TRIALS

Total or Partial Knee Arthroplasty Trial - TOPKAT: study protocol for a randomised controlled trial

Beard *et al.*

BioMed Central

Beard *et al. Trials* 2013, **14**:292
http://www.trialsjournal.com/content/14/1/292

Beard et al. Trials 2013, 14:292
http://www.trialsjournal.com/content/14/1/292

TRIALS

STUDY PROTOCOL Open Access

Total or Partial Knee Arthroplasty Trial - TOPKAT: study protocol for a randomised controlled trial

David Beard[1*], Andrew Price[1], Jonathan Cook[3], Ray Fitzpatrick[2], Andrew Carr[1], Marion Campbell[3], Helen Doll[4], Helen Campbell[2], Nigel Arden[1], Cushla Cooper[1], Loretta Davies[1] and David Murray[1]

Abstract

Background: In the majority of patients with osteoarthritis of the knee the disease originates in the medial compartment. There are two fundamentally different approaches to knee replacement for patients with unicompartmental disease: some surgeons feel that it is always best to replace both the knee compartments with a total knee replacement (TKR); whereas others feel it is best to replace just the damaged component of the knee using a partial or unicompartment replacement (UKR). Both interventions are established and well-documented procedures. Little evidence exists to prove the clinical and cost-effectiveness of either management option. This provides an explanation for the high variation in treatment of choice by individual surgeons for the same knee pathology.
The aim of the TOPKAT study will be to assess the clinical and cost effectiveness of TKRs compared to UKRs in patients with medial compartment osteoarthritis.

Methods/Design: The design of the study is a single layer multicentre superiority type randomised controlled trial of unilateral knee replacement patients. Blinding will not be possible as the surgical scars for each procedure differ. We aim to recruit 500 patients from approximately 28 secondary care orthopaedic units from across the UK including district general and teaching hospitals. Participants will be randomised to either UKR or TKR. Randomisation will occur using a web-based randomisation system. The study is pragmatic in terms of implant selection for the knee replacement operation. Participants will be followed up for 5 years. The primary outcome is the Oxford Knee Score, which will be collected via questionnaires at 2 months, 1 year and then annually to 5 years. Secondary outcomes will include cost-effectiveness, patient satisfaction and complications data.

Trial registration: Current Controlled Trials ISRCTN03013488; ClinicalTrials.gov Identifier: NCT01352247

Keywords: Medial compartment osteoarthritis, Total knee replacement, Unicompartmental knee replacement, Equipoise, Expertise

Background

Osteoarthritis in the knee affects different people in different ways. In the majority of patients with osteoarthritis of the knee the disease originates in the medial compartment [1]. There are varying forms of treatment for this and each aim to relieve pain and discomfort, to reduce stiffness and to minimise further damage to the joint. Such approaches include physiotherapy, drug therapy and surgery [2-5]. One of the surgical options is to replace the diseased joint with a prosthesis (arthroplasty) and there are different approaches in common use. Some surgeons feel that it is always best to replace both the knee compartments with a total knee replacement (TKR). Others feel it is best to replace just the damaged component of the knee with a partial or unicompartmental knee replacement (UKR). There is disagreement among knee surgeons with the majority supporting TKR and the minority UKR. Fewer than 5% of knee replacements worldwide are unicompartmental, although it is thought that up to 30% of patients requiring knee replacements have only unicompartmental disease that would be suitable for a UKR [1,6,7]. This variation in decision-making for patients with medial compartmental

* Correspondence: david.beard@ndorms.ox.ac.uk
[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Botnar Research Centre, University of Oxford, Headington, Oxford OX3 7LD, UK
Full list of author information is available at the end of the article

arthritis has been well illustrated in a recent linked study [8]. The study showed a high variation in decision-making (TKR or UKR) between four different surgeons (up to 59%). Reassuringly, the consistency of treatment choice (test re-test repeatability) for each individual surgeon remained high. The conclusions were that surgeons, given identical information, do not concur on treatment for patients with the same pathology and that consensus treatment for medial osteoarthritis of the knee remains in question.

There are arguments for both approaches. Both interventions are established and well-documented procedures. Each intervention is considered standard care. There exists little evidence, however, to prove the clinical and cost-effectiveness of either management option and decisions on treatment tend to have a large personal opinion component of the surgeon. The TKR supporters believe that the operation is less complex than UKR and thus, in the short-term TKRs are less susceptible to early problems and failures. They also believe that in the longer term the joint disease will progress to the other, normal, compartments of the knee [9,10], thus a UKR will ultimately fail and require revision to TKR anyway [11,12]. In contrast, the UKR supporters believe the UKR gives faster recovery [7,13], fewer complications [14], superior function[15], is more cost-effective than TKR [16], and it is associated with long-term survival of the joint [6,17].

Current patient management for medial osteoarthritis is based on limited evidence. There have been several individual cohort studies, indirect comparisons and retrospective studies but these have addressed specific aspects and many involve only short-term assessments. Such studies include a comparison between TKR and UKR of the kinematics [18], proprioception [19], ability to kneel [15], ease of revision [20-22] and success or revision after various procedures [23-26], appropriateness for specific pathology [27], accuracy of implantation [28-30] and complications [31,32]. No large, well-powered, multicentre randomised controlled trial has been undertaken to directly compare UKR with TKR. The only other previous attempt at comparing these operations on a large scale was that from one of the comparisons in the Knee Arthroplasty Trial (KAT) [33,34]. However, this comparison failed due to slow patient recruitment. The primary reason for this was that a new minimally invasive technique was introduced for UKR between trial design and recruitment - surgeons chose to learn the new technique rather than recruit for the trial. Joint registry data has shown a trend towards TKR having better survival (as assessed by the rate of revision surgery) [11,12], but other studies are characterised by low level evidence, consensus and peer influence [35-38]. In order to test the validity of these results, further investigation is required. Using an appropriate patient population and long-term assessments, the clinical and cost-effectiveness of both treatment options can be examined.

