UKUFF STUDY

The Clinical and cost- effectiveness of surgical (arthroscopic or open) versus Rest then Exercise management for tears of the rotator cuff.

PROTOCOL

A UK Collaborative Study funded by the
NHS HTA Programme

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PROTOCOL SUMMARY

AIM

To assess the clinical and cost effectiveness of three forms of management of rotator cuff tears – arthroscopic surgery, open surgery and a non-surgical/conservative treatment.

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 600 patients from 70 centres throughout the United Kingdom.

INTERVENTIONS

Open surgery
Arthroscopic surgery
Rest then Exercise Programme

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 (for those randomised to surgical arm only)

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
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UKUFF PERSONNEL

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Other Information
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The clinical and cost-effectiveness of surgical (arthroscopic or open) versus Rest then Exercise management 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, open surgery and a Rest then Exercise program in the management of rotator cuff tears. For the surgical arms the surgeons will undertake their usual and preferred surgical techniques while the conservative management arm will comprise of a month of rest and then up to 12 weeks of specialised shoulder exercises. This conservative programme has been designed specifically for the trial with the help of consumers, physiotherapists and shoulder surgeons.

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 three 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 age1. In addition, it is estimated that disorders of the rotator cuff account for between 30 and 70% of the shoulder pain cases that are reported2,3.

1.1 The problem

The clinical evidence available, regarding both the natural history and management of rotator cuff tears, is limited and conflicting4,5,6,7,8,9,10,11. 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). They also found that higher volume surgeons were generally less enthusiastic about conservative care.

1.2 Treatment for rotator cuff tears

Rotator cuff tears can be treated both surgically (arthroscopic and open) and nonsurgically (for example by injection and exercises). In the UK there is wide variation in the treatment practice for rotator cuff tears and it is unclear which approach provides the best results for the patient.

1.2.1 Treatment by 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 three approaches are available for surgical repair. These include:

(a) Open
Open surgery involves the rotator cuff being repaired under direct vision (through an incision in the skin). During this procedure the deltoid muscle in the shoulder is detached from the bone.

(b) Mini-open
Mini-open surgery is an arthroscopically assisted repair. The sub-acromial decompression is performed arthrscopically and the repair is performed under direct vision (through a longer incision in the skin). During this procedure the deltoid muscle is split but not detached from the bone.

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

For the purposes of the UKUFF trial, the open and mini-open surgical techniques are classified together as open surgery.

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 surgery. Other potential disadvantages of the arthroscopic approach include increased technical difficulty and longer time in theatre. Only a few, small, randomized controlled trials directly compare procedures and, therefore, there is a need to compare the outcome of the two surgical techniques13.

1.2.2 Non-surgical treatment

In 2007 a systematic review was conducted by Ainsworth and Lewis14 to review the evidence for the effectiveness of therapeutic exercises for the treatment of full thickness tears of the rotator cuff. They concluded that there was some evidence to support the use of exercise in the management of full thickness rotator cuff tears but that there was a definite need for a well planned randomised controlled trial to investigate this further.

2. STUDY DESIGN

2.1 Aim

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

A A parallel group randomised controlled comparison of three forms of management of Rotator Cuff injuries (arthroscopic surgery, open surgery, and Rest then Exercise management), to assess their relative clinical effectiveness.

B An economic evaluation of these three forms of treatment to compare the cost effectiveness of the three management policies, to identify the most efficient provision of future care, and to describe the resource impact that various policies for rotator cuff repair would have on the NHS.

