Surgery versus PhysiothErapist-leD exercise for traumatic tears of the rotator cuff: a multi-site pilot and feasibility randomised controlled trial (the SPeEDy study)

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SIGNATURE PAGE

For Keele University sponsored studies, the sponsor will confirm approval of the protocol by signing the IRAS form and therefore a signature on the protocol is not required. The sponsor must be notified of all amendments to the protocol, both substantial and non-substantial. Review of amendments by the sponsor will act as the confirmation that the sponsor confirms approval of the amended protocol.

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol, GCP guidelines, the Sponsor's SOPs, and other regulatory requirements as amended.

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

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

Chief Investigator:

Signature: Date:

05/08/2019

.....

Name (please print):

.....Chris Littlewood.....

Sponsor statement:

Where Keele University takes on the sponsor role for protocol development oversight, the signing of the IRAS form by the sponsor will serve as confirmation of approval of this protocol.

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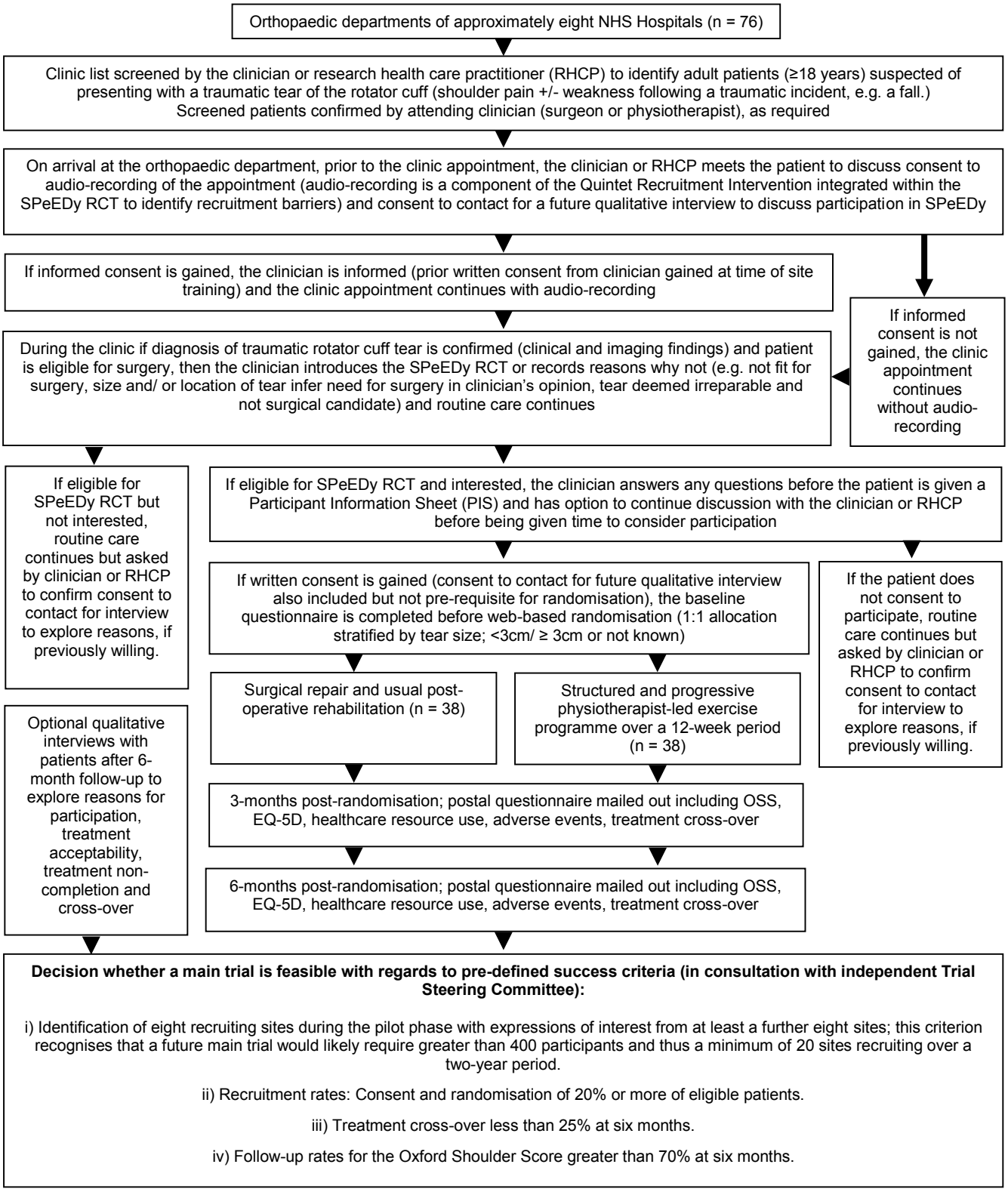
STUDY SUMMARY