Objectives

The primary objective for TOPKAT will be to assess the clinical and cost-effectiveness of TKRs compared to UKRs in patients with medial compartment osteoarthritis of the knee.

Secondary objectives include investigation of complications, patient satisfaction, and the cost implications of the knee replacements for patients and employers as well as healthcare providers.

Methods/Design

Study design

The design of the study is a single layer multicentre superiority type randomised controlled trial of unilateral knee replacement patients. The randomised controlled trial design will help reduce and prevent potential bias influencing the evaluation.

Participants will be randomised to either UKR or TKR. The trial has a combined equipoise/expertise approach. It enables surgeons who are not in equipoise to deliver only one of the two operations while also allowing surgeons in equipoise to provide both operations. A surgeon who is in equipoise ('equipoise surgeon') and has sufficient experience to perform both TKR and UKR will deliver the allocated operation (UKR or TKR). The same surgeon will perform the operation for both arms of the study.

Not all surgeons are able to exhibit this equipoise. They may hold a preference for one treatment over the other often due to experience/expertise with one type of operation. Interestingly, a surgeon may also believe the patient may benefit from one particular operation even though they may not be able to perform it themselves.

Equipoise is difficult to investigate or establish. Self declaration has been used as the main approach but in order to sufficiently secure this state the following aspects are important:

- The equipoise considered must be patient- or individual-based equipoise rather than an overall or general category equipoise based on operation type. The surgeon must consider their position for each individual patient. Only if they believe that either operation will be suitable for an individual patient can the patient then be recruited.
- No surgeon will ever knowingly perform what they consider a substandard surgical procedure.

In order to complete the trial by seeking to maximise surgeon participation, an 'expertise'-based delivery of the

intervention will also occur. For this approach there must be a surgeon with expertise in TKR and a surgeon with expertise in UKR in the same centre who will act together as a 'delivery unit'. Patients recruited to the study who are under the care of such a surgeon ('expertise surgeon') will be randomised to one of the two groups and treated by the appropriate surgeon. This 'expertise' approach allows for those UKR surgeons who work alongside TKR surgeons to team up and participate in the study. Subsequent surgery may be carried out by a surgeon different to that at the initial consultation. In such cases the patient is internally referred to the other surgeon's operating list. A study flowchart is detailed in Figure 1. No restriction is made upon the number of delivery units within a centre. A surgeon can only be in one delivery unit, that is, they are either an 'equipoise surgeon' or an 'expertise surgeon'.

To ensure participating surgeons have appropriate expertise, a simple audit of participating surgeons' routine practice will be undertaken. UKR surgeons must have had appropriate training, been practising the technique for at least 1 year and have performed the operation at least 10 times in the past year. They must also be aware of their clinical results and these must be acceptable to the study team. Implants used by UKR surgeons in the study must have good clinical results and be a commonly used knee system which does not require patella dislocation. TKR surgeons must satisfy similar criteria.

