 (0)	5 (114)	Regress, match. Utility at 1 year is conditional on being alive at 3 months. Subsequent utilities conditional on being alive at the end of previous year	Full model	QALY component
eq5d_3m		0 (0)	12 (274)			
eq5d_1y		1 (16)	12 (277)			
eq5d_2y		3 (59)	15 (339)			
eq5d_3y		5 (88)	16 (352)			
eq5d_4y		7 (130)	17 (372)			
eq5d_5y		10 (182)	17 (390)			
eq5d_6y		14 (253)	19 (427)			
eq5d_7y		18 (323)	19 (421)			
eq5d_8y		22 (395)	20 (448)			
eq5d_9y		26 (467)	21 (480)			
eq5d_10y		34 (551)	28 (623)			
eq5d_11y		60 (614)	54 (1223)			

CCU, critical care unit; comp, complication; CT, computed tomography; LOS/los, length of stay; Op, operation; US, ultrasound.
a Percentage of observed values that equal zero (where appropriate).
b Cost of readmissions includes the inpatient stay, operation time, knee components, transfusions, US and CT.

Appendix 4 Committee membership

Project management group

Marion K Campbell (Aberdeen), Nick Fiddian (Bournemouth), Ray Fitzpatrick (Oxford), Adrian M Grant (Aberdeen), Alastair M Gray (Oxford), Richard W Morris (London), David W Murray (chairperson, Oxford) and David Rowley (Dundee).

Additional members (over the lifetime of the trial)

Graeme S MacLennan (Aberdeen), Suzanne Breeman (Aberdeen), Helen A Dakin (Oxford), Linda Johnston (Dundee), Kirsty McCormack (Aberdeen), Craig Ramsay (Aberdeen), Allan Walker (Aberdeen), Susan Campbell (Aberdeen), Mark Kelaher (Aberdeen), Anne Langston (Aberdeen), Sue Ross (Aberdeen) and Luke Vale (Aberdeen).

Data monitoring committee (with affiliations at time of data monitoring committee meeting)

Gordon Murray (chairperson, University of Edinburgh), Rajan Madhok (South Manchester Primary Care Trust) and Hamish Simpson (University of Edinburgh).

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