2.2 Design

A detailed survey of 126 surgeons from the British Elbow & Shoulder Society (BESS), carried out in preparation for this study, showed that the majority of surgeons practice only open surgery for rotator cuff repairs. A number of surgeons did indicate a willingness to randomise between arthroscopic and open surgery although the majority showed no equipoise for the two different techniques. Reflecting this lack of individual uncertainty around certain comparisons, randomisation will be organised within three strata depending on the surgeons' preparedness to randomise. The three strata are:

StratumA	arthroscopic surgery versus open surgery versus Rest then Exercise
StratumB	arthroscopic surgery versus Rest then Exercise
StratumC	open surgery versus Rest then Exercise

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 crosssection 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 an eligibility check-list (Appendix I). If the patient is interested then the surgeon will provide them with a copy of the Patient Information Sheet (PIS Appendix I), 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 (Appendix I) 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 (Appendix II), the full Patient Information Sheet (Appendix I), a full consent form (Appendix I), a baseline questionnaire (Appendix IV) 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 allow 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 management programmes. A copy of the signed consent form will be returned to the patient. 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.

3.3.2 Local recruitment
At some of our clinical centres a research nurse is available to complete the full consent process. The eligibility of the patient will initially be assessed by the local consultant orthopaedic surgeon who will introduce the trial to the patient using the prompt sheet and complete an eligibility check-list. If the patient is interested a research nurse will provide

them with a copy of the Patient Information sheet, which summarises what the study involves and answer any questions they may have.

The research nurse will organise a time for the patient to come back in to the clinic to sign the full consent form and complete the patient assessment form. The patient will also receive a baseline questionnaire to complete at home and return to the study office in Oxford. When these details have been returned to the study office in Oxford the patient will officially enter the trial and be randomised to one of the management programmes. A copy of the signed consent form will be returned to the patient.

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 management programmes. 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 performed by the surgeon (open and/or arthroscopic) and minimised using centre, 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.

3.4.1 Randomisation to surgical arm

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

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 (Appendix IV). If circumstances dictate that the allocated surgical technique can not 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.

3.4.2 Randomisation to conservative arm

The study office in Oxford will send an allocation letter to the participant along with an information pack containing a self-help CD, self-help booklet and a sling (Appendix II). The participants will be asked if they have access to a DVD player or computer, although the information contained on the CD is identical to the information in the booklet. To ensure the participants receive the information pack, a reply slip will be enclosed with the pack asking the participants to check the contents and then return the slip to the study office in Oxford. The consultant surgeon and the participants GP will also receive letters outlining that their patient has been randomised to the conservative management programme (Appendix II). All participants randomised to the conservative arm will receive the same information and advice. If they require further information about non-surgical care they will have access to a

telephone free-call help-line where clinical staff and/or the research physiotherapist will be available to answer questions and provide advice. The patients GPs will also be asked to inform the study office if the patient consults them regarding any physiotherapy treatments. This information is important as attending a physiotherapy session may alter the outcomes of the programme and so all sessions need to be documented.

The Rest then Exercise participants will be placed on the NHS waiting list for surgery at the same time as the surgical arm participants. Due to the length of most of the Trust's NHS waiting lists, they should be able to complete the Rest then Exercise programme before they would be due for surgery. However, it is anticipated that a few participants may have their date of surgery delayed while they complete the programme, although this is not anticipated to be a regular occurrence. Surgeons are asked to contact the study office if their patients decline surgery after the completion of the Rest then Exercise Programme.

4. DATA COLLECTION AND PROCESSING

Outcome assessments are primarily from patient based questionnaires and the 12 month post surgeryMRI 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 (Appendix IV):

- Baseline questionnaire – completed before randomisation
- 2 and 8 weeks post treatment – questionnaire completed over the phone and includes a conservative programme compliance questionnaire if applicable
- 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 (Appendix III). 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.

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 outcome15. In addition, MRI scanning has been shown to have high sensitivity and specificity (85-95%) in the detection of full thickness tears16. For these reasons, participants randomised to surgery 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 practise. 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:

i. all those allocated arthroscopic surgery versus all those allocated rest and exercise (Strata A & B)
ii. all those allocated open surgery versus all those allocated rest and exercise (Strata A & C)
iii. all those allocated open versus all those allocated arthroscopy surgery (Strata A, B & C)

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 at 12 months after randomisation
- Eq-5d at 12, 24 months after randomisation
- MHI-5 at 12, 24 months after randomisation
- Shoulder pain and disability index (SPADI) at 12, 24 months after randomisation
- Participant's pleasure with shoulder symptoms at 12, 24 months after randomisation
- Participant's view of state of shoulder at 12, 24 months after randomisation
- Surgical complications (intra and post-operative) at 12, 24 months after randomisation
- Economic outcomes

The way in which this data will be analysed is set out in Appendix V (Dummy Tabulations).