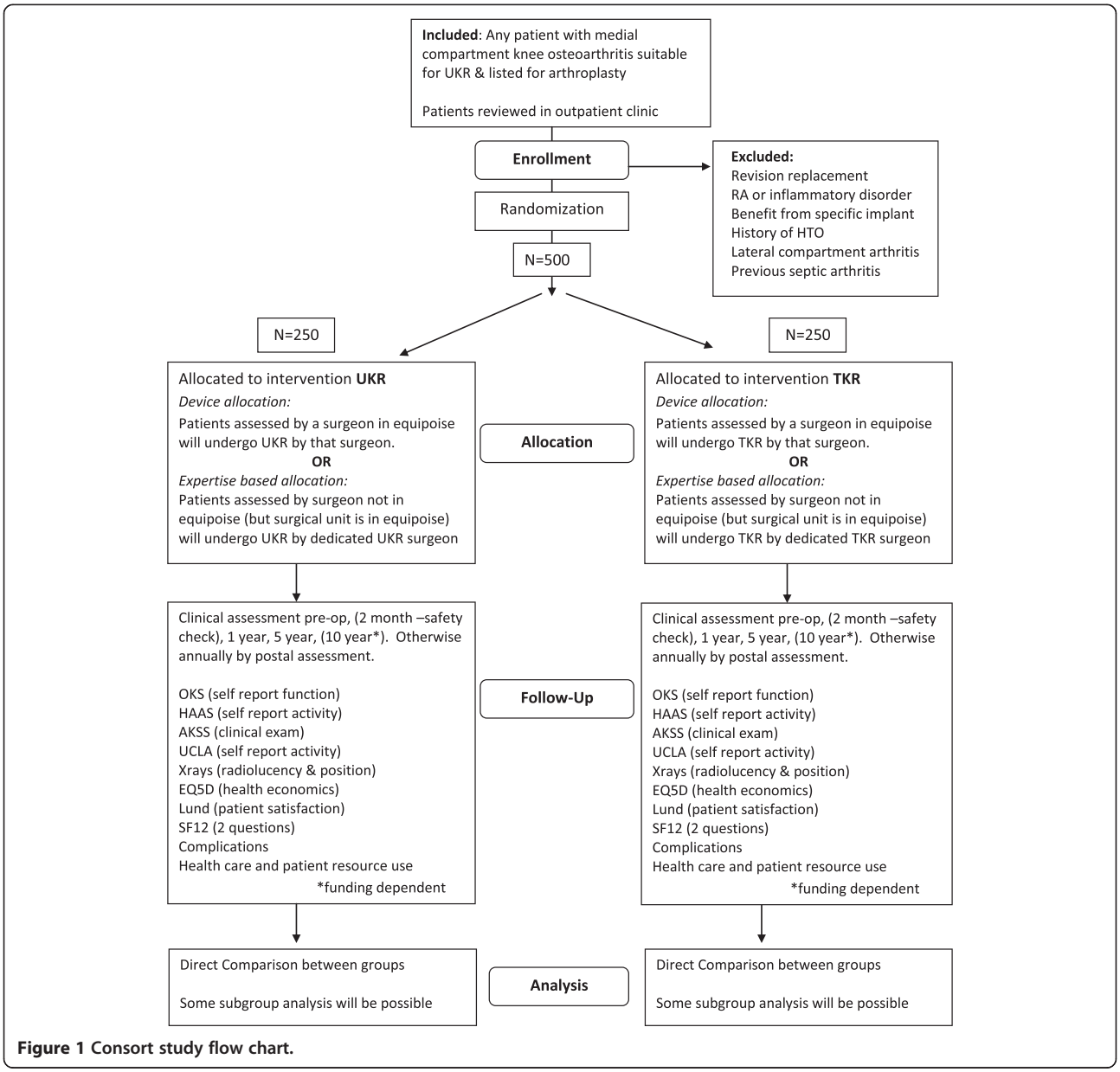

Figure 1 Consort study flow chart.

They must have had many years experience with TKR and will use a conventional approach with patella dislocation. 'Equipoise surgeons', who deliver both operations, are required to satisfy the criteria for both operations, that is, they will have appropriate training in both operations and have performed a minimum of 10 UKR and 10 TKR procedures.

Primary outcome measure

The primary outcome measure for TOPKAT is the Oxford Knee Score (OKS). This is a patient-reported outcome questionnaire specifically designed and developed to assess function and pain after TKR surgery; it is a validated and effective measure of change over time [39]. Although patients will be contacted annually, the primary analysis will be at 5 years (and 10 years (subject to additional funding) post randomisation. An early analysis at 1 year is also planned.

Secondary outcome measures

- American Knee Society Score [40] - measures range of motion and function of the knee
- UCLA Activity Score [41] - measurement of patient activity level in arthroplasty patients with mid/lower level activity
- High Activity Arthroplasty Score (HAAS) [42] - measurement of patient activity accounting for patients with potentially higher levels of activity
- Radiographic features including signs of potential failure, that is, loosening
- EuroQol EQ-5D [43] - evaluation generic measure of health-related quality of life to be used for the economic evaluation
- Lund Score [44] - measurement of patient satisfaction
- Complications
- Length of hospital stay
- Re-operation rate (minor revision, major revision and other related procedure)
- Composite outcome assessment - combination of re-operation frequency and poor outcome in terms of OKS. The anchor based minimally important change (MIC) of the OKS will be used to identify poor outcome ('lack of success') for functional outcome [45]
- Adjunct score to the OKS (for younger/active patients)

Health economics

The health economic evaluation proposed will take the form of a cost-utility analysis. Health outcomes will be assessed at each trial follow-up point using the EuroQol EQ-5D questionnaire and each patient's resulting utility profile will be used to calculate the number of quality-adjusted life years (QALYs) they experience over the duration of the trial.

To estimate the direct healthcare costs associated with both types of knee replacement, information will be collected for each patient in the trial on the resources consumed during initial surgery (including time in theatre, implants used and hospital inpatient stay), and on any subsequent related healthcare use (for example, relating to complications and/or surgical re-operation including revision). Data on costs patients may incur as a result of their knee condition, including rehabilitation, will be recorded. Information will also be collected from patients on return to paid employment.

Study setting

Five hundred patients will be recruited from approximately 28 secondary care orthopaedic units from across the UK including district general and teaching hospitals over a period of 3 years.

Study participants

Participants with osteoarthritis of the medial compartment of the knee will be included in the study. Patients must satisfy general requirements for a medial UKR which are listed below as the inclusion criteria to be recruited to TOPKAT. It should also be noted that if patients meet the inclusion criteria with both their knees, only one knee (designated the study knee) will be operated on according to the randomised allocation assigned as the patient enters into the study. Knee specific measures will be collected (primarily) for the study knee. TOPKAT will not recruit patients with simultaneous bilateral knee replacements. Subsequent knee replacement on the other, non study, knee will be recorded but the subsequent operation will not lead to a further random allocation.

Inclusion criteria

- Medial compartment osteoarthritis with exposed bone on both femur and tibia
- Functionally intact anterior cruciate ligament (superficial damage or splitting is acceptable)
- Full thickness and good quality lateral cartilage present
- Correctable intra-articular varus deformity (suggestive of adequate medial collateral ligament function)
- Medically fit showing an ASA of 1 or 2

Exclusion criteria

- Require revision knee replacement surgery

- Have rheumatoid arthritis or other inflammatory disorders
- Are unlikely to be able to perform required clinical assessment tasks
- Have symptomatic foot, hip or spinal pathology
- Previous knee surgery other than diagnostic arthroscopy and medial menisectomy
- Previously had septic arthritis
- Have significant damage to the patella-femoral joint especially on the lateral facet.

