RAPSODI-UK TRIAL PROTOCOL

Full title: Reverse or Anatomical replacement for Painful Shoulder Osteoarthritis, Differences between Interventions (RAPSODI): a multi-centre, pragmatic, parallel group, superiority randomised controlled trial

Acronym: RAPSODI-UK

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Sponsor: Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust

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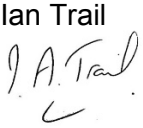
Signature:		**Date:**	24 April 2023
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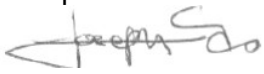
Signature:		**Date:**	24 April 2023
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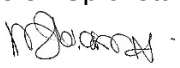
Signature:		**Date:**	24 April 2023

Amendment history

Amendment number	Revised protocol version number and date	Details of key changes made (including if justification required)
1	V2.0 Date 2022.11.12	Clarified our wording about the type of replacement that is permitted to include any “off the shelf” replacements.
2	V3.0 Date 2023.04.24	(1) Remote consent has been introduced because of the long distances that patients live from hospitals. (2) There is clarification of the wording to the protocol about all imaging to be collected is routine and when radiographic assessment of the implant will be performed. (3) We have modified how we will approach participants who are interested in being interviewed. (4) A paragraph has been added to the statistical analysis section to describe how we will handle participants who complete multiple baseline SPADIs. (5) We have added about participants receiving a £20 gift voucher at the two year follow-up. (6) We have added about the blinded assessment of baseline shoulder range of movement and strength when this is collected post-randomisation.

Abbreviations

AE	Adverse event
API	Associate Principal Investigator
CI	Chief Investigator
CONSORT	Consolidated Standard of Reporting Trials statement
CRF	Case Report Form
CT	Computerized Tomography
CTIMP	Clinical Trial of an Investigational Medicinal Product
EQ-5D-5L	EuroQoL 5 dimension 5 level
GDPR	General Data Protection Regulation
HRA	Health Research Authority
HTA	Health Technology Assessment
IDMC	Independent Data Monitoring Committee
ISF	Investigator Site Files
ISRCTN	International Standardised Randomised Controlled Trial Number
MHRA	Medicines and Healthcare Regulatory Authority
MRI	Magnetic Resonance Imaging
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NJR	National Joint Registry
NHS	National Health Service
OA	Osteoarthritis
OMERACT	Outcome Measures in Rheumatoid Arthritis Clinical Trials
OSS	Oxford Shoulder Score
PI	Principal Investigator
RAPSODI	Reverse or Anatomical replacement for Painful Shoulder Osteoarthritis, Differences between Interventions
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
ROM	Range of movement
SAC	Specialty Advisory Committee
SAE	Serious Adverse Event
SIV	Site Initiation Visit
SPADI	Shoulder Pain and Disability Index
SWAT	Study Within A Trial
TSC	Trial Steering Committee
TSR	Total shoulder replacement
US	Ultrasound Scan
WWL	Wrightington, Wigan and Leigh
YTU	York Trials Unit

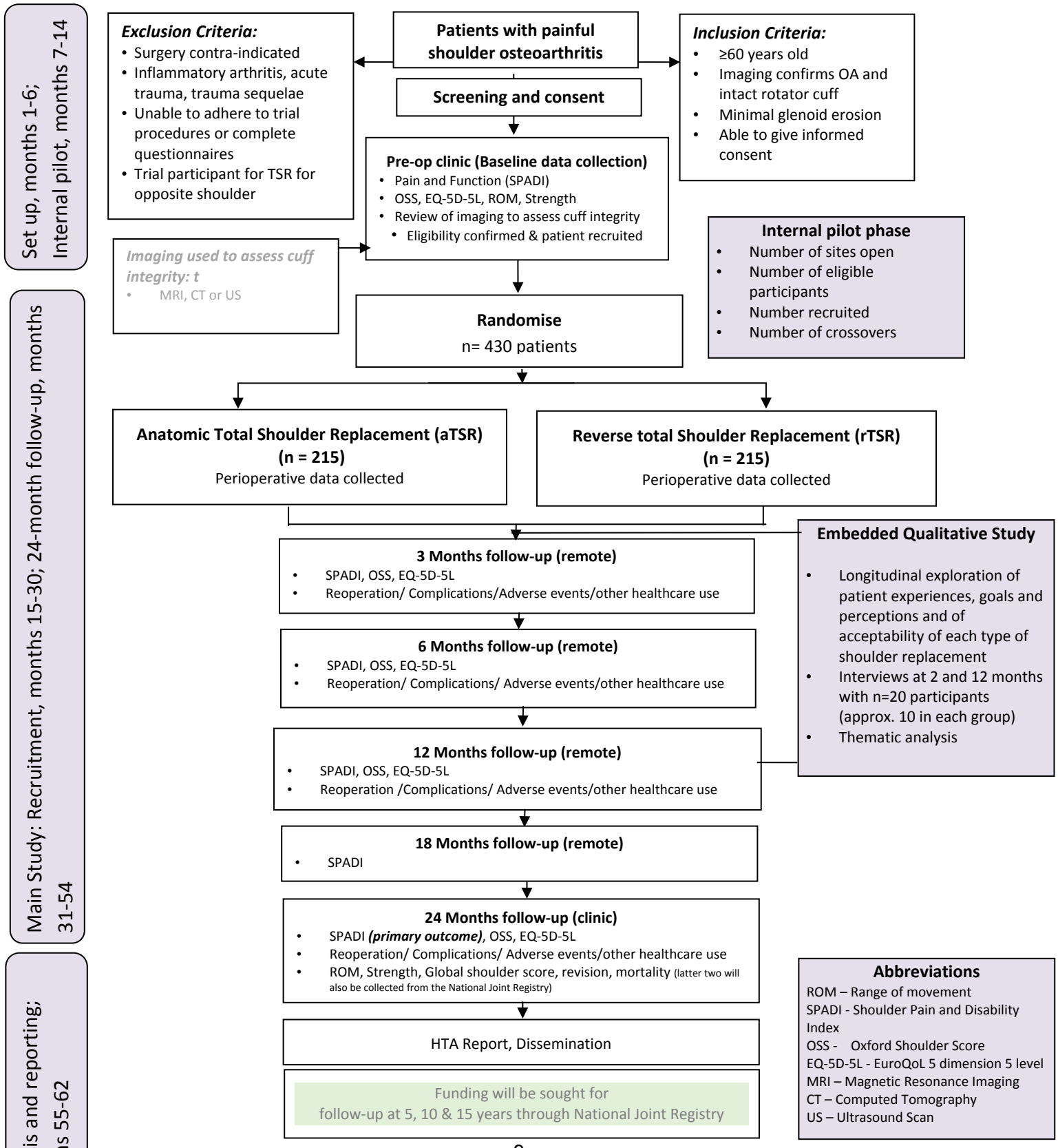
Contents

Trial Synopsis

Acronym	RAPSODI-UK
Long title	Reverse or Anatomical replacement for Painful Shoulder Osteoarthritis, Differences between Interventions (RAPSODI): a multi-centre, pragmatic, parallel group, superiority randomised controlled trial
Type of trial	Non-CTIMP
Study design	A multi-centre, pragmatic, two-arm, parallel group, individually randomised, superiority trial with blinding of patients and assessors
Setting	Orthopaedic Departments of NHS Hospitals in England, Wales and Northern Ireland
Target population	Adults ≥60 years of age with painful OA of the shoulder joint with an intact rotator cuff and bone stock suitable for shoulder arthroplasty
Intervention	Reverse total shoulder replacement (rTSR)
Comparator	Anatomical total shoulder replacement (aTSR)
Primary outcome	Patient-reported shoulder pain and function (combined SPADI [Shoulder Pain and Disability Index] score) at 24 months
Secondary outcomes	Total SPADI score at 3, 6, 12, and 18 months, and over 24 months; individual subscales of pain and disability from the SPADI, Oxford Shoulder Score, EQ-5D-5L, resource use, re-operations and complications at 3, 6, 12, 18 (SPADI only) and 24 months; range of movement, strength and global shoulder score at 24 months; revisions and mortality over 24 months.
Estimated recruitment period	24 months (1 September 2022 to 30 August 2024)
Duration per patient	24 months
Estimated total trial duration	62 months (1 March 2022 to 30 April 2027)
Planned trial sites	28 sites (up to a maximum of 35)
Planned sample size	430 patients (215 in each group)
Eligibility criteria	**Inclusion criteria** • Aged 60 years and over. • Diagnosis of painful osteoarthritis of the glenohumeral joint using routine radiographs not controlled by previous interventions. • An intact rotator cuff determined by pre-operative advanced imaging (Ultrasound, MRI, or CT). • Minimal glenoid erosion determined by pre-operative CT or other imaging in whom an off the shelf replacement is appropriate. • Able to give informed consent. **Exclusion Criteria**

	• Shoulder replacement surgery contra-indicated. • A diagnosis of inflammatory arthritis, acute trauma or trauma sequelae. • Evidence that the patient would be unable to adhere to trial procedures or complete questionnaires. • Trial participant for TSR for opposite shoulder.

RAPSODI-UK trial flowchart



Study Assessment Schedule

Assessment (M=month)	**Baseline**[1] (Clinic)	**Randomisation**	**Treatment delivery**	**M3** (Remote)	**M6** (Remote)	**M12** (Remote)	**M18** (Remote)	**M24** (Clinic)
Enrolment								
Screen	X							
Assess eligibility	X[2]							
Informed consent	X							
Baseline data collection	X							
Randomisation		X						
Treatment								
Treatment allocation			X					
Operation data[3]			X					
Physiotherapy data			X					
Follow-up assessment								
SPADI (primary outcome)	X			X	X	X	X	X
OSS	X			X	X	X		X
EQ-5D-5L	X			X	X	X		X
Resource use				X	X	X		X
Re-operations				X	X	X		X
Complications				X	X	X		X[4]
Global shoulder score								X
Revision								X
Mortality								X
Range of movement	X							X
Strength	X							X
Adverse events				X	X	X		X

[1]Baseline assessments will be prior to randomisation except for baseline Range of Movement and Strength to allow planning for surgery and collected by an independent assessor.