Study Title	Surgery versus PhysiothErapist-leD exercise for traumatic tears of the rotator cuff: A multi-site pilot and feasibility randomised controlled trial.
Internal Ref. Number (or short title)	The SPeEDy study.
Study Design	Two-arm, parallel group, pilot and feasibility RCT with integrated Quintet Recruitment Intervention (QRI) and qualitative interviews.
Trial Intervention	Surgical repair of the rotator cuff with usual post-operative rehabilitation.
Study Participants	Adults with traumatic tears of the rotator cuff, eligible for surgery.
Planned Sample Size	76
Treatment duration	12 weeks
Follow up duration	6 months post-randomisation
Planned Trial Period	RCT 36 months (fellowship total 48 months)

Objectives:	Outcome Measures
1) Determine feasibility of recruiting patients	*Numbers of patients screened, number eligible, number approached, number consenting, number randomised, and number accepting allocation*
2) Determine feasibility of retaining participants	*Numbers of participants continuing in allocated treatment* *Follow-up response rates to questionnaires*
3) Determine zone of clinical equipoise	*Data from screening logs, including reasons for not approaching potentially eligible patients* *Integrated qualitative interviews*
4) Determine proportion and reasons for treatment cross-over	*Numbers of participants receiving treatment (surgery or PT-led exercise) other than that which was allocated* *Integrated qualitative interviews*
5) Estimate the number of potential and willing sites for the future main trial.	*Feasibility of recruiting current and future participating sites*
6) Identify barriers and facilitators to recruitment and retention	*Audio recording, integrated qualitative interviews*
7) Determine participant satisfaction with the interventions	*Satisfaction using a questionnaire on a five-point ordinal scale*
8) Determine the number and nature of adverse events.	*Data from self-report questionnaire at 3 and 6 months post-surgery* *Clinician report*

STUDY FLOW CHART



1 BACKGROUND

Shoulder pain presents a significant personal, social and economic burden and impacts on work, difficulty undertaking tasks, including leisure and household activity, and disturbed sleep [1]. Tears of the rotator cuff are regarded as a significant cause of shoulder pain and the rates of surgery to repair the torn rotator cuff have risen approximately 200% over recent years across Europe and the USA [2–5]. In the NHS, 9 189 surgical repairs of the rotator cuff were undertaken in 2015/ 2016 with approximately one-third undertaken for traumatic tears [6]. Depending on complexity, the cost of this procedure ranges from £2 897 to £5 593 [7] meaning that direct NHS treatment costs alone range from £26.6 to £51.4 million annually, and £9.6 to £18.5 million specifically for traumatic rotator cuff tears.

To date three RCTs (n = 252) comparing surgery to conservative treatment have been undertaken and synthesised in a systematic review [8]. The review concluded there is limited evidence that surgery is not more effective than conservative care. Hence the rise in the number of operations has occurred without evidence of comparative benefit. But, of the 252 patients included in the systematic review, only 40 (16%) were diagnosed with traumatic tears of the rotator cuff (24 randomised to surgery; 16 to physiotherapist-led exercise). So, there is a lack of evidence from RCTs to support clinical decision-making.

Different treatment pathways are proposed in the current British Elbow & Shoulder Society and British Orthopaedic Association guidelines [9] for patients presenting with non-traumatic or traumatic rotator cuff tears. The reasons for these different treatment pathways, in part, relate to suggestions that, for traumatic tears, a delayed surgical repair is more technically challenging and delay risks poorer clinical outcomes. Several non-randomised studies have evaluated the impact of time to surgery. Findings vary considerably with some recommending surgery within four months of symptom onset [10], some six months [11], and some 24 months [12] yet others conclude that time to surgery is not a critical factor [13]. Given that asymptomatic rotator cuff tears are also very common, it is also difficult to attribute tears of the rotator cuff to the recent trauma with confidence [14]. Imaging for shoulder pain following trauma might actually just be identifying an existing asymptomatic rotator cuff tear.