Recruitment and consent

Potential patients will be identified and approached in outpatient and at pre-assessment clinics by the participating surgeon (or their late stage trainee). At this stage patients will be provided with an 'Invitation letter' and information sheet which will explain why they have been approached and will provide further details about the study. Patients will indicate if they are willing to be contacted again by the research team, using the TOPKAT Yes/No ('opt in') form. Those patients who indicate 'Yes' will be contacted by local study staff to arrange a screening visit to assess their eligibility for the study. If the patient is identified during an outpatient appointment the screening visit could coincide with their pre-assessment clinic appointment. The pre-assessment appointments are routinely scheduled for a short time before their scheduled operation date. If patients were identified at their pre-assessment clinic appointment, an extra visit will have to be coordinated for the screening to take place before the patient's operation date. Contact with the patient must be made at least 48 hours following introduction to the study.

Potential patients may also be identified from local databases. These patients will be sent a letter and a TOPKAT YES/NO form to return documenting if they are willing to be contacted subsequently.

During the screening visit patients will be asked to sign a consent form. This allows their details to be entered into the TOPKAT web-based data collection system. Patient details and all preoperative assessments will be recorded and a study number will be allocated.

Patients will be given sufficient time to accept or decline involvement. They will be free to withdraw from the study at any time without affecting their routine perioperative care.

Study assessments

Preoperative assessments will include a patient reported questionnaire examining pain and function (OKS), activity level and healthcare resource use. In addition, the American Knee Society Score (AKSS), a clinical assessment of range of motion and function of the knee, will be carried out. Routine preoperative X-rays will also be collected.

Operative details will be recorded and routine postoperative X-rays collected.

Patients will be required to attend a clinic appointment for the AKSS assessment at 2 months, 1 and 5 years post operation. The first two visits will coincide with routine hospital follow-up visits for these knee replacement procedures.

A postal questionnaire (containing the OKS, UCLA, HAAS, EQ-5D, Lund, healthcare and patient resource use) will also be sent out at years 1 to year 5 post randomisation. Additional clinical and postal questionnaire assessments are planned for years 7 and 10 subject to funding. The components of follow-up are shown in Table 1.

Due to the variation in waiting times for surgery at participating sites, it is possible that a small number of participants may receive their 1 year follow-up questionnaire (which is sent post randomisation) at a time point much earlier than 1 year post surgery when the clinical assessment is carried out. These patients will have their 1 year assessment too early in their recovery for the results to be valid and there will be great variation in follow-up time. In cases where there is more than 12

Table 1 Components of follow-up time points

	Pre	2 months	1 year	2 years	3 years	4 years	5 years	7 years	10 years
OKS (self-report function)	▲	○	○	○	○	○	○	○	○
AKSS (clinical exam)	▲	▲	▲				▲		▲
UCLA (self-report activity)	▲	○	○	○	○	○	○	○	○
High Activity Arthroplasty Score	▲	○	○	○	○	○	○	○	○
X-rays	▲	▲*					▲		▲
EQ-5D	▲	○	○	○	○	○	○	○	○
Lund (patient satisfaction)		○	○	○	○	○	○	○	○
Complications		▲	▲	○	○	○	▲	○	▲
Healthcare and patient resource use	▲	○	○	○	○	○	○	○	○

▲ = Collected at clinic visit ○ = Postal Questionnaires * = Immediately Post Op.

weeks between randomisation of a patient to treatment and their operation date, an additional OKS will be administered at the clinical assessment 1 year post surgery.

Randomisation procedures

Randomisation will occur using a web-based randomisation service at the Centre for Healthcare Randomised Controlled Trials (CHaRT), Health Services Research Unit, University of Aberdeen.

The minimisation algorithm will incorporate gender, age and baseline OKS and 'delivery unit'. A delivery unit is either an 'equipoise surgeon' or a pair of 'expertise surgeons' with complementary expertise (that is, one TKR-focused and one UKR-focused).

This factor is included to ensure balance is maintained for individual equipoise surgeons and more generally by centre. Participating surgeons will be discouraged from changing practice during the course of the trial. Within a centre there may be a mixture of delivery unit types. Local recruitment officers at each site will undertake the randomisation. The randomised treatment will be recorded in the patient's hospital notes and study notes and the surgeon will be notified. If the allocated operation is not provided by the recruiting surgeon (for example, they are an 'expertise surgeon' who provide the other operation), an 'internal referral' to their delivery unit colleague will be initiated. A standard letter informing the admissions department/care-pathway coordinators will be sent. Local study staff will oversee this referral. Patients' GPs will also be notified at this time.

Interventions

TOPKAT will be pragmatic in terms of implant selection for the knee replacement operation. Providing the above conditions are met, surgeons will be entirely free to use an implant of their choice or will use the current implants used at their institution. Implant type used on each patient will be recorded.

Total knee replacement

A total knee replacement involves all surfaces of the knee being replaced. The procedure involves excising both diseased and normal femoral condyles, the tibial plateau and often the patella. This is done through a large skin incision which provides easy access to the knee joint. Each component will be replaced with an artificial implant, which may be cemented in position.

Partial knee replacement

A partial knee replacement or UKR involves only the diseased area of the joint being replaced. The healthy compartment of the knee is retained and artificial implants are inserted in place of the diseased area. This is done via a minimally invasive surgical procedure.

Safety

The TOPKAT trial involves routine knee replacement surgery for medial compartmental osteoarthritis. There are no additional risks to patients. They will undergo knee replacement as per standard management regime. The benefits will be to future patients although involvement in the trial with specific outcome measurement may be perceived as a benefit by some patients. Patients will be informed of the standard risks associated with anaesthetic and knee replacement operations.

