NETSCC, HTA

25 August 2010

UKUFF STUDY

The clinical and cost-effectiveness of arthroscopic versus open surgical repair for tears of the rotator cuff.

PROTOCOL Version 4

A UK Collaborative Study funded by the NIHR HTA Programme

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PROTOCOL SUMMARY

AIM	To assess the clinical and cost effectiveness of two forms of management of rotator cuff tears – arthroscopic surgery and open/mini-open surgery
DESIGN	Multi-centred, parallel group, randomised control trial
PATIENT ELIGIBILITY	Full thickness, degenerative rotator cuff tear Tear diagnosed by MRI or Ultrasound scan Tear suitable for surgical repair ≥50 years old with the ability to consent
RECRUITMENT	The eligibility of the patients will be assessed by the consultant orthopaedic surgeon, with full consent being obtained either locally by a research nurse or remotely by the study office in Oxford. The aim would be to recruit over 270 patients from 20 centres throughout the United Kingdom.
INTERVENTIONS	Open surgery Arthroscopic surgery
OUTCOME ASSESSMENT	Telephone questionnaire at 2 and 8 weeks post treatment Postal questionnaire at 8, 12 and 24 months post randomisation MRI scan at 12 months post surgery
ORGANISATION	**Local:** by Consultant Orthopaedic Surgeon **Central:** by Study Office in Oxford (clinical co-ordination and health economic evaluation) and Study Office in Aberdeen (data entry and statistical analysis) **Overall:** by the UKUFF Management Group and overseen by the Trial Steering Committee and the Data Monitoring Committee
FUNDING	NHS Health Technology Assessment Programme Start date: July 2007 Reconfiguration Date March 2010 Planned finish date: Sep 2013- Jan 2014 Planned reporting date: March-June 2014

UKUFF PERSONNEL

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Other Information

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The clinical and cost-effectiveness of arthroscopic versus open surgical repair for tears of the rotator cuff

This protocol describes a major multi-centre UK trial to assess the clinical and cost effectiveness of arthroscopic surgery and open/mini-open surgery in the management of rotator cuff tears. The surgeons will undertake their usual and preferred surgical techniques . The eligibility of the patient will be assessed by the local consultant orthopaedic surgeon, with consent being obtained either locally by a research nurse or remotely by the study office in Oxford. Only when the consent form and the baseline questionnaire are returned will the participant enter the trial and be randomised to one of the two management arms. The patients will continue to be followed up at 2 and 8 weeks post treatment and 8, 12, and 24 months post randomisation.

1. BACKGROUND OF ROTATOR CUFF TEARS AND TREATMENT

In 2000, an assessment of the prevalence and incidence of consultations for shoulder problems in UK primary care (based on a three year longitudinal study of over 650,000 patients aged 18 and over) estimated the annual prevalence to be 2.4%, with the rate increasing linearly with age[1]. In addition, it is estimated that disorders of the rotator cuff account for between 30 and 70% of the shoulder pain cases that are reported[2,3].

1.1 The problem

The clinical evidence available, regarding both the natural history and management of rotator cuff tears, is limited and conflicting[4,5,6,7,8,9,10,11]. Most reports are small scale, (<50 cases), single centre, retrospective cohort studies.

In one recent report, the surgical management of rotator cuff tears was reviewed by Dunn *et al*[12]. They surveyed members of the American Academy of Orthopaedic Surgeons (AAOS) and found there to be considerable variation in their surgical decision making. This included the type of surgery, the surgical techniques (for example, use of anchors, and type of suture) and also the type and duration of conservative treatment (including cortisone injections, physiotherapy, rest, advice, and analgesia and home exercises).

1.2 Treatment for rotator cuff tears

Rotator cuff tears can be treated both surgically (arthroscopic and open) and non surgically (for example by injection and exercises). The majority of patients selected for surgery have tried and failed conservative care and their symptoms persist. Of the 470 patients randomized to the UKUFF trial so far 89% have received conservative care prior to the decision that surgery was indicated and they were recruited to the trial. Of the 11% who have not received conservative care the decision to operate was commonly based on severity of symptoms or sudden tear progression where conservative care was deemed inappropriate or unlikely to be of value. In the UK there is variation in the surgical treatment (open and arthroscopic) for rotator cuff tears and it is unclear which approach provides the best results for the patient.

