Trials

STUDY PROTOCOL

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ARC (Australian Rotator Cuff) trial: study protocol for a randomised placebo-controlled trial comparing rotator cuff repair to no repair during arthroscopic shoulder surgery for people with shoulder pain and non-acute rotator cuff tears

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Abstract

Background Degenerative rotator cuff tears are common and are often treated with surgical repair. Randomised trials have not shown a clear advantage to surgery over non-surgical treatment, but there have been no published placebo-controlled trials investigating rotator cuff repair. This study aims to compare arthroscopic shoulder surgery with rotator cuff repair to surgery without rotator cuff repair (placebo) for improving shoulder pain and function in people with shoulder pain and full-thickness degenerative rotator cuff tears.

Methods The study is a multicentre two-parallel arm, blinded, individually randomised controlled trial (RCT). Participants will be people aged 40–75 years (inclusive) with more than 6 months of shoulder pain, a degenerative (non-traumatic) full thickness rotator cuff tear 1 to 4 cm in length for whom surgery is recommended and repair of the tear is the main reason for surgery. The intervention is arthroscopic surgery (including—as indicated—bursectomy, debridement, acromioclavicular joint resection, acromioplasty and biceps tenodesis or tenotomy) with rotator cuff repair. The control is the same arthroscopic shoulder surgery without rotator cuff repair. Participants will be randomised to cuff repair or no cuff repair in a 1:1 ratio intra-operatively, after all other surgical procedures have been performed. Participants, follow-up surgeons, physiotherapists, study staff and statisticians will be blinded. Post-surgical rehabilitation will be usual care for rotator cuff repair in both groups. The primary outcome will be shoulder pain and function measured using the Western Ontario Rotator Cuff Index at 6 months post-surgery.

Discussion The ARC trial will provide low bias evidence on a common surgical procedure: rotator cuff repair for degenerative tears.

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Trial registration The trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12620000789965) on 5 August 2020 and the WHO International Clinical Trials Registry Platform (universal trial number U1111-1251-6599).

Keywords Clinical trials, Rotator cuff, Shoulder, Surgery, Placebo

Introduction

Background and rationale {6a}

Rotator cuff pathology is common and increases with age, affecting many people over the age of 45 years and most people over the age of 60, with more than half having shoulder pain [1, 2]. Shoulder pain is common (22% prevalence in adults) and makes up approximately 1% of all primary care presentations, 85% of which will have rotator cuff pathology [3–6]. Large acute tears may occur as a result of significant trauma (such as a shoulder dislocation) but most tears are not acute.

The two most common surgical procedures for patients with shoulder pain are subacromial decompression and rotator cuff repair (suturing and anchoring the torn tendon to the humeral head insertion), either separately or in combination.

Subacromial decompression is performed arthroscopically and involves removal of bursal tissue and the bony under-surface of the acromion to decompress the passage of the rotator cuff tendons through the subacromial space. The effectiveness of subacromial decompression as stand-alone treatment for rotator cuff disease (excluding full thickness tears) has been called into question based upon high-certainty evidence that it provides no clinically important benefits over placebo in pain or function [7–9] with a BMJ guideline panel making a strong recommendation against use of this surgery for shoulder pain [10].

The Australian Rotator Cuff (ARC) study investigates the effectiveness of a strategy to surgically repair full thickness, non-acute tears. Such lesions make up over 75% of all tears [11] and are often treated with surgery following failed non-operative management. Rotator cuff repair is the most common surgical procedure performed in the shoulder, with rates increasing [12–17]. The rationale for surgical repair is to improve symptoms (pain and function) which are believed to arise from the tear and to prevent the tear from becoming larger.

In contrast to subacromial decompression, results from a randomised placebo-controlled trial of rotator cuff repair have not been reported. A 2019 Cochrane review that included nine randomised trials involving 1007 participants comparing rotator cuff repair with or without decompression to other (non-surgical) active interventions noted that all trials were at high risk of bias, most notably for selection and performance bias due to failure to blind both participants and study personnel to treatment allocation [18]. The review found low certainty evidence that rotator cuff repair provides little or no benefit in pain, function and quality of life compared to non-operative treatment and no added benefit over subacromial decompression alone. In addition, there are high rates of re-tears (following repair) at 1 to 2 years [19–21], the structural integrity of the cuff after surgical repair does not correlate with clinically important differences in pain or function, and many tears do not progress if left unrepaired [22–24].

Uncertainty around the effectiveness of surgical rotator cuff repair is also reflected in variation in rates of surgery and surgeon preference [25, 26]. As a result of practice variation and evidence uncertainty, high-quality trials for rotator cuff tears were listed in the top ten research priorities for shoulder surgery in a multidisciplinary priority setting exercise using the James Lind Alliance Priority Setting Partnership methods in 2016 [27].

Objectives {7}

The ARC trial aims to determine the effectiveness, safety and cost-effectiveness of arthroscopic shoulder surgery with rotator cuff repair compared with arthroscopic shoulder surgery without rotator cuff repair, for improving shoulder pain and function, and quality of life in people with symptoms attributed to non-acute, full-thickness rotator cuff tears. The study hypothesis is that in people aged 45 to 75 years with at least 6 months of shoulder symptoms and a complete, surgically reparable rotator cuff tear, arthroscopic surgery with repair of the tear is superior to arthroscopic surgery without repair in improving shoulder pain and function at 6 months post-surgery.