[2]This includes radiographs (typically anteroposterior and axial) to confirm osteoarthritis; CT or other imaging to assess glenoid erosion; and CT, MRI or US to assess the rotator cuff.

[3]Assessment of cuff integrity in theatre before operating and the possible use of fluoroscopy during surgery.[4]This includes an assessment of implant problems using post-operative radiographs and radiographs at 24 months or earlier if not available. The radiographs will typically be anteroposterior and axial.

1 Background and rationale

1.1 General introduction

Osteoarthritis (OA) of the 'ball' (humerus) and 'socket' (glenoid) joint of the shoulder is common with advancing age. A shoulder joint replacement (or arthroplasty) may be appropriate when other options no longer provide adequate pain relief. The number of shoulder replacements is increasing, with 7,294 primary cases recorded in England, Wales and Northern Ireland in 2019, of which 55% are for shoulder OA.(1)

There are two broad types of Total Shoulder Replacement: anatomical (aTSR) and reverse (rTSR). aTSR retains the normal anatomy of the joint and is used for patients who have functional shoulder muscles (intact rotator cuff) that enable them to lift the arm above shoulder height. rTSR reverses the orientation of the components (the 'ball' is put on the glenoid and the 'socket' on the humerus) and is suitable for patients with a damaged or dysfunctional rotator cuff, as it relies on the deltoid muscle to enable the patient to lift the arm. One of the leading causes of revision of aTSR is subsequent rotator cuff failure. Therefore, in recent years more patients aged 60 years and over with an intact rotator cuff are having their shoulder replaced using rTSR, despite a lack of evidence of superiority over aTSR and a lack of evidence regarding the cost-effectiveness of the two procedures. Some data from the American healthcare system suggests that there may be higher hospital costs associated with rTSR, therefore it is also important to understand more about the relative benefits.(2, 3)

Shoulder pain and disability is a major reason for disruption to work, social and domestic activity.(4) The 2015 James Lind Alliance highlighted that patients want a shoulder replacement to give the best improvement in pain and function with least risk of repeat surgery. In 2020, a commissioned literature review by the National Institute for Health and Care Excellence (NICE) found no studies of either clinical or cost-effectiveness comparing aTSR to rTSR for OA patients with intact rotator cuff and called for a randomised controlled trial (RCT) to address this uncertainty.(5)

A survey of United Kingdom (UK) shoulder surgeons when developing the protocol revealed that 20/23 (87%) surgeons would or do perform rTSR in patients with shoulder OA who have an intact rotator cuff. The surgeons indicated that while aTSR can produce a better range of movement they worried about later cuff failure requiring revision of aTSR. In their view, the outcomes of rTSR are more reproducible. However, concerns were expressed about the ability to revise rTSR. 17/23 (74%) surgeons expressed willingness to change practice based on high quality evidence and two already use rTSR as first choice.

1.2 Review of existing evidence

Currently no RCTs compare aTSR with rTSR in adults with OA and an intact rotator cuff. A Cochrane review in 2020 reported a lack of high-quality studies and it is uncertain whether rTSR has better outcomes than aTSR.(6) Simovitch and Levy in comparative case series both report

that aTSR gives more reliable recovery of range of movement.(7, 8) While Schoch et al in a retrospective study of 187 shoulders reported that rTSR has a lower reoperation and complication rate with more satisfied patients.(9) Young et al (10) observed radiological signs of rotator cuff failure evidenced by proximal migration of the humeral head in 29.7% of 518 patients after aTSR in a retrospective multicentre review with mean follow-up of 103.6 months. Wright(11) found 11 of the 14 complications experienced by patients with aTSR were rotator cuff tears, with seven having repeat surgery at an average of 28 months. Data from the National Joint Registry (NJR) (1) indicates that the risk of revision of aTSR for cuff failure is 0.42 per 100 prosthesis years compared to rTSR with a rate of 0.02 per 100 prosthesis years. More recently a systematic review and meta-analyses has been undertaken of six retrospective studies of 447 patients with intact rotator cuffs for primary shoulder OA having either aTSA or rTSA.(12) Range of movement (ROM) was better (specifically external rotation, although trend towards better ROM in all tested directions) for aTSA than for rTSA, function scores were not different, glenoid loosening was more common with aTSA, and scapula notching more common with rTSA. Overall revision rate was no different. Importantly, no long-term follow-up was available from the eligible studies. Therefore, considerable uncertainty remains as to whether rTSR leads to better and more enduring outcomes over aTSR in this patient group.

Core outcome domains for shoulder RCTs have been agreed using the OMERACT framework and include pain, function and global effect(13) but a core outcome measurement set has not been agreed. In choosing the primary outcome instrument for this trial we have followed the guidance of the DELTA (Difference ELicitation in TriAls) group, and DELTA-2.(14) The Shoulder Pain and Disability Index (SPADI), is very reliable, has low floor and ceiling effects, is valid for use in shoulder arthroplasty research and, because it is the most sensitive to change, best enables us to answer the question of superiority of rTSA over aTSA in the two key domains identified by both the PPI group and OMERACT, that is pain and function.(15) There is also a strong correlation between SPADI score and range of shoulder movement.(16) The Oxford Shoulder Score (OSS) is included as a secondary outcome to enable comparison of the trial population with the NJR dataset (where OSS is used) to confirm external validity; however, the NJR evidenced ceiling effects of the OSS in shoulder arthroplasty, and lower responsiveness to change, making it unsuitable as the primary outcome instrument.(1) NICE have recommended the primary outcome should be collected at 24 months after surgery.(5)

In determining the age of patients eligible for the trial we have considered the NICE NG157 (Appendix J) recommendation for a different research question for patients under the age of 60 years, and the surgeons reported bias against rTSR in this age group, because of concerns about more challenging revisions.(5) The NICE research recommendation states that all patient groups are equally likely to suffer with pain and disability from shoulder OA and therefore we will involve centres nationwide and monitor diversity in partnership with VOCAL, a not-for-profit PPIE organisation hosted by the University of Manchester.

2 Research question and objectives

2.1 Research question

In patients aged 60 years and over, with painful OA of the shoulder with an intact rotator cuff and suitable bone stock, is reverse total shoulder replacement (rTSR) superior, in terms of clinical and cost-effectiveness, to anatomical total shoulder replacement (aTSR)?

2.2 Primary objective

To determine whether rTSR is superior to aTSR for the treatment of painful OA of the shoulder joint with an intact rotator cuff and suitable bone stock in patients aged 60 years and over as measured by patient-reported pain and function using the Shoulder Pain and Disability Index (SPADI) at 24 months.

2.3 Secondary objectives

- Confirm feasibility of the trial in an 8-month internal pilot, in particular site set-up, recruitment rate, assumptions regarding cuff integrity and whether this leads to cross-overs from aTSR to rTSR.
- Compare shoulder pain and disability using the SPADI at 3, 6, 12 and 18 months, and over the whole 24 months, between rTSR and aTSR.
- Compare rTSR to aTSR in other secondary outcomes including OSS, EQ-5D-5L, resource use, re-operations and complications at 3, 6, 12 and 24 months.
- Compare rTSR to aTSR in shoulder range of movement (ROM), shoulder strength and global shoulder score at 24 months.
- Compare the mortality and revision rates over 24 months between rTSR and aTSR including through NJR linkage.
- Evaluate the cost-effectiveness of rTSR and aTSR from the NHS perspective up to 24 months.
- Explore patients' perceptions of acceptability of rTSR and aTSR, patients' goals, and their experiences of recovery, within and across trial groups.

3 Trial design

RAPSODI-UK is a pragmatic, patient and assessor blinded, multi-centre, parallel group, superiority RCT to evaluate the clinical and cost effectiveness of rTSR compared to aTSR for patients with painful OA of the shoulder joint with an intact rotator cuff. There will be an 8-month internal pilot to assess the assumptions about site set-up, recruitment and cuff integrity. The trial will include a full health economic evaluation, NJR data linkage and an embedded qualitative interview study.

3.1 Internal pilot

We will select a minimum of 28 high and medium volume hospital sites and prioritize sites that have performed at least 130 shoulder arthroplasties in the three years to 2019.

Recruitment and monitoring data will be discussed with the Independent Data Monitoring Committee (IDMC) and the Trial Steering Committee (TSC) who will recommend to the funder about proceeding to the main trial. The pilot will last 1/3 of the recruitment period (8/24 months) and aim to recruit 1/5 (20%) of the total target (n=86/430), due to the large number of sites and staggered set-up, based on Herbert et al(17) and a target to set up 16 of the overall target of 28 sites. A proportion of recruits (we estimate up to 5%) may not have an intact rotator cuff when visually inspected at the time of surgery, despite appearing intact on pre-operative imaging. When this occurs patients randomised before the planned operation to aTSR would cross-over to rTSR, whereas those randomised to rTSR would proceed as allocated. This could lead to unbalanced cross-over. This risk could be mitigated by randomising at the time of surgery but this would be more challenging for the surgical team to be prepared to undertake either intervention and have both prosthesis kits available for use and may increase theatre time. We therefore plan to randomise before surgery. The number and proportion of participants, in both groups, seen not to have an intact rotator cuff during surgery, and the resulting number of cross-overs in the aTSR group, will be assessed during the pilot phase to inform whether to continue or not with randomisation before the planned surgery. We may need to continue to monitor this beyond the pilot depending on whether there are sufficient patients at that time to make a decision, also as new sites are enrolled it will be important to monitor that this does not change. Any patients who are identified as having non-intact rotator cuff during surgery will remain in the trial and be followed-up and analysed following the principles of intention-to-treat. We will also monitor, in both groups, whether there are cancellations or postponements in surgery post-randomisation, and the time between randomisation and surgery. Routine imaging done within six months before surgery will be used, or earlier imaging if not routinely available, to assess the integrity of the cuff to reduce the risk of time dependent changes in cuff status.

Progression criteria for recruitment will be: Green (recruit ≥100% of target [n≥86]); Amber (60%-99% [n=52-85]), review and implement methods to increase recruitment, if feasible, otherwise stop trial); Red (<60% of target [n<52]) stop unless mitigating circumstances. This and other progression criteria are detailed in Table 1.