1.2.1 Surgery

A rotator cuff repair operation aims to re-attach the tendons to the bone. The repair involves sewing the torn tendon into a groove on the bone, releasing a ligament and excising a prominence on the bone (sub-acromial decompression) to give the repaired muscle more space in which to move.

In general two approaches are available for surgical repair. These include:

(a) Open/mini-open surgery involves the rotator cuff being repaired under direct vision

(through an incision in the skin and a sub-acromial decompression performed either arthroscopically or also via an open method)

(b) Arthroscopic surgery involves both a sub-acromial decompression and the repair being performed through arthroscopic portals inserted into the shoulder.

1.2.1.1 Arthroscopic v open surgery

Proponents of arthroscopic rotator cuff surgery suggest that the procedure may have advantages over standard open procedures in terms of less trauma to shoulder muscles (smaller incisions and theoretically less soft tissue damage), less post-operative patient discomfort together with decreased morbidity and early return of movement. The success of the repair, however, depends on the ability of the surgeon to achieve a secure attachment of tendon to bone. This may be more easily and reliably achieved by open/mini-open surgery. Other potential disadvantages of the arthroscopic approach include increased technical difficulty and longer time in theatre. Only a few, small, non-randomized controlled trials directly compare procedures and, therefore, there is a need to compare the outcome of the two surgical techniques[13].

2. STUDY DESIGN

2.1 Aim

The aim of this study is to assess the clinical and cost effectiveness of arthroscopic surgery, and open surgery in the management of rotator cuff tears. There are two complementary components:

A	A parallel group randomised controlled comparison of two forms of management of Rotator Cuff injuries (arthroscopic surgery and open surgery) to assess their relative clinical effectiveness.
B	An economic evaluation of these two forms of treatment to compare the cost effectiveness of the two management policies, to identify the most efficient provision of future care, and to describe the resource impact that various policies for surgical rotator cuff repair would have on the NHS.

2.2 Design

Our experience with the UKUFF trial so far has revealed that 20 surgeons in the UK are willing to randomize patients between open and arthroscopic surgery: The study will be a 2 way parallel group design

3. TRIAL RECRUITMENT

3.1 Surgeons eligibility

The study will require a 'minimum level of expertise' for the types of surgery undertaken. For both surgical techniques only consultant orthopaedic surgeons with a minimum of two years experience in consultant practice can participate. For those surgeons performing arthroscopic surgery, only those who have been trained to the levels defined by the education committee of BESS will be eligible. As such training standards do not exist for open surgery, only those who perform a minimum of 5 cases per year will be considered. The participating surgeons will represent a cross-section of high, medium and low volume practitioners undertaking both arthroscopic and open surgery.

3.2 Patient eligibility

3.2.1 Inclusion criteria

The patient must satisfy all the following criteria to be eligible for the study:

- Aged over 50 years
- Suffer from a degenerative rotator cuff tear
- Have a full thickness rotator cuff tear
- Rotator cuff tear diagnosed using MRI or Ultrasound scan
- Patient able to consent

3.2.2 Exclusion criteria

- The patient may not enter the study if ANY of the following apply:
- Previous surgery on affected shoulder
- Dual shoulder pathology
- Significant problems in the other shoulder
- Rheumatoid arthritis/Systemic disease
- Significant osteoarthritis problems
- Significant neck problems
- Cognitive impairment or language issues
- Unable to undergo an MRI scan for any reason

Although there is no formal age limit, it is expected patients aged 85 years and over might not be eligible to participate.

Patients are free to withdraw at any time without consequence to the health care they receive.

3.3 Recruitment

Patients attending out-patient clinics with a rotator cuff tear diagnosed using either an MRI scan or an ultrasound scan, which is deemed suitable for surgical repair, will be approached. The patient must also have agreed to be placed on the NHS waiting list for surgery.