Whether treatment pathways for traumatic rotator cuff tears should be different to non-traumatic tears remains unclear. A previous cohort study of 1300 patients with traumatic (n = 811) and non-traumatic (n = 489) rotator cuff tears reported no difference in clinical outcomes according to the nature of onset of the tear [12].

Another concern relates to increasing size of the rotator cuff tear if not operated on [15]. It has been reported that 42 to 47% of symptomatic tears increase in size up to 100 months follow-up [15,16] with greatest rate of increase in those with full-thickness tears; observed in 82% versus 26% of those with partial-thickness tears [16]. Hence, some rotator cuff tears do increase in size over time, but it is apparent that some do not and, importantly, these increases in the size of tear are not consistently associated with poorer clinical outcome in terms of pain and function [16,17].

To further highlight the uncertainty in this area, the recent NIHR HTA funded UKUFF trial [1] reported a 40% re-tear or failed-healing rate following surgical repair but the outcomes for these patients were not significantly different from those patients who did not re-tear their rotator cuff. Similar findings have also been reported in a systematic review and meta-analysis of 14 studies (n = 861) [18]. Considering that surgical intervention is largely justified through implication that the rotator cuff tear is the source of symptoms and therefore the tear should be repaired to improve symptoms, this is an interesting finding that challenges the assumed mechanism of action of surgery. It also raises questions as to whether surgical repair is required to effect good clinical outcomes and whether, instead, physiotherapist-led exercise might be a credible treatment option just as it currently is for patients with non-traumatic tears [19].

A recent RCT comparing surgical interventions for tears of the cartilaginous shoulder labrum reported no benefit of surgery over sham surgery [20]. Another RCT (ACCURATE Trial/ NCT02885714), identified through a clinical trials registry search, currently recruiting (estimated study completion September 2019), compares surgical repair of the traumatic rotator cuff tear with sham surgery. The ACCURATE trial has the potential to offer useful information regarding the mechanism of action of surgical repair but will not inform clinical decision-making with regard to a credible alternative treatment.

In the context of finite NHS resources, there are cost implications to consider. Cost of surgery ranges from £2 897 to £5 593 depending on complexity with a further £115 to £204 for a course of post-operative rehabilitation with a NHS physiotherapist. The cost of post-operative rehabilitation is similar to the cost of out-patient NHS physiotherapist-led exercise (up to six sessions). In the UK, post-operative rehabilitation typically consists of immobilisation in a sling for up to six weeks followed by an exercise programme to regain movement, strength and function over a three to six-month period [21]. Based on data from sites who have expressed interest in being involved in SPeEDy, 36% of operations to repair the rotator cuff are for traumatic tears which equates to 3 308 operations in the NHS in 2015/2016 with direct costs (surgery and post-operative physiotherapy) of £10 to £19.2 million. Two previous studies have evaluated the impact of physiotherapy on the need for surgery with one reporting that 75% of patients with non-traumatic tears of the rotator cuff did not subsequently require surgery [22]. A RCT evaluating the impact of physiotherapist-led exercise [23] on the need for subacromial decompression surgery reported that 80% of participants did not subsequently require surgery. Cautiously extrapolating this data, if an out-patient physiotherapist-led exercise programme resulted in 50% of patients not requiring surgery, for an outlay of £380 420 to £674 832 (3 308 x £115 to £204), there would be considerable NHS treatment cost savings per year of £4.8 to £9.3 million. If societal costs are added to this calculation, including work costs, this figure would rise considerably. This cost-saving is in the context of rising incidence of rotator cuff tears over time.

Hence, in relation to this common and burdensome problem there is considerable uncertainty and lack of evidence from RCTs to inform decision-making. Beyond the ACCURATE Trial (NCT02885714), a clinical trials registry search identified two further ongoing RCTs (NCT01498198; NCT02059473). The

first of these is not restricted to traumatic rotator cuff tears, where most uncertainty exists, and the latter, in Sweden (n= 50), will not give answers to the feasibility of a future main RCT in the UK. Therefore, considering issues relating to cost, surgical risk (including infection and post-operative stiffness [24]) and patient and NHS burden associated with surgical intervention there is a strong ethical argument to urgently conduct high-quality research in this area. In a resource limited context, it is not acceptable to continue to provide invasive and expensive interventions without evidence of comparative effectiveness. Furthermore, the James Lind Alliance have identified this idea as a research priority in upper limb orthopaedic research [25].

