RaCeR 2	
Clinical and cost-effectiveness of individualised (early) patient-directed rehabilitation versus standard rehabilitation after surgical repair of the rotator cuff of the shoulder: a multi-centre, randomised controlled trial with integrated Quintet Recruitment Intervention (RaCeR 2)	
Version and Date of Protocol:	V3.0 05 MAR 2025
Sponsor:	University Hospitals of Derby & Burton NHS Foundation Trust
Chief Investigator:	Professor Chris Littlewood
Local Study Reference:	UHDB/2020/102
IRAS Number:	318438
ISRCTN number:	11499185
Funder(s):	National Institute of Health and Care Research (NIHR) Health Technology Assessment (HTA)
This protocol has regard for the HRA guidance	

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SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Derby CTSU's SOPs, and other regulatory requirements.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Protocol v3.0 05/MAR/2025 authorisation signatures:

Chief Investigator:

Signature: Signed by: Chris Littlewood EE55BDBF3C614F5... Date: 27-03-25

Name (please print): Chris Littlewood

For and on behalf of the Study Sponsor (if required):

Signature: DocuSigned by: Teresa Grieve 1D8BA63002344B4... Date: 03-04-25

Name (please print): Teresa Grieve

Position:

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STUDY SUMMARY

Study Title:	Clinical and cost-effectiveness of early individualised patient-directed rehabilitation versus standard rehabilitation after surgical repair of the rotator cuff of the shoulder: a multi-centre, randomised controlled trial with integrated Quintet Recruitment Intervention
Local Study Reference:	UHDB/2020/102
Study Design:	Pragmatic, multi-centre, open label, randomised controlled trial (RCT) with internal pilot phase using a parallel group design with 1:1 allocation ratio, with full economic evaluation, and integrated Quintet Recruitment Intervention (QRI)
Study Participants:	Adults awaiting arthroscopic surgical repair of a full-thickness rotator cuff tear
Planned Number of Sites:	24-30
Planned Sample Size:	638 randomised
Treatment Duration:	Approximately 12 weeks following surgery
Follow Up Duration:	12 months with primary endpoint at 12-weeks post-randomisation
Planned Start Date:	1st June 2023
Planned Recruitment End Date:	30th September 2025
Planned Study End Date:	30th November 2026
Research Question:	What is the clinical and cost-effectiveness of individualised (early) patient-directed rehabilitation (EPDR) versus standard (delayed) rehabilitation after surgical repair of the rotator cuff of the shoulder?

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Funder(s)	Financial and Non-Financial Support Given
National Institute for Health and Care Research (NIHR) National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre University of Southampton Alpha House, Enterprise Road Southampton SO16 7NS Email: netspostawardsetup@nihr.ac.uk	£1,737,837.84

Sponsor

The Sponsor, University Hospitals of Derby & Burton NHS Foundation Trust (UHDB), take on overall responsibility for appropriate arrangements being in place to set up, run and report the research project. The sponsor is not providing funds for this study but has taken on responsibility for ensuring finances are in place to support the research.

Funder

The study is funded by the National Institute for Health & Care Research (NIHR). The NIHR have approved this protocol prior to the study commencing.

Study Management Committees

Trial Management Group

The trial management group (TMG) will meet regularly to oversee the day-to-day management of the trial and ensure it is conducted according to the protocol. Any problems with study conduct and participating centres will be raised and addressed during TMG meetings.

Trial Steering Committee

The Trial Steering Committee (TSC) will oversee and supervise the progress of the trial and ensure that it is being conducted according to the protocol and the applicable regulations. The TSC is an independent body that includes majority members (including lay members) who are not involved with the running of the trial. Meetings will take place remotely, at least annually, or more frequently if required. Given the nature of this study, a separate Data Monitoring Committee (DMC) will not be convened and the TSC will be asked to take on the data monitoring role, as agreed by the funder.

Project Management

Full clinical trials unit support will be provided by Derby Clinical Trials Support Unit (DCTSU). DCTSU is a UKCRC registered unit. DCTSU support will include a dedicated trial manager, administrative support, set-up and management of the online randomisation system and database, statistical services, monitoring, and quality assurance.

Protocol Contributors

Several protocol contributors have been involved in the development of this protocol, these include the Chief Investigator, Statistician, all co-applicants, Data Manager and Trial Manager. Protocol contributors are responsible for inputting into the design of the study, ensuring that it is designed transparently and efficiently.

CONTENTS

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LIST OF ABBREVIATIONS

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
DM	Data Management
EPDR	Individualised (early) Patient-Directed Rehabilitation
GCP	Good Clinical Practice
ICF	Informed Consent Form
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials
MDC	Minimum Data Collection
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QRI	Quintet Recruitment Intervention
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Data Verification
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TMG	Trial Management Group
TSC	Trial Steering Committee
TMF	Trial Master File

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STUDY FLOW CHART

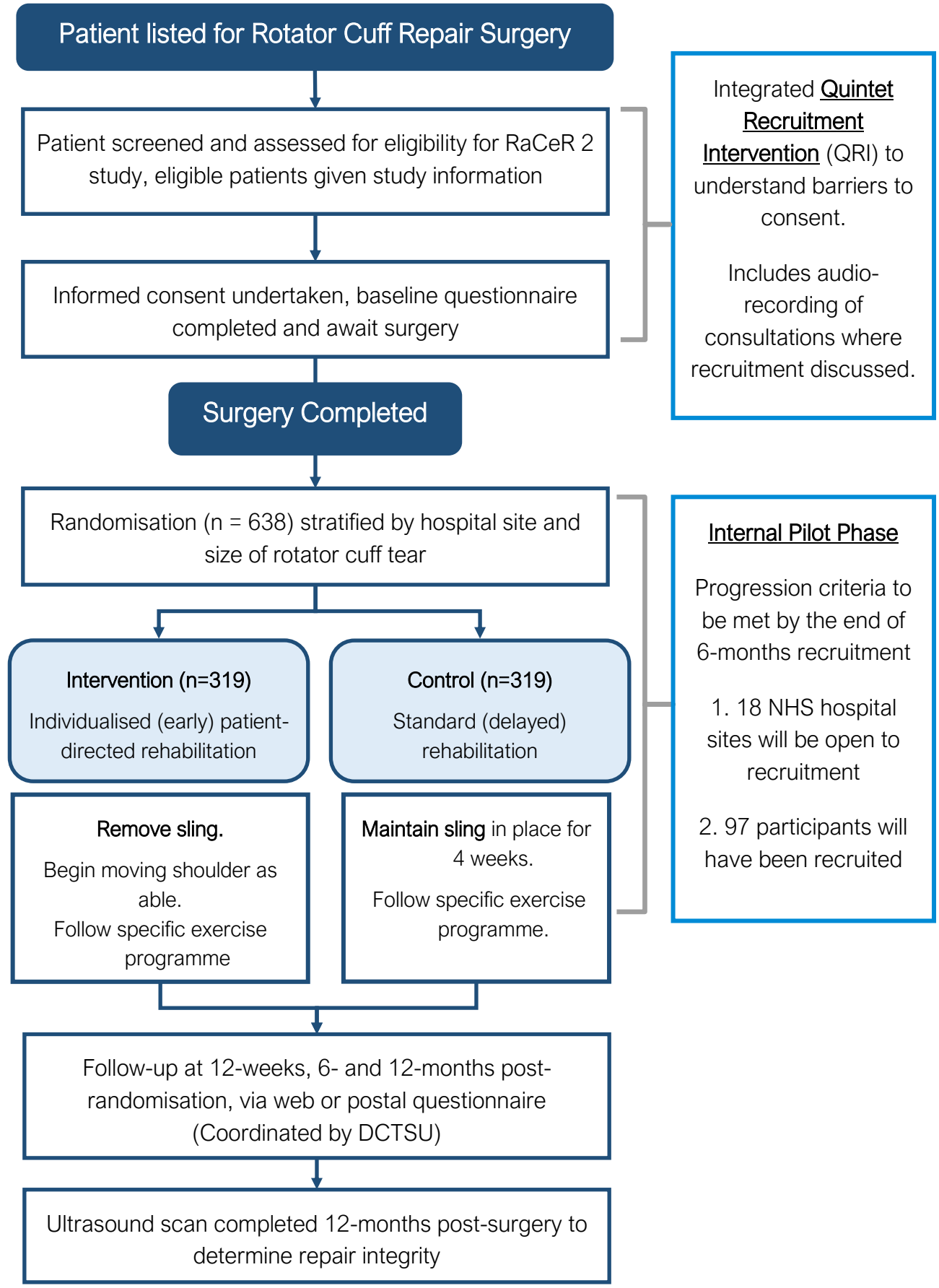

Figure 1: Study Flowchart

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1 BACKGROUND

Tears of the tendons of the shoulder (rotator cuff) are a significant cause of shoulder pain. A painful shoulder caused by a torn rotator cuff can have a significant effect on a person's life including ability to self-care, undertake usual activities, including working and driving, and sleep (1). Shoulder pain can also affect mood, social participation and significantly reduce quality of life. Shoulder pain caused by rotator cuff tears is common and in 2018/2019, almost 9,000 surgical repairs of the rotator cuff were undertaken in the NHS costing up to £56.7 million in direct NHS treatment costs alone (2).