3.3.1 Remote recruitment

In most of the clinical centres, recruitment of the participants will be a two-step process. The patient's eligibility will be assessed by the local consultant orthopaedic surgeon who will introduce the trial to the patient using the prompt sheet and complete a patient assessment form. If the patient is interested then the surgeon will provide them with a copy of the Patient Information Sheet, which summarises what the study involves and answer any questions they may have.

If the patient is willing to enter the trial then the initial consent form will be signed, which allows the patients details to be forwarded to the study office in Oxford. The office will then issue an invitation letter, the full Patient Information Sheet, a full consent form, a baseline questionnaire and a pre-paid return envelope to the participant by post, encouraging them to contact the office or their surgeon if they have any further questions or concerns. Patients who have not returned their questionnaire and consent form within a week will be telephoned by a member of the UKUFF team in Oxford. This contact will allow the patient to ask questions about the study and permit the team to assess if the patient is still willing to participate. When the full consent form and baseline questionnaire have been returned to the Oxford office the patient will then officially enter the trial and be randomised to one of the surgical options. A copy of the signed consent form will be returned to the patient. Appendix I contains the forms and information sheets for the Recruitment phase.

3.3.2 Local recruitment

It is anticipated that some surgeons will have an extended scope practitioner or a research nurse working with them to help with this initial consenting process. Under these circumstances the participants may receive the invitation letter, the full Patient Information Sheet, a full consent form, a baseline questionnaire and a pre-paid return envelope from the clinical centre to return to the study office in Oxford.

3.4 Randomisation procedures

When the full consent form and the baseline questionnaire have been received by the study office in Oxford the participant will be randomised to one of the surgical options.

Randomisation will be by computer allocation using the service provided by the Health Services Research Unit, University of Aberdeen. Allocation will be stratified by the surgical technique (open or arthroscopic) and minimised using age and size of tear. After randomisation the participant is considered irrevocably part of the trial for the purpose of the research, irrespective of what occurs subsequently.

The study office in Oxford will send an allocation letter to the participant, detailing the surgical procedure to which they have been randomised too, along with the Post Operation Guideline Booklet (unless instructed otherwise by the local consultant surgeon). The consultant surgeon and the participants GP will also receive letters outlining which the surgical procedure to which their patient has been randomised too. It is expected that the intervention will be undertaken within four months of randomisation.

3.4.1 Randomised Surgery

The participating surgeon will be expected to perform the type of surgery that the patient has been randomised to. Details of the surgical technique used (including method of repair and theatre equipment used e.g. types of suture) will be recorded, as well as the size of the tear, the appearance of the tendons involved, the ease of repair and the completeness of the repair. If circumstances dictate that the allocated surgical technique cannot be carried out then an alternative procedure should be conducted, in accordance with the UKUFF intention to treat principle. The surgeon is also asked to contact the study office if their patient is unwilling or unable to have the operation on the arranged date. The randomization letters and forms are enclosed in Appendix II.

4. DATA COLLECTION AND PROCESSING

Outcome assessments are primarily from patient based questionnaires and the 12 month post surgery MRI scan.

4.1 Questionnaires

A combination of the Oxford Shoulder Score (OSS), the shoulder pain and disability index (SPADI), the mental health inventory (MHI-5) and the EQ-5D will be used to assess functional outcome and patient quality of life. These will assess a range of symptoms often experienced with rotator cuff tears e.g. pain, weakness and a loss of function. Outcome assessment is conducted by participant self-completion questionnaires and as such, interviewer bias and clinical rater bias is avoided. This form of outcome measurement has consistently performed well in comparison to clinician based assessments and general health status measures. All participants, including those who have withdrawn from their allocated intervention but who still wish to be involved in the study, will be followed up, with analysis based on the intention to treat principle.

Participants will receive questionnaires at the following time points :

- Baseline questionnaire – completed before randomisation

- 2 and 8 weeks post treatment – questionnaire completed over the phone
- 8, 12 and 24 months post randomisation

The baseline, 12 and 24 month post randomisation questionnaires will also incorporate a cost-effectiveness analysis. Questions relating to information on primary care consultations, other consultations, out-of-pocket costs and work-impact of the intervention received will be included.