2 RATIONALE

Despite being such a common and burdensome problem, the optimal treatment pathway for patients with symptomatic rotator cuff tears is unclear and a current research priority [25]. Clinically a distinction is made between type of rotator cuff tear; traumatic or non-traumatic and this sub-classification currently informs the treatment pathway [9]. Traumatic rotator cuff tears are diagnosed when onset of shoulder pain can be attributed to a specific event thought to be sufficient to tear the rotator cuff, e.g. a fall or sudden awkward movement of the shoulder, and non-traumatic or degenerative rotator cuff tears where a specific cause cannot be identified but a tear is identified on a scan, e.g. MRI or diagnostic ultrasound [9]. Reflective of the research evidence, patients with shoulder pain attributed to non-traumatic tears typically undergo conservative care, or more specifically physiotherapist-led exercise in the first instance, and surgery is only considered if this intervention fails [9,19]. This is not the case for traumatic rotator cuff tears where it is currently recommended that patients are fast-tracked for surgical opinion [9].

Despite these different pathways, there is a case for uncertainty about the most clinical and cost-effective treatment pathways for patients with symptomatic traumatic rotator cuff tears [8,25]. Given this uncertainty, in tandem with the cost and risk, for example infection, associated with surgery, and reports that approximately 40% of repaired rotator cuffs fail to heal or re-tear [1], a high-quality, adequately powered, randomised controlled trial (RCT) comparing surgery with physiotherapist-led exercise is needed to inform clinical decision making with potential for direct patient benefit and efficiency savings for the NHS.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary objective

In adult patients diagnosed with traumatic tears of the rotator cuff, is it feasible to conduct a future, substantive, multi-site RCT to test the hypothesis that physiotherapist-led exercise is not inferior to surgical repair of the rotator cuff in terms of clinical outcomes but is more cost-effective.

Objectives

1) Determine feasibility of recruiting patients

2) Determine feasibility of retaining participants

3) Determine zone of clinical equipoise, i.e. the range of patient characteristics (including age, size and location of rotator cuff tear, level of functioning) where clinicians are prepared to randomise or not

4) Determine proportion and reasons for treatment cross-over

5) Estimate the number of potential and willing sites for the future main trial

6) Identify barriers and facilitators to recruitment and retention

7) Determine participant satisfaction with the interventions

8) Determine the number and nature of adverse events.

3.2 Secondary objectives

Not applicable.

3.3 Outcome measures/endpoints

Feasibility outcomes:

1) Numbers of patients screened, number eligible, number approached, number consenting, number randomised, and number accepting allocation

2) Numbers of participants continuing in allocated treatment

3) Follow-up response rates to questionnaires at three and six months post-randomisation (including Oxford Shoulder Score and EQ-5D-5L)

4) Data from screening logs, including reasons for not approaching potentially eligible patients to inform determination of zone of clinical equipoise

5) Numbers of participants receiving treatment (surgery or PT-led exercise) other than that which was allocated to determine proportion of participants who cross-over

6) Feasibility of recruiting participating sites and numbers of additional sites who are interested in participating in the main trial

7) Participant satisfaction with the interventions on a five-point ordinal scale; Very Satisfied/Satisfied/Neutral/Dissatisfied/Very Dissatisfied

8) Barriers and facilitators to recruitment, retention and treatment cross-over (qualitative data; audio recording and individual interviews).

Clinical outcomes:

1) Pain and disability assessed using the Oxford Shoulder Score (OSS) at baseline, three and six months post-randomisation by post with telephone call for minimum data collection if no response to reminder postal questionnaire

2) Health related quality of life assessed using the EQ-5D-5L at baseline, three and six months post-randomisation by post with telephone call for minimum data collection if no response to reminder postal questionnaire

3) Days lost from work due to the shoulder problem at three and six months post-randomisation via postal questionnaire

4) Time taken to return to driving, if applicable, via questionnaire at three and six months post-randomisation via postal questionnaire

5) Number and type of adverse events for up to six months post-randomisation via patient self-report questionnaire or telephone Minimal Data Collection (MDC) at three and six months and via surgeon, physiotherapist or GP report.

Self-report data relating to further health care resource use, including NHS- and private borne service and medication costs will also be collected.