Table 1: Progression criteria for the internal pilot

	Red	***Amber***	***Green***
Total number of participants recruited	*<52*	*52-85*	*≥86*
Recruitment rate/site/month	*<0.64*	*0.64-<1.06*	*≥1.06*
Number of sites opened	*<10*	*10-15*	*≥16*
Percentage randomised to aTSR that receive it	*<70%*	*70-<95%*	*≥95%*

Screening logs will be used to monitor the number screened, eligible, approached and randomised.(18) The extent to which eligible patients are not given the opportunity to participate in the trial and whether there are any trends in the characteristics of patients not approached will be monitored. We will also monitor the reasons why patients decline participation in the trial (if they agree to provide this information). We will explore whether any factors under our control can be addressed during the pilot.(17)

The age cut-off of 60 years in our patient population is consistent with the threshold for equipoise for consideration of rTSR amongst clinicians which was informed from a survey of surgeons when designing the study. Below this age there are concerns that the patient will require revision of the implant during their lifetime and that this may be more complicated after rTSR than aTSR. We will monitor the proportion of the sample that are in the 60-69 age group and above using the screening logs. We will closely monitor if the recruited patient group is similar in characteristics to the population included in the NJR from data published in their annual report. We will use this information to inform the ongoing support and training provided by York Trials Unit (YTU) to recruitment staff at individual sites and at cross site meetings to share good recruitment practice from other orthopaedic surgical trials.(19)

At the end of the pilot phase, data required to assess the trial against the pre-specified progression criteria will be summarised descriptively. No formal hypothesis testing will be undertaken, nor will this involve looking at any primary or secondary outcome data. The IDMC and TSC will review progress and recommend that the trial continue without amendments, continue with major/minor amendments, or discontinue.

4 Methods

4.1 Setting

Orthopaedic departments of NHS Hospitals in England, Wales and Northern Ireland that routinely treat shoulder OA with both anatomic and reverse shoulder replacement.

4.2 Target population

Patients aged 60 years or over with painful OA of the shoulder and an intact rotator cuff presenting to secondary care and through shared decision making, having completed non-surgical treatments, proceeding to shoulder replacement.

4.2.1 Inclusion criteria

- Aged 60 years and over.
- Diagnosis of painful OA of the glenohumeral joint using routine radiographs not controlled by previous interventions.
- An intact rotator cuff determined by pre-operative advanced imaging (Ultrasound, MRI, or CT).
- Minimal glenoid erosion determined by pre-operative CT or other imaging in whom an off the shelf replacement is appropriate.(20)
- Able to give informed consent.

4.2.2 Exclusion Criteria

- Shoulder replacement surgery contra-indicated.
- A diagnosis of inflammatory arthritis, acute trauma or trauma sequelae.
- Evidence that the patient would be unable to adhere to trial procedures or complete questionnaires.
- Trial participant for total shoulder replacement for the opposite shoulder.

4.3 Interventions

Patients will be assessed for eligibility via review of existing radiographs (typically anteroposterior and axial views), CT or other imaging. Once identified as meeting the above criteria, eligible and consenting patients will be randomly allocated to either anatomical total shoulder replacement (aTSR) or reverse total shoulder replacement (rTSR). Only commercially available off the shelf implants will be used. We define “off the shelf” as not designed or made to order but taken from existing stock or supplies. If glenoid erosion requires custom made prosthesis then these patients will be excluded. Some hospitals will use fluoroscopic imaging during surgery, as part of their standard practice.

4.3.1.1 <u>Anatomical total shoulder replacement (aTSR)</u>

The aTSR is a conventional shoulder replacement which mimics the natural ball and socket structure of the joint and relies on the presence of an intact rotator cuff for useful range of movement. The choice of implant will depend on local practice at recruiting sites but will include any anatomical shoulder implant from any manufacturer licensed for use in the UK implanted using techniques consistent with manufacturer instructions. We will record and report the implants used. The advantage is the potential for better function but with a risk of revision for failure of the rotator cuff.

4.3.1.2 Reverse total shoulder replacement (rTSR)

For the rTSR, the arrangement of the ball and socket component parts are reversed making use of the deltoid muscle for movement of the arm: it does not rely on an intact or functioning rotator cuff. The advantage is that this may reduce complications and re-operations(9) and it does not depend on the rotator cuff to function, but the implant may be more costly. However, the range of movement from a rTSR compared with an aTSR does not appear to be as good and scapula notching is more common.(12) The choice of implant will depend on local practice at recruiting sites but will include any reverse shoulder implant from any manufacturer licensed for use in the UK implanted using techniques consistent with manufacturer instructions. We will record and report the implants used. Other surgical risks are similar for the two types of implant.

4.3.2 Surgeon's level of experience

To reflect the pragmatic design of this trial a required level of experience of the operating surgeon will not be defined, but all surgeons performing shoulder arthroplasty on patients within the trial will be required to be familiar with the techniques and equipment that they are using. Data will be collected on the level of primary and secondary surgeon through the NJR minimum data set.

4.3.3 Surgical approach

The surgical approach will depend on local practice at recruiting sites and will not be mandated in the protocol in keeping with the pragmatic design but will be recorded and may include a deltopectoral or deltoid splitting approach. The treatment of the rotator cuff during the surgical approach and repair on completion of the surgery will be recorded but will be left to the discretion of the operating surgeon.

4.4 Post-surgical rehabilitation

Both groups will receive usual post-operative care including physiotherapy which can be delivered in person, remotely or using a hybrid model (as per current practice). We will provide an update to physiotherapists at each site with the best available evidence on rehabilitation after TSR, including evidence where available about post-operative rehabilitation following aTSR and rTSR. The timing and frequency of the physiotherapy will follow usual care at participating sites. Data on the post-operative physiotherapy programme including the content and number of physiotherapy sessions will be recorded and described. We will also collect and summarise documents from participating sites that describe their typical physiotherapy protocols for patients having TSRs including exercise leaflets or templates.

4.5 COVID-19 mitigation

We have planned data collection methods to mitigate against any ongoing COVID-19 disruption. The trial is designed with minimal patient contact using postal questionnaires for the primary and many secondary outcome measures. No additional research-related hospital visits are required for participants in the trial outside of routine care.

In some NHS hospitals elective shoulder replacement surgery may be provided in local private hospital facilities. Where possible, and after ensuring that patients are still covered by NHS indemnity, local agreements will be put in place to include these facilities. Assessments will be made during Site Initiation Visits (SIVs), contracting and monitoring.

Whilst patients testing positive for coronavirus on admission are not specifically excluded from the study, it may be that these patients will not be considered suitable for surgery. The decision will be that of the treating surgeon in line with any local restrictions.

4.6 Outcomes

The follow-up timepoints in this trial are 3, 6, 12, 18 (SPADI only) and 24 months post-randomisation. Early time-points are required to assess change in outcomes over time. The rationale for the 18-month SPADI assessment is that we hope this will reduce both loss to follow-up between 12 and 24 months, and the impact of loss to follow up if participants complete data at 18 months but not 24 months.

4.6.1 Primary outcome

The primary outcome is the combined pain and disability score measured using the Shoulder Pain and Disability Index (SPADI) at 24 months. These two domains are deemed ‘mandatory’ for shoulder disorder trials by OMERACT.(13) The 13-item SPADI is a validated and sensitive instrument for use in shoulder arthroplasty that assesses two domains; pain (5 items) and functional activities (8 items) on numerical rating scales.(15, 21)

4.6.2 Secondary outcomes

- **Combined pain and disability score:** measured via the combined SPADI score at 3, 6, 12 and 18 months, and over 24 months.
- **Individual pain and disability scores:** measured via the subscale scores of the SPADI at 3, 6, 12, 18 and 24 months, and over 24 months.
- **Pain and function:** measured via the Oxford Shoulder Score (OSS), which is a 12-item patient-reported outcome measure of shoulder pain and function with 5 response categories and overall scale ranging from 0 (worst) to 48 (best).(22) The OSS will be collected at 3, 6, 12 and 24 months. The OSS is also collected by the NJR in patients undergoing shoulder arthroplasty; this will enable comparison of the trial participants’ OSS with the NJR cohort as reported in their annual progress reports.
- **Change in shoulder:** patient opinion about the change in their shoulder will be assessed using the global shoulder score at 24 months via the question “Compared with just before the operation for your shoulder replacement at the start of the study, how would you say that your shoulder is now?”. Responses will be on a 5-point Likert scale with the following options: much improved, improved, same, worse, and much worse.(23)
- **Health-related quality of life:** measured at 3, 6, 12 and 24 months via the EQ-5D-5L, 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.(24) The EQ-5D-5L will be used to calculate quality-adjusted life years (QALYs) according to NICE best practice guidance at the time of the analysis.

- **Range of shoulder movement**: The range of shoulder flexion, abduction, internal and external rotation will be assessed by a suitably trained blinded assessor at 24 months using a hand-held goniometer following trial specific instructions and recorded as continuous measurements except for internal rotation that will be assessed according to the position of the thumb to the spine.(25)
- **Strength of shoulder:** Shoulder strength will be measured at 24 months using a spring balance as described for the Constant Murley Score by a suitably trained blinded assessor.(25) This will be done for both shoulders and repeated three times and will only be completed if the arm can be elevated to 90 degrees (abduction).
- **Complications:** Expected complications related to the affected shoulder will be recorded and will include (but are not limited to) deep and superficial wound infection (using Centers for Disease Control (CDC) and Prevention definition),(26) re-hospitalisation, implant, nerve and skin problems. These complications will be recorded at 3, 6, 12 and 24 months. Complications specific to the arthroplasty implant (i.e. glenoid loosening (keeled and pegged), scapula notching and lucency of the humeral stem)(27-29) will be reviewed by the local surgeon using post-operative radiographs (typically anteroposterior and axial views) and two year radiographs (typically anteroposterior and axial views) or the most recent radiographs if not available at two years. This assessment will be performed using routinely taken radiographs and where feasible by a local surgeon who did not operate on the participant. Depending on the availability of funding, these radiographs will be anonymised of personal data and collected for central review independent of the surgeons at the local hospital.
- **Re-operations:** An operation to correct the complications of a previous operation due to, for example, an infection or dislocation. Re-operations will be recorded at 3, 6, 12 and 24 months.
- **Revision and mortality:** Rates of implant revision and patient mortality over the 24-month follow-up will be collected from hospital and the NJR records to identify patients in whom revision was undertaken elsewhere or death that is not recorded in the hospital records. A revision will be defined as for all joints in the NJR which is any operation where one or more components are added to, removed or modified in a joint replacement or if a Debridement And Implant Retention (DAIR) with or without modular exchange is performed.(30)
- **Resource use:** Data on resource use will be collected to inform the economic evaluation (e.g. length of hospital stay, re-hospitalisation, physiotherapy). Data will also be recorded about use of private care, and days lost to work and normal activities. These data will be collected from participants and hospital records at 3, 6, 12 and 24 months.