Following rotator cuff repair surgery, patients undergo a programme of rehabilitation, which is crucial to recovery. Despite this and the high number of operations and surgical advancement, rehabilitation after rotator cuff repair has not advanced for over 20 years (3). The traditional cautious approach, where patients use a shoulder sling for about 1 month, might be contributing to sub-optimal outcomes (3–7). In our NIHR-funded pilot RaCeR randomised controlled trial, we worked with 5 NHS hospitals and recruited 73 participants. Patients were randomly allocated to early patient-directed rehabilitation or standard rehabilitation. Those participants allocated to early patient directed rehabilitation reported less shoulder pain and disability and returned to driving 18 days faster than patients offered standard rehabilitation, and also reported 4 fewer days lost from work over 12-weeks (5). However, due to the small number of participants in the study there was considerable uncertainty with these findings which is why we now need a larger study. In this context, it is remiss that we still do not have a better understanding of the optimal approach to rehabilitation that maximises outcomes, including early and safe return to usual activities (7,8).

We will now aim to find the most clinically and cost-effective approach to rehabilitation after surgical repair of the shoulder rotator cuff tendons. Specifically, we and patients want to know if moving the shoulder as soon as patients feel able is better than current standard rehabilitation methods which includes delayed mobilisation where patients use a shoulder sling for a month after surgery. Patients waiting for shoulder surgery to repair their rotator cuff will be recruited. After surgery, these patients will receive one of two treatments. One group of patients will be advised to remove their sling and start to move their shoulder as soon as they feel able. The second group of patients will follow the current standard approach to rehabilitation and use a sling for one month after surgery. All patients will be supported by a physiotherapist during their rehabilitation programmes.

2 RATIONALE

Our systematic review of 20 previous randomised controlled trials reported no difference in terms of shoulder pain or disability over 12-months, but early mobilisation significantly improved range of movement (6). Critically, there was no difference in repair integrity (6), which is a concern for clinicians and one of the reasons that underpins cautious approaches to rehabilitation (9). However, we found variation in treatment protocols with most introducing early mobilisation via passive (fully supported) movement at variable time-points more reflective of standard (delayed) UK practice rather than the early patient-directed rehabilitation approach we describe here. In contrast, early patient-directed rehabilitation encourages early active movement and is

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progressed according to patient's ability, so is quite different from other 'early' mobilisation programmes tested in the randomised controlled trials included in our review.

The research question: "Does early mobilisation after shoulder surgery improve patient outcome compared to standard immobilisation?", ranked as 4th research priority from the James Lind Alliance Priority Setting Partnership for shoulder surgery (9) . Through our extensive PPI, it is clear this is an important research question for patients and the public.

We also surveyed 76 surgeon members of the British Elbow and Shoulder Society (BESS):

- 87% agreed/strongly agreed that there is uncertainty about postoperative rehabilitation
- 81% agreed/strongly agreed that early patient-directed rehabilitation might benefit recovery
- 57% were neutral/disagreed that early patient-directed rehabilitation risks re-tear after surgery
- 72% agreed/strongly agreed that they would be interested in taking part in a definitive randomised controlled trial

Thus, we propose a definitive randomised controlled trial, RaCeR 2, to address this key area of clinical uncertainty with potential to provide substantial health benefits and change clinical practice.

3 OBJECTIVES AND OUTCOME MEASURES/ ENDPOINTS

3.1 Aims

The primary aim is to assess whether individualised (early) patient-directed rehabilitation results in less shoulder pain and disability at 12-weeks post randomisation after surgical repair of full-thickness tears of the rotator cuff compared to current standard (delayed) rehabilitation.

Secondary aims include:

- Within-trial cost consequence analysis from an NHS and personal social services perspective and model-based long-term cost-effectiveness analysis
- Estimates of treatment effects across a range of secondary outcomes including shoulder pain and disability at 6 and 12-months, quality of life, time to return to usual activities including work, further healthcare use (including number of physiotherapy sessions), repair integrity, and adverse events to 12-months
- Understanding and mitigating barriers to recruitment and informed consent.

3.2 Primary Outcome

- Shoulder pain and disability at 12-weeks post-randomisation will be measured using the total Shoulder Pain and Disability Index (SPADI) score. The SPADI is a validated self-

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report measure of shoulder pain and disability (10) and was more responsive than the Oxford Shoulder Score in our RaCeR pilot RCT (11).

3.3 Secondary Outcome measures and endpoints

- Shoulder pain and disability at 6- and 12-months post-randomisation will be measured using the total SPADI score. (10)(11) Health-related quality of life at 12-weeks, 6- and 12-months post-randomisation will be measured using the EQ-5D-5L. The EQ-5D-5L is a validated measure of health-related quality of life in terms of 5 dimensions (mobility, ability to self-care, ability to undertake usual activities, pain and discomfort, anxiety and depression) each with 5 levels of severity (28).
- Time to return to usual activities, including work and driving, will be measured via self-report questionnaire at 12-weeks, 6- and 12-months.
- Healthcare resource use at 12-weeks, 6- and 12-months will be measured via self-report questionnaire.
- Rotator cuff repair integrity (evidence of full-thickness re-tear; yes/ no) at 12-months will be assessed via diagnostic ultrasound scan.
- Number and nature of adverse events at 12-weeks, 6- and 12-months will be measured via self-report questionnaire and clinician report. Adverse events might include an increase in shoulder pain requiring additional care, e.g. prescribed medication or injection; infection up to 12-weeks post-surgery; other shoulder disorders, e.g. stiffness; rotator cuff re-rupture requiring additional care, e.g. injection, physiotherapy or surgery.
- Self-report time out of sling, measured in hours, over 4 weeks post-surgery via self-report diary.

4 STUDY DESIGN

A pragmatic multi-centre, open label, randomised controlled trial with internal pilot phase using a parallel group design with 1:1 allocation ratio, with full economic evaluation, and integrated Quintet Recruitment Intervention (QRI).

4.1 Internal Pilot Phase

Our internal pilot phase will last 6 months. Table 1 describes the progression criteria:

Progression criteria	Red (Stop) **< 66%**	Amber (Amend) **≥ 66%**	Green (Go) **100%**
Average recruitment rate/ site/ month	< 0.7	0.7 - 1.0	1.1
Sites open	< 12	12 - 17	18
Participants recruited	< 50	50 - 96	97

Table 1 Internal pilot progression criteria

At the end of the internal pilot phase, in consultations with the Trial Steering Committee, we will assess study progress against Table 1 and act accordingly:

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- Green: no action required, continue to main study
- Amber: review areas of weakness and make amendments accordingly
- Red: halt, do not progress to main study

The TMG will monitor the following during the internal pilot phase of the study, and thereafter if the study progresses:

- The number of patients screened, eligible, approached and consented (randomised), and reasons if these do not happen.
- Uptake of translated patient information; frequency and languages used.
- The number of withdrawals post consent due to patients not having arthroscopic surgery.
- The number and reasons of missing total SPADI scores at 12 weeks.

Findings will be discussed by the TMG and appropriate action will be taken (if any).

4.2 Details of the intervention

a. Intervention

EPDR includes advice to the patient from a physiotherapist within 24-hours following surgery to remove their shoulder sling and gradually begin actively using their arm as they feel able and within acceptable limits of their pain. Participants record their time out of the sling in a diary to monitor and support their progress following hospital discharge. The advice to remove the sling is complemented by a specific exercise programme supervised by a physiotherapist and practised at home.

It is important to recognise that EPDR is an individualised approach where shoulder movement, sling removal, and exercise are progressed over time within the context of the participant's own pain experience and tolerance (5,12). Rather than rehabilitation, which is progressed according to pre-set timescales, EPDR reflects that individual patients have different biological, psychological and social profiles that influence progress.

After the first session with the physiotherapist, participants will access follow-up with a physiotherapist according to usual care agreements either face-to-face or via remote consultation as mutually agreed. It is expected that approximately 5 follow-up appointments will be scheduled over the 12-week period following surgery but, again, this will be mutually agreed between the patient and physiotherapist and there will be no pre-specified upper limit.

b. Comparator

Current standard (delayed) rehabilitation includes advice to the patient from a physiotherapist within 24-hours following surgery to keep their shoulder sling in place for four weeks, except for when eating, washing, dressing, or undertaking the specific exercise prescribed (3–5).

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As with the intervention, after the first session with the physiotherapist, participants will access follow-up with a physiotherapist according to usual care agreements either face-to-face or via remote consultation as mutually agreed. It is expected that approximately 5 follow-up appointments will be scheduled over the 12-week period following surgery but, again, this will be mutually agreed between the patient and physiotherapist and there will be no pre-specified upper limit. This means that both treatments will be delivered within the parameters of current NHS physiotherapy provision. Within the follow-up appointments, the specific exercise programme, reflective of current UK practice (3) will be staged as follows:

Stage 1: Fully assisted (passive) shoulder movement

Stage 2: Partially assisted (active assisted) with progression to full non-assisted (active) shoulder movement

Stage 3: Resisted static exercises (isometric)

Stage 4: Resisted exercises through shoulder range of movement (dynamic).

The key difference between the two approaches is that the intervention aims to promote a more individualised approach to rehabilitation which reflects individual patient factors including pain, pre-operative levels of function, psychological well-being, and aims to promote self-efficacy whereby the patients feel they have increased control over their recovery. Both groups will start with stage one of the specific exercise programme, but the intervention group will be supported to progress through the stages as they feel able, whereas the control group will remain at stage one for a minimum of 4 weeks, as per current standard care.

In this individually randomised controlled trial, surgeons and physiotherapists will treat patients in both arms of the trial and multiple clinicians will be involved in patients' treatment in each arm in each site. The risk of contamination is low due to the protocolised nature of standard rehabilitation but will be monitored throughout the trial through review of treatment case report forms and feedback provided to sites.