4 STUDY DESIGN

4.1 Interventions/Treatments

Intervention/ comparator:

1) Intervention; structured and progressive physiotherapist-led exercise programme. Reflective of current guidance for exercise programmes for people with rotator cuff disorders, an individualised programme developed in relation to the participant's specific goals will be prescribed by the physiotherapist and supported over approximately six contact sessions across a 12-week period.

During the first contact session, the physiotherapist will ask the participant about treatment related goals linked to functional activities. For example, participants might have difficulty reaching to a shelf at home, lifting at work, or sports-related difficulties, including serving at tennis etc. Once these have been identified, the physiotherapist will break down the identified functional activities in to component parts. For example, if the participant complains of difficulty reaching to a shelf, predominantly an activity of forward-flexion of the shoulder, initial assessment of exercise capacity will commence in relation to forward-flexion of the shoulder.

To highlight this, the assessment commences with testing of active-assisted forward flexion starting with the arm by the side and moving to 30º (Figure 1). Given the lack of research evidence supporting an

optimal number of repetitions and sets and considerable variation in clinical practice [26,27], a self-dosed approach will be taken where the participant is advised that the exercise should always be challenging to them. The participant could be challenged in relation to pain response, fatigue or perceived exertion, or a combination but this challenge should always be at a level that is acceptable to the individual participant. The level of acceptable response is likely to vary between participants but they will be re-assured that such challenge does not equate to damage and they should be guided by what is acceptable to them rather than with reference to generic guidance that might not be acceptable to them and hence would serve as a barrier to exercise adherence. So, for example, a participant might commence repeated active-assisted forward flexion with the arm by the side and moving to 30º. The first 20 repetitions might be perceived as challenging but acceptable, but repetitions beyond this become unacceptable. Then, the participant records the type of exercise performed and the number of sets and repetitions. This record sets the target for the participant to meet and exceed during their next exercise session. Such an approach facilitates progressive exercise. Participants will be advised to aim for a minimum of one exercise session per day, a minimum of five days per week, and up to three different exercise series will be prescribed, e.g. forward-flexion, abduction (reaching out to the side away from the body), and reaching behind back. Given the self-dosed nature of this programme, no upper limit will be prescribed providing the response remains within an individually acceptable limit. For example, participants would be asked to re-consider their approach to self-dosing if it was felt the number of exercises undertaken was contributing to pain that impaired sleep.

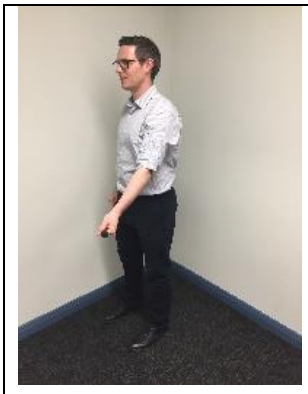


Figure 1 Active-assisted forward flexion starting with the arm by the side and moving to 30º

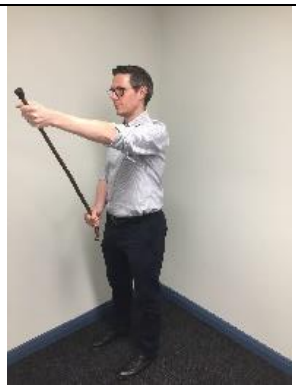


Figure 2 Active-assisted forward-flexion of the shoulder with the aim of reaching 90º

If stage one exercises are perceived as not challenging, the participant will be able to move on to stage two exercises. Multiple exercise prescriptions and progressions will be detailed in relation to various functional difficulties. These prescriptions and progressions will be detailed in an information and exercise booklet with photographs and descriptive text in sufficient detail to enable replication, informed by the TIDieR checklist [28]. In this example, stage two exercise would be active-assisted forward-flexion of the shoulder with the aim of reaching 90º (Figure 2). Following the same principles of progression, stage three would incorporate active-assisted flexion to 180º. Although we expect that

many participants will have exercise capacity greater than these initial stages, this assessment process is important in the context of exercise prescription because it teaches the participants how to progress but also regress their own exercise. This means that if the response to exercise becomes unacceptable when exercising away from the physiotherapist, the participant has the understanding of how to regress the exercise to maintain acceptable levels. Similarly, the patient also has understanding of how to progress the exercise, as they feel able. Such progression is an important component of effective exercise prescription [26]

Stages four, five and six, would include progression to active exercise; up to 30º for stage four, up to 90º for stage five (Figure 3), and then up to 180º for stage six (Figure 4).