The study office in Aberdeen will contact participants whose questionnaires have not been returned. In the first instance this will be through a reminder letter by post or email, depending on the participant's preference. If the questionnaire is still not returned by the specified time-frame, the study office in Aberdeen will telephone the participant and address any administrative issues that may have arisen, such as change of address, loss of questionnaire. If any clinical issues are identified the study office in Oxford will contact the participant, if appropriate, and address these issues. The time period allocated to the follow-up checks will depend on which outcome assessment it relates to. The covering letters and questionnaires are enclosed in Appendix III.

4.2 MRI scan

A number of authors have reported high rates of re-rupture of the rotator cuff tear (20-54%) after surgery, with some reporting a significant correlation between re-rupture and poor outcome[15]. Rates of re-rupture may differ between the two surgical techniques. In addition, MRI scanning has been shown to have high sensitivity and specificity (85-95%) in the detection of full thickness tears[16]. For these reasons, participants will be asked to have an MRI scan at 12 months post operation to assess the state of the rotator cuff repair. These will take place locally and will be arranged by the study office in Oxford, at a time agreed to by the Trust and the participant. The MRI scans will be collected centrally and read by an independent consultant radiologist who is unaware of the type of surgery that was performed. Any re-tears will not be reported to the participating surgeons, so as not to deviate from their normal practice. However, if patients represent to surgeons with symptoms of a re-tear, the surgeon may contact the UKUFF office in Oxford to ask for the MRI scan results. Incidental abnormalities will be routinely reported to the surgeon.

5. ANALYSIS

Statistical analyses will be based on all people randomised, irrespective of subsequent compliance with the randomised intervention. The principal comparisons will be all those allocated arthroscopic surgery versus all those allocated open surgery.

5.1 Measure of outcome

The primary outcome measure is:

- Oxford Shoulder Score at 24 months after randomisation

The primary measure of cost effectiveness is:

- Incremental cost per quality-adjusted life years

Secondary outcome measures include:

- Oxford Shoulder Score (OSS) at 12 months after randomisation
- EQ-5D at 8, 12, 24 months after randomisation
- MHI-5 at 8, 12, 24 months after randomisation
- Shoulder pain and disability index (SPADI) at 8, 12, 24 months after randomisation

- Participant's rating of pleasure with shoulder symptoms at 12, 24 months after randomisation
- Participant's view of state of shoulder at 8, 12, 24 months after randomisation
- Surgical complications (intra and post-operative) at 2 and 8 weeks post surgery and 12, 24 months after randomisation
- Economic outcomes

5.2 Planned subgroup analyses
(i) Size of tear (small versus medium/large);
(ii) Age <65 or >65;

Stricter levels of statistical significance ($p<0.01$) will be sought, reflecting the exploratory nature of these subgroup analyses.

5.3 Statistical analysis
Reflecting the possible clustering in the data, the outcomes will be compared using multilevel models, with adjustment for minimisation variables and participant baseline values. Statistical significance will be at the 2.5% level with corresponding confidence intervals will be derived. All participants will remain in their allocated group for analysis (intention to treat).

An independent Data Monitoring Committee (DMC) will agree the terms of reference and other procedures and will review confidential interim analyses of accumulating data at least annually as directed.

5.4 Economic evaluation
A cost-effectiveness analysis will be performed. A simple patient cost-related questionnaire will be sent out at baseline and at 12 and 24 months post randomisation, to obtain information on primary care consultations, other consultations, out-of pocket costs, work-impact of the intervention received and return to work. Unit costs will come from national sources and participating hospitals. The patient questionnaire will also be used to administer the EQ-5D, which will also be obtained at baseline. The main health economic outcome will be within-trial and extrapolated quality adjusted life-years, estimated using the EQ-5D.

Incremental cost-effectiveness will be calculated as the net cost per quality-adjusted life year gained, for arthroscopic surgery versus open surgery. Power calculations (see following section) are based on clinical rather than cost-effectiveness outcomes, which will be estimated rather than used in hypothesis testing. Cost-effectiveness ratios and net-benefit statistics will be calculated. We will report within-trial cost-effectiveness; if the trial produces sufficient evidence to plausibly model future quality of life or costs (e.g. based on projected failure rates) we will also extrapolate long-term cost-effectiveness beyond the trial period.