4.6.3 Baseline data

The SPADI, OSS, EQ-5D-5L, range of shoulder movement and shoulder strength will be collected at baseline. Other validated measures to be included at baseline will be a patient-reported 5-item frailty scale,(31-33) a five-stage grading of muscular fatty degeneration (34), a co-morbidity index(35) and an assessment of glenoid erosion.(36) Other data collected at baseline will include socio-demographic characteristics of participants and moderators of prognosis. Baseline data will be collected prior to randomisation. The range of shoulder movement and shoulder strength, however, may be collected by a blinded assessor (and the participant will be blinded) after randomisation to allow planning for surgery.

4.7 Sample size

The primary outcome is pain and disability (combined SPADI score) at 24 months. As two approaches to surgery are being compared, we need to power the trial to detect a small to moderate difference between the groups at 24 months. The smallest difference classed as clinically important on the SPADI is 8 points.(37) We conservatively assume a group standard deviation (SD) of 25 points, based on 3 non-randomised studies.(9, 38, 39) We plan to use a linear mixed-effects model in the primary outcome analysis, which uses data from all study time-points, to obtain an estimate of the between-group difference at 24 months. However, due to a lack of reported data in the literature that can be used to inform our assumed between-visit correlations, we instead calculate the sample size estimate based on an ANCOVA ('baseline-as-a-covariate') model which uses only the baseline and 24-month visit estimates as a conservative upper bound on the required sample size, knowing that a linear mixed-effects model will likely achieve the greater statistical power for a chosen number of participants.

Assuming a baseline/24-month SPADI score correlation of 0.35(40), we need 182 participants per group (364 total) with 24-month SPADI data to give 90% power to detect a difference of 8 points (SD 25) between rTSR and aTSR, using ANCOVA and a 5% significance level. Allowing for 15% loss to follow-up at 24 months(41) we need to randomise 430 participants.

The OSS is our key secondary outcome measure to allow direct comparison of the trial population to the NJR in order to confirm external validity. Assuming a between-group difference of 2.7 points (the smallest available relevant, validated important difference), an expected SD of 8.80, and a baseline correlation of 0.35, the sample size of 430 would achieve 87.5% power for the OSS using a similar ANCOVA analysis method and the same underlying assumptions.

Based on NJR data for 2019, there were 7294 shoulder arthroplasty procedures, 55% (~4000) of which were for OA. Our 28 selected sites perform around 1916 TSRs per year (so approximately 1054 will be for OA). Assuming 60% of OA cuffs are intact, a conservative estimate based on the proportion of patients from the NJR with a diagnosis of OA having aTSR or hemiarthroplasty, and an expected minimum 55% recruitment (consent amongst those eligible, based on similar surgical trials with two surgical arms of equal intensity (DRAFFT HTA 08/116/97)), we can recruit 347 per year (an average 1.03 per site per month) from these sites once all are open to recruitment. We will set up sites in a staggered formation over 14 months,

prioritising the high-volume sites, resulting in an expected recruitment rate of 1.06 per site per month during the internal pilot. We expect to achieve the target sample size with a 24-month recruitment period. The Trial Management Group will regularly monitor the number screened, eligible, approached and randomised and take appropriate mitigating action, including recruiting additional sites (up to a maximum of 35), as necessary.

4.8 Participant recruitment

The research team will work closely with the hospital staff at each participating site to optimise the local screening and recruitment processes for local circumstances. Screening to identify patients eligible for the trial will be those attending an out-patient clinic or already on the waiting lists for shoulder arthroplasty prior to the pre-operative clinic.

Routine radiographs (typically anteroposterior and axial views) to confirm OA of the shoulder (glenohumeral) joint will have been taken as part of routine care. More detailed routine imaging with CT, MRI or ultrasound done within six months of surgery will be used to assess the integrity of the rotator cuff or using earlier imaging if not routinely available. A routine CT scan or other imaging will confirm minimal erosion of the glenoid and the morphology of the glenoid and be recorded.(42, 43) All this imaging will be part of standard care prior to the patient being enrolled into the study and will not require their consent. Delegated hospital staff will approach eligible patients to take part in the trial at the earliest opportunity. For new patients this would be at their out-patient appointment clinic. For those patients already on a waiting list that will depend on the local practice of participating sites. This could include bringing the patient in for an out-patient appointment, calling the patient and/or posting the RAPSODI-UK trial patient information leaflet to the patient. Posters about the study will also be displayed in clinics. Informed consent will be confirmed and baseline data collected when the patient has been determined to be fit and ready for surgery such as at the pre-operative assessment clinic or consent to surgery clinic by a suitably qualified and delegated member of the research team. Where feasible, this will be done within 6 weeks from the planned surgery. Participants will have the right to withdraw from the study at any time but we will keep all data collected on them up until that time. The reason for withdrawal will be recorded, if the participant is willing to provide this, in the Case Report Form.

An Associate Principal Investigator (API) scheme will be available to involve aspiring researchers to coordinate trial recruitment. The APIs will be trained in trial processes and supervised by the PI at the site.

4.8.1 Remote consent

Where feasible, face-to-face consent is the preferred option. However, at some participating hospitals, patients already confirmed fit for surgery live a considerable distance away and therefore it is only feasible to confirm their written consent and collect baseline data when they attend on the day of the operation. This can be burdensome for both the patient and the hospital staff. It is also possible that new patients, not already on a waiting list, may not be able to be consented, such as at the pre-operative assessment clinic or consent to surgery clinic, because delegated hospital staff are not available.

In these instances, the patient will be called and/or posted the RAPSODI-UK trial patient information leaflet. If a patient agrees to consider the study further, a remote meeting would be organised (e.g. telephone call or video call) to discuss the study and do the consent and baseline data collection (except for the shoulder range of movement and strength assessment which will still need to be done in person) on that call. The remote consent clinic will be performed by both a nurse and a witness nurse (or other appropriately authorised staff who are GCP trained). The nurse taking verbal consent will read out the statements on the consent form and add their initials on behalf of the patient. Both the nurse taking the verbal consent and a witness nurse will sign the consent form and record the date this was done. The patient will need to sign the consent form and will be provided with a copy. Where feasible, this remote consent should be done within 6 weeks of the planned surgery.

The potential participant will have the opportunity to ask questions and where possible be given time to consider options. If the patient requires further information or does not agree to consent then the patient will proceed with the agreed standard of care as would occur during normal clinical practice.

At the remote clinic, the patient will have the option to verbally consent and be posted the baseline forms to complete and return to York Trials Unit in a pre-paid envelope provided.
In all instances, it is possible that the planned surgery may be cancelled and the patient needs re-listing. Therefore, if the patient has not been randomised (which should ideally be done within 2 weeks before the planned surgery date) within three months of the baseline data being collected then the SPADI only (primary outcome) will be collected again. The reassessment of the SPADI will be done remotely or by post. As the patient will have already consented to take part and provided contact details, then authorised staff at York Trials Unit will do this. If a SPADI is to be collected a second time (or more), the original consent will still apply and the participant will not need to be re-consented.Equality, diversity and inclusivity of patients

It is important that for the recruitment of patients in the study that we reach out to underserved and vulnerable populations.(44, 45)

Other than for the stated exclusion criteria, all patients who are identified as being eligible will be approached regardless of gender, disability, gender reassignment, marriage and civil partnership, ethnicity, religion or belief, sexual orientation, access to health care, or socio-economic status.

We acknowledge that we have limited control over the referral process from primary care or musculoskeletal interface services, or if underrepresented groups lack awareness of shoulder replacement surgery. While full investigation of these issues is outside the scope of this study we will make every attempt to ensure equal access and monitor this where feasible in eligibility screening reports.

We will make our teams aware to help identify barriers to recruitment and retention and we will mitigate these where possible. Ethnic minority communities appear to be underrepresented in those having shoulder replacement surgery but we do not know the prevalence of OA in this

population, and other communities sharing protected characteristics defined by the Equality Act 2010.

We have set up a designated team, with appropriate resources, to steer our efforts to ensure equality and diversity, and access for eligible participants. We plan to create information resources to be shared at SIVs to introduce the PPI team, provide contact details and inform site research teams of resources available. This will help them support participants who face difficulties joining or remaining in the study.

We will use information from screening to explore whether there are any trends in the characteristics of individuals being approached to participate in the trial or who decline participation, for example, age as outlined above. We will also investigate whether deprived areas are adequately represented using the participant's postcode and collect gender and ethnicity data at screening to monitor recruitment into the trial. Our team will advise the TMG of any unforeseen barriers to recruitment by particular sections of populations served that can feasibly be overcome. Capturing, evaluating and reporting this activity will be supported by the PPI lead who will attend TMG meetings. As part of the dissemination of RAPSODI-UK we will report on our experiences using these approaches.

4.9 Randomisation

Allocation will be 1:1, using random permuted blocks of random block size, stratified by age (60-69; 70+) as a surrogate of deteriorating shoulder rotator cuff function. The allocation schedule will be generated by a trial statistician, otherwise not involved in the recruitment or randomisation of participants. It will be implemented using a secure web-based randomisation service managed by York Trials Unit (YTU), ensuring allocation concealment. The research team at the site will confirm patient eligibility and consent and access the online service to perform the randomisation ideally two weeks before surgery but no earlier than the pre-operative clinic to confirm the patient is fit for surgery.