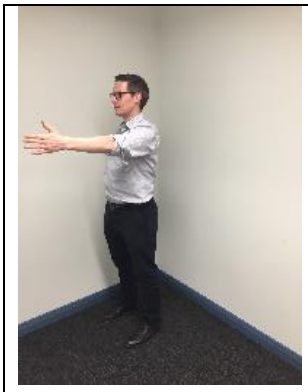
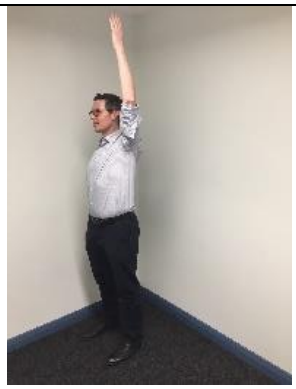
	

Figure 3 Active forward-flexion of the arm reaching to 90º	**Figure 4** Active forward-flexion of the arm reaching to 180º

Stages seven, eight and nine, would include progression to resisted exercise; up to 30º for stage seven, up to 90º for stage eight (Figure 5), and then up to 180º for stage nine (Figure 6).

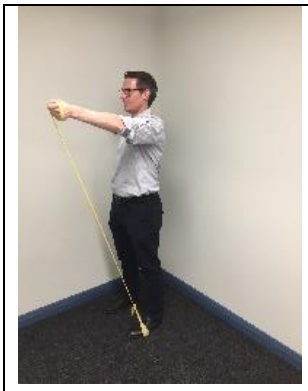


Figure 5 Resisted forward-flexion of the arm reaching to 90º	**Figure 6** Resisted forward-flexion of the arm reaching to 180º

The final stage of the physiotherapist-led exercise programme will include functional restoration with exercise prescribed by the physiotherapist in relation to the specific functional difficulty rather than isolated movements. In this example, the participant would be encouraged to undertake repeated

reaching to the shelf, initially with assistance, then without and then against resistance provided through an elastic training band or hand-weight.

The exercise approach described here enables adaptation to the individual participant who, in the context of this SPeEDy trial, are likely to present with quite different levels of exercise capacity at the outset. The programme will be prescribed and supported within existing NHS physiotherapy services where, following an initial consultation and exercise prescription, the patient will maintain responsibility for undertaking the exercise but will return to the physiotherapist, at individually negotiated and agreed time points over approximately six sessions across a 12-week time period, for follow-up self-management support and advice regarding exercise progression [29,30]. Adherence to the exercise programme will be recorded in an exercise diary provided to the patient and monitored by the physiotherapist. Alongside the exercise programme there will be an educational component, supported by the physiotherapist, that will further emphasise the study specific information, including a balanced view of the two interventions and uncertainty about the most effective approach. This aspect of the educational component will aim to identify and further discuss any subsequent concerns about being randomised to what might be perceived as a simple intervention, i.e. physiotherapist-led exercise, compared to a surgical intervention. This educational component will also include clear advice that improvement with exercise takes time and will involve asking the participants to identify barriers to exercise, e.g. time, and discuss ways of managing this.

Delivery of the physiotherapist-led exercise programme will be supported by a manual for the physiotherapists, other clinicians involved, and patient participants. Intervention fidelity will be determined via case note review with reference to the important components of the exercise programme and the number of physiotherapy contact sessions attended.

2) Comparator; surgical repair plus usual post-operative rehabilitation. Surgical repair will be guided by the size and location of the tear and also surgeon preference, the details of which will be recorded on a specific case report form and reported accordingly. Similarly, the content of post-operative rehabilitation is variable across the UK [21] but typically begins with a period of immobilisation using an arm sling for up to six weeks. After this period, rehabilitation progresses gradually with the aim of restoring movement, strength and function. The content of the post-operative rehabilitation programme (in-patient and out-patient) will also be recorded on a case report form following case note review and reported accordingly.

4.1.1 Intervention delivery

Appointments for the participants and follow-up physiotherapy appointments will be managed through the normal service channels at the participating sites, including arrangements for participants who do not attend appointments (DNAs) for treatments.