Difference between current and planned care pathways: EPDR supports an individualised (early) patient directed approach to rehabilitation where removal of the postoperative sling and introduction of movement is encouraged according to the acceptable symptom response of the patient. Patients undergoing EPDR are invited to resume activities in line with their individual progress rather than pre-set timescales, as with current standard rehabilitation. The number of sessions with the physiotherapist is as would be the case in usual care and no other aspects of the standard treatment pathway are affected.

4.3 Quintet Recruitment Intervention (QRI)

We will implement the QuinteT Recruitment Intervention (QRI) in RaCeR 2 with the aim of optimising recruitment. Rather than simply increasing the numbers of patients recruited, the QRI will aim to reduce 'missed opportunities' for enrolling eligible patients, while safeguarding informed consent. We will draw on insights from previous application of QRI methods in randomised controlled trials, and the latest recruitment related evidence to develop materials and training which will support participant accrual from the outset of RaCeR 2. Once centres open to

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recruitment, the QRI will investigate and address recruitment issues that transpire 'in real time' throughout the remainder of the scheduled recruitment period.

Pre-emptive training and materials to support recruitment to RaCeR 2

The QRI team will work closely with the TMG to support recruitment including:

- Contributions to writing patient-facing documentation (e.g., PIS) and the design of screening logs to monitor recruitment.
- Designing and delivering pre-emptive recruitment training that will be tailored to RaCeR 2 based on issues identified in the RaCeR pilot (5) and survey of surgeons' clinical equipoise (13), including reduced willingness to recruit patients as rotator cuff tear size increases. Drawing on evidence from previous QRIs, this training will provide strategies for conveying equipoise, explaining trial concepts (e.g., randomisation) and engaging with patients' views and preferences about treatment. The training will be integrated into Site Initiation Visits (SIVs)
- Providing pre-emptive 'tips and guidance' sheets for recruiters to reinforce this training and provide early support for explaining the trial to eligible patients.

Understanding Recruitment Issues that Transpire in RaCeR 2 (Phase 1)

Once sites open to recruitment, we will use mixed-methods to investigate actual (rather than anticipated) issues hindering recruitment as the trial proceeds. A flexible approach will be taken to investigate these issues in real-time, as follows:

- Semi-structured interviews with individuals involved in recruitment ('recruiters')
- Audio-recording discussions between recruiters and potential participants about RaCeR 2
- Mapping of recruitment pathways and screening log analysis

Findings from the above sources will be triangulated to generate an in-depth understanding of the 'root-causes' of any recruitment issues in RaCeR 2. This will provide a foundation for designing and implementing recommended 'actions' to optimise recruitment.

Development and Implementation of 'actions' to address recruitment challenges (Phase 2)

The QRI team will work closely with the TMG and PPI group to design and implement 'actions' to optimise recruitment. These actions will be tailored to address the root-causes of recruitment issues, based on Phase 1 findings. Actions may be applicable to all sites, specific sites, or individual recruiters, and will aim to increase the number of eligible patients approached, and/or improve conversion rates whilst safeguarding informed consent.

- Cross-site actions may include disseminating 'tips' documents with suggestions on how to explain the trial design and convey equipoise – a skill that is often trial-specific, as it requires an appreciation of the distinct advantage/disadvantages of the trial arms and

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patients' perceptions of these arms. Cross-site actions may also entail changes to patient-facing materials (e.g., to address commonly held patient misconceptions). Group 'feedback sessions' will also be organised, to address recruitment issues that are rooted in clinicians' variable interpretations of eligibility criteria and different perceptions of equipoise. Bringing recruiters together to air these issues can be a powerful means of challenging ingrained views and practices.

- Site-specific interventions may entail changes to how recruitment is organised and delivered in a particular site, facilitated by sharing examples of 'good practice' from other sites that have more efficient and effective recruitment models. These interventions will be delivered through site visits conducted in person or remotely (e.g. using web conferencing software).

A core component of Phase 2 will focus on delivering feedback on recruiters' communication with patients. Interactive 'feedback sessions' will be delivered to recruiters. These sessions will use anonymised extracts from audio-recorded consultations to illustrate how recruiters' communication can influence patients' responses to invitations of trial participation. Training videos showing simulated recruiter-patient interactions may also be developed. Individual confidential feedback will be offered to recruiters who provide recordings of their consultations.

Iterative Nature of QRI Phases

The QRI phases described above will run iteratively. New avenues of enquiry will emerge throughout the conduct of the QRI, through discussion in feedback meetings and continued monitoring of screening logs. We will pay close attention to screening log data before/after QRI-actions to formatively evaluate the impact of actions, and the need for further investigation (Phase 1) or actions (Phase 2). As mentioned above, part of the QRI will entail up-front training for sites as they open to recruitment. This training will evolve to become increasingly trial-specific as we develop our understanding of recruitment issues, with a view to ensuring sites that open in the latter stages of the trial benefit from the QRI insights that have emerged to date.

5 STUDY SETTING

This is a multi-centre randomised controlled trial, taking place in orthopaedic and physiotherapy services in NHS hospitals across the UK. We expect to open 24 sites, with a scope to increase this number if required. To ensure inclusivity we will work with a range of NHS hospitals serving diverse communities in rural and urban communities.

All sites are expected to be recruiting sites, undertaking all activities, unless individual Trusts determine that operating as a Participant Identification Centre (PIC) site is more appropriate in line with their service.

6 ELIGIBILITY CRITERIA

6.1 Inclusion Criteria

- Adults awaiting arthroscopic surgical repair of a full thickness tear of their shoulder rotator cuff, of any size

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- Able to return (remote or in-person consultation) to the recruiting centre or affiliated site for rehabilitation supported by a physiotherapist trained to deliver the study interventions

6.2 Exclusion Criteria

- No full thickness tear at surgery and/ or arthroscopic repair not undertaken
- Unable to provide informed consent
- Patients taking part in another research study that mandates the post-operative rehabilitation pathway.

7 STUDY RECRUITMENT

Recruitment processes in the study will be closely linked to the QRI, as described in Section 4.3. Involvement in the QRI is subject to consent from the recruiter (defined as anyone involved in recruitment to RaCeR 2) as well as consent from the patient.

7.1 Patient Identification and Screening

Local site staff, including surgeons, will be provided with a neutral statement to introduce the study to patients at early, initial conversations about their surgery and rehabilitation. Posters and flyers with brief information about the study will be available for sites to display in clinics if they choose, to raise awareness of the study and support recruitment.

Patients listed for rotator cuff repair surgery will be screened and assessed against the RaCeR 2 eligibility criteria by local site staff, as per local arrangements for assessing eligibility for research studies.

For each patient screened, age, ethnicity, diagnosis, and size and location of rotator cuff tear, will be collected. This is to monitor inclusivity and identify any groups that may be disproportionately excluded early in the screening process. This will be monitored by the QRI team and will be regularly reviewed by the TMG. These data are collected for screening purposes but minimised to protect patient anonymity and avoid approaching the same patient again.

Screening data will be collected on the eCRF to aid monitoring of recruitment and will capture:

- Number of patients screened
- Numbers of patients eligible
- Reasons for ineligibility (if applicable, e.g. not listed for arthroscopic repair)
- Numbers of patients approached and invited into the trial
- Reasons not approached (if applicable, e.g. treating clinician not in equipoise)
- Numbers of patients consenting
- Reasons for decline (if applicable, e.g. unable to complete outcome measures in English)
- Randomisation (Y/N)
- Randomisation allocation
- Reason not randomised (if applicable, e.g. arthroscopic repair not completed)

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Once an eligible patient has been identified and has been allocated a date for surgery, they will be provided with a participant pack containing information about the study (including the QRI) and consent forms.

7.2 Consent

7.2.1 QRI Consent Process

- *Recruiter consent*

Recruiters will be invited to take part in a QRI interview and/or audio-recording of recruitment conversations, as is appropriate to their role. Individuals will be informed about the QRI study processes via a dedicated QRI information sheet, which will be disseminated at Site Initiation Visits. This will explain the QRI processes for interviews and audio-recording of recruitment consultations. Local site staff or the QRI researcher will obtain written consent from recruiters, which will seek permission for each of the individual QRI elements (interviews and audio-recording consent discussions). Recruiters may opt to participate in just one, both, or neither of the QRI activities. Consent may be taken remotely where necessary. All QRI consent forms will be stored in the Investigator Site File (ISF).

- *Patient consent*

Details of the QRI process will be provided to patients within the main study information. Verbal consent to the audio recording of discussions relating to the study will be sought, prior to the first discussion.

7.2.2 Study Consent Process

Patients will be offered written participant information sheets and be given the opportunity to discuss RaCeR 2 with support from an interpreter as required. We will also provide sites with translated information sheets (translated according to the most common non-English languages reported across involved sites).

Whilst recruiting, details of the QRI will be included in the study information given to patients, but consent for this will be optional. Patients will be informed that their decision about QRI participation will have no bearing on their decision to participate in the RaCeR 2 randomised controlled trial, and that patients may participate in either, neither or both. Separate QRI clauses relating to recording of discussions about the study will be included within the consent form.

Recruiters will follow up in-person or with a phone call to the patient to discuss the study further and answer any questions they may have. They will have ample time to consider participation, which may mean more than one follow-up conversation. Patients will have plenty of opportunities to ask any questions they may have before deciding on their participation.

If the recruiter has consented to take part in the QRI, this follow-up conversation with the patient will be audio-recorded, provided the patient agrees to this. This will provide direct insight into how the trial is presented by recruiters and interpreted by patients. We will pay particular attention to: i) whether the trial interventions are described in a clear, accurate and balanced way; ii) ways in

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which recruiters manage patients' treatment preferences; and iii) explanations of trial processes (e.g., randomisation, follow-up).

The process of gaining informed consent may be wholly or partly undertaken remotely or in-person depending on local site and patient circumstances.

Where consent is taken remotely, the recruiter must read through the consent form with the patient and ensure understanding, as would be the case if the conversation were in person. Usually, the patient will be asked to sign the consent form and return this to the site (either by post or at their next visit). The recruiter will then receive the signed consent form, verify it has been completed correctly, sign as the person taking consent, and indicate that consent was taken remotely. If the patient does not return a signed consent form to site, the recruiter will sign the consent form, indicate that consent was taken remotely, and send it to the participant.

If it is not possible to get written consent, for example if the patient is not returning to the site prior to their surgery date, verbal consent will be acceptable to avoid unnecessary burden for the patients and site staff. The consent form must be completed by the recruiter indicating that consent was taken verbally, and a copy provided to the participant. This is the same for patients who consent to the audio recording of their discussion (QRI) but not to participating in RaCeR 2. Page 1 of the consent form must be completed to indicate consent was taken verbally (unless written consent can be obtained).

In all cases, consent must also be fully documented within the patient's medical notes, including the method of consent (remote, in-person and verbal).

It will be the responsibility of the local site Principal Investigator (PI) to ensure that all staff taking consent are appropriately trained and on the delegation log for the study. Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study. The consent process must be recorded in the patient's medical records.

Reasons for declining participation, where given, will be recorded on the screening log.

Subject to their consent, a letter will be sent to each (randomised) participant's General Practitioner (GP) to notify them of their participation in the study and allocation.

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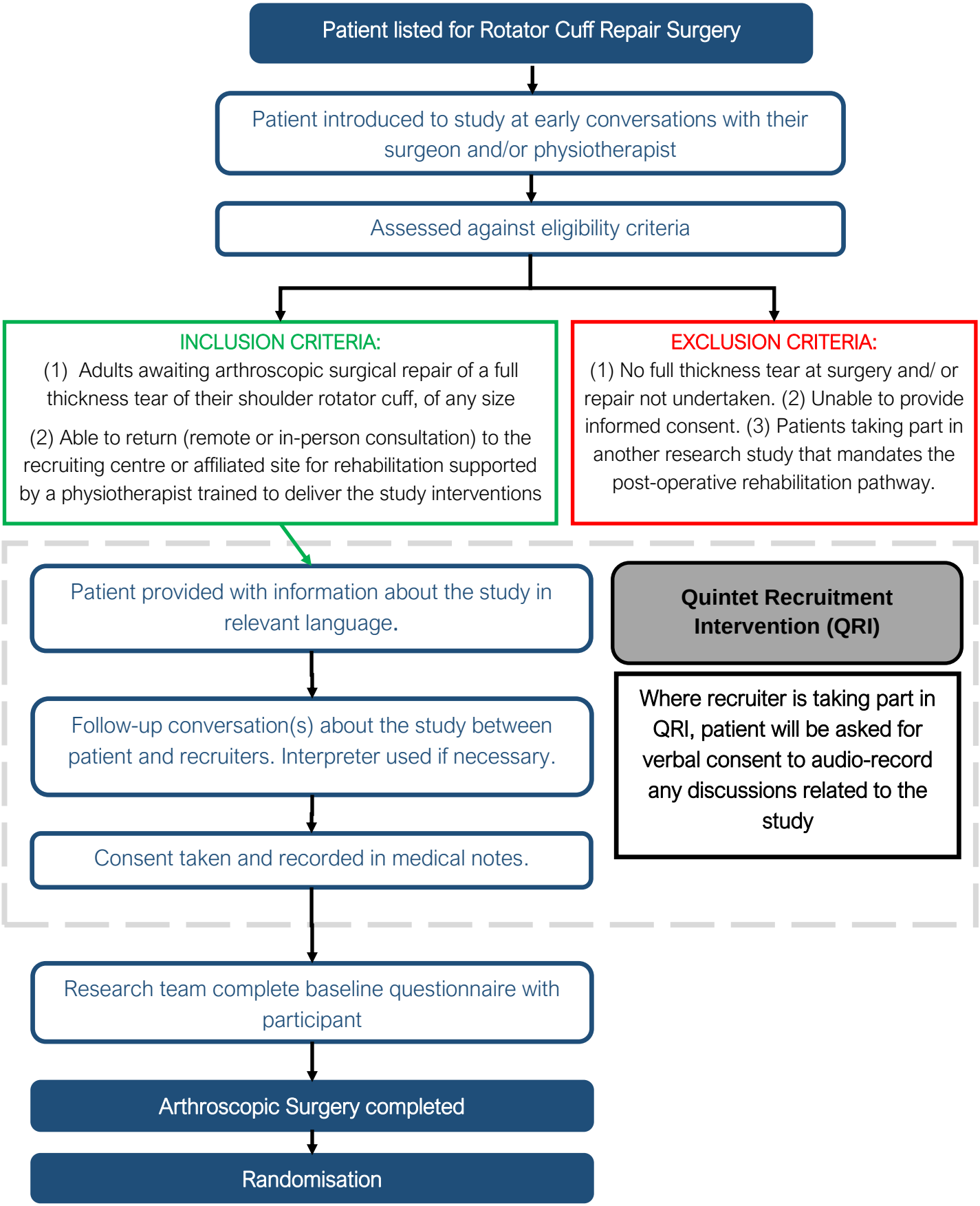

Figure 2: Summary of Recruitment Process

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7.3 Recruiter interviews

QRI researchers will conduct interviews with recruiters (i.e., research and/or clinical personnel involved in trial recruitment) (n≈10-25) to investigate perceptions of equipoise, interpretations of the RaCeR 2 rationale and underpinning evidence, recruitment challenges encountered (where relevant), and how recruitment is organised within and across sites. Numbers of interviews will be guided by intentions to achieve information power (i.e., sample holds sufficient information for a responsible analysis) (14) and pragmatic factors (i.e., finite numbers of recruiters).

Interviews are anticipated to take up to 45 minutes, and will be conducted remotely, via telephone or secure web-conferencing platforms that have been approved by the study sponsor at the time of data collection. As guidance around recommended platforms can vary, we will ensure that the QRI researchers are attuned to the latest guidance and policies to ensure secure data collection throughout the project.

Should concerning information (e.g. relating to medical malpractice) be shared in interviews, the researcher conducting the interview will discuss the information with the PI in the first instance. The PI may subsequently take appropriate steps, according to their local procedures, which may require a break in confidentiality.

8 RANDOMISATION

Consent to participate will be obtained prior to surgery, but random allocation will occur after surgery. This reflects learning from our RaCeR pilot randomised controlled trial where we randomised before surgery.

8.1 Method of Implementing the Allocation Sequence

Participants will be randomly allocated using minimisation via an online randomisation system, stratified by hospital and rotator cuff tear size (small (<1cm), medium (1cm to 3cm), large/massive (>3cm), unknown), set up by Derby Clinical Trials Support Unit (DCTSU) to ensure balanced allocation concealment. Tear size, in the antero-posterior direction, will be taken from records of pre-operative scanning, or if this is not available, from measurements taken and recorded during surgery where available.

Access to the online randomisation system will be via personal username and password, and specific to role. The study is open label and as such an urgent unblinding process is not required. Details of the randomisation method and implementation will be included in the Randomisation Specification.

If participants are no longer eligible for randomisation (i.e. they have not undergone arthroscopic surgery), they will be considered “consented, but not randomised” and will not contribute to the required sample size.

9 STUDY ASSESSMENTS

A schedule of assessments is provided on page 27.

9.1 Baseline & Post-Op Visits

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Following consent, the baseline questionnaire will be completed prior to surgery in-person or remotely.

Completion of the baseline questionnaire will require input from local site staff and participants, and site staff will work to support participants to ensure all requested data are collected.

The questionnaire will include the SPADI and EQ-5D-5L validated questionnaires as well as other demographic data including:

- date of birth
- sex,
- ethnicity,
- height and weight
- postcode,
- level of education,
- work status'
- duration of their shoulder problem,
- treatment preference,
- expected date of surgery,
- size, thickness, and location of rotator cuff tear.

Following confirmation that arthroscopic rotator cuff repair surgery has been undertaken, the participant will be randomised in advance of the first consultation with the physiotherapist. Participants must only be randomised once arthroscopic surgical repair has been completed.

If a participant does not undergo arthroscopic repair as per inclusion criteria or is deemed not to have a rotator cuff tear during surgery, they will not be randomised.

The local site team will explain to the participant their randomised allocation as well as other routine post-operative requirements. An exercise manual will be provided, along with a diary documenting time out of sling (for the first 4 weeks post-op) and a postcard to summarise the follow-up schedule.

- Control group: Those allocated to the control group will follow usual current practice, with the participant's shoulder immobilised in a sling for 4 weeks.

- Intervention group: Those allocated to the intervention will be advised to remove their shoulder sling and gradually begin actively using their arm as they feel able and within acceptable limits of their pain.

9.2 Diary to record time out of sling

Participants will be asked to complete a self-report diary daily for 4 weeks and return this to Derby CTSU via a pre-paid envelope. Participants will record in the diary for how long they were not wearing the sling at regular periods throughout the day.

9.3 Treatment Logs

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PIs (or delegates) will be asked to record information about the physio sessions delivered as part of the study to monitor treatment. The logs will record:

- Whether participants were advised to keep their arm in the sling (control group).
- Whether participants were advised to remove the sling and move their arm as able (intervention group)
- Whether participants were advised regarding the exercise programme.
- Whether participants were provided with an exercise manual and diary.
- The number of sessions attended.
- The physiotherapist who delivered most of the sessions.
- The band of the physiotherapist.