Trial design {8}

The ARC trial is a multicentre, two-parallel group, blinded, randomised, placebo-controlled superiority trial. All eligible patients at participating sites will be approached to participate. Those who consent will undergo shoulder arthroscopy to confirm eligibility (size and location of rotator cuff tear) and address other pathology (e.g. acromial pathology, see below), and then randomised intra-operatively by online randomisation service to either arthroscopic surgical rotator cuff repair

or no repair in a 1:1 ratio. Concomitant arthroscopic procedures (see "Interventions", below) will be performed as per current usual practice and prior to randomisation.

Patient involvement

The trial was discussed in a focus group of rotator cuff surgery patients. The consumers understood the need for the trial and were comfortable with the use of placebo surgery. Furthermore, they were comfortable with the use of a common rehabilitation protocol, follow-up by a surgeon not involved in their operation, and maintenance of blinding. They considered it important to have no costs to the participants (as planned) and felt that the closer follow-up associated with trial participation, the avoidance of any costs, and contributing to the evidence that will assist with the management of future patients were strong drivers to participate.

The trial protocol has also been reviewed by the Consumer Advisory and Scientific Committees of the Australia and New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network and feedback has been incorporated. The ANZMUSC Executive Committee has endorsed the trial. The study includes two people with shoulder pain as investigators.

Methods: participants, interventions and outcomes

Study setting {9}

The study setting will parallel usual practice. Operating surgeons will be specialist (fellowship-trained) shoulder surgeons. The consultations and surgery will be performed in healthcare sites (public and/or private) normally used by the study surgeons, including all usual personnel (physiotherapists, nurses, trainee surgeons, anaesthetists, etc.).

Eligibility criteria {10}

Inclusion criteria

- Age 45–75 years inclusive (older patients are usually treated non-operatively and younger patients are less likely to have non-acute tears)
- At least 6 months duration of shoulder symptoms
- Complete tear of supraspinatus tendon on magnetic resonance imaging (MRI)
- Rotator cuff repair is considered the primary reason for surgery
- English speaking
- Available for post-operative rehabilitation and follow-up for at least 6 months
- Complete tear of the supraspinatus tendon confirmed at arthroscopy as being 1 to 4 cm in anteroposterior length with or without extension into infraspinatus and allowing tearing of the superior 1/3 of subscapularis tendons and considered arthroscopically reparable

Exclusion criteria

- Pregnancy
- Tear extending beyond superior 1/3 of subscapularis tendon
- Prior rotator cuff surgery of the affected shoulder
- Stage 3 or higher fatty atrophy of the rotator cuff muscles and a positive Tangent sign (relative contraindication to repair due to low success rate) [28]
- Glenohumeral osteoarthritis (Outerbridge Grade III or higher measured during arthroscopy) [29] or loss of joint space or osteophyte on pre-operative imaging
- Frozen shoulder (>50% loss global passive range) and/or proposed capsular release
- A traumatic tear (an acute event that is more than a fall from standing height) that has occurred within the last 6 months
- Current use of oral glucocorticoids, immunosuppressants; there will be no exclusion based on prior therapies
- Rheumatoid arthritis or other autoimmune inflammatory arthropathy
- Shoulder instability (history of dislocation)
- Osteonecrosis of the humeral head
- Resident of a residential aged care facility
- Shoulder condition covered by workers' compensation insurance (this is associated with poor results and may bias against any effectiveness of surgery [30])
- Limited English proficiency or cognitive impairment precluding fully informed consent

Who will take informed consent {26a}

Potential participants will be identified from the participating sites (private and public settings) where study surgeons work. If the surgeon considers rotator cuff repair surgery to be indicated and the cuff repair to be the main reason for surgery, patients will be approached to participate, informed of the trial, given written information and contacted by the research team prior to deciding whether to participate. Consent will be collect using an online consent form.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

No additional consent procedures will be used and no specimens will be taken as part of the study.

Interventions

Explanation for the choice of comparators {6b}

By comparing arthroscopic surgery with rotator cuff repair to arthroscopic surgery without rotator cuff repair, the only difference between study groups will be the presence or absence of the active component of the intervention being tested (i.e. rotator cuff repair). Isolating the active ingredient of the procedure being studied allows the study to provide the least biased estimate of efficacy of rotator cuff repair in the study population.

Intervention description {11a}

The active intervention is arthroscopic shoulder surgery with rotator cuff repair. The surgical technique will be according to surgeon preference. The type of repair (e.g. double row versus single row) will be recorded. Surgery will be performed within 90 days of consent where possible, and baseline data will be collected within 42 days of surgery in all cases.

The control intervention (placebo) is arthroscopic shoulder surgery without rotator cuff repair. In both groups, concomitant procedures will be allowed prior to intra-operative randomisation.

For both groups, anaesthesia and surgical set-up will be according to local standard practice. Arthroscopy will use standard portals with full visualisation to allow diagnostic arthroscopy. Exposure of the rotator cuff tear will be sufficient to allow visualisation, measurement and recording (site, size and reparability) of the tear to confirm eligibility, and subsequent repair if randomised to that arm of the trial. At the conclusion of the procedure, the arm will be placed in a shoulder immobiliser sling in both groups. Intra-operative images will be taken as per usual practice and will be used for inclusion criteria and treatment verification.

Allowing concomitant procedures more closely resembles usual practice, making the study more pragmatic and generalisable. It also increases acceptability by participants and surgeons. Further, by retaining all elements of the procedure with the exception of the active ingredient of the study intervention (rotator cuff repair), the requirements for high-fidelity placebo surgery are met [31].

The permitted concomitant procedures will be bursal debridement, acromioplasty, biceps tendon tenodesis or tenotomy and acromioclavicular joint resection. Concomitant procedures will be performed prior to randomisation and will not require any change to the post-operative rehabilitation. Concomitant procedures will be balanced between groups (through randomisation alone or the minimisation algorithm used in the randomisation process).

Post-operative analgesia (including nerve blocks) will be as per usual care for each treating surgeon. Whilst the focus of this trial is the surgery, participants and their physiotherapists will receive written guidance on good quality post-operative rehabilitation which includes a graded programme divided into phases, informed by recommendations from the recent consensus statement of the American Society of Shoulder and Elbow Therapists [32] and the protocol of the current ACCURATE placebo RCT [33].

Physiotherapists will be guided to follow four phases of rehabilitation that represent a consensus of current best practice recommendations:

- Phase 1 (0–4 weeks): arm placed in sling, passive and assisted range of motion (ROM).
- Phase 2 (5–8 weeks): active-assisted ROM unloading rotator cuff.
- Phase 3 (9–12 weeks): active-unloaded exercises, isometric cuff strengthening.
- Phase 4 (13–20 weeks): active ROM, dynamic strengthening exercises for cuff and scapula.

Physiotherapists will be guided to progress to each phase dependent on time and milestone achievement.

Participants will be followed up directly (electronically or by telephone/ mail) for study data collection at 1–2 weeks, 6–8 weeks, 3 months, 6 months, 12 months and 24 months. Five- and ten-year follow-up will be subject to additional funding. Participants will be followed in person by a blinded surgeon other than their operating surgeon at 1–2 weeks, 6–8 weeks, 3 months and 6 months. If further surgical reviews are required beyond 6 months, this will be dependent on the participant's post-surgical progress.

Criteria for discontinuing or modifying allocated interventions {11b}

The interventions are one-off procedures and cannot be discontinued or modified after being provided. Surgeons are allowed to modify the technique of rotator cuff repair according to usual preference.

Strategies to improve adherence to interventions {11c}

Participant adherence to the interventions is not applicable as the intervention is applied during their surgical procedure, under anaesthetic. Surgeon adherence will be monitored by inspection of intra-operative imaging. Participant adherence to the post-operative physiotherapy programme will be monitored by surveying all participants regarding attendance.

Table 1 Baseline variables

Variable	Unit of measurement
Age at time of consent	Years
Sex	Male, female
Hand dominance	Left, right
Educational attainment	No schooling, primary, high school, vocational training, bachelor, masters, doctorate, other
Medical history	High blood pressure, diabetes, osteoporosis, neck pain, heart condition, stomach disorder, bowel or intestinal disorder, depression anxiety, chronic respiratory illness, kidney disease
Current medications	Yes, no
WORC	Numeric: 0–100, higher scores representing better pain and function
EQ-5D-5L	Numeric, higher scores representing better health-related quality of life
EQ-VAS	Numeric: 0-100, higher scores representing better health
Shoulder pain at rest	Numeric rating scale 0–10, higher scores indicating more pain
Shoulder pain with activity	Numeric rating scale 0–10
Height	Centimetres
Weight	Kilograms
Current smoker	Yes, no
Duration of symptoms	6–12 months, more than 12 months
Work status	Normal duties, restricted duties/hours, not working
Strength tests (Geelong and Finland sites)	Shoulder abduction and external rotation power (Newtons)
Size of complete tear on MRI	Centimetres to one decimal place (mm) in antero-posterior plane

Table 2 Surgical variables

Variable	Units of measurement
ASA grade	I, II, II, IV
Date of surgery	Date
Length of tear	Centimetres to one decimal place (mm) in antero-posterior (length) and medial-lateral (width) planes
Involvement of infraspinatus	Yes, no
Biceps condition	Normal, tendinosis, subluxation, ruptured (choose highest applicable)
Biceps surgery	None, tenotomy, tenodesis
Biceps fixation	None, screw, button
Glenoid osteoarthritis	Outerbridge grade 0, 1, 2, 3, 4
Humeral osteoarthritis	Outerbridge grade 0, 1, 2, 3, 4
Cuff repair	No repair, repair (single vs double row, number of anchors)

Relevant concomitant care permitted or prohibited during the trial {11d}

Concomitant surgical procedures are listed above, under "Intervention description" and these will be performed prior to randomisation. All participants (in both groups) will undergo routine care associated with rotator cuff repair surgery, including anaesthesia, post-operative pain relief and post-operative rehabilitation.

Provisions for post-trial care {30}

Participants will be managed by the post-operative surgeon and physiotherapists according to usual care, including the management of any complications.

Outcomes {12}

Baseline data (Table 1) will be collected up to 6 weeks prior to surgery. Surgical data (Table 2) will be collected at the time of surgery.

The primary outcome is the Western Ontario Rotator Cuff Index (WORC) measured at 6 months post-surgery. The WORC is a self-administered condition-specific health questionnaire specifically designed for rotator cuff disease and its treatment [34]. It consists of 21 questions encompassing 5 domains: symptoms, sport and recreation, work, social function and emotions and can be presented in a summary score on a scale from zero (no symptoms or limitations) to 2100 (each question

is scored on a 0–100 scale). The raw score will be converted to the final WORC, which ranges from 0 to 100, with higher scores indicating worse pain and function. The final WORC score is calculated by subtracting the raw WORC score from 2100 and dividing the result by 21 to create a score out of 100. The WORC was chosen because it is widely used for studies of rotator cuff repair, has been validated in that population, has better internal consistency, reliability, content validity and responsiveness than other shoulder outcome tools [35], has no floor or ceiling effect [36], and is the primary outcome in the current (ACCURATE) placebo rotator cuff repair trial (thereby enabling direct comparison) [33]. WORC was recommended by the surgeon investigators and was developed with direct patient input [34].