4.2 Study Training

Clinicians responsible for confirming potentially eligible patients (surgeons and physiotherapists, where appropriate), clinicians responsible for delivering study-related treatments, and research heath care practitioners (RHCP) will be trained at each of the participating sites in relation to the participant eligibility criteria, approach to recruitment and consent, completion of all study paperwork requirements, Good Clinical Practice (GCP) as applicable to research and the maintenance of the study site file and study records. Reporting of serious adverse events and adverse events will also be covered.

In addition, the clinical physiotherapists who deliver the physiotherapist-led exercise intervention will be trained prior to the start of recruitment and treatment. The focus of this training will be on individualised exercise prescription and progression and will be supplemented by a comprehensive manual providing clear guidance. This training will also cover study processes, including adverse event reporting. The training will take the form of a workshop consisting of information provision and practical application of the exercise intervention.

For pragmatic reasons relating to limited workforce capacity, the same clinical physiotherapists might treat participants in both groups. However, given the protocolised nature of post-operative rehabilitation, we do not anticipate any problems or expect a significant contamination effect but details of the exercise/ rehabilitation programmes delivered in both treatment arms will be recorded on case report forms, as described, and compared.

5 STUDY SETTING

Patients will be recruited from orthopaedic departments of the participating NHS hospitals. The study interventions will be delivered through their associated orthopaedic and physiotherapy services.

6 ELIGIBILITY CRITERIA

6.1 Inclusion criteria

1) Adult patients (≥18 years)

2) Diagnosed with a symptomatic tear of the rotator cuff following a traumatic incident thought to be of sufficient force to induce a tear.

3) Rotator cuff tear confirmed by diagnostic ultrasound or MRI scan undertaken as part of routine diagnostic work-up

4) Eligible for rotator cuff repair surgery or a programme of physiotherapist-led exercise as determined by the attending clinician (surgeon or physiotherapist, where appropriate)

5) Able to return to the participating NHS hospital or associated orthopaedic and physiotherapy services (where physiotherapists have been trained in trial interventions) for post-operative rehabilitation or the programme of physiotherapist-led exercise.

6) Able to understand English.

6.2 Exclusion criteria

1) Not eligible for rotator cuff repair surgery **or** a programme of physiotherapist-led exercise as determined by the attending clinician (surgeon or physiotherapist, where appropriate)
2) Patients who are unable to give full informed consent.

7 STUDY PROCEDURES

7.1 Patient identification and recruitment

Potential participants will be identified at the point when the diagnosis of symptomatic traumatic rotator cuff tear is made (sudden onset of shoulder pain and weakness following a traumatic incident with a tear confirmed by ultrasound or MRI) and surgery is considered as a treatment option. The pathway to this point in the care pathway is variable between sites but, typically, this diagnosis and treatment offer will be made by an orthopaedic surgeon, or physiotherapist where appropriate, who will subsequently introduce the trial to the patient. If the patient expresses interest, further discussion will ensue between the patient and the clinician or RHCP (depending on availability) who will provide them with a study information pack, by hand or in the post, and follow this up with a discussion, face-to-face or over the telephone. Building on a successful six-step model to promote recruitment to RCTs that resulted in 57% recruitment of eligible patients in the orthopaedic setting [31], this discussion will include: (1) an explanation of the condition, (2) reassurance about receiving treatment, (3) establishment of uncertainty as to the optimum treatment, (4) an explanation of the study purpose, (5) a balanced view of the two interventions and (6) an explanation of study procedures.

7.2 Consent

Interested and eligible patients will be required to provide written informed consent before participating (see reference below to optional Quintet Recruitment Intervention (QRI) and optional six month qualitative interviews). Typically, written informed consent will be sought at the time of attendance at the orthopaedic clinic or other convenient time prior to the surgery if the patient requests more time to consider participation in the trial. A clinician or RHCP, who will have received appropriate training and is authorised on the trial delegation log, will obtain informed consent. A record of the consent process and a copy of the consent form will be kept in the patients' medical records. The original consent form will be retained in the Study Site File and a copy will be given to the participant. A copy will also be sent to Keele CTU for monitoring purposes. Participants in the SPeEDy RCT have the right to withdraw from treatment and/ or completion of outcome measures at any time without any consequence to any future care they receive. The GP of each trial participant will be sent a letter to confirm that their patient is taking part in the research study.