9.4 Follow-up Questionnaires

Follow-up questionnaires, including SPADI, EQ-5D-5L, self-report questionnaire for healthcare resource use, time to return to usual activities, and any adverse events, will be completed at 12 weeks, 6 and 12 months after randomisation (-1 week/ +4 weeks visit window). This process will be co-ordinated centrally by the Derby CTSU, who will ensure participants are provided access to the questionnaires and conduct follow up calls where required.

Follow up questionnaires will be available in paper or electronic format, according to participant preference. These will be posted, or a link to the electronic questionnaire sent via email or SMS ahead of the expected completion date. For each timepoint, the method of completion will be collected on the eCRF.

For those participants who have verbally consented due to difficulties reading and/ or writing, Derby Clinical Trials Support Unit will contact them via telephone at the appropriate time to complete the questionnaires.

Participants will be given a £5 voucher when the 12-week, 6- and 12-month questionnaires are completed and returned to Derby CTSU, as an incentive to encourage completion.

If participants do not complete their questionnaires at the expected timepoints, the following process will be followed:

If after 2 weeks, participants have not returned their questionnaires, a member of Derby CTSU will contact them to find out if they need any assistance and to remind them to complete them. If the questionnaire has not been received, a repeat questionnaire will be sent. If after 3-weeks the questionnaires have still not been returned, minimum data collection (per Section 9.7) will be attempted. The visit window expires at 4-weeks and attempts to contact will be made until this timepoint.

If a questionnaire is completed outside the visit window, then the responses will be recorded in the eCRF. If a participant requests to complete a questionnaire outside of the visit window, but no longer has access to the original questionnaire, then a further copy (paper or electronic) will be sent.

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Unless the participant explicitly withdraws their consent to be contacted for further follow up timepoints, they will continue to be sent the questionnaires at the next planned timepoints and the missed visit will be marked as "missed" in the eCRF.

If participants return their 12-week questionnaire and the SPADI is incomplete (i.e. less than 10 questions answered), Derby CTSU will attempt minimum data collection to obtain this primary endpoint data. Attempts to contact will be made until the visit window expires.

9.5 Ultrasound / 12-Month Visit

Local site staff will contact participants and arrange for them to return to the hospital 12-months following surgery to undergo an ultrasound scan to assess the integrity of the rotator cuff repair. The results of the ultrasound scan will be discussed with them by the clinical team and reported on the CRF.

9.6 Participant reimbursement

Participants will be reimbursed for reasonable travel expenses incurred from attendance at the 12 month follow up visit, up to £30 (exceptional circumstances will be considered). All other visits are expected to be in line with routine care visits.

9.7 Study within a trial (SWAT)

This study will be a host trial for a study within a trial (SWAT) which aims to identify and compare the characteristics of participants who choose to complete either electronic or paper participant reported outcomes (PROs) to support future trial decision making. The secondary aim is to explore the impact of patient's choice on the number of unanswered questions, the number of data queries, crossovers and return rates of PROs. Previous research acknowledges that electronic means of collecting PROs can be advantageous over the traditional paper-based methods, offering higher data quality and lower costs (15). However there remains some reticence due to technological barriers and the "digital divide", and therefore paper methods continue to be used.

For the SWAT, participants will be given the choice to complete questionnaires via paper or electronic means.

To meet the primary and secondary aims of the SWAT, we will collect data and compare, according to their choice of ePRO or paper-based questionnaire, the participant's characteristics: age, sex, ethnicity, post code, deprivation, educational status, type of rotator cuff tear, reading/writing difficulties and reasons for their preference (ePRO or paper).

Participants characteristics (sex, ethnicity, educational status, type of rotator cuff tear, reading/writing difficulties) will be compared between patient's choices using Chi-squared test. Age and deprivation score will be compared between patient's choices using Independent T-test. Logistic regression will be undertaken to compare age, sex, ethnicity, deprivation score, educational status, type of rotator cuff tear and reading/writing difficulties, between electronic and paper PROs. Linear regression will be used to compare patient's choice of electronic or paper PROs for predicting the number of unanswered questions, and the number of data queries

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(resolved and unresolved). Logistic regression will be used to compare participant's choice of electronic or paper PROs for predicting the PROs return and crossover rates.

The method of PRO completion at each timepoint will be recorded in the eCRF. This will allow us to note any changes to the choices participants may make during the study.

Table 2 Schedule of Assessments

Assessment	Timepoint					
	Screening	Baseline	Post Op	12 weeks	6 months	12 months
Eligibility assessment	X		X			
Participant invitation	X					
Screening data collected	X					
Recording of recruitment appointment/ Informed consent		X				
Baseline questionnaire completed by participant and site staff		X				
SPADI		X		**X***	**X***	**X***
EQ-5D-5L		X		X*	X*	X*
Randomisation			X			
Physiotherapy session			X			
Sling-use Diary completion+			X			
Adverse event questionnaire				**X***	**X***	**X***
Adverse event assessments (by PIs/physios)			X	X	X	X
Follow up questionnaire including details on healthcare resource use				X*	X*	X*
Ultrasound to assess repair integrity						X
Treatment log (by PIs or a delegated individual)			X			

[1]Text in **underlined bold** represents minimum data collection (MDC) for that timepoint

*co-ordinated by Derby CTSU

+required daily for 4 weeks post-surgery only

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9.8 Withdrawal Criteria

Participants will be able to withdraw from the RaCeR 2 trial at any time without affecting the clinical care they receive.

However, to minimise missing data, participants should be given the option to modify their involvement, whilst remaining in the study. Options are:

- Withdraw from or alter the allocated rehabilitation program but continue to provide follow up data
- Reduce questionnaire burden and be contacted by phone to complete the questionnaires, either in full or provide minimum data as follows:
    - SPADI
    - Adverse events

Any change in the level of participation will be documented on the Participation Change Form, and a copy provided to the participant. Change in participation and/or withdrawal from the study will also be documented on the appropriate form on Dacima. Participants moving away from the region of the site where they had surgery and initial rehabilitation do not need to be withdrawn from the trial for this reason.

It is always within the remit of the local care team responsible for a patient to withdraw a patient from the study for appropriate medical reasons.

9.9 End of Study

The end of study will be defined as the last participant's received questionnaire or visit for ultrasound scan at 12 months (whatever is latest). Derby CTSU will notify the Sponsor, participating sites, and REC within 90 days of the end of study. The final report required by the REC and HRA will be submitted within 12 months of the end of study.

10 SAFETY REPORTING

Adverse Event (AE) definitions can be found in Appendix 2.

10.1 Reportable (S)AEs

Participants will be asked if they have experienced any of the following adverse events (AEs):

- An increase in shoulder pain requiring additional care, e.g. prescribed medication or injection;
- Infection up to 12-weeks post-surgery requiring additional anti-biotic prescription;
- Other shoulder disorders, e.g. stiffness, requiring additional care, e.g. injection, physiotherapy or surgery;
- Rotator cuff re-rupture requiring additional care, e.g. injection, physiotherapy or surgery.

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- Any reaction to sling use which results in discontinuation of the sling
- Any problems with wound healing
- Any other serious health problem

Any individual who is delegated AE recording and reporting duties is responsible for reporting all SAEs to the Derby CTSU using the eCRF within 24 hours of becoming aware of the event.

The following AEs/ SAEs are not required to be recorded in the eCRF:

- Transient increase in shoulder pain that the participant manages without need for clinical consultation
- Any clinical consultations for pre-existing health conditions

10.2 Process for Reporting (S)AEs

All reportable AEs will be reported from the time of randomisation until completion of the 12-month follow-up point, on the eCRF unless specified otherwise in 10.1.

Where AEs are identified by the site, the PI, or other delegated individual, will report these on the eCRF. This may be through discussions with the participant, or through review of the participant's medical records.

Participants will self-report AEs at the follow-up questionnaire timepoints.

When AEs are entered onto the eCRF, the Chief Investigator, Associate Investigator or delegated individual with appropriate medical training (as determined by the CI) will be alerted and required to categorise each AE and assess for seriousness, causality, and expectedness (SAEs only), per Section 10.3 (participants will complete assessment of severity at the point of entry).

When an AE is identified as being serious (SAE), an additional SAE form will be completed via the eCRF for reporting to the Sponsor.

If an SAE is deemed related and unexpected, the 'non-CTIMP safety report to REC form' available from the HRA website is to be completed by Derby CTSU and submitted to REC within 15 days of becoming aware of the event. Safety information will be reviewed during TMG/TSC meetings.

10.3 Assessment of (S)AEs

Assessment of severity is completed by the individual completing the initial AE details on the CRF.

Severity	
Mild	no interference with daily activities.
Moderate	moderate interference with daily activities.
Severe*	considerable interference with daily activities (e.g. inability to work).

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* To avoid confusion or misunderstanding the term “severe” is used to describe the intensity of the event, which may be of relatively minor medical significance, and is NOT the same as “serious” which is described in the safety definitions.

Seriousness
An AE is considered serious if it meets any of the following criteria: • results in death • is life-threatening+ • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other ‘important medical events’ may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

+ "life-threatening" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Causality	
Clinical judgement should be used to determine the relationship between the study procedures and the occurrence of each AE.	
Not related:	There is no evidence of a causal relationship between the event and study procedures.
Related:	There is evidence of a causal relationship between the event and study procedures i.e. a relationship to the study procedures cannot be completely ruled out.