4.9.1 Allocation concealment and blinding

Patients will be blinded to treatment group allocation so will not be told which replacement they have received. The surgical wound is the same for both surgical approaches. Patients will be provided with a card to remind them about their blinding and to show health care professionals at appointments about being blinded. Sites will also be provided with a generic leaflet about helping patients to gain the maximum benefit from their operation as some sites provide these specific to the type of shoulder replacement. To help prevent unblinding of patients from occurring we will ask sites to list patients as a 'RAPSODI-UK Total Shoulder Replacement' so it is clear that an individual is a trial participant. Were a patient to be unblinded to their treatment allocation this will be recorded. Surgeons performing the surgery cannot be blinded to allocation. Outcome assessors who will undertake the shoulder range of movement and strength of shoulder measurements, will not be told which replacement the patient has had. There is a risk that staff who have sight of postoperative radiographs will be unblinded due to the appearance of the prosthesis on the radiograph but treating clinicians including

physiotherapists delivering post-operative rehabilitation will be asked not to disclose the type of replacement to the patient during follow-up visits. Blinded outcome assessors will be asked not to access radiographic records of the patient as these do not form part of the outcome assessment for the patient. The primary outcome is a patient-reported measure (SPADI), helping mitigate surgeon influence. Patients will be informed which type of surgery they had after primary outcome data are collected at 24 months. We will remind site staff on hospital Case Report Forms not to unblind patients and to record if it does happen. Trial participants will also be asked at 24 months whether they have been informed of the type of replacement they have had during the study and what they thought that was.

5 Data management

5.1 Data collection methods

Data will be collected from the participants at baseline, 3, 6, 12, 18 and 24 months post-randomisation. Baseline data will be collected at recruiting sites by a delegated member of staff. All follow-up data collection from participants will be by postal questionnaire with supplemental telephone/video conference follow-up for non-responders or collected in clinic when attending at these time-points as part of their routine care. Delegated staff will also collect data from hospital records at 3, 6, 12 and 24 months. This includes a local assessment of routine post-operative radiographs and those routinely taken at 24 months (or earlier if not available then) to assess complications specific to the arthroplasty implant. Final follow-up data collection will include a routine out-patient clinic attendance at 24 months to assess shoulder range of movement and strength by a blinded assessor.

YTU will manage the postal and telephone/video conference data collection, and the scanning and processing of all data collection forms. All reporting of data collection will be undertaken in line with the Consolidated Standards of Reporting Trials (CONSORT) statement.(46)

To minimise attrition, we will use multiple methods to maintain contact with patients. We will ask patients for full contact details (including mobile phone number and email address if available) to be used to contact them. For all the postal data collections, two reminders will be sent to non-responding participants (at 2 and 4 weeks past the due date), with a final attempt to obtain data by a telephone/video conference interview (at 6 weeks). Newsletters will be circulated to participants during the trial to keep them informed and engaged.(47) At some hospitals, the 24 month follow-up clinic is not a routine appointment. All trial participants will, therefore, receive a £20 gift voucher for attending the clinic and as a thank you for completing study questionnaires.

On their immediate return to YTU, participant questionnaires will be checked for missing data. Where this happens, a patient will be called to complete any missing primary outcome data, and other missing data as feasible, over the telephone/video conference call. As a duty of care, questionnaires will be checked immediately for anything that indicates that the participant could be at risk of harm. Where this occurs, the hospital team will be notified via email. To maximise data quality, on their return to YTU, key variables in the hospital CRFs will be reviewed by a

research data administrator for completion and accuracy, who will resolve any queries with staff at the relevant site. Following these initial checks, all CRFs will undergo a scanning process within Teleform software, followed by second checking and validation against predetermined rules.

A data management system will be used to track participant recruitment and study status as well as CRF returns. Data from CRFs will be processed by administrative personnel. Data will be verified through cross checking of the data against the hard copy of the CRF. The YTU Data Manager will write a Validation Plan for each CRF in consultation with the trial manager/coordinator and statistician. The Plan will include detailed coding for the CRF and data query resolution rules/procedures. Quality Control will be applied at each stage of data handling to ensure that all data are reliable and have been processed correctly.

For the purposes of ongoing data management and statistical analysis, each participant will be identified by a unique trial identification number.

5.2 Data entry

The patient questionnaires and hospital CRFs will be designed using Teleform software.(48) The data collected by trial participants and sites using paper CRFs, will be mailed (original paper CRFs) to YTU to be entered/scanned using Teleform. When necessary, a site can securely return the CRF electronically. Data collected via telephone or video call will be collected onto paper CRFs.

All data will be stored and transferred following YTU standard operating procedures. The staff involved in the trial (both at the sites and YTU) will receive training on data protection. The staff will be monitored to ensure compliance with privacy standards.

5.3 Data storage

Each site will hold data according to the General Data Protection Regulation (GDPR) as implemented in the Data Protection Act 2018.(49) Data will be collated in CRFs identified by a unique identification number (i.e. the participant trial identification number) only. A Trial Enrolment Log at the sites will list the participant identification numbers. YTU will maintain a list of participant identification numbers for all trial patients at each site.

All YTU data recorded electronically will be held in a secure environment at the University of York, with permissions for access as detailed in the delegation log. The Department of Health Sciences, in which YTU is based at the University of York, has a backup procedure approved by auditors for disaster recovery. Full data backups are performed nightly using rotational tapes, to provide five years' worth of recoverable data. The tapes are encrypted and password protected and stored in a locked fire-proof safe in a separate secured and alarmed location. All study files will be stored in accordance with Good Clinical Practice guidelines. Study documents (paper and electronic) returned to YTU will be retained in a secure University managed storage location for the duration of the trial.

All essential documents (i.e. the documents which individually and collectively permit evaluation of the conduct of a clinical trial and the quality of the data produced) will be kept with the Trial Master File and Investigator Site Files and retained for a minimum of five years after the conclusion of the trial to comply with standards of Good Clinical Practice. CRFs will be used to record all the information required from the protocol and will be stored for a minimum of 10 years after the conclusion of the trial as paper records in a secure University managed storage facility or off-site. The separate archival of electronic data on a password protected server will be performed at the end of the trial, to safeguard the data for the period(s) established by relevant regulatory requirements. All work will be conducted following the University of York's data protection policy which is publicly available.(50)

5.4 Data quality assurance and quality control

Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust will be the Sponsor for this trial and take overall responsibility for the quality of study conduct. The study will be fully compliant with the Research Governance Framework and MRC Good Clinical Practice Guidance.(51) Detailed instructions and guidance will be agreed relevant to database set up, data entry, validation, review, query generation and resolution, quality control processes involving data access and transfer of data to the Sponsor at the end of the trial, and archiving.

A rigorous programme of quality control will be undertaken. The day-to-day management of the trial will be the responsibility of the Trial Manager at YTU. Regular meetings with the Trial Management Group will be held and will monitor adherence to the trial protocol at the trial sites. Quality assurance checks will be undertaken by YTU to ensure integrity of randomisation, study entry procedures and data collection. YTU will undertake remote monitoring of participating hospitals to ensure the integrity of the trial such as the correct version of the protocol is being adhered too, the most recent CRFs are being used, the delegation log is up-to-date, data are being stored securely, and site staff are aware of the necessary safety reporting requirements. YTU will develop study-specific procedures and training of staff to ensure the rigor with which telephone/videoconference calls are undertaken with trial participants to collect data (both to check missing data from returned CRFs and to collect data that is not returned) and any actions that are required to safeguard participants that arise from data collection.

5.4.1 Direct access to source data/documents

A statement of permission to access source data by study staff and for regulatory and audit purposes will be included within the participant consent form with explicit explanation as part of the consent process and participant information sheet. This will also apply to seeking permission from patients to consent to using anonymised trial data for further research. Notably we plan to undertake an analysis of merged data from the two parallel trials that are being undertaken in the UK and Australia which includes both the qualitative and quantitative data. Management of qualitative data is addressed in Section 8.2.

Once YTU has completed the analysis and published in all intended scientific journals, the anonymised trial data will be available for other researchers if requested. In principle, anonymised trial data will be made available for meta-analysis and where requested by other

authorised researchers and journals for publication purposes. Requests for access to data will be reviewed by the joint Chief Investigators and trial team.

The Investigator(s)/Institutions will permit monitoring, audits, and REC review (as applicable) and provide direct access to source data and documents.

5.5 Embedded Study Within A Trial (SWAT)

A SWAT will be conducted around participant retention with an embedded 1:1 RCT to investigate the impact of a newsletter sent 6 weeks prior to each of the 18 and 24-month follow-ups on completed SPADI follow-up rates at these time-points (primary outcome 24-month SPADI completion), as a replication of registered SWAT 28.(47)

5.6 National Joint Registry Linkage

Rates of implant revision and patient mortality at 24 months will be collected from hospitals and the NJR records to identify patients in whom revision was undertaken elsewhere (to the recruiting site) or death not recorded in the hospital records. An expression of interest has been registered with the NJR of England, Wales and Northern Ireland to embed the trial for collection of this data. Separate funding will be sought to investigate survival outcomes up to 5, 10 and 15 years in our trial participants and to further confirm that our recruited population reflects that in the NJR.

The OSS is included as a secondary outcome to enable comparison of the trial population with the NJR dataset (where OSS is used) as reported in annual progress reports to confirm external validity. Other characteristics of our trial population will be compared with the NJR cohort such as age and gender. Patients will be asked if they agree to consent to complete questionnaires at future time-points beyond the 24-month follow-up (subject to the progress of this study and future funding) to further investigate long term outcomes.

Data will be collected on the level of primary and secondary operations performed by participating surgeons through the NJR minimum data set.

6 Statistical methods

Full analyses will be detailed in a Statistical Analysis Plan (SAP), to be finalised prior to the end of data collection, and approved by the Trial Steering Committee.

6.1 Descriptive and summary statistics

For the analysis of the full trial (assuming continuation from the internal pilot phase) a CONSORT flow diagram will be provided to display the flow of participants through the trial. The number of participants withdrawing from the trial will be summarised with reasons where available. Baseline characteristics will be presented overall and by intervention group. All trial

outcomes will be reported descriptively by group at all time-points at which they were collected. Continuous data will be summarised as means, standard deviations, medians and ranges, and categorical data as frequencies and percentages.

Outcomes will be illustrated graphically over time, including 95% confidence intervals (CIs) where appropriate.(15) We will present, by group, the number and proportion of participants who become unblinded to their treatment allocation over the follow-up.

6.2 Definition of analysis population

Statistical analyses will be on an intention to treat (ITT) basis, with participants analysed in the groups to which they were randomised.