On receipt of written informed consent, the baseline questionnaire will be completed prior to randomisation. The participant will then access the interventions as per usual treatment pathways, including being placed

on a waiting list for surgery or physiotherapy. Time to intervention will be variable between treatment arms and between treatment sites and will be recorded and reported accordingly, including the proportion of participants who have not commenced their allocated treatment at the three and six month follow-up time points. Should this pilot and feasibility trial prove feasible, the statistical analysis plan for any future main trial will not control for this variation but it will be accounted for, as a co-variate. The current median wait for surgery in the NHS is 74 days and between 14 to 42 days for physiotherapy.

7.3 The randomisation scheme

Participants will be allocated on a 1:1 ratio, stratified by tear size (large tear ≥3cm/ small to medium sized tear < 3cm/ or not known), using mixed blocks randomisation. Tear size is usually obtained as part of usual diagnostic work-up prior to confirming eligibility but where this is not known, for whatever reason, this will not preclude randomisation. Randomisation will be undertaken remotely using web-based randomisation to ensure allocation concealment provided by Derby CTU.

Following confirmation of eligibility, receipt of a correctly completed and signed consent form and completed baseline questionnaire, participants will be randomised to one of the two treatment arms. The randomisation will be performed using random permuted blocks, stratified by tear size (1:1 ratio) to ensure that patients with a similar tear size have an equal chance of receiving either treatment. The participant will be informed of the allocation by the clinician or RHCP and will then access the interventions as per usual treatment pathways, including being placed on a waiting list for surgery or physiotherapy.

7.4 Blinding

No measures to blind participants, clinicians, research team or oversight committees will be implemented in this external pilot and feasibility RCT.

7.5 Unblinding

Not applicable.

7.6 Baseline data

To meet the pre-specified objectives, the following baseline data will be collected:

Measure	Description
Patient descriptors	
Demographics	Gender, date of birth, height, weight
Duration of shoulder pain	Patient self-report in months: 1 question
Smoking status	Patient self-report: 1 question (current tobacco smoker/ past tobacco smoker / current e-cigarette vaper / past e-cigarette vaper/ never smoked or vaped)
Diabetes	Patient self-report: Yes/ No
Employment	Patient self-report: Current employment status : 1 question
Preference for treatment intervention	Patient self-report: 1 question with 3 options
Clinical status	
Shoulder Pain (Patient self-report)	Oxford Shoulder Score (OSS); 12 items, 5 discrete responses per item
Shoulder Function (Patient self-report)	Oxford Shoulder Score (OSS); 12 items, 5 discrete responses per item
Health related quality of life (Patient self-report)	EuroQol: EQ-5D-5L
Diagnosis	
Size & location of rotator cuff tear	Size according to imaging (USS or MRI): 1 question with 5 options (small <1cm, medium ≥1 but <3cm, large ≥3 but <5cm, massive ≥5cm, not known). Location according to imaging (USS or MRI): 1 question with 5 options – more than one can apply (supraspinatus, infraspinatus, subscapularis, teres minor, not known)

Consenting patients will complete the baseline questionnaire, including demographic data and GP details, the Oxford Shoulder Score (OSS), and EQ-5D. The participant will be given adequate time and a suitable location to complete the baseline questionnaire. It will be checked for completeness before proceeding to randomisation. The original baseline questionnaire will be returned to Keele CTU and a copy retained in the Study Site File. Once the baseline questionnaire is completed and checked the participant will be randomised to either the intervention or comparator.

The OSS is a 12-item shoulder-specific self-report measure of shoulder pain and function primarily for the assessment of outcome of shoulder surgery in RCTs [32]. The OSS is reliable, valid, responsive and acceptable to patients [1,32,33]. The items refer to the past 4 weeks with five ordinal response options scored from 0 to 4, with 4 representing the best outcome. When the 12 items are summed, this produces an overall score ranging from 0 to 48, with 48 being the best outcome.

The EQ-5D-5L is a generic measure of health related quality of life that provides a single index value for health status that can be used for the purpose of clinical and health economic evaluation [34]. The EQ-5D-5L consists of questions relating to five health domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and respondents rate their degree of impairment using five

response levels (no problems, slight problems, moderate problems, severe problems and extreme problems) [34]. EQ-5D is the National Institute for Health & Care Excellence's (NICE) preferred measure of health-related quality of life in adults.

7.7 Trial assessments

To meet the pre-specified objectives, the following data will be collected:

Assessment	Description
Feasibility of recruiting patients	Numbers of patients screened, number eligible, number approached, number consenting, number randomised, and number accepting allocation
Retention and follow-up rