kat

PROTOCOL

VERSION 4 – June 2001

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 - David Rowley) and Oxford (Nuffield Orthopaedics Centre - David Murray. 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: 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

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 1 and 2). Information will also be sent to their general practitioners in case they are consulted (Appendix 3). 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 4). 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.

6. 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.

7. 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 5). 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 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).

Follow-up is planned for at least ten years.

8. 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.

9. 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.

10. CLINICAL CO-ORDINATION

The clinical co-ordinating centres are in Dundee (Department of Orthopaedics and Trauma Surgery - David Rowley) and Oxford (Nuffield Orthopaedics Centre - David Murray). 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.

11. 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 3 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 Rowley (Dundee), Ray Fitzpatrick and David Murray (Oxford), and Adrian Grant (Aberdeen), together with Richard Morris (London), Alasdair Gray (Oxford), Marion Campbell (Aberdeen) and a representative from each participating centre. Meetings will be held annually, and the chair will alternate between David Rowley and 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 Rowley (Dundee), Ray Fitzpatrick David Murray (Oxford), and Adrian Grant (Aberdeen), together with Richard Morris (London) and 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. Again, the chair will alternate between David Rowley and 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.

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).

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 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 7. 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.

APPENDICES

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

---

[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.*

study, we will ask you to fill in a short questionnaire before your operation. We will write to 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

Appendix 2

kat

Knee Arthroplasty Trial

PATIENT INFORMATION LEAFLETS

Appendix 3

kat

Knee Arthroplasty Trial

INFORMATION SHEET & LETTERS FOR GENERAL PRACTITIONERS

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 01224 551126: 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 01224 551126: 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

kat

Knee Arthroplasty Trial

CONSENT FORM

kat

Knee Arthroplasty Trial

PARTICIPANT QUESTIONNAIRES

& LETTERS

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 (01224 551126). 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 (01224 551126). 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

kat

Knee Arthroplasty Trial

SURGEON FORM, PARTICIPANT DETAILS AND HOSPITAL CARE FORM

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.*

Appendix 8

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	**Non-metal backed**
	N =	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	**Non-metal backed**
	N =	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).