Secondary outcomes are:

- *Health-related quality of life*: EuroQoL 5 Domain (EQ5D-5L) & EuroQoL Visual Analogue Scale (EQ-VAS), a validated generic quality of life questionnaire. Comprises of five questions on mobility, self-care, pain, usual activities and psychological status with five possible answers for each item and a VAS to indicate general health status.
- *Shoulder patient global perceived effect*: a 5-point Likert Scale measuring "How is your shoulder now compared to before the surgery?": much worse, a little worse, about the same, a little better, much better.
- *Shoulder pain at rest*: a Numerical Rating Scale from 0 to 10 with "0" representing no pain and "10" representing the worst pain imaginable in the preceding week.
- *Shoulder pain with activity*: a Numerical Rating Scale from 0 to 10 with "0" representing no pain and "10" representing the worst pain imaginable in the preceding week.
- *Work status*: normal duties, restricted duties/hours, not working.
- *Post-operative physiotherapy attendance at 6 months*: 0–4 sessions, 5–9 sessions, equal to or greater than 10 sessions.
- *Presence and size of complete rotator cuff tear on MRI at 12 months*: measured in centimetres to one decimal place
- *Acromio-humeral distance on MRI at 12 months*: measured in millimetres
- *Osteoarthritis on MRI at 12 months*: according to modified Samsilon & Prieto Score [37].
- *Muscle wasting of rotator cuff on MRI at 12 months*: measured using Goutallier classification (Stages 0–4) [28].
- *Complications*: death, frozen shoulder, infection requiring treatment, repeat surgery.

The outcomes include the four mandatory clinical trial domains (pain, function, patient global assessment of the shoulder and adverse events including death) and the majority of the four "important but optional" domains (participation (recreation/work), sleep, emotional wellbeing and condition-specific pathophysiological manifestations) in the OMERACT Core Domain Set for Clinical Trials of Shoulder Disorders [38].

Participant timeline {13}

Table 3 provides the schedule of participant contact.

Sample size {14}

The sample size used during initial trial registration was based on detecting a 0.5 standard deviation (SD) difference between groups. Recent research has reported the Smallest Worthwhile Effect (SWE) for the ARC study, specifically comparing the two groups used in this trial [39]. The median SWE for improvement in pain and function within 6 months for rotator cuff repair surgery over subacromial decompression alone was 40% and the lower limit of the interquartile range was 20%. We chose to power the study based on the lower estimate of 20% improvement in the raw WORC score, which converts to 14% change in the final (0–100) WORC based on baseline values in this population (both the SWE study and the ARC study to date). The minimum important difference in the WORC has been reported at similar levels of 13 and 14 points [40–42]. The SD of the WORC post-rotator cuff tear has been estimated at 17–20 [43–45]. Using a 14-point between-group difference in the WORC at 90% power and a p value of 0.05 and assuming a conservative estimate of 20 for the SD, 86 participants are required (43 in each group). Therefore, we aim to recruit until we have primary outcome (6 months) data for 86 participants.

Recruitment {15}

At least 8 centres will be included to ensure achievement of the sample size. Surgeons will be asked to complete screening logs and complete screening forms for potential participants. Monthly newsletters will be provided to investigators and these will include recruitment rates and targets.

Assignment of interventions: allocation

Sequence generation {16a}

Randomisation will occur by use of the computer-generated interactive web response system of the Griffith University Randomisation Service. Randomisation will be 1:1 between groups and will use the technique of minimisation to balance groups for age, surgeon and concomitant procedures.

Table 3 Schedule of study procedures

	Enrolment	Baseline	Visit 1 -Surgery	PS-1 1–2 weeks	PS-2 6–8 weeks	PS-3 3 months	PS-4 6 months	PS-5 12 months	PS-6 24 months	PS-7 5 years	PS-8 10 years
Informed consent	X										
Inclusion / exclusion criteria		X	X								
Copy of clinical MRI		X						X[a]			
Medical history/demographics		X									
Surgery / randomisation			X								
Operation reports			X								
Surgeon follow up				X	X	X	X	X	X		
Blinding fidelity				X			X	X	X		
Shoulder strength		X					X	X			
Work status		X					X	X			
Physiotherapy attendance							X				
Outcome questionnaires		X					X	X	X	X	X
AE/ SAE /Complications				X	X	X	X	X	X	X[b]	X[b]

PS post surgery

[a] 11–18 months

[b] Only complications will be recorded (not adverse events)

Concealment mechanism {16b}

Use of the online interactive web response system will ensure concealment of the allocation until it is assigned.

Implementation {16c}

The allocation sequence will be computer-generated and allocated by the interactive web response system. The system will be accessed by the operating surgeon or their delegate intra-operatively. The intervention will be assigned by the operating surgeon.

Assignment of interventions: blinding

Who will be blinded {17a}

Operating surgeons will not be blinded. Participants, the post-surgical care team, including follow-up surgeons, rehabilitation physiotherapists and the study management team will remain blinded for the duration of the study. Participants will be followed up by a different surgeon to the operating surgeon (a blinded trial surgeon at the same site).

Maintenance of blinding will be supported by information provided in patient study cards (to be carried with participants and presented to treating practitioners), and letters provided to treating general practitioners and physiotherapists informing them of the trial procedures.

Operation reports will be standardised as "Treatment according to the ARC study protocol". An unblinded operation report (standard report) will be produced and kept by the treating surgeon and only released if unblinding is deemed necessary (e.g. further surgery required) or at the end of the study.

Blinding fidelity will be tested during follow-up (see Table 3 for timing) by asking each participant which group they believe they are in: rotator cuff repair, no rotator cuff repair, or unsure.

The statisticians responsible for the analyses will programme all the analyses indicated in the statistical analysis plan using a masked treatment allocation performed by an independent statistician. The statisticians will provide the Writing Committee with blinded results from the analyses, with the two arms labelled A and B. The Writing Committee will then meet to consider the interpretations of the results until a consensus is reached for each alternative interpretation (based on the two possible treatment allocations), prior to unblinding.

Procedure for unblinding if needed {17b}

If the participant's treating clinicians at any time during the study period deem a change in treatment is needed and unblinding may be necessary, the Trial Management Group (TMG) will decide if the patient will be unblinded. Participants will be encouraged to remain blinded for the first 2 years, after which time those who wish to know their treatment allocation will be unblinded.

Data collection and management

Plans for assessment and collection of outcomes {18a}

Data will be collected directly in a REDCap [46, 47] database. Participants will be directed to the REDCap interface for consent and entering survey responses. Surgical data will be entered into REDCap by the research team based on case report forms completed intra-operatively by the surgeons.

Plans to promote participant retention and complete follow-up {18b}

The use of electronic links to online surveys is expected to improve participant follow-up. Participants who do not respond to electronic (email and text) reminders will be contacted by telephone but directed to enter the data directly where possible. Follow-up will continue regardless of protocol adherence.

Data management {19}

The REDCap database is provided, hosted and backed up regularly by the University of New South Wales, on a secure network. Data will be password protected and with separate access, depending on the study role, with no one able to access the random treatment allocation except the unblinded statistician responsible for providing reports to the independent Data Safety and Monitoring Committee (DSMC) and an assigned unblinded study team member. Data access will be restricted to the TMG that will oversee day-to-day trial management. The Steering Committee (SC) will oversee study progress, data collection and integrity and will approve the statistical analysis plan and research protocol.

The integrity of trial data will be monitored by regular (monthly) review of data for omissions and errors. The database will be constructed with restricted ranges to reduce errors in data entry.

Confidentiality {27}

Personal information in the database will be password protected on a secure network. No identifying information will be used in any analysis, report or publication.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Biological specimens will not be collected in this study.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

The study will be reported according to the CONSORT statement and will include a CONSORT flowchart [48].

Baseline data will be described for each group separately and the total cohort. Baseline differences between groups will not be formally tested. The primary outcome (difference in WORC between groups at 6 months) will be analysed on an intention to treat basis using multivariable regression, adjusted for baseline WORC. The effect of the intervention will be estimated as the adjusted mean difference and its 95% confidence interval. The p value for the primary analysis will be reported based on the null hypothesis of no difference in shoulder pain and function at 6 months post-surgery between the two groups.

Other outcomes and timepoints for the primary outcome will be reported using regression adjusted for baseline scores where applicable. Dichotomous outcomes (e.g. complications) will be reported using logistic regression with no adjustments.

A secondary analysis including all WORC measurements will be conducted using a repeated-measures linear mixed model including the treatment allocation, the visit (timepoint), the treatment-by-visit interaction and baseline WORC. A random subject effect or a repeated effect will be included to model within-subject correlations. A detailed Statistical Analysis Plan will be developed and published prior to unblinding and database lock.

Eligible patients who decline inclusion in the randomised trial will be invited to participate in a parallel observational study. Those treated surgically will be treated as per the intervention arm of the randomised trial. The non-operative group will be treated as per usual care. The observational cohort will be followed as per the randomised study (time points and outcomes) with the following differences:

- Baseline assessments must be completed within 6 weeks of enrolment, rather than within 6 weeks of the scheduled surgery.
- Adverse events will not be collected as participants will not be assigned any study intervention and will be provided with unblinded "usual care". Pre-determined complication outcomes as specified in secondary outcomes will still be obtained.

Data from this observational cohort will provide information on the generalisability of the results of the randomised trial and allow comparison between the control group and matched non-operative care.

Interim analyses {21b}

Unless requested by the DSMC, no interim analysis is planned.

Methods for additional analyses (e.g. subgroup analyses) {20b}

Exploratory analyses will be performed to analyse the effect of tear size, concomitant procedures, surgeon and repair type on the primary outcome (interaction).

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

As randomisation occurs intra-operatively and the primary outcome is at 6 months, no crossovers and minimal loss to follow-up are expected. A per-protocol analysis and imputation for missing data will only be performed if crossovers or loss to follow-up at 6 months (primary endpoint) are greater than 5%.

Plans to give access to the full protocol, participant-level data and statistical code {31c}

The protocol will be published and the full protocol made available on request. De-identified study data and the statistical code will be made available upon reasonable request, after publication.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

The SC oversees overall study design and conduct and comprises all investigators based in Australia. The SC will meet at least every 6 months. The coordinating centre at the Whitlam Orthopaedic Research Centre, supported by the Ingham Institute for Applied Medical Research and the University of New South Wales, oversees the trial's overall management, including protocol adherence, site coordination, ethics and data management. It provides organisational support and facilitates communication between trial sites and oversight committees. The central trial coordinator supports the trial's daily operations.

The TMG oversees day-to-day trial management and consists of 5 of the study's investigators, including the Coordinating Principal Investigator (CPI) the study's two second co-investigators and the central trial coordinator. The TMG initially met monthly during trial set-up and will meet every second month during recruitment and until trial close-out. The TMG review trial conduct, focusing on recruitment progress, data management, protocol adherence, safety reporting and site performance. Any protocol or site-specific issues identified will be addressed through corrective actions to ensure compliance and trial integrity.

Composition of the data monitoring committee, its role and reporting structure {21a}

The DSMC oversees data management and safety and comprises a statistician, a shoulder surgeon and a rheumatologist. The DSMC will provide medical oversight and expertise concerning recommendations for the continuation, modification or termination of the trial. The DSMC will be independent of the study sponsor, will not be involved in the study, will declare any competing interests and will not benefit in any way from the results of this trial. The DSMC will monitor AEs and SAEs to ensure the safety of participants. The DSMC will meet annually or as required to provide study oversight. The DSMC charter is available from the corresponding author upon reasonable request.

Adverse event reporting and harms {22}

Adverse events (AE) (non-serious AEs / serious adverse events (SAE)/ unexpected related serious adverse events), Significant Safety Issues and Urgent Safety Measures) will be collected, monitored and reported accordingly to the Sponsor's Delegate, relevant ethic committee(s) and Research Governance Office(s). The safety reporting procedures will follow the latest version of The ARC Trial Safety Management Plan.

An independent DSMC will conduct an annual review of the trial data to assess participant safety and study integrity, providing recommendations on whether to continue, modify or stop the trial.

The DSMC will have access to unblinded data and data on the primary outcome, AEs (after coding) and SAEs. Data on complications will be recorded as outcomes, and the DSMC will assess their severity and frequency.

Frequency and plans for auditing trial conduct {23}

Regular central monitoring of recruitment rates, withdrawals, protocol deviations, safety reports and data quality concerns by the study officer is planned and will be discussed by the TMG and/or the SC or DSMC meetings, with the outcomes of all meetings documented via meeting minutes. A yearly monitoring report will be submitted to the trial Sponsor.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Any protocol amendments are approved by the TMG, which is chaired by the Sponsor's delegate, the Coordinating Principal Investigator. All significant changes to the protocol will be submitted to the relevant human research ethics committee and communicated to all sites and investigators once approved. All protocol amendment submission and approvals are filed in the Investigator Site Files as per GCP. Any protocol changes are updated in the ANZCTR registry.

Dissemination plans {31a}

The Writing Committee will draft all manuscripts prior to review by other investigators and comprises IAH, RSP, RB, and JD. Authorship of all manuscripts will be granted according to ICJME guidelines.

Study results will be published in a scientific journal and presented at international meetings. Media coverage will be promoted and sought to more widely communicate the results. The trial involves many opinion leaders in shoulder surgery nationally and internationally and has been endorsed by the Shoulder and Elbow Society of Australia (surgeons) and ANZMUSC (a musculoskeletal clinical trials network of clinicians, researchers and consumers); working with members of these groups will facilitate incorporation into practice guidelines and the day-to-day practice of clinicians.

Discussion

The ARC trial will generate new, low bias evidence on the efficacy of rotator cuff repair for patients with chronic shoulder pain and non-acute (degenerative) rotator cuff tears by using a high-fidelity placebo control to isolate the active ingredient of the surgery (cuff repair) and by maximising blinding of patients, carers, health care providers and investigators.

Trial status

This manuscript is based on Version 16 of the protocol (15 July 2024). Recruitment began in April 2021 and is expected to be complete by April 2026.

Abbreviations

AE	Adverse event
ANZMUSC	Australia and New Zealand Musculoskeletal Clinical Trials Network
ARC	Australian Rotator Cuff (trial)
DSMC	Data Safety and Monitoring Committee
EQ-5D-5L	EuroQol 5-domain, 5-level quality of life survey
EQ-VAS	EuroQol visual analogue scale
MRI	Magnetic resonance imaging
RCT	Randomised controlled trial
SAE	Serious adverse event
TMG	Trial Management Group
WHO	World Health Organization
WORC	Western Ontario Rotator Cuff Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-025-08822-w.

Supplementary Material 1.

Supplementary Material 2.

Acknowledgements
Not applicable.

Authors' contributions {31b}
IAH is the Principal Investigator and conceived the study and drafted the protocol. JD is the study statistician and contributed to the statistical analysis. All authors contributed to and approved the final version of the manuscript.

Funding {4}
The study is funded by the Whitlam Orthopaedic Research Centre, a not-for-profit charitable gift recipient organisation. The funding organisation has no role in the design of the study and collection, analysis and interpretation of data and in writing the manuscript.

Data availability {29}
All investigators will have access to the final dataset. There are no contractual agreements limiting access for investigators. The final dataset will be available after study publication upon reasonable request. The protocol and statistical analysis plan will be published.