Expectedness	
The assessment of expectedness is only required if the event is serious **and** deemed to be related to study procedures.	
Expected:	• Other shoulder disorders, including Frozen shoulder, requiring hospital admission for treatment, e.g. surgical release • Rotator cuff re-rupture requiring hospital admission for treatment, e.g. revision rotator cuff repair surgery • Deep shoulder or systemic infection requiring hospital admission for treatment, e.g. further surgery • Pulmonary embolism or deep vein thrombosis • Pneumonia • Myocardial infarction

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	• Cerebrovascular event, e.g. stroke
Unexpected:	Event not previously described in the protocol. N.B. Unexpected (related) SAEs must be reported to REC as per Section 10.1

10.4 Reporting Urgent Safety Measures

If any urgent safety measure is taken the research team should inform the Derby CTSU within 24 hours using the Derby CTSUs safety incident reporting form. The Derby CTSU will inform the REC and participating sites of the measures taken and the circumstances giving rise to those measures within 3 days on implementation of the urgent safety measure.

11 DATA HANDLING

A Data Management Plan will be written with more detail on the data handling for the study, the following section serves as a summary.

11.1 System and Compliance

An electronic software platform will be used to store participant study data as detailed in section 11.3. Data entry will be via a web-based, fully validated system, compliant with 21 CRF Part 11; Electronic records; Electronic signatures and EU Commission Directive 2005/28/EC with comprehensive audit trials. Derby CTSU will be responsible for database build and system validation. Data will be hosted externally according to General Data Protection Regulation guidance.

Entry into the database will vary per participant, but will be performed by site staff, participants themselves via ePRO, DCTSU staff from paper questionnaires, diaries and phone calls with the participant.

11.2 Source Data

Source data is the term used to mean the place where data are first recorded. This will include medical records containing key eligibility data, as well as paper study documents including the consent form, questionnaires, and PROs. The eCRF may also serve as source data.

Source data must be kept in line with the archiving requirements outlined in section 11.6.

Where any original paper documentation is required to be sent to Derby CTSU from the participating sites, sites must keep a copy for their ISF.

11.3 Data Handling and Record Keeping

The DCTSU Data Management (DM) team will design the database to capture the clinical data in accordance with the best principles of clinical data management and the relevant SOP on Case Report Form and Database Selection, Development & Release developed by Derby CTSU.

When data are entered into the EDC (by site staff, the participant or DCTSU staff), validation checks will be performed on the data to ensure accuracy and consistency according to the study Data Validation Plan. All data queries generated as a result of these checks will be available for resolution by the site online. After data entry is complete, all data queries have been resolved,

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any required coding is complete and all forms have been signed by the PI, the database will be locked and released for statistical analysis.

All clinical data will be collected, stored, processed, and archived in accordance with the Data Management Plan for this trial and in line with the relevant SOPs on Data Entry, Data Closeout Activities and Archiving developed by the Derby CTSU and any relevant legislation.

11.4 Coding

The MedDRA coding dictionary will be used to code adverse events. When an event is entered into the database, the system will attempt to auto-code the reported term. If the term is able to be auto-coded, the term can be approved by the individual delegated to perform coding. If the term is not able to be auto-coded, the delegated individual must manually code the term. More detail around coding will be recorded in the Data Management Plan.

11.5 Audio recordings – QRI

Recordings of discussions where the trial is discussed will be taken using an encrypted digital recorder and regularly uploaded by site staff onto the study database. Access to the recordings will be granted to appropriate University of Bristol employees who will be able to download the recordings (following confirmation of consent). All data will be stored in a password protected drive maintained by the University of Bristol.

Recordings will be transcribed in full or part by University of Bristol employees or University approved transcription services as soon as possible after each recording has been received. If an approved external transcription service is used, the transfer of recordings and transcripts will adhere to the secure transfer of recordings/transcripts procedure specified by the University. Transcripts will be labelled with a study-assigned participant number, edited to ensure anonymity of respondents and stored adhering to the University's secure data storage policies.

11.6 Data Access and Security

Direct access will be granted to authorised representatives from the Sponsor, Derby CTSU, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections.

All documents will be stored safely in confidential conditions. With the exception of regulatory authorities, only authorised members of the study team will have access to source documents.

Access to the study database will be role-specific and password protected. DCTSU DM will control access, granting access to sites as recorded on the Delegation Log(s). The CI, PI, DCTSU staff and University of Bristol staff will be given appropriate access dependent on their role, which will be recorded in a study Attributes file.

Each participant will be assigned a participant ID for use on study forms, other study documents and the electronic database. The investigator and trial team will ensure that the participant's identity is protected at every stage of their participation within the trial. If any patient information needs to be sent to a third party the trial team will adhere to maintaining pseudo-anonymous participant parameters in correspondence.

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11.7 Archiving

At the end of the study, following completion of the end of study report, Derby CTSU will ensure that study related documentation is securely archived for a minimum of 10 years. After this, arrangements for confidential destruction will be made. It is the responsibility of each PI to ensure that data and all essential documents relating to the study are retained securely for a minimum of 10 years after the end of study, and in accordance with national legislation. Derby CTSU will notify sites when study documentation held at sites may be archived, and then destroyed. All archived documents must continue to be available for inspection by appropriate authorities upon request.

12 STATISTICS AND DATA ANALYSIS

The statistical analysis will be undertaken by the study statistician. Analysis of the QRI data will be undertaken by the QRI researchers. The study statistician will draft the Statistical Analysis Plan (SAP) according to CTU-SOP-019 Statistical Analysis Plan, which will be reviewed by the Chief Investigator, and the Trial Steering Committee (TSC). Full details will be developed and agreed in the final SAP. The finalised SAP will be approved and signed by the CI and the study statistician.

12.1 Sample Size Calculation

Based on total SPADI score at 12-weeks with MCID of 8 points (16), standard deviation of 30 (the upper 80% confidence limit from the pilot RCT (5)), power 90%, and significance level 5%, using an independent T-Test, 297 participants per group (594 in total) are required [Stata command: "power twomeans 37, diff(8) sd(30 power (0.9)"]. However, using ANCOVA (primary analysis), adjusting for the baseline SPADI score, where correlation (r) between baseline and 12-weeks = 0.2 (data from pilot Racer RCT), then the sample is adjusted by $(1-r^2)$ plus one extra participant per group (16). Adjusting for 10% non-response of SPADI questionnaire at 12 weeks, then 319 participants per group (638 in total) should be randomised.

12.2 Planned Recruitment Rate

We expect to work with a range of recruiting sites with different recruitment potential. Our projections for the internal pilot phase, which inform the progression criteria in section 4.1, are detailed in Table 3.

	SITE 1	SITE 2	SITE 3	SITE 4	SITE 5	SITE 6	SITE 7	SITE 8	SITE 9	SITE 10	SITE 11	SITE 12	SITE 13	SITE 14	SITE 15	SITE 16	SITE 17	SITE 18
Recruitment start date	Jun-23			Jul-23			Aug-23			Sep-23			Oct-23			Nov-23		
Months to reach min recrutiment	3	3	1	3	1	1	3	1	1	3	1	1	3	1	1	1	1	1
Min recruitment per month	3	3	1	3	1	1	3	1	1	3	1	1	3	1	1	1	1	1
Total recrutiment at 6 m (97 patients)	15	15	6	12	5	5	9	4	4	6	3	3	3	2	2	1	1	1

Table 3 Recruitment forecast for the internal pilot phase. Recruitment is defined as the time of randomisation.

Through the internal pilot phase, we would aim to recruit both large and small recruitment sites. This is reflective of real-world clinical practice and so will help with generalisability of trial findings but will also ensure geographical diversity. The large sites have a recruitment target of three

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participants per month and the small sites have a recruitment target of one participant per month with a specified run-in period before recruiting to the monthly target. For example, University Hospitals Derby and Burton NHS Foundation Trust, considered a large recruiting site, have a recruitment target of three participants per month and we would expect them to reach that monthly target by month three.

Over the entire recruitment period (24 months) we have also factored in a staged setup of recruiting sites (3 sites per month), and a recruitment plateau to recognise that recruitment to pragmatic trials reduces towards the end of such recruitment periods.

12.3 Analysis of QRI Data

QRI researchers will compare recruitment pathways with screening data to identify points where patients are lost, and practices that are conductive or counter-productive to efficient and effective recruitment.

Screening data for RaCeR 2 will include information about each patient screened, including whether they were eligible, approached, consented, randomised, accepted/declined their allocation, and the allocated treatment. Screening data will be analysed and summarised descriptively.

Audio-recorded interviews and recruitment consultations will be transcribed and labelled with a study-assigned participant number, edited to ensure anonymity of respondents, and stored securely adhering to the University's data storage policies. Data will be managed using qualitative data analysis software (such as NVivo). The interviews with recruiters (above) will be used to map out the recruitment pathway for each site, noting processes for screening and identifying eligible patients, how patients are approached, and the personnel involved in these activities

Interviews and recruitment consultations, along with screening data and study documentation, will be subject to simple counts, content, thematic and targeted conversation analyses. There will be a focus on aspects of information provision that are unclear, disrupted, or potentially detrimental to recruitment and/or adherence. Standard approaches to enhancing rigour, such as double-coding, triangulating, and seeking out 'negative cases', will be employed throughout the conduct of the QRI. A detailed description of how the QRI methodology achieves rapid analysis whilst maintaining rigour is detailed elsewhere(17).

12.4 Summary of Baseline Data and Flow of Patients

Analyses will be reported in line with the CONSORT statement. Descriptive statistics will be presented to summarize the distribution of baseline variables across each of the randomisation groups. The continuous baseline variables (age, height, weight, deprivation score, duration of shoulder problem, size of tear, length of shoulder pain) will be reported with means & Standard Deviations, if shown to be normally distributed, using a combined skewness and kurtosis test, otherwise will be reported with medians & Interquartile Ranges (IQR). The categorical variables (size of tear, sex, ethnicity, level of education, location of tear, work status, treatment preference) will be reported with frequencies & percentages.