An important component of this trial will be assessment of cost. Therefore, an accurate record of procedures at each of the proposed centres is essential. To evaluate costs of each type of surgery, information from the operating theatres will be collected. Theatre managers will be contacted and visited at each site. Resources used, equipment costs and standard procedures for rotator cuff repairs will be looked at. Per case information will also be analysed. A checklist of equipment, consumables, implants, time and staff utilized during each case will be completed by theatre staff. Information from theatres will be collected by the Oxford UKUFF office and used in a cost comparison between the arthroscopic and open surgery.

6. SAMPLE SIZE AND FEASIBILITY

6.1 Sample size sought

In the original UKUFF trial with 3 randomised strata, the sample size that was funded was constructed to detect a difference in OSS score of 0.38 of a SD for the comparison of arthroscopic versus open surgery. We do not propose any amendment to that clinically important difference. It was based on our experience of using and developing the OSS score in a variety of settings., a 3 point difference (0.33 of a SD) would be deemed a clinically important change. In the original UKUFF trial the detectable difference of 0.38 was constructed by combining evidence from a direct randomised comparison with indirect (non-randomised) comparison data from the other strata. Incorporating indirect effects is a suboptimal approach to measuring the effectiveness because unmeasured confounders can bias the outcomes. The proposed change in this proposal is to achieve the detectable difference of 0.38 of an SD by direct randomised comparison data only.

Attrition is expected to be low (10%) as are the effects of clustering of outcomes within surgeon[19,20] (intra cluster correlation less than 0.03). Whilst we do not have a direct estimate from a shoulder trial, other orthopaedic datasets available to our team (e.g. KAT) support this low ICC estimate. Both these factors require the sample size to be inflated; however, the primary analysis adjusts for baseline OSS score which conversely allows the sample size to be decreased by a factor of (1-correlation squared)[21]. Our previous studies showed that the correlation in the OSS score pre surgery to 6 months post surgery in patients similar to potential trial participants was 0.57. Assuming a conservative correlation of 0.5 implies that the sample size could be reduced by 25% and still maintain the same power. Therefore, a study with a total of 267 participants will still have sufficient power to detect a clinically important change in each comparison assuming attrition and clustering accounts for approximately 25% of variation in the data.

6.2 Recruitment rate

Fifteen trial centres have been recruited with twenty surgeons. Recruitment has been at a steady stady state of 10 patients per month for the past 6 months. We have recruited 87 patients to the surgical arms of the study. We estimate a further 18 months recruitment is required (180 cases and 10 cases per month) to reach our target.

7. ORGANISATION of THE RECONFIGURATION

7.1 In summary

From approval of the reconfiguration it would be as follows – 1-4 months: set up and obtain amendment to ethical approval;: 19-22 months identify and recruit ADDITIONAL participants into the study (recruitment is currently stopped); 27-30 months: 8 month post-randomisation follow-up complete; 31-34 months: 12 month post-randomisation follow-up complete, including one year post-operative MRI scan; 43-46 months: 24 month post-randomisation follow-up complete and database closure; 49-51 months: complete data collection, analysis and dissemination.

7.2 Local organisation in centres

The trial is designed to limit the extra work required by the collaborating clinicians to tasks that only they can do. The research teams in Oxford and Aberdeen will facilitate the trial remotely and initiate site visits as required.

7.2.1 Lead consultant surgeon

Each collaborating centre will identify a lead consultant surgeon who will be the point of contact for that centre. The responsibility of this person will be to:

- establish the study locally (e.g. facilitate local research ethics committee approval, liaise with the local R&D manager and inform all relevant local staff about the study)

- take responsibility for the conduct of the research locally
- notify the study office in Oxford of any unexpected clinical events which might be related to study participation
- provide support and supervision for the local research nurse if applicable
- represent the centre at UKUFF collaborators meetings
- initiating recruitment of participants
- maintaining communication with the study office in Oxford regarding allocated surgical treatment, date of operation, discharge instructions and surgery withdrawal

7.2.2 Research nurse (if applicable)

Some centres have CLRN research nurses to organise the recruitment of the participants. We have found that the presence of a CLRN research nurse doubles the rate of recruitment The responsibility of this person will be to:

- keep regular contact with the lead consultant surgeon and notify them of any problem or unexpected development
- maintain regular contact with the study office
- keep local staff informed of the progress of the study
- assist the lead surgeon to inform the participants about the study and
- answer any questions they may have
- obtain written consent from the participant
- supply participant with the invitation letter, full consent form (if applicable), baseline questionnaires and a pre-paid envelope for their return to the study office in Oxford
- represent the centre at collaborators meetings

7.3 Central organisation of the study

Reflecting the complex nature of the trial, trial functions will be divided between the Oxford coordinating team and the Aberdeen coordinating team.

7.3.1 Study co-ordination in Oxford

The UKUFF study team in Oxford is divided between the Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences (NDORMS) and the Department of Public Health and Primary Care (DPHPC). Both departments are a part of the University of Oxford with NDORMS having very strong links with the Nuffield Orthopaedic Centre NHS Trust.

7.3.1.1 NDORMS

The NDORMS team will be responsible for all clinical aspects of the trial including; the recruitment and education of surgeons, recruitment of participants, daily management and troubleshooting of clinical issues from staff and participants in the trial and the coordination of the 12 month post operative MRI scans.

7.3.1.2 DPHPC

The UKUFF team in DPHPC are responsible for the design, conduct and analysis of the concurrent economic evaluation and outcome questionnaires.

7.3.1.3 Timing of meetings

All members of the management team in Oxford will aim to meet quarterly to review trial progress. NDORMS members will aim to meet weekly to discuss site, surgeon and patient recruitment.

7.3.2 Study co-ordination in Aberdeen

The Aberdeen team are based at the Centre for Health and Randomised Trials within the Health Services Research Unit at the University of Aberdeen. They will be responsible for all data aspects of the trial including: the design and set-up of trial databases, the randomisation system, the management of postal participant follow-up, data management and verification

and the conduct of final trial analysis.

7.3.2.1 Timing of meetings

The management team in Aberdeen will meet weekly and a conference call with the CI and trial coordinator in Oxford will occur fortnightly.

7.3.3 Production of reports

The production of all interim reports for the trial steering committee, data monitoring committee, and progress reports required by the funding body, sponsor and ethical committees will be completed in collaboration with all teams and coordinated by the trial managers in Oxford and Aberdeen.

7.4 UKUFF Management Group

The trial management group will oversee all aspects of the conduct and progress of the trial and ensure that the protocol is adhered to. They will be responsible for the daily management of the trial and will meet at 6 monthly intervals to review the progress of the trial. The group consists of the grant holders and representatives from both the study office in Oxford and Aberdeen

7.5 UKUFF Steering Committee

The study is overseen by an independent Steering Committee. The chairman is Professor Jane Blazeby, with Miss Jo Gibson and Mr Dair Farrar-Hockley acting as the other independent members. The study grant holders, along with Mr David Stanley, complete the Steering Committee. This committee will meet annually or more frequently if circumstances dictate. They will take responsibility for any major decisions, such as the need to close recruitment or more parts of the study or to change the protocol for any reason.

TSC Guidelines are detailed in Appendix IV.

7.6 Data and Safety monitoring

7.6.1 UKUFF Data Monitoring Committee

The Data Monitoring Committee is independent of the study organisers. The chairman is Professor Roger Emery, a Professor in Orthopaedic Surgery, along with Dr Jeremy Lewis (Reader in Physiotherapy) and Dr Richard Morris (Senior Lecturer in Medical Statistics). During the period of recruitment to the study, interim analyses will be supplied, in the strictest 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 light of these interim analyses, the Data Monitoring Committee will advise the Steering Committee if, in its opinion, the trial has provided both:

a) proof beyond reasonable doubt that for all or some types of participants one intervention is clearly indicated in terms of clinical and cost effectiveness
b) evidence that might reasonably be expected to influence materially the care of the people with rotator cuff tears 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. Unless this happens, the Steering Group, Management Group, consultant surgeons and study office staff (except those you supplied the confidential analyses) will remain ignorant of the interim results.