Declarations

Ethics approval and consent to participate {24}
The study protocol version 6.0 28 May 2020 was approved by the Human Research Ethics Committees of the South Western Sydney Local Health District on 15 June 2020 (reference number 2020/ETH00754) and St John of God Health Care on 18 August 2020 (reference number 1704). Each update to the protocol has been approved by the relevant ethics committee.
The study will be performed according to the National Statement on Ethical Conduct in Human Research [49, 50]. As per the National Statement (2018 and 2023, section 3.1.5), placebo controlled trials are ethically acceptable where the current standard of care includes the absence of the intervention being tested and there is no risk of significant harm in the absence of the intervention. All investigators will undergo training in Good Clinical Practice for clinical trials and will complete a study start up site or remote visit that involves training of the site principal investigator and all delegated personnel, on the approved versions of the trial protocol, standard operating procedures and/or relevant essential documents. The protocol and a statistical analysis plan will be published in an open-access journal. The protocol complies with SPIRIT guidelines [51] and the study will be reported according to the CONSORT guidelines [48].

Consent for publication {32}
A model consent form and participant information sheet have been provided as Supplementary Material.

Competing interests {28}
The authors declare that they have no competing interests.

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References

1. Sher JS, Uribe JW, Posada A, et al. Abnormal findings on magnetic resonance images of asymptomatic shoulders. J Bone Joint Surg Am. 1995;77:10–5.
2. Yamamoto A, Takagishi K, Osawa T, et al. Prevalence and risk factors of a rotator cuff tear in the general population. J Shoulder Elbow Surg. 2010;19:116–20.
3. Chard MD, Hazleman R, Hazleman BL, et al. Shoulder disorders in the elderly: A community survey. Arthritis Rheum. 1991;34:766–9. https://doi.org/10.1002/art.1780340619.
4. Hill CL, Gill TK, Shanahan EM, et al. Prevalence and correlates of shoulder pain and stiffness in a population-based study: the North West Adelaide Health Study. Int J Rheum Dis. 2010;13:215–22.
5. Östör AJK, Prevost AT, Hazleman BL, et al. Diagnosis and relation to general health of shoulder disorders presenting to primary care. Rheumatology. 2005;44:800–5.
6. Luime JJ, Koes BW, Hendriksen IJ, et al. Prevalence and incidence of shoulder pain in the general population; a systematic review. Scand J Rheumatol. 2004;33:73–81.
7. Beard DJ, Rees JL, Cook JA, et al. Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): a multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial. Lancet. 2018;391:329–38.
8. Karjalainen TV, Jain NB, Page CM, et al. Subacromial decompression surgery for rotator cuff disease. Cochrane Database Syst Rev. 2019;1:CD005619.
9. Paavola M, Malmivaara A, Taimela S, et al. Subacromial decompression versus diagnostic arthroscopy for shoulder impingement: randomised, placebo surgery controlled clinical trial. BMJ. 2018;362:k2860.
10. Vandvik PO, Lähdeoja T, Ardern C, et al. Subacromial decompression surgery for adults with shoulder pain: a clinical practice guideline. BMJ. 2019;364:l294.
11. Aagaard KE, Abu-Zidan F, Lunsjo K. High incidence of acute full-thickness rotator cuff tears. Acta Orthop. 2015;86(5):558–62.
12. Colvin AC, Egorova N, Harrison AK, et al. National trends in rotator cuff repair. J Bone Joint Surg Am. 2012;94:227–33.
13. Ensor KL, Kwon YW, Dibeneditto MR, et al. The rising incidence of rotator cuff repairs. J Shoulder Elbow Surg. 2013;22:1628–32.
14. Jo YH, Lee KH, Kim SJ, et al. National trends in surgery for rotator cuff disease in Korea. J Korean Med Sci. 2017;32:357–64.
15. Mather RC 3rd, Koenig L, Acevedo D, et al. The societal and economic value of rotator cuff repair. J Bone Joint Surg Am. 2013;95:1993–2000.
16. Thorpe A, Hurworth M, O'Sullivan P, et al. Rising trends in surgery for rotator cuff disease in Western Australia. ANZ J Surg. 2016;86:801–4.
17. Yanik EL, Chamberlain AM, Keener JD. Trends in rotator cuff repair rates and comorbidity burden among commercially insured patients younger than the age of 65 years, United States 2007–2016. JSES Rev Rep Tech. 2021;1:309–16.
18. Karjalainen TV, Jain NB, Heikkinen J, et al. Surgery for rotator cuff tears. Cochrane Database Syst Rev. 2019;12:CD013502.
19. Kukkonen J, Joukainen A, Lehtinen J, et al. Treatment of non-traumatic rotator cuff tears: A randomised controlled trial with one-year clinical results. Bone Joint J. 2014;96:75–81.
20. Lambers Heerspink FO, van Raay JJ, Koorevaar RC, et al. Comparing surgical repair with conservative treatment for degenerative rotator cuff tears: a randomized controlled trial. J Shoulder Elbow Surg. 2015;24:1274–81.
21. Moosmayer S, Lund G, Seljom U, et al. Comparison between surgery and physiotherapy in the treatment of small and medium-sized tears of the