A Consolidated Standards of Reporting Trials (CONSORT) flow diagram will be produced, showing the frequency of patients/ participants;

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- Screened for eligibility,
- Reason for not being eligible,
- Found eligible,
- Reasons not approached,
- Approached,
- Excluded before consent and reason for exclusion
- Consented
- Excluded before randomisation and reason for exclusion,
- Randomised,
- Allocated to each randomisation group,
- That received each allocated intervention,
- That did not receive each allocated intervention,
- Lost to follow-up (and the frequency of each reason for loss to follow-up) for each analysis group,
- Analysed for each analysis group,
- Not analysed (and the frequency of each reason for not being analysed) for each analysis group.

12.5 Primary Outcome Analysis

Primary analyses will be conducted according to intention-to-treat analysis group. ANCOVA will be used to compare total SPADI scores between EPDR and standard rehabilitation at 12 weeks adjusting for baseline SPADI score.

12.6 Secondary Outcomes Analysis

Among other secondary analyses, time to return to usual activities (work & driving) will be analysed using Kaplan-Maier curves and log rank test. Logistic regression will be undertaken to test the association between treatment groups and re-tear at 12 months. Linear regression will be used to test the association between treatment groups and time out of sling over 4 weeks. Mixed effects models will be used to test any between groups differences up to 12 months in terms of SPADI. ANCOVA will be used to compare total SPADI and EQ-5D-5L scores between the treatment groups at 6 and 12 months adjusting for the baseline scores.

Safety analysis will be undertaken based on the per protocol analysis group. Presence of AEs / SAEs (related and non-related) and problems after surgery will be compared between the two groups at 12 weeks, 6- and 12-months using Chi-Squared test.

12.7 Subgroup Analyses

Subgroup analysis will be undertaken for the primary endpoint including an interaction term in the ANCOVA model of “rotator cuff tear size” by “treatment group”.

12.8 Interim Analysis and Criteria for the Premature Termination of the Study

The Derby CTSU and/or Sponsor may suspend or prematurely terminate either the entire study, or the study at an individual site, for significant reasons that must be documented (e.g. an unacceptable risk to participants or serious repeated deviations from the protocol/ regulations). If

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this occurs the Derby CTSU/ Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e. participants, investigators, participating sites, REC, regulatory bodies).

Interim descriptive analysis will be undertaken at 6 months from the start of recruitment in order to assess the progression criteria of the internal pilot phase. The average recruitment rate / site / month, and number of participants recruited will be presented per group and aggregated for both groups. The number of sites open in total and per month will be presented. The results will be presented to TSC for their decision. Recruitment will not be suspended during the interim analysis stage.

12.9 Analysis Groups

Intention-to-treat Analysis Group: Including patients in their initially randomised group regardless of any protocol deviations.

Per Protocol Analysis Group: This is a subset of the ITT Analysis group. Including:

- Participants who received the randomised treatment allocation as planned and per protocol,
- For participants randomised to EPDR this means including those with total time out of sling of 222.6 hours or more over 4 weeks,
- For participants randomised to the comparator group those with total time out of sling less than 222.6 hours based on the cut-off values from the pilot RACER study (5). Missing values in the diary will not be included in the analysis. Participants discovered after the event, not to be eligible at the time of consent, will be excluded from the per protocol analysis group.

12.10 Procedure(s) to Account for Missing or Spurious Data

Follow up reminders and phone calls will be undertaken to minimise the missing SPADI scores at 12 weeks, 6 and 12 months, as described in Section 9.3. Complete cases analysis will be undertaken as part of the primary endpoint analyses, where cases with missing values or those completed outside the 4 weeks visit window will be excluded in each analysis. This supports our approach in the sample size estimations where the sample size was adjusted for 10% non-response of SPADI questionnaire at 12 weeks. The non-response rate will be monitored throughout the trial and remedial actions will be undertaken if it is approaching the 10%. If substantial missing data (>10% and <20%) are observed in the primary endpoint or a key prognostic covariate for the primary analysis, then multiple imputation using chained equations will be applied. Otherwise, complete cases analysis will be undertaken as part of the primary endpoint analyses. Complete cases analysis will be undertaken for the secondary study outcomes.

12.11 Sensitivity Analyses

Sensitivity analyses of the primary endpoint will be undertaken:

1. based on the Per Protocol group,

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2. where the missing total SPADI scores and those outside the 4 weeks visit window will be imputed using chained equations,

3. where the missing total SPADI scores will be imputed using chained equations, and the actual values outside the 4 weeks visit window will be used,

4. where the use of any concomitant medication for pain relief (yes / no) and the total number of concomitant medications for pain relief following randomisation will be used as a covariate in the ANCOVA model.

12.12 Economic Analysis

The economic analysis will be implemented in three phases. In the first phase, we will develop an initial conceptual cost-effectiveness model to inform the estimation of the long-term costs and QALYs of EPDR and standard rehabilitation in RaCeR2. The initial model will be populated with parameters derived from the RaCeR pilot data, integrated with information from published sources where relevant. The second phase of the economic evaluation will be a within-trial cost-consequences analysis to quantify the healthcare resource use, costs and health benefits observed during the RaCeR2 trial period for each treatment group. In the third phase, a model-based economic evaluation will be carried out to estimate the long-term cost-effectiveness of EPDR versus standard rehabilitation. This will update the initial value of information analysis (pre-trial) using the data collected in the RaCeR2 trial.

Primary data from the RaCeR pilot study on changes in health-related quality of life (HRQoL) measured using the EQ-5D-5L, Oxford Shoulder Score (OSS) and Shoulder Pain and Disability Index (SPADI) will be used to inform the model parameters. Relevant clinical events relating to rehabilitation following rotator cuff repair will be determined through a search of published literature and consultation with clinicians. These will be used to develop an initial state transition (Markov) decision analytic cost-effectiveness model. The uncertainty associated with the parameters will be characterised using probability distributions.

Value of information analysis will be conducted to estimate the level of decision uncertainty associated with RaCeR2's cost-effectiveness given the existing evidence base and determine whether the cost of the main trial is likely to be offset by its contribution to reducing the current level of uncertainty with RaCeR2's cost-effectiveness.

12.13 Within trial cost consequence analysis

A within-trial cost consequence analysis will be performed comparing EPDR and standard rehabilitation with data collected alongside RaCeR2. Health benefits will be quantified in terms of changes in health-related quality of life (HRQoL) as measured by the EQ-5D-5L instrument, the health benefit measure recommended by NICE for use in economic evaluation studies. Healthcare resource use will be estimated from data collected in the RaCeR2 trial. Healthcare resource use will be costed using national average figures (e.g., BNF for drugs, PSSRU unit costs and NHS reference costs for other healthcare resources). We will follow current guidelines in conducting and reporting economic evaluation for this (18).

Descriptive statistics (e.g., mean, standard deviation, interquartile range) for health care resource use, total costs and EQ-5D will be reported at baseline (EQ-5D only), 12 weeks, 6- and 12-months

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follow-up. Uncertainty analysis will comprise the estimation of 95% confidence intervals around incremental costs and health outcomes. The impact of patients' baseline characteristics on healthcare resource use, costs and EQ-5D will be assessed using regression models (e.g., two-part or GLM models for costs(19–21); Beta-based regression (22) and adjusted limited-dependent variable mixture models(23) for EQ-5D if required. Given that the trial follow-up is 12 months, costs and health benefits in the within-trial analysis of RaCeR-2 will be left undiscounted. Clinical primary outcomes will be analysed as part of the statistical analysis plan as described in sections 12.5 and 12.6.

12.14 Model-based economic analysis

In addition to the within-trial analysis, results will be combined with prior data on costs and health outcomes of the EPDR and standard rehabilitation following rotator cuff repair. The long-term costs and health outcomes of EPDR and standard rehabilitation (beyond the trial duration) will be modelled in terms of their impact on clinically relevant events (e.g., re-tear, re-operation). For this, we will update the state-transition model developed in the pre-RCT phase with parameters derived from data collected in RaCeR-2 and (where relevant) the published literature. Transition probabilities between health states and the occurrence of the clinical events of interest will be governed by a series of risk equations estimated from the RaCeR2 trial data and linked to the costs and EQ-5D- regression equations developed for the within-trial analysis. The final structure of the cost-effectiveness model will be informed by the initial phase (e.g., model conceptualisation, analysis of RaCeR pilot data). For these reasons we are unable to prespecify at this stage the details of the model's features. One possibility will be to define individual membership of health states on the basis of changes in the primary clinical outcomes as observed during the study period. More details will be provided at a later stage once the model conceptualisation work is complete, and the analysis of RaCeR pilot data has been conducted.

The costs and EQ-5D regression models will be reformulated (to reflect the longitudinal nature of the outcomes of interest) and re-estimated to derive input parameters for the state-transition model (e.g., the cost and EQ-5D associated with the membership of a given health state; the impact of an undesirable clinical event on the mean cost and EQ-5D). The results will be presented in terms of incremental mean costs per incremental QALYs gained, if appropriate. Probability distributions will be used to characterise sampling uncertainty for each model input parameter (e.g., Beta for probabilities, Gamma for costs). The impact of parameter uncertainty on decision uncertainty will be propagated using probabilistic sensitivity analysis (PSA), and structural uncertainty (e.g., incidence of retear beyond study follow-up) will be assessed using scenario analyses, the results of which will be represented using cost-effectiveness acceptability curves. This curve depicts the probability associated with recommending EPDR as a cost-effective therapy for different cost per QALYs threshold values. Furthermore, the results of the PSA will be used to conduct a value of information analysis to identify which parameters are associated with the greatest source of uncertainty and thus quantify the value of further research.