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

DMC Guidelines are detailed in Appendix IV.

7.6.2 Safety concerns

The UKUFF trial involves two interventions that are well established in clinical practicse, although unproven for clinical and cost effectiveness. There are safety concerns surrounding the surgical treatments. These include:

- surgical site infection
- frozen shoulder
- complications relating to anaesthetic and or theatre equipment
- uncontrolled bleeding

As the techniques are standard treatments for rotator cuff tears, and because the surgeons are performing their usual and preferred surgical procedures, the trial participants would not be put at any more risk than is normally associated with the treatment. It is anticipated that none of these events would be classified as a serious adverse event but we would respond appropriately to any notification.

Collaborators and participants may contact the chairman of the Steering Committee through the trial office in Aberdeen or Oxford about any concerns they may have about the trial. If concerns arise about procedures, participants or clinical or research staff (including risk to staff) these will be relayed to the Chairman of the Data Monitoring Committee.

Safety Reporting is detailed in Appendix V.

7.6.3 Data handling and record keeping

All data collected and stored as a result of the study will comply with the data protection act.

8. FINANCE

The UKUFF trial is funded by the UK NIHR Health Technology Assessment Programme (Ref: 05/47/02). The Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences in Oxford will manage the finances and budget.

Participating sites invoice the UKUFF study quarterly in order to receive the payment of £200 per randomised patient. The trial coordinator will supply each site with their recruitment numbers at the end of each quarter so the invoice can be raised for the correct amount. Participating sites invoice the UKUFF study as required in order to receive the payment for the required MRI scan. The cost of these scans is negotiated with each site before the first scan is undertaken. This cost is entered into the Clinical Trial Agreement implemented between the site and the University of Oxford.

8.1 Costing of Reconfiguration

Of the original grant allocation £610,000 remains at February 2010 in the NDORMS Budget. Our reconfigured costs are £590,801 representing a saving of £19,199. By stopping recruitment into the conservative arm of the trial and by reducing the number of surgeons from 90 to 20 we have been able to reduce the overall costs by approximately £42,000. This includes the costs for reconfiguring the trial to recruit for a further 18 months into the modified stratum A group (open versus arthroscopic surgery).

9. SATELLITE STUDIES

The funds provided by the HTA Programme are to conduct the main trial as described in this

protocol. Nevertheless, it is recognised that the value of the UKUFF 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 Management Group.

Protocols for each of these are attached in Appendix VI.

10. INDEMNITY

The UKUFF study is sponsored by the University of Oxford. Indemnity and/or compensation for negligent harm arising specifically from an accidental injury for which the University is legally liable as the Research Sponsor will be covered by the University of Oxford.

The University of Oxford have authority to audit the process of the UKUFF trial. Authorised University staff may review aspects of the trial, such as; the consenting process, data collection and storage. UKUFF state that a period of 10 working days notice must be given before these reviews occur.

The NHS will owe a duty of care to those undergoing clinical treatment, with Trust Indemnity available through the NHS Litigation Authority Scheme.

11. PUBLICATION

The success of the trial depends entirely on the wholehearted collaboration of a large number of health care workers. 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 trials' publication policy is described in Appendix IX. The results of the trial will be reported first to trial collaborators. The main report will be drafted by the UKUFF Management Group, and the final version will be agreed by the Trial Steering Committee before submission for publication, on behalf of the UKUFF collaborators.

To safeguard the integrity of the main trial, reports of satellite studies will not be submitted for publication without prior agreement from the UKUFF Management Group.

We maintain interest in the study by publication of UKUFF newsletters at three monthly intervals for collaborators and annually for participants. The newsletters inform their audience of how the study and recruitment is progressing and any relevant interim results. UKUFF have deemed it important to communicate with the collaborators so that common problems may be addressed and protocol adherence may be monitored.

Authorship and Publication guidelines are detailed in Appendix VII.

12. REFERENCE LIST

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