rotator cuff: A randomised controlled study of 103 patients with one-year follow-up. J Bone Joint Surg Br. 2010;92:83–91.
22. Jeong HJ, Nam KP, Yeo JH, et al. Retear After Arthroscopic Rotator Cuff Repair Results in Functional Outcome Deterioration Over Time. Arthroscopy. 2022;38(8):2399–412.
23. Kim YS, Kim SE, Bae SH, et al. Tear progression of symptomatic full-thickness and partial-thickness rotator cuff tears as measured by repeated MRI. Knee Surg Sports Traumatol Arthrosc. 2017;25:2073–80.
24. Russell RD, Knight JR, Mulligan E, et al. Structural integrity after rotator cuff repair does not correlate with patient function and pain: a meta-analysis. J Bone Joint Surg Am. 2014;96(4):265–71.
25. Dunn WR, Schackman BR, Walsh C, et al. Variation in orthopaedic surgeons' perceptions about the indications for rotator cuff surgery. J Bone Joint Surg Am. 2005;87:1978–84.
26. Wang A, Mackie K, Bain G, et al. Variation in treatment of rotator cuff injury within a subspecialist shoulder society. Shoulder and Elbow Society of Australia (SESA) Biennial Meeting. SESA, Perth, 2018.
27. Rangan A, Upadhaya S, Regan S, et al. Research priorities for shoulder surgery: results of the 2015 James Lind Alliance patient and clinician priority setting partnership. BMJ Open. 2016;6:e010412.
28. Somerson JS, Hsu JE, Gorbaty JD, et al. Classifications in Brief: Goutallier Classification of Fatty Infiltration of the Rotator Cuff Musculature. Clin Orthop Relat Res. 2016;474(5):1328–32.
29. Slattery C, Kweon CY. Classifications in Brief: Outerbridge Classification of Chondral Lesions. Clin Orthop Relat Res. 2018;476:2101–4.
30. Harris I, Mulford J, Solomon M, et al. Association between compensation status and outcome after surgery: a meta-analysis. JAMA. 2005;293:1644–52.
31. Beard DJ, Campbell MK, Blazeby JM, et al. Considerations and methods for placebo controls in surgical trials (ASPIRE guidelines). Lancet. 2020;395:828–38.
32. Thigpen CA, Shaffer MA, Gaunt BW, et al. The American Society of Shoulder and Elbow Therapists' consensus statement on rehabilitation following arthroscopic rotator cuff repair. J Shoulder Elbow Surg. 2016;25:521–35.
33. Ryosa A, Kukkonen J, Bjornsson Hallgren HC, et al. Acute Cuff Tear Repair Trial (ACCURATE): protocol for a multicentre, randomised, placebo-controlled trial on the efficacy of arthroscopic rotator cuff repair. BMJ Open. 2019;9:e025022.
34. Kirkley A, Alvarez C, Griffin S. The development and evaluation of a disease-specific quality-of-life questionnaire for disorders of the rotator cuff: The Western Ontario Rotator Cuff Index. Clin J Sport Med. 2003;13:84–92.
35. Huang H, Grant JA, Miller BS, et al. A systematic review of the psychometric properties of patient-reported outcome instruments for use in patients with rotator cuff disease. Am J Sports Med. 2015;43:2572–82.
36. de Witte PB, Henseler JF, Nagels J, et al. The Western Ontario rotator cuff index in rotator cuff disease patients: a comprehensive reliability and responsiveness validation study. Am J Sports Med. 2012;40:1611–9.
37. Buscayret F, Edwards TB, Szabo I, et al. Glenohumeral arthrosis in anterior instability before and after surgical treatment: incidence and contributing factors. Am J Sports Med. 2004;32:1165–72.
38. Ramiro S, Page MJ, Whittle SL, et al. The OMERACT core domain set for clinical trials of shoulder disorders. J Rheumatol. 2019;46:969–75.
39. Hansford HJ, Buchbinder R, Zadro JR, et al. The smallest worthwhile effect on pain and function for rotator cuff repair surgery: a benefit-harm trade-off study. medRxiv, 2024.https://www.medrxiv.org/content/10.1101/2024.07.24.24310953v1. Accessed 5 Sep 2024.
40. Braun C, Handoll HH. Estimating the Minimal Important Difference for the Western Ontario Rotator Cuff Index (WORC) in adults with shoulder pain associated with partial-thickness rotator cuff tears. Musculoskelet Sci Pract. 2018;35:30–3.
41. Jones IA, Togashi R, Heckmann N, et al. Minimal clinically important difference (MCID) for patient-reported shoulder outcomes. J Shoulder Elbow Surg. 2020;29:1484–92.
42. Ekeberg OM, Bautz-Holter E, Keller A, et al. A questionnaire found disease-specific WORC index is not more responsive than SPADI and OSS in rotator cuff disease. J Clin Epidemiol. 2010;63:575–84.
43. Bejer A, Płocki J, Probachta M, et al. A comparison study of the Western Ontario Rotator Cuff Index, and the Constant-Murley Score with objective assessment of external rotator muscle strength and pain in patients after arthroscopic rotator cuff repair. Int J Environ Res Public Health. 2023;20:6316.
44. Herring MJ, White M, Braman JP. The WORC Index and Predicting Treatment Failure in Patients Undergoing Primary Arthroscopic Rotator Cuff Repair. Orthop J Sports Med. 2019;7(7):2325967119859518.
45. Sugaya H, Maeda K, Matsuki K, et al. Functional and structural outcome after arthroscopic full-thickness rotator cuff repair: single-row versus dual-row fixation. Arthroscopy. 2005;21:1307–16.
46. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–81.
47. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software partners. J Biomed Inform. 2019;95:103208.
48. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c332.
49. National Health and Medical Research Council, Australian Research Council, Universities Australia. National Statement on Ethical Conduct in Human Research 2007 (updated 2018). Canberra: National Health and Medical Research Council, 2018.
50. National Health and Medical Research Council. Australian Research Council. National Health and Medical Research Council: Universities Australia. National Statement on Ethical Conduct in Human Research. Canberra; 2023.
51. Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158:200–7.

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