Possible (expected) complications and consequences are:

- All substantive surgical procedures (including knee replacement) whether primary or revision procedures carry a risk of anaesthesia-related problems, death, morbidity including wound infection, bleeding intra- and postoperatively, thrombo-embolic complications and complications secondary to existing co-morbidity, for example, ischaemic heart disease.
- Specific complications following knee replacement procedures include loosening of components - tibia/femur/both, dislocation of knee/bearing, superficial and deep infection, unexplained knee pain, knee stiffness, haematoma, mechanical failure of replacement, periprosthetic fracture. These complications may result in the need for further surgery such as revision operations, arthroscopy, washout, manipulation under anaesthetic, debridement (open), aspiration, above knee amputation, patella resurfacing.

For the purpose of TOPKAT, a serious adverse event (SAE) is defined as any adverse event during the course of the study resulting from the administration of any of the research procedures required by the protocol that:

- Results in death,
- Is life-threatening†,
- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Other important medical events*

† The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

*Other events that may not result in death, are not life-threatening, or do not require hospitalisation, may be considered a SAE when, based upon appropriate

medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

All SAEs will be notified to the appropriate authorities (Research Ethics Committee (REC) and Sponsor) within the timelines specified.

When the web-based SAE form is completed detailing any possible related and unexpected SAEs, the Chief Investigator (CI) or deputy will be notified automatically. If, in the opinion of the local surgeon and the CI, the event is confirmed as being related and unexpected (that is, not listed as a possible expected occurrence), the CI will submit a report to the main REC and the study sponsors within 15 days of the CI becoming aware of it.

The reporting procedures for all study-related adverse events are detailed in accordance with the guidance from the National Research Ethics Service (NRES).

Reporting of postsurgical complications

The annual postal self-report questionnaires will ask patients if they have been admitted to hospital at any point over the last 12 months. Any readmissions will be followed up by the trial coordinator in Oxford who will contact the recruitment officers at the patient's hospital and ask them to collect further information about the readmission event. Details of any readmissions that are study-related (that is, result from administration of any of the procedures required by the trial protocol) and are expected (that is, listed as a possible expected occurrence) will be collected.

At the routine follow-up clinical visits, patients will also be asked if they have experienced any complications related to their study knee since their last scheduled TOPKAT visit, which resulted in them visiting a healthcare practitioner. This information will be recorded.

Statistics and analysis

Sample size

The sample size for the trial (250 in each arm, 500 overall) has been based on a number of considerations, drawing on what previous research has suggested is both plausible and the likely size of difference that is clinically significant.

Primary outcome - OKS score

Table 2 shows the number of subjects required in each randomised group to give either 80% or 90% power to detect differences in the OKS of 2.0, 3.0 and 4.0, at either the two-sided 1% or 5% significance level and with SD of 8.0, 9.0 or 10.0.

The minimal clinically significant difference of the OKS is judged to be 2.0, and the likely SD of the OKS is 8.0 [46]. A sample size of 500 patients (250 in each group) would provide 80% power to detect a difference of 2.0 at 5% (two-sided) significance level. Since it is possible that the SD of the OKS could be >8.0 [13], this size of sample would allow for the detection of a difference of 3.0 in OKS with a SD of 10.0 at 5% (two-sided) significance level and 90% power and also a difference of 3.0 at 1% (two-sided) significance level with 80% power.

Indeed, almost all of the above scenarios are detectable if the difference in OKS is 3.0 rather than 2.0. This difference of 3.0 in the OKS is equivalent to a typical category change in the American Knee Society Score [40]. Furthermore, a difference in the OKS of 4.0 would, with 250 patients per group allow for some subgroup analyses. As previous research (the Bristol RCT) suggests that the difference between the groups is indeed likely to be >2.0 [6], a sample size of 250 in each arm would allow for some non-response yet still detect differences. As the statistical analysis will adjust for the baseline value and account for the surgical delivery unit this will likely increase precision. Offsetting this will be any missing data which would have the reverse impact.

Re-operation (including revision) of the device

UKR may be associated with higher re-operation rates, including revision. The re-operation rate after TKR is anticipated to be approximately 5% at 5 years [47]. A sample size of 250 patients per group would give 80% power at P <0.05 to detect an increase to 12% (compared to just under 5%), and 90% power at P <0.05 to detect

Table 2 Sample size scenarios

Number in each group		Mean difference in OKS					
		2.0		3.0		4.0	
Power	SD	1% sig level	5% sig level	1% sig level	5% sig level	1% sig level	5% sig level
90	8.0	480	340	215	150	120	85
	9.0	600	430	270	190	150	110
	10.0	740	520	330	235	190	130
80	8.0	375	250	170	110	100	60
	9.0	470	320	210	140	120	80
	10.0	590	390	260	175	150	100

an increase to 14%. Analysis based on the time to re-operation using survival analysis will likely be more than sufficient.

Statistical analysis

Principle analyses will be based on an 'intention to treat' basis where participants will be analysed according to the allocated group using all available participant data. Statistical significance will be judged at the two-sided 5% level with corresponding 95% confidence interval presented. A short summary of the proposed analyses is given below. Further details of the planned statistical analyses are contained in the Statistical Analysis Plan, which will be finalised, prior to the unblinding of data.

Three sets of analyses are planned, based on the anticipated follow-up period. By 2 years, all patients are anticipated to have received surgery. Analyses are planned at 1 year post operation (3 years into the trial), at 5 years randomisation (7 years into the trial) and 10 years post randomisation (12 years into the trial).