6.3 Presentation and interpretation of treatment effects

Between-group treatment differences will be reported in the form of point estimates with 95% CIs and p-values. Statistical significance will be declared at the 5% level.

6.4 Analysis software

Analyses will be conducted in the latest available version of Stata or similar statistical software.

6.5 Analysis of primary outcome measure

The primary comparison of interest is the between-groups difference in SPADI score at 24 months. To make use of all available observations from all time-points in the trial, the estimate for the difference at 24 months will be derived from a constrained longitudinal data analysis (cLDA) model.(52) The model will be a linear mixed-effects model, featuring SPADI score as the outcome, intervention group, time-point (coded as dummy variables to denote the baseline, 3, 6, 12, 18, or 24-month time-points), age and gender as fixed effects, and participant identifier and study site as random effects. A series of group-by-time point interaction effects will be included as fixed effects, thereby making no assumptions about the shape of the SPADI score trajectory over time. The model will be constrained so that the baseline SPADI scores are equal between groups.(52) The model will use maximum likelihood estimation, with an unstructured covariance matrix. The between-groups difference in SPADI score at 24 months will be extracted from this model as the primary outcome and reported with a 95% CI and p-value.

6.6 Analysis of secondary outcome measures

The between-group differences for combined SPADI score at 3, 6, 12 and 18 months, and over 24 months will also be extracted from the primary analysis model as secondary outcomes. The other secondary continuous outcomes (e.g. SPADI pain and function subscale scores, OSS) will be analysed using an identical mixed-effects model to the primary outcome analysis, with the same covariates and covariance structure. The outcome in these models will be replaced with each of the secondary outcomes of interest. The OSS model will not feature an 18-month time

point, as this outcome is not collected at this time. While also a continuous secondary outcome, the EQ-5D-5L will exclusively be used in the economic evaluation.

Range of movement and strength are collected at two time-points (baseline and 24 months). The 24-month outcomes for these measures will be compared via a mixed-effects linear regression model with intervention group as the predictor variable, as well as age, gender and baseline value of the outcome, and site as a random effect.

The ordinal outcome of global shoulder score at 24 months will be analysed using mixed-effects ordinal logistic regression, adjusting for age, gender, and baseline combined SPADI score, with site as a random effect.

Time-to-event outcomes (time to revision/re-operation/death) will be explored by comparing restricted mean survival times between intervention groups (as we suspect that proportional hazards-type analyses may be inappropriate for these outcomes).

Safety outcomes (adverse event rate, complication rate and types of complication) will be summarised across all time-points at which they are collected.

6.7 Methods for additional planned analyses

Age is considered a key moderating factor on the effects of recovery from shoulder arthroplasty,(53) and from our survey of surgeons informs clinical decisions about whether to use aTSR or rTSR. We therefore will directly compare aTSR and rTSR in two specific subgroups, for differential treatment effects: age 60-69 years (where the two implants are provided in approximately even numbers in routine practice), and 70+ years (where clinically, rTSR are generally given in greater numbers than aTSR). We shall include an interaction term between age and treatment group in the primary analysis model, and will model the primary outcome in each of the two subgroups separately. Other moderators will be presented in the detailed SAP.

There is the potential for patients in this trial not to receive their allocated intervention (e.g. surgery not performed, or they cross-over). To account for this, a complier average causal effect (CACE) analysis will be considered as a sensitivity analysis, using an instrumental variable (IV) approach with randomised treatment assignment as the IV.(54)

For participants who complete the SPADI more than once at baseline (pre-randomisation), their first assessment score shall be used as a covariate in the primary analysis model. However, in sensitivity analyses, their second SPADI baseline scores will be substituted in place of their first score, and the primary analysis rerun to see if there is any impact on the treatment estimates. Likewise, if anyone completes the SPADI for a third (or more) time.

6.8 Methods to handle missing data

If observations are missing at random (MAR), rather than missing completely at random (MCAR), we will use multiple imputation to reduce the risk of bias in the primary analysis models.

We will consider performing a series of sensitivity analyses for the primary outcome analysis under plausible missing not at random (MNAR) assumptions.

6.9 RAPSODI-AUS

The RAPSODI-UK trial group support a linked application through the NIHR-NHMRC collaboration to run a parallel trial to the same protocol in Australia. Australia's national growth in shoulder replacement surgery over the last 12 years is amongst the highest globally with a 338% increase since 2008 (lifetime risk 1:57 males / 1:35 females). A similar number of replacements are undertaken annually compared to the UK despite a smaller population. Internationally, Australia has one of the highest ratios of rTSR (accounting for >80% of total shoulder replacements according to Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) 2019 data).(55) A parallel trial in Australia will inform whether the findings of RAPSODI-UK can translate to other healthcare settings (Australia has a mixed public and private healthcare setting). An analysis of the merged data, which would be funded through a separate funding application, will increase the precision for the primary outcome, improve the power for secondary outcomes and allow for moderator analysis to explore whether some patients benefit more from either of the TSRs. We also plan to share the qualitative data collected from the two countries to further explore similarities and differences in patient experience. A memorandum of understanding between UK and Australia will confirm arrangements regarding the governance and expectations of the collaboration.

7 Economic analysis

The economic evaluation will comprise (i) a within-trial analysis over the trial's 24-month time horizon and (ii) a decision analytic model to extrapolate beyond the trial, to evaluate the longer term cost-effectiveness of rTSR versus aTSR.

Data from the American healthcare system suggests that there may be higher hospital costs associated with rTSR.(2, 3) If this finding is replicated in the NHS setting in this trial it will be important to determine if this difference is justified by an improvement in quality adjusted life years (QALYs).

The economic analysis will be conducted as per NICE Guide to the Methods of Technology Appraisal(56) and Decision Modelling for Health Economic Evaluation.(57) The perspective of the cost-effectiveness analysis will be of the UK NHS and personal social services, over a time horizon of 24 months. Health and social care resource use, including that associated with the index surgery (for which we will consider using a micro-costing approach), adverse events, revisions, and physiotherapy will be used alongside published national unit costs and other

sources to estimate the costs associated with both surgical approaches. The EQ-5D-5L will be used with an area under the curve approach to estimate QALYs accrued during the trial. QALYs will be derived according to best practice guidance at the time of the analysis. Regression analysis, adjusted for key covariates, will be used to estimate net costs and QALYs (on an ITT basis) by arthroplasty allocation. These will be combined into an incremental cost-effectiveness ratio (cost per QALY). Bootstrapping and cost effectiveness acceptability analysis will be used to explore uncertainty and estimate the probability that rTSR is cost-effective (compared to aTSR) at different willingness to pay thresholds. Similarly, given the implication of the painful shoulder for the patient in terms of loss of earnings and lost days of normal activity, as well as private care costs, a sensitivity analysis from a broader perspective will be conducted.

A secondary analysis will explore the costs and benefits associated with the surgical approaches over a longer time horizon, using a probabilistic decision analytic model. The model will be informed by trial data and existing literature including the NJR which reports data on surgery revision rates. Future costs and benefits will be discounted following NICE guidance,(56) with sensitivity analyses undertaken to explore uncertainty around model parameters and assumptions.

Full details of the economic analyses will be provided in a pre-specified Health Economics Analysis Plan (HEAP), which will be developed prior to the end of data collection and agreed with the Trial Steering Committee.

8 Embedded qualitative study

8.1 Design

We plan an embedded longitudinal qualitative study, with semi-structured interviews conducted with participants from each trial group approximately 2 and 12 months after surgery. These time-points have been selected as they are key in the recovery process: at 2 months, patients are anticipated to starting regaining use of their arm and at 12 months functional recovery is starting to plateau for most patients.(7, 8)

8.1.1 Participants and sampling

Approximately 20 individuals will be recruited (10 from each trial arm). We may need to recruit more individuals at 2 months after surgery as there is anticipated drop-out at 12 months after surgery. We may also need to recruit patients only at 12 months if there is a shortfall at this time-point. This will result in approximately 40 interviews (two per participant). It is anticipated that this sample size will be large enough to gain a range of perspectives and for a rich understanding of participants' experiences and perceptions to be gained, whilst being small enough for the dataset to be effectively managed given the expected level of detail and depth.

Purposive sampling will be conducted to ensure approximately equal numbers from each trial group, and to ensure variation in age (individuals aged 60-69 and 70+) and geographical location (we will sample from a minimum of 4 trial sites). We will also aim to include variation in

gender and ethnicity within the sample. We would like to ensure inclusion of participants with variation in pain and function. If the sample lacks such variation, we may recruit additional participants at 12 months, using trial pain/function data to inform selection.

8.1.2 Recruitment

The interview study will be briefly mentioned in the trial PIS. In the trial consent form, participants will have the option to express willingness to be contacted about the interview study. The interview study researcher will have access to demographic information for individuals willing to be contacted, and also information about trial groups (sufficient information for the researcher to sample approximately even numbers from each group but without knowing which group is receiving which type of shoulder replacement).

Close to the time of the first interview (approximately 6 weeks after surgery), the researcher will send potential participants the interview study PIS. A week later they will contact them by telephone to establish that they received the PIS and to determine whether they would like to proceed with an interview. If the participant did not yet receive the PIS, the researcher will either 1) ring back in 48 hours time or 2) email it to the participant and ring in at least 24 hours time. If individuals wish to proceed, a time for the interview will be agreed that is at least 8 weeks after surgery. Interviews will take place at a time that is convenient to the patient and when clinical support would be available to the researcher if needed, in line with distress policy/safety procedures.

Consent will be taken verbally immediately prior to the interview. The researcher will first review the PIS with participants, check their understanding and answer any further questions. The interviewer will then audio record the consent process: the interviewer will ask participants to state their name before reading out each consent statement. Participants will be asked if they agree with each point. The audio-recorder will then be stopped, and a new audio-recording commenced for the interview.

On completion of each interview the participant will be sent a card thanking them for their involvement.