5.2 Planned subgroup analyses

(i) Size of tear (small versus medium/large);
(ii) Age <65 or ³65;

Stricter levels of statistical significance (2p<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). Comparisons (i) and (ii) will be based upon the respective direct randomised evidence only. For comparison (iii), a meta analysis will be used to combine the results from the direct comparison (using stratum A) and an indirect comparison (using strata B and C). A secondary analysis will investigate the impact of surgical expertise level (learning curve effects)17. All study analyses will be according to a statistical analysis plan that will be agreed in advance by the Trial Steering Committee. A single main analysis will be performed at the end of the trial when all follow up has been completed. An independent Data Monitoring Committee (DMC) will meet early in the trial to agree its 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-ofpocket 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 Rest then Exercise, open surgery versus Rest then Exercise, either surgical versus Rest then Exercise and 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

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. Using the informal survey of surgeons' preferences, we aim to recruit at least 8 surgeons to stratum A, 10 to stratum B and 40 to stratum C. From this we have assumed the following numbers of participants in each strata: Stratum A – 70 participants in each group; stratum B - 120 arthroscopic surgery : 120 Rest then Exercise management and stratum C - 120 open surgery : 120 Rest then Exercise management (see Table 1) giving 690 participants in total.

Table 1 – Proposed number of randomised participants

	Arthroscopic surgery	Open surgery	Rest then Exercise
Stratum A	70	70	70
StratumB	120	None	120
StratumC	None	120	120

For comparison (i), results from the arthroscopic surgery and Rest then Exercise groups in strata A and B can be combined without introducing any systematic bias (resulting in 190 arthroscopic:190 Rest then Exercise). Such a study has greater than 80% power at 2.5% significance level (to account for multiple testing) to detect a difference in mean OSS of 0.33 of a SD, using a two sample two-sided t-test. With an SD of about 9, this would translate to having adequate power to be able to detect a difference in mean OSS score between two groups of about 3 units.

For comparison (ii), the same power (>80%) and detectable difference (0.33 of a SD) as given above are obtained by combining the open surgery and Rest then Exercise management groups in strata A and C (n=190 in each arm).

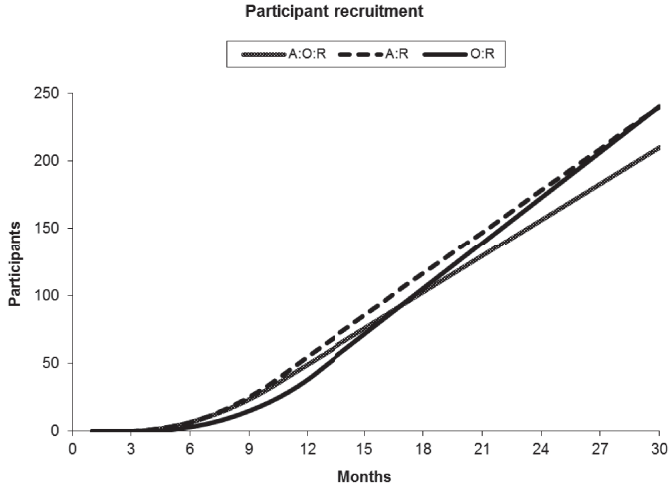
For comparison (iii), due to the small numbers of surgeons willing to randomise to this comparison we propose to use a mixture of direct (randomised) and indirect (non randomised) comparisons. The direct comparison is in stratum A where 70 arthroscopic: 70 open surgeries have 80% power at 2.5% significance to detect a difference of 0.5 of a SD. An indirect comparison using only the results from strata B and C would have 80% power (at 2.5% significance level) to detect a difference of 0.55SD18. Combining the direct and indirect comparison estimate (using recognised meta analysis techniques) gives approximately 80% power at 2.5% significance to detect a difference of 0.38SD.