Under the principal analysis of the primary outcome, the OKS score will be compared at each assessment point alone (multiple linear regression analysis adjusted for minimisation factors). The impact of adjusting for delivery unit will be explored using multilevel modelling. A stratified analysis (and associated interaction effect) will be performed to allow for a difference between expertise versus equipoise delivery of the treatments and the potential impact upon the comparison. Secondary analyses will explore the potential impact of missing data and alternative analytic approaches. In addition to the analyses planned once 5 and 10 year follow-up has matured, a complementary analysis will also compare the OKS over all assessments (the follow-up period) using multilevel modelling to allow for repeated measurements for participants. One secondary analysis, using an external comparative cohort, will also evaluate whether trial patients are representative, in terms of age, patient demographics and operative findings, of patients undergoing UKR and TKR in the general population.

Secondary outcomes will be analysed in a similar manner adjusting for minimisation factors where appropriate within a generalised linear models framework. Confidential interim analysis will be performed as requested by the Data Monitoring Committee.

For the health economic evaluation within-trial cost-effectiveness will be assessed at 5 years (and at 10 years - subject to additional funding). Costs and QALYs in each trial arm will be expressed using means and standard deviations. Incremental analysis will be performed. If appropriate, results will be expressed as an incremental cost per QALY gained, with uncertainty around this ratio determined through the use of non-parametric bootstrapping and cost-effectiveness acceptability curves [48,49]. Longer-term extrapolation of results will also be conducted and will use trial data, for example surgical re-operation rates will be projected using a simple parametric model and will be assigned appropriate event costs and utility scores.

Ethics

The study obtained approval from the National Research Ethics Service, Oxfordshire REC C in September 2009 (09/H0606/88).

Trial status

Recruitment to the TOPKAT trial commenced in January 2010 and is ongoing at the time of manuscript submission. To date, 478 patients have been randomised (May, 2013). Recruitment was originally scheduled to end in December 2011. Early indications were that recruitment targets would not be met due to early delays with R&D approval process and time taken to incorporate the study procedures into the routine practice of participating sites. An extension to recruitment was discussed and recommended by the TMG and TSC which was agreed upon by the funders. The recruitment phase was extended to September, 2013.

Abbreviations

AKSS: American knee society score; HAAS: High activity arthroplasty score; KAT: Knee arthroplasty trial; OKS: Oxford Knee Score; QALYs: Quality adjusted life years; TKR: Total knee replacement; UCLA: University of California Los Angeles; UKR: Unicompartment replacement.

Competing interests

Professor David Murray receives royalties from Biomet (the company who make the Oxford Unicompartmental Knee Replacement system). Professor Andrew Price receives consultancy fees from Biomet. However, TOPKAT does not actively promote the use of one unicompartmental system over another. All unicompartmental systems may be used as part of the study.
Jonathan Cook holds a Medical Research Council Methodology Fellowship (G1002292). The Health Services Research Unit is core funded by the Chief Scientist Office of the Scottish Government Health Directorates. Views expressed are those of the authors and do not necessarily reflect the view of funders.

Authors' contributions

DB as Chief Investigator, AP, JC, RF, AC, MC, HD, HC, NA and DM were co-applicants on the grant application to the NIHR HTA, and were involved in the design of the study and its implementation, as was CC. LD is the study co-ordinator. DB, JC, DM, HC and LD were responsible for writing this manuscript. All authors read and approved the final manuscript.

Authors' information

David Beard is the Chief Investigator of the study, Professor of Musculoskeletal Sciences and Director of OSIRIS (Orthopaedic Surgical and Interventional Trials Unit) within the Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences at the University of Oxford. Andrew Price is co-first author, Professor of Orthopaedic Surgery within the Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences at the University of Oxford.

Acknowledgements

The TOPKAT study is funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) Programme (project number 08/14/08) and will be published in full in Health Technology Assessment. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health.

Management of the study is divided between the Oxford coordinating team OSIRIS and the Aberdeen data centre, Centre for Healthcare Randomised Trials (CHaRT).
Trial steering committee - Professor Simon Donell (Chair), Professor David Beard, Mr Jonathan Waite, Mr Shawn Tavares, Ms Donna Dodwell, Professor Marion Campbell, Professor Ray Fitzpaterick, Dr Helen Campbell.
Data monitoring committee - Professor Gordon Murray (Chair), Professor Hamish Simpson, Dr Karen Barker.
The authors would like to thank all participants for their involvement in the study and all the principal investigators and their teams at each of the TOPKAT sites (TOPKAT Study Group).
The authors would also like to acknowledge and thank the TOPKAT Study Group and the DMC/TSC for their contributions to any modification and amendments to the protocol since inception.

Author details
[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Botnar Research Centre, University of Oxford, Headington, Oxford OX3 7LD, UK. [2]Department of Public Health, University of Oxford, Rosemary Rue Building, Old Road Campus, Headington, Oxford OX3 7LF, UK. [3]Health Services Research Unit, University of Aberdeen, 3rd Floor, Health Sciences Building, Foresterhill, Aberdeen AB25 2ZD, UK. [4]Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ, UK.