8.1.3 Data collection

Semi structured interviews will be conducted in English by telephone or video conference. Interview topics will include patients' priorities and expectations, experiences of recovery (including pain and functioning) and thoughts on the acceptability of each type of shoulder replacement. Patients' experiences of the trial will also be explored. The interview schedule will also be informed by the PPI group, the research literature and relevant theory (e.g. the Theoretical Framework of Acceptability).(58). The interviewer will be blinded to intervention allocation (they will be unblinded after participants have completed both interviews). If a patient has become unblinded, it is possible that they may reveal this during an interview. If this occurs it will be acknowledged during reporting and taken into account during analysis of the qualitative data.

Interviews will be audio-recorded and transcribed verbatim by a YTU researcher or a YTU-approved professional transcription service. All professional transcriptions will be checked for accuracy by a YTU researcher and during this process, transcripts will be pseudonymised: identifying details such as people and place names will be removed.

8.1.4 Analysis

An inductive, data-driven, thematic analysis will be conducted to identify and understand patterns in the data using the Framework approach.(59, 60) Framework is a systematic and transparent approach and includes the use of matrices to summarise data whilst maintaining flexibility enabling careful understanding and interpretation of the dataset. These matrices are used to interrogate and make sense of the data, aiding consideration of issues that are identified both within and across participant datasets. In an iterative process, preliminary findings will be shared with PPI contributors and clinical research team members in order to gain and incorporate their insights into the analysis. The analysis will aim to gain a deep understanding of patients' experiences and perceptions both within and across trial groups. Potential similarities and differences in experience by trial group will be explored to help explain the main trial findings. We will collaborate with the Australian qualitative team during analysis phases to explore cross-country similarities and differences within the data.

During the running of the trial, should issues be identified within qualitative interviews which may be relevant to the conduct of the trial, these will be shared with the trial team. This process will be carefully managed to ensure that the participant confidentiality for the qualitative study (as described in 8.2 and 8.3) is not compromised.

8.2 Ethical considerations

Confidentiality and anonymity

In discussing their experiences of shoulder replacement, recovery, and of trial involvement, some individuals may discuss their experiences with care teams, and such information could be valuable within the dataset. In order to be comfortable talking about these issues, it may be important to individuals that members of their care team are not able to identify them. After removing identifying details such as names and dates from transcripts, contextual information and/or descriptions of experiences may mean that transcripts could be identifiable to individuals who know the participant – such as members of their care team. To address this issue, restrictions will be placed on access to interview transcripts. During the study access will be restricted to the UK and Australian RAPSODI qualitative research team members, none of whom are care team members. After the study, sharing of data will be restricted to research teams who will follow the same data management rules as the RAPSODI team (see Data Management, below).

During or after interviews, it may be necessary to break confidentiality if the researcher is concerned that any individual might be at risk of harm or discloses information about criminal activities. The research team would inform the patient's care team of such concerns.

Distress

The topics being discussed in interviews are not anticipated to cause distress but it is possible that patients could talk about topics they find upsetting or worrying – for example, pain or difficulties with activities. Should a participant show signs of distress, the study distress policy will be followed.

Fatigue

It is possible that some participants could be experiencing fatigue. It will be made clear to participants, in the PIS and in verbal information at the start of the interview, that they can take breaks if they need to, and/or split the interview over more than one day. Part way through the interview, the researcher will check whether the participant is feeling well and able to continue, or if they would like to take a break.

Withdrawal

All participants will be informed that they are free to withdraw from the interview without giving a reason and without detriment, at any time before or during an interview. Data already provided up to the point of withdrawal will usually be retained for analysis. Participants will also be free to withdraw from the study up to 2 days after their participation in an interview, such that the data they provided in that interview would not be retained nor used in analysis. After this time, participants' data will be integrated into the analysis process.

If a participant loses capacity to consent after being interviewed, the information they provided during the interview will still be used in analysis.

8.3 Data management

During the study, the qualitative research team will need records of participant names and contact details in order to carry out interviews at two time points and to link interview datasets. Such details will be securely stored until completion of the study and then destroyed. Audio consent files will be stored separately to interview data, and details which might link consent files with interview data will be removed from the data set on completion of the study.

Interview audio-recordings will be securely stored until the completion of analysis and then destroyed.

Interview transcripts will be pseudonymised: identifying details such as names and dates will be removed and will be kept in a secure University managed storage facility for a minimum of ten

years. Remaining contextual information and/or descriptions of experiences may mean that transcripts could be identifiable to individuals who know the participant – such as members of their care team. During the RAPSODI study, full transcripts will only be available to the UK and Australian RAPSODI qualitative research team members (none of whom are members of participants' care teams); clinician members of the research team will not have access to full transcripts. Discussion of findings within the full team will be facilitated using documents summarising issues and quotes which are carefully selected to ensure participants will not be identifiable to anyone, including clinician members of the research team. The pseudonymised interview transcripts will be encrypted and securely shared with the Australian qualitative team using the University of York Drop Off system. After completion of the RAPSODI study, sharing of qualitative data (transcripts) will be restricted to reputable research teams who will work with the same rules surrounding data confidentiality and secure management as the RAPSODI team.

9 Project management

RAPSODI-UK will be sponsored by Wrightington, Wigan & Leigh Teaching Hospitals NHS Foundation Trust. The day-to-day running of the trial will be undertaken by the Trial Manager based at YTU supported by senior staff. Trial Coordinators will be responsible for the day-to-day support to trial sites, data handling, and the management of the administrative trial team. The team at YTU will meet weekly during the trial and will work closely with the Joint Chief Investigators (JCIs) throughout, including regular meetings to ensure that all aspects of preparation of study material, study site setup and the start of recruitment progress smoothly. YTU staff will keep in close contact via email, telephone or videoconferencing throughout. Each site will have a Principal Investigator (PI) who will be responsible locally for the trial and be encouraged to have an Associate PI (API).

YTU is experienced in working with local investigators at recruitment sites to ensure ethical and efficient delivery of trials in compliance with the trial protocol. In addition to regular TMGs, the trial team will keep in regular contact with sites and use joint local investigator meetings, newsletters and other forms of communication to monitor progress, support any struggling sites, and to share good practice across sites.

9.1 Trial Management Group

A Trial Management Group (TMG) will monitor the day-to-day management (e.g. protocol and ethics approvals, set-up, recruitment, internal pilot data evaluation and success criteria, data collection, analysis plan, data management, analysis, interpretation, dissemination) of the trial chaired by the JCIs. Membership will include the JCIs, co-investigators and research staff on the trial. Throughout the trial there will be regular tele/videoconference contact supplemented by face-to-face meetings where required. Frequency of meetings will vary depending on the stage of the trial.

The TMG comprises a multidisciplinary team that includes expertise in surgical management of patients with replacements of the shoulder in both techniques being tested; expertise in the involvement of the public and patients in research; physiotherapy; design, delivery and statistical analysis of RCTs; and design, delivery and analysis of qualitative research.

Prof Page and Prof Foster as co-applicants will be part of RAPSODI-UK TMG and RAPSODI-AUS TMG and will be fully informed of planned amendments via the two co-applicants and the sharing of study reports. Prof Trail and Prof Dias as JCIs will provide UK representation on the RAPSODI-AUS TMG as well as a representative(s) of YTU. At the TMG meetings in both countries there will be a standing item about updates to the protocol to ensure this is discussed as well as progress updates, safety reporting and other regulatory details as required. The Trial Managers for UK and Australia will also correspond about protocol amendments to ensure that there is timely sharing of this information.

9.2 Trial Steering and Independent Data Monitoring Committee

A Trial Steering Committee (TSC) will monitor progress of the trial, provide independent advice and the independent chair will make recommendations to the funder. An Independent Data Monitoring Committee (IDMC) will monitor the data arising from the trial and make recommendations to the TSC on whether there are any ethical or safety reasons why the trial should not continue. The TSC and IDMC will meet regularly to provide oversight to the trial. The trial will also be monitored by the Sponsor and a representative will be invited to attend the TMG and TSC meetings.

10 Safety monitoring

In the context of the lack of robust evidence to determine the best surgical approach for shoulder OA with an intact rotator cuff the risks are not increased through trial participation.

10.1 Definitions

Adverse events (AE) will be defined as any untoward medical occurrence in a trial participant to whom a treatment has been administered and which does not necessarily have a causal relationship with the treatment. Only medical occurrences related to treatment for the shoulder condition that are ‘unexpected’ and up until the 24-month follow-up will be classified as events. This is because ‘expected’ events are well known complications for the two routine treatment options that will be recorded on CRFs and which the specialist clinical care teams will be experienced in managing.

Serious adverse events (SAEs) will be defined as any untoward medical occurrence that:

- Results in death.
- Is life threatening (that is it places the participant, in the view of the Investigator, at immediate risk of death).

- Requires hospitalisation or prolongation of existing inpatients' hospitalisation (unplanned refers to emergency hospitalisations resulting in an inpatient stay; prolonged hospitalisation is deemed to be where a patient's stay is longer than expected).
- Results in persistent or significant disability or incapacity.
- Any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed.

10.2 Collection, recording and reporting of adverse events

A delegated member of the research team at the site will record all AEs or SAEs on the appropriate CRF for routine return to YTU. In addition, sites should follow their own local procedures for the reporting of any adverse events linked to clinical care.

AEs and SAEs will be reported to YTU within five days or 24 hours respectively of the site investigator becoming aware of them. Once received, causality and expectedness will be confirmed by either of the JCIs. SAEs that are deemed to be unexpected and related to the trial will be notified to the Research Ethics Committee (REC) and Sponsor within 15 days.

SAEs that may be expected as part of the surgical interventions and that do not need to be reported to the main REC include: complications of anaesthesia or surgery (e.g. wound complications, infection (superficial and deep), damage to a nerve or blood vessel and thromboembolic events), skin problems, implant problems (e.g. fracture, rotator cuff tear, and instability), and secondary operations for or to manage instability, infection, fracture, non-union or for symptoms related to the prothesis.

Follow-up reports a month later of all AEs and SAEs will be reviewed by either of the JCIs to ensure that adequate action has been taken and progress made.

AEs and SAEs will be monitored regularly at TMG meetings and reported to the TSC and IDMC when they meet. Members of the RAPSODI-UK team and RAPSODI-AUS team will attend both countries respective TMG meetings and be informed of these events. Both countries IDMC will also correspond with each other about trends observed in the reporting of these events.