Attrition is expected to be low (10%) as are the effects of clustering of outcomes within surgeon19,20 (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 (section 3.2) 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 maintains the same power. Therefore, a study with 690 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

Trial centres will be recruited in a staggered way, bringing on 3 centres in each of months 4 and 5, and then 6 or 7 centres per month during months 6 through 13, making a total of 58 centres (8 in menu A:O:R; 10 in menu A:R, and 40 in menu O:R). Steady state will be achieved by month 11 for the two menus involving arthroscopy, and by month 13 for the O:R option. We anticipate having in aggregate 188 centre months for A:O:R (steady state monthly rate of 9 to achieve 210 participants), 233 centre months for A:R (steady state monthly rate 10 to achieve 240 participants, and 856 centre months for O:R (steady state monthly rate 11 to achieve 240 participants), or 690 randomised participants in total. The Hospital Episode Statistics data for 2004/2005 indicates that 1295 rotator cuff repairs took place in NHS hospitals in England alone giving a mean of 15 per trust. With fifty eight centres recruited there is a potential recruitment rate in the order of 75 patients per month. In steady state we will need to be recruiting 30 patients per month, or 40% of the available throughput. Expected recruitment milestones will be 16 (month 6); 142 (month 12); 320 (month 18); 507 (month 24) and 690 (month 30).

Participant recruitment



We anticipate that the trial will require the participation of 58 centres. If the recruitment of patients is failing to meet targets and cannot be increased at participating centres then we would increase the number of centres in the trial.

7. ORGANISATION

7.1 In summary

A detailed plan and timetable of study organisation is given in the Gantt chart (Appendix VI). In summary, it is as follows – 1-4 months: set up office, assemble team, obtain ethical approval and establish first centre; 5-13 months: establish study in all centres; 4-30 months: identify and recruit participants into the study; 12-38 months: 8 month post-randomisation follow-up complete; 16-42 months: 12 month post-randomisation follow-up complete, including one year post-operative MRI scan; 28-54 months: 24 month post-randomisation follow-up complete and database closure; 54-60 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 trail 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 will identify a research nurse to organise the recruitment of the participants. 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 Orthopaedic Surgery (NDOS) and the Department of Public Health and Primary Care (DPHPC). Both departments are a part of the University of Oxford with NDOS having very strong links with the Nuffield Orthopaedic Centre NHS Trust.

7.3.1.1 NDOS
The NDOS team will be responsible for all clinical aspects of the trial including; the recruitment and education of surgeons, recruitment of participants, the coordination of the Rest then Exercise Programme, 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. NDOS 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 Jeremy Fairbank, 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.

7.6 Data and Safety monitoring

7.6.1 UKUFF DataMonitoring Committee

The Data Monitoring Committee is independent of the study organisers. The chairman is Mr Roger Emery, a Reader 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.

7.6.2 Safety concerns

The UKUFF trial involves three interventions that are well established in clinical practise, although unproven for clinical and cost effectiveness. Two of these interventions are surgical and so inevitably there are safety concerns surrounding them. 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 (Appendix VII).

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.

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 NHS Health Technology Assessment Programme (Ref: 05/47/02). The Nuffield Department of Orthopaedic Surgery in Oxford will manage the finances and budget.

Participating sites will be asked to 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 will also be asked to invoice the UKUFF study quarterly in order to receive the payment for the required MRI scan. The cost of these scans will be 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.

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. Details of all satellite studies are outlined in Appendix VIII.

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 plan to maintain interest in the study by publication of UKUFF newsletters at three monthly intervals for collaborators and annually for participants. The newsletters will 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.

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