Received: 3 June 2013 Accepted: 23 August 2013
Published: 12 September 2013

References

1. White SH, Ludkowski PF, Goodfellow JW: **Anteromedial osteoarthritis of the knee.** *J Bone Joint Surg Br* 1991, **73:**582–586.
2. Bellamy N, Campbell J, Welch V, Gee TL, Bourne R, Wells GA: **Viscosupplementation for the treatment of osteoarthritis of the knee.** *Cochrane Database Syst Rev* 2006, **2**, CD005321.
3. Brouwer RW, van Raaij TM, Jakma TT, Verhagen AP, Verhaar JAN, Bierma-Zeinstra SMA: **Braces and orthoses for treating osteoarthritis of the knee.** *Cochrane Database Syst Rev* 2005, **1**, CD004020.
4. Fransen M, McConnell S: **Exercise for osteoarthritis of the knee.** *Cochrane Database Syst Rev* 2008, **4**, CD004376.
5. Brouwer RW, Jakma TS, Bierma-Zeinstra SM, Verhagen AP, Verhaar J: **Osteotomy for treating knee osteoarthritis.** *Cochrane Database Syst Rev* 2007, **3**, CD004019.
6. Newman JH, Ackroyd CE, Shah NA: **Unicompartmental or total knee replacement? Five-year results of a prospective, randomised trial of 102 osteoarthritic knees with unicompartmental arthritis.** *J Bone Joint Surg Br* 1998, **80:**862–865.
7. Cameron HU, Jung YB: **A comparison of unicompartmental knee replacement with total knee replacement.** *Orthop Rev* 1988, **17:**983–988.
8. Beard DJ, Holt MD, Mullins MM, Malek S, Massa E, Price AJ: **Decision making For knee replacement: variation In treatment choice for late stage medial compartment osteoarthritis.** *Knee* 2012, **19:**886–889.
9. Weale AE, Murray DW, Baines J, Newman JH: **Radiological changes five years after unicompartmental knee replacement.** *J Bone Joint Surg Br* 2000, **82:**996–1000.
10. Khan OH, Davies H, Newman JH, Weale AE: **Radiological changes ten years after St. Georg Sled unicompartmental knee replacement.** *Knee* 2004, **11:**403–407.
11. Pearse AJ, Hooper GJ, Rothwell A, Frampton C: **Survival and functional outcome after revision of a unicompartmental to a total knee replacement: the New Zealand National Joint Registry.** *J Bone Joint Surg Br* 2010, **92:**508–512.
12. Baker PN, Petheram T, Jameson SS, Avery PJ, Reed MR, Gregg PJ: **Deehan: Comparison of patient reportd outcome measures following total and unicondylar knee replacement.** *J Bone Joint Surg Br* 2012, **94:**919–927.
13. Price AJ, Webb J, Topf H, Dodd CA, Goodfellow JW, Murray DW: **Rapid recovery after oxford unicompartmental arthroplasty through a short incision.** *J Arthroplasty* 2001, **16:**970–976.
14. Brown NM, Sheth NP, Davis K, Berend ME, Lombardi AV, Berend KR, Della Valle CJ: **Total knee arthroplasty has higher postoperative morbidity than unicompartmental knee arthroplasty: a multicenter analysis.** *J Arthroplasty* 2012, **27:**86–90.
15. Hassaballa MA, Porteous AJ, Newman JH: **Observed kneeling ability after total, unicompartmental and patellofemoral knee arthroplasty: perception versus reality.** *Knee Surg Sports Traumatol Arthrosc* 2004, **12:**136–139.
16. Willis-Owen CA, Brust K, Alsop H, Miraldo M, Cobb JP: **Unicondylar knee arthroplasty in the UK National Health Service: an analysis of candidacy, outcome and cost efficacy.** *Knee* 2009, **16:**473–478.
17. Newman J, Pydisetty RV, Ackroyd C: **Unicompartmental or total knee replacement. The 15-year results of a prospective randomised controlled trial.** *J Bone Joint Surg Br* 2009, **91:**52–57.
18. Dennis D, Komistek R, Scuderi G, Argenson JN, Insall J, Mahfouz M, Aubaniac JM, Haas B: **In vivo three-dimensional determination of kinematics for subjects with a normal knee or a unicompartmental or total knee replacement.** *J Bone Joint Surg Am* 2001, **83:**104–115.
19. Isaac SM, Barker KL, Danial IN, Beard DJ, Dodd CA, Murray DW: **Does arthroplasty type influence knee joint proprioception? A longitudinal prospective study comparing total and unicompartmental arthroplasty.** *Knee* 2007, **14:**212–217.
20. Gill T, Schemitsch EH, Brick GW, Thornhill TS: **Revision total knee arthroplasty after failed unicompartmental knee arthroplasty or high tibial osteotomy.** *Clin Orthop Relat Res* 1995, **321:**10–18.
21. Padgett DE, Stern SH, Insall JN: **Revision total knee arthroplasty for failed unicompartmental replacement.** *J Bone Joint Surg Am* 1991, **73:**186–190.
22. Saldanha KA, Keys GW, Svard UC, White SH, Rao C: **Revision of Oxford medial unicompartmental knee arthroplasty to total knee arthroplasty - results of a multicentre study.** *Knee* 2007, **14:**275–279.
23. Cameron HU, Park YS: **Total knee replacement following high tibial osteotomy and unicompartmental knee.** *Orthopedics* 1996, **19:**807–808.
24. Jackson M, Sarangi PP, Newman JH: **Revision total knee arthroplasty. Comparison of outcome following primary proximal tibial osteotomy or unicompartmental arthroplasty.** *J Arthroplasty* 1994, **9:**539–542.
25. Johnson S, Jones P, Newman JH: **The survivorship and results of total knee replacements converted from unicompartmental knee replacements.** *Knee* 2007, **14:**154–157.
26. Levine WN, Ozuna RM, Scott RD, Thornhill TS: **Conversion of failed modern unicompartmental arthroplasty to total knee arthroplasty.** *J Arthroplasty* 1996, **11:**797–801.
27. Myers TG, Cui Q, Kuskowski M, Mihalko WM, Saleh KJ: **Outcomes of total and unicompartmental knee arthroplasty for secondary and spontaneous osteonecrosis of the knee.** *J Bone Joint Surg Am* 2006, **3:**76–82.
28. Fisher DA, Watts M, Davis KE: **Implant position in knee surgery: a comparison of minimally invasive, open unicompartmental, and total knee arthroplasty.** *J Arthroplasty* 2003, **1:**2–8.
29. Jenny JY, Boeri C: **Accuracy of implantation of a unicompartmental total knee arthroplasty with 2 different instrumentations: a case-controlled comparative study.** *J Arthroplasty* 2002, **17:**1016–1020.
30. Manzotti A, Confalonieri N, Pullen C: **Unicompartmental versus computer-assisted total knee replacement for medial compartment knee arthritis: a matched paired study.** *Int Orthop* 2007, **31:**315–319.
31. Engh GA, Dwyer KA, Hanes CK: **Polyethylene wear of metal-backed tibial components in total and unicompartmental knee prostheses.** *J Bone Joint Surg Br* 1992, **74:**9–17.
32. Weale AE, Murray DW, Newman JH, Ackroyd CE: **The length of the patellar tendon after unicompartmental and total knee replacement.** *J Bone Joint Surg Br* 1999, **81:**790–795.
33. Johnston L, MacLennan G, McCormack K, Ramsay C, Walker A, Campbell M, Fiddian N, Fitzpatrick R, Grant A, Gray A, Morris R, Murray D, Rowley D: **KAT Trial Group: The Knee Arthroplasty Trial (KAT) design features, baseline characteristics, and two-year functional outcomes after alternative approaches to knee replacement.** *J Bone Joint Surg Am* 2009, **91:**134–141.
34. Breeman S, Campbell M, Dakin H, Fiddian N, Fitzpatrick R, Grant A, Gray A, Johnston L, Maclennan G, Morris R, Murray D: **KAT Trial Group: Patellar resurfacing in total knee replacement: five-year clinical and economic results of a large randomized controlled trial.** *J Bone Joint Surg Am* 2011, **93:**1473.
35. Amin AK, Patton JT, Cook RE, Gaston M, Brenkel IJ: **Unicompartmental or total knee arthroplasty?: Results from a matched study.** *Clin Orthop Relat Res* 2006, **451:**101–106.
36. Laurencin CT, Zelicof SB, Scott RD, Ewald FC: **Unicompartmental versus total knee arthroplasty in the same patient. A comparative study.** *Clin Orthop Relat Res* 1991, **273:**151–156.