11 Research governance

11.1 Ethical considerations and approval

The trial will be conducted to protect the human rights and dignity of the patients as reflected in the Declaration of Helsinki.(61)

Formal NHS REC approval will be sought via the Health Research Authority (HRA) specific to the individual countries. Local R&D approvals (confirmation of capacity and capability) will be obtained for participating sites. Any further amendments to the trial protocol will be submitted and approved by the appropriate regulatory authorities where required.

The participant information sheet for the trial will be developed with the involvement of service users and will give a balanced account of the possible benefits and known risks of the interventions. It will state explicitly that quality of care will not be compromised if the participant decides to a) not enter the trial or b) withdraw their consent. Written informed consent will be obtained from all participants who agree to take part in the trial after they have had sufficient time to read the study materials and ask any questions. The earlier section (8.1.2) explains consent to take part in the qualitative interviews.

A potential ethical concern for this study is the blinding of participants to their treatment allocation. This is to minimise bias in the collection of data that may occur from unconscious or intentionally perceived beliefs about the effectiveness of either treatment.(62) As both groups of patients will receive a total shoulder replacement we judge that it is ethically acceptable to blind them to their treatment allocation and we will explicitly seek permission for participants to be blinded when they are consented to the trial. During the trial, if there is a clinical need to do so, or they no longer consent to be blinded or take part in the study, then their treating clinician (or other delegated member of the clinical team) will inform the participant of their treatment allocation and this will be recorded. On completion of the 24-month follow-up, a participant will be notified of their treatment allocation by their treating clinician (or other delegated member of the clinical team) or by the research team as appropriate.

11.2 Competent authority approvals (proposed action to comply with the medicines for human use (clinical trials) regulations 2004)

The techniques under investigation are well-recognised and internationally accepted surgical procedures using CE-marked implants and medical devices. We do not require prior authorisation by the UK Competent Authority, the MHRA, under the Medical Devices Regulations (2002).(63)

11.3 Regulatory compliance

The trial will comply with the approved protocol and adhere to the Research Governance Framework and MRC Good Clinical Practice Guidance(64). An agreement will be in place between the site PI and the Sponsor, setting out respective roles and responsibilities.

All deviations from the protocol or GCP will be reported by PIs or designated site staff to YTU. The site must inform the PI as soon as they are aware of a possible serious breach of compliance, so that the sites can report this breach to the trial Sponsor (via YTU) with onward reporting to ethics and regulatory bodies as necessary. For the purposes of this regulation, a 'serious breach' is one that is likely to affect to a significant degree:

- The safety, physical or mental integrity of the participants in the trial, or
- The scientific value of the trial.

Processing of all trial data will comply with GDPR as implemented in the Data Protection Act 2018(49) and in accordance with the Australian Privacy Act 1988 for the purposes of future sharing of data between UK and Australia.

11.4 Patient confidentiality

The researchers and clinical care teams must ensure that patient confidentiality will be maintained and that their identities are protected from unauthorised parties. Patients will be assigned a unique participant identification number which will be used on CRFs. Sites will securely keep and maintain the patient Enrolment Log showing participant identification numbers and names of the patients. This unique participant number will identify all CRFs and other records.

All records will be kept in locked locations. All paper copies of consent forms will be secured safely in a separate compartment of a locked cabinet. Electronic copies will be stored separately to clinical information and access restricted to study personnel. Clinical information will not be released without written permission, except as necessary for monitoring purposes.

11.5 Trial closure

The end of the trial will be defined as the last patient last contact which will occur at 24 months after the end of the recruitment period (end of follow-up for the last patient) and after all the data are entered, checked and queries resolved.

An end of study declaration form will be submitted to the REC and Sponsor within 90 days of trial completion and within 15 days if the trial is discontinued prematurely. A summary of the trial report and/or publication will be submitted to the REC, Sponsor and Funders within one year of the end of the trial.

11.6 Annual progress reports

An Annual Progress Report (APR) will be submitted to the REC that gave the favourable ethics opinion 12 months after the date on which the favourable opinion was given and thereafter until the end of the trial (if applicable).

11.7 Urgent safety measures

The site PI may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. These safety measures should be taken immediately and may be taken without prior authorisation from the REC.

11.8 Access to data

The Investigator(s)/institution(s) will permit authorised representatives of the Sponsor and applicable regulatory agencies direct access to source data/documents to conduct trial related monitoring, audits and regulatory inspection. Trial participants are informed of this during the informed consent discussion. Participants will consent to provide access to their medical notes.

The participating site will archive the trial essential documents generated at the site for the agreed archiving period in accordance with the signed Clinical Trial Site agreement or Organisational Information Document.

11.9 Indemnity

This trial will be sponsored by Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust. If there is negligent harm during the trial, when the NHS Trust owes a duty of care to the person harmed, NHS Indemnity covers NHS staff and medical academic staff with honorary contracts only when the feasibility of the trial has been approved by the R&D department. NHS indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm.

12 Patient and public involvement

Our Patient and Public Involvement (PPI) group emphasised that patients want to be confident that any surgery offered is the best choice for pain relief and provides the best long-term functional outcome but is also informed by research evidence. The avoidance of further surgery and shared decision making were also extremely important. The PPI prioritisation of pain and function as important outcomes for them has driven our choice of primary outcome measure. They were supportive of a RCT (13 of 14 patients surveyed affirming they would be open to randomisation in a trial) and patient blinding during the two years. They were also supportive of aligning outcome measures with the NJR so long-term outcomes could be efficiently captured.

In line with DELTA-2 recommendations(14), the PPI group reviewed three commonly used outcome instruments and independently reported that the SPADI was the most relevant to them, the easiest to understand and the least burdensome. The PPI group identified pain relief as the most important goal of shoulder arthroplasty with improved function the next most important goal. It is our view that the pain and disability subscales of the SPADI will most easily enable us to report the trial results in a way that will be meaningful to patients and to clinicians, including pain relief and functional improvements between the interventions over time. This will facilitate the translation of findings into clinical shared decision making and will help impact realisation.

The PPI group also proposed gaining in-depth information about the acceptability of surgery, patients' experiences (including pain and function), and how these issues change over time. These findings would provide information to help explain the RCT findings. A literature search for qualitative research exploring patient experiences of shoulder arthroplasty revealed no relevant studies.

The PPI group will input into patient documentation, the topic guide for the qualitative interviews and materials for sharing the results to different audiences. We will also seek input from our PPI group about recruitment and retention challenges that arise during the trial as well as how to give participants a choice of how they would prefer to receive updates and messages of thanks for their participation.

13 Plan of investigation and timetable

The start date is 1 March 2022 with a 62-month total duration. The timetable for the trial is summarised below.

Activity	Duration	Time period
Trial set up including relevant approvals (REC, HRA)	6 months	1 Mar 2022 to 31 Aug 2022
Recruitment for internal pilot phase	8 months	1 Sep 2022 to 30 Apr 2023
Recruitment for main trial phase	16 months	1 May 2023 to 31 Aug 2024
Final follow-up data collection	24 months	1 Sep 2024 to 31 Aug 2026
Statistical analysis and write up of HTA report	8 months	1 Sep 2026 to 30 Apr 2027

14 Finance

The financial arrangements for the trial will be as contractually agreed between the funder (HTA), and the Sponsor (Wrightington, Wigan and Leigh NHS Foundation Trust). There will be a separate collaboration agreement between the Sponsor and the collaborating organisations.

15 Dissemination, Outputs and Anticipated Impact

This trial has the potential to improve decision making about which type of shoulder replacement to offer patients aged 60 years and over with OA and an intact rotator cuff. The use of the SPADI as the primary outcome will allow a clear discussion between surgeons and patients regarding the benefits of one surgical approach over the other in terms of pain relief and function gains. A publication plan will be developed by the trial team and approved by the Trial Steering Committee.

The executive summary and copy of the trial report will be sent to NICE and other relevant bodies, including to Integrated Care Systems, so that the study findings can inform their deliberations and be translated into clinical practice nationally. We will also work with the relevant National Clinical Director in the Department of Health to help ensure the findings of the trial are considered when implementing policy and will work with the Specialty Advisory Committees (SAC) to incorporate the findings into the training curriculum for clinicians who will undertake shoulder arthroplasty. The British Elbow and Shoulder Society have adopted the trial into their research portfolio which will facilitate dissemination of findings to relevant stakeholders.

A number of dissemination channels will be used to inform clinicians, patients and the public about the results of the study. The projected outputs are listed below:

- The study protocol will be published in a peer-reviewed, open access journal, after the study commences. The Statistical Analyses Plan will also be made publicly available.
- An HTA monograph will be produced.

- On completion of the trial, the findings of the HTA report will be presented at national and international meetings of organisations such as the British Orthopaedic Association Annual Congress, the British Shoulder and Elbow Society, European Federation of National Associations of Orthopaedics and Traumatology (EFORT), European Shoulder and Elbow Society (SECEC) and American Academy of Orthopaedic Surgeons.
- The trial report will be published in peer reviewed high impact general medical and orthopaedic journals, such as Lancet, the BMJ, the Journal of Bone and Joint Surgery or similar. The findings of the qualitative study will also be published on completion.
- The trial results (including the combined findings across UK and Australia) will be shared with relevant evidence synthesis teams (including within the Cochrane Collaboration) in order to ensure that results are incorporated in future systematic reviews.
- A summary of the trial report, written in lay language will be produced and made available to participants, members of our user group and relevant patient-focused websites.
- As part of the trial an information booklet on the condition, the likely recovery process and post-operative rehabilitation will be produced. We will explore making this more widely available to patients following the trial.
- We will also report on our findings about ensuring equality, diversity and inclusivity of patients into the trial.
- The findings of the SWAT will be disseminated in a relevant journal read by trialists such as BMC Trials or BMJ Open and disseminated at relevant conferences such as the International Clinical Trials Methodology Conference.
- Dissemination activities will be undertaken throughout the trial starting with the publication of the trial protocol. The trial protocol and updates on trial progress will also be presented at relevant surgical meetings (see above). This will create established pathways for dissemination of the findings when they become available.

Participants will be kept informed of the progress of the trial and trial outcome via newsletters annually. Information resources will be available to participants on webpages. After acquisition of 24-month follow-up, the participant will be informed of which implant was used.

16 Funding acknowledgement and disclaimer

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