The perspective for both within-trial and model-based analyses will be that of the NHS and Personal Social Services (PSS). Following NICE guidelines, long-term costs and benefits will be discounted at 3.5%(24).

13 MONITORING, AUDIT AND INSPECTION

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The Investigator(s) must ensure that source documents and other documentation for this study are made available to study monitors, the REC or regulatory authority inspectors. Authorised representatives of the Derby CTSU/ Sponsor may visit the participating sites to conduct audits/ inspections.

Monitoring and source data verification will be conducted by the Derby CTSU according to the risk assessment and study monitoring plan. The extent and nature of monitoring will be determined by the study objectives, purpose, design, complexity, blinding, number of patients and sites, and endpoints. Audits will be conducted by the Sponsor according to their audit plan; these may be central or site audits and may be study or process-level audits.

14 ETHICAL AND REGULATORY CONSIDERATIONS

14.1 Assessment and Management of Risk

This study has been risk assessed by the Sponsor and Derby CTSU according to their Standard Operating Procedures (SOPs). A full risk assessment has been completed by Derby CTSU to identify any risks and mitigating actions, which have fed into the study design, development of the protocol and the study monitoring plan.

14.2 Peer review

This study has been peer reviewed as part of the NIHR application process. The protocol has been reviewed by the NIHR and RaCeR 2 TSC prior to submission for approval.

14.3 Public and Patient Involvement/Engagement (PPI/E)

With support from patients and the public, we have already completed a pilot study (funded by NIHR) which has informed the design of this protocol. We have continued to work with patients, who have experience of rotator cuff tears and surgical repair who have helped us design this definitive study. One of the patients is a co-applicant and will join the Trial Management Group. PPI members will also co-produce patient-facing materials and help with dissemination of our findings.

14.4 Research Ethics Committee (REC) & Regulatory Considerations

The study outlined in this protocol is developed from a previous pilot randomised controlled trial and integrated qualitative study for which REC and HRA approval was granted (REC Ref 18/WA/0242 and IRAS Project ID 232678),

The study will be conducted in compliance with the approved protocol, the Declaration of Helsinki and the UK Framework for Health and Social Care Research. The protocol and all related documentation (e.g. informed consent form, participant information sheet, questionnaires) have been reviewed and received approval by a Research Ethics Committee (REC) and Health Research Authority (HRA). Participant activities must not begin until approval from the HRA and REC has been obtained and documented. All documentation and correspondence must be retained in the trial master file/investigator site file.

It is the responsibility of the Derby CTSU to ensure that an annual progress report (APR) is submitted to the REC within 30 days of the anniversary date on which the favourable opinion was

given, annually until the study is declared ended. The Derby CTSU is also responsible for notifying the REC of the end of study (see Section 6.9) within 90 days. Within one year of the end of study, the Sponsor will submit a final report with the results, including any publications/abstracts to the REC.

Before any site can enrol a patient into the study confirmation of capacity must be sought from the site's research and development (R&D) department.

14.5 Amendments

If changes to the study are required these must be discussed with the Sponsor, who is responsible for deciding if an amendment is required and if it should be deemed substantial or non-substantial. Substantial amendments will be submitted to the relevant regulatory bodies (REC, HRA) for review and approval. The amendments will only be implemented after approval and a favourable opinion has been obtained. Non-substantial amendments will be submitted to the HRA for their approval/ acknowledgment. Amendments will not be implemented until all relevant approvals are in place. All amendments must be notified to participating sites prior to implementation.

14.6 Protocol Compliance & Non-Compliance Reporting

The Principal Investigator at each site is responsible for ensuring that the study is conducted in accordance with the procedures described in this protocol. Prospective, planned deviations and/or waivers to the protocol are not acceptable, however accidental protocol deviations (non-compliances) may happen and as such these must be recorded on the eCRF. All non-compliances should be reviewed and assessed by the trial manager and Senior Trial Manager to determine if they meet the criteria of a "serious breach" (Section 12.6). Non-compliances which are found to frequently recur are not acceptable, will require immediate action, and could potentially be classified as a serious breach.

14.6.1 Notification of Serious Breaches to GCP and/or the Protocol

A "serious breach" is a departure from the protocol, Sponsor procedures (i.e. SOPs), or regulatory requirements which is likely to effect to a significant degree –

→ The safety or physical or mental integrity of the subjects of the study; or

→ The scientific value of the study.

If a serious breach is identified the Derby CTSU must be notified immediately (i.e. within 1 working day) using the 'Non-CTIMP Notification of a Serious Breach' form. The report will be reviewed by the Derby CTSU and CI, and where appropriate, the Derby CTSU will notify the REC within 7 calendar days of being made aware of the breach.

14.7 Data Protection and Patient Confidentiality

The study will be conducted in accordance with the Data Protection Act 2018. The investigator must ensure that participant's anonymity is maintained throughout, and following completion of, the study. Participants will be identified on all study specific documents, (except for the informed consent form, enrolment log and questionnaires (where necessary), only by the participants study specific identifier. This includes both electronic and paper documents. Participants' contact

details will be recorded and stored securely by Derby CTSU for the purposes of administering the follow up questionnaires. This includes their name, address and/or email address and telephone number. Access to this will be restricted to the members of the Derby CTSU who require this to fulfil study requirements.

Transcripts from recordings will be anonymised, and where audio clips are used, these will be voice-modified to protect anonymity.

All documents (paper and electronic) will be stored securely with access restricted to study staff and authorised personnel.

The Chief Investigator will act as the custodian of the data generated in the study.

14.8 Indemnity

As UHDB is acting as the research Sponsor for this study, NHS indemnity applies. NHS indemnity provides cover for legal liabilities where the NHS has a duty of care. Non-negligent harm is not covered by the NHS indemnity scheme. UHDB, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional circumstances an ex-gratia payment may be offered.

14.9 Access to Final Study Dataset

Data produced from the study will be made available to other researchers upon request, subject to approval by the Sponsor, where this is not already covered in a data sharing agreement or collaboration agreement.

Anonymised quotations and parts of voice modified audio-recordings may be used for training, teaching, research and publication purposes for RaCeR 2 and future studies. Anonymised transcripts may be made available to other researchers (including those outside of the Universities) by controlled access if they secure the necessary approvals for purposes not related to this study, subject to consent from participants.

15 DISSEMINATION POLICY

As the Sponsor, UHDB NHSFT will own data and results arising from the study. On completion of the study, a final study report will be prepared and shared with the NIHR as the Funder of the study. A report will also be shared with REC per the conditions of favourable opinion.

In all outputs, the Funder and Sponsor will be duly acknowledged.

We anticipate a range of outputs from the RaCeR 2 trial, including:

- Trial data that will influence patient decision-making, clinical practice, and clinical guidelines
- Data that will help understand approaches to optimising informed consent in orthopaedic trials
- Manuals to guide rehabilitation after rotator cuff repair, for patients and clinicians.
- Videos describing the trial results to support patient and clinical decision making

- NHS workshop events to disseminate the results of the trial and the approaches to rehabilitation evaluated in the RaCeR 2 trial
- National and international conference presentations
- Peer-reviewed publications including the study protocol, reports of the results of the trial in terms of clinical- and cost-effectiveness, economic modelling, and findings of the Quintet Recruitment Intervention.
- Blogs and social media posts from the research team describing the progress of RaCeR 2, the results, and signposting to study-related resources.
- Key stakeholders to inform and engage include patients undergoing rotator cuff repair, surgeons performing rotator cuff repair surgery, physiotherapists supporting rehabilitation after surgical repair, the British Elbow and Shoulder Society (BESS) and the Chartered Society of Physiotherapy (CSP).

15.1 Authorship Eligibility Guidelines and any Intended Use of Professional Writers

Authorship will be determined as per the criteria outlined the International Committee of Medical Journal Editors(25).

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17 APPENDICES

17.1 Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
-	2.0	22/MAR/2023	RS, CL, AR	Changes made following HRA and REC review of the study, prior to approval
-	2.1	05/APR/2023	RS, CL	Changes made to follow up with further information requested from REC
1	2.2	14/APR/2023	AF	Addition of "unknown" tear size for randomisation stratification
12	2.3	22/MAR/2024	RS, KI, AF, ZC	Clarification around treatment logs, questionnaire visit windows, statistics and staffing updates.
15	2.4	09/MAY/2024	KI	Minor update to safety reporting process and non-compliance reporting.
18	3.0	05/MAR/2025	KI	Update to contact details for CL and VGc, extension to recruitment and study end date, clarification around receiving out of window questionnaires and inclusion of postcard in participant post-surgery pack

Detail all protocol amendments. Protocol amendments must be submitted to the Derby CTSU & Sponsor for approval prior to submission to the REC.

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17.2 Appendix 2 – Adverse Event Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant, including occurrences which are not necessarily caused by or related to study procedures.
Related (S)AE	An untoward and unintended response in a participant to a study procedure. This means that a causal relationship between the study procedure and an (S)AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Related & Unexpected SAE	A serious adverse event that; • is believed with reasonable probability to be due to one of the study procedures. • the nature and severity of which is not consistent with the information provided in the protocol i.e. it is not listed as an expected occurrence.

The following circumstances are usually not considered SAEs:

- Routine treatment or monitoring of the studied indication not associated with any deterioration in condition.
- Treatment, which was elective or pre-planned, for a pre-existing condition not associated with any deterioration in condition.
- Any admission to hospital or other institution for general care where there was no deterioration in condition.
- Treatment on an emergency, outpatient basis for an event not fulfilling any of the definitions of serious as given above and not resulting in hospital admission.

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