37. Soohoo NF, Sharifi H, Kominski G, Lieberman JR: **Cost-effectiveness analysis of unicompartmental knee arthroplasty as an alternative to total knee arthroplasty for unicompartmental osteoarthritis.** *J Bone Joint Surg Am* 2006, **88:**1975–1982.
38. Slover J, Espehaug B, Havelin LI, Engesaeter LB, Furnes O, Tomek I, Tosteson A: **Cost-effectiveness of unicompartmental and total knee arthroplasty in elderly low-demand patients. A Markov decision analysis.** *J Bone Joint Surg Am* 2006, **88:**2348–2355.
39. Dawson J, Fitzpatrick R, Murray D, Carr A: **Questionnaire on the perceptions of patients about total knee replacement.** *J Bone Joint Surg Br* 1998, **80:**63.
40. Insall JN, Dorr LD, Scott RD, Scott WN: **Rationale of the Knee Society clinical rating system.** *Clin Orthop Relat Res* 1989, **13:**248.
41. Zahiri CA, Schmalzried TP, Szuszczewicz ES, Amstutz HC: **Assessing activity in joint replacement patients.** *J Arthroplasty* 1998, **13:**890–895.
42. Talbot S, Hooper G, Stokes A, Zordan R: **Use of a new high-activity Arthroplasty score to assess function of young patients with total hip or knee Arthroplasty.** *J Arthroplasty* 2010, **25:**268–273.
43. Brooks R: **EuroQol: the current state of play.** *Health Policy* 1996, **37:**53–72.
44. Robertsson O, Dunbar M, Pehrsson T, Knutson K, Lidgren L: **Patient satisfaction after knee arthroplasty: a report on 27,372 knees operated on between 1981 and 1995 in Sweden.** *Acta Orthop Scand* 2000, **71:**262–267.
45. Beard DJ, Dawson J, Harris K, Doll H, Murray DW, Carr A, Price AJ: *Minimal important change or difference for the Oxford Hip and Knee scores following joint replacement surgery.* Toronto: ISAKOS conference proceedings; 2013.
46. Murray D, Fitzpatrick R, Rogers K, Pandit H, Beard D, Carr A, Dawson J: **The use of the Oxford hip and knee score.** *J Bone Joint Surg Br* 2007, **89:**1010–1014.
47. Labek G, Thaler M, Janda W, Agreiter M, Stockl B: **Revision rates after total joint replacement. Cumulaive results from worldwide joint register datasets.** *J Bone Joint Surg Br* 2011, **93:**293–297.
48. Efron B, Tibshirani R: **Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy.** *Stat Sci* 1986, **1:**54–77.
49. Fenwick E, Byford S: **A guide to cost-effectiveness acceptability curves.** *Br J Psychiatry* 2005, **187:**106–108.

doi:10.1186/1745-6215-14-292
Cite this article as: Beard *et al.*: Total or Partial Knee Arthroplasty Trial - TOPKAT: study protocol for a randomised controlled trial. *Trials* 2013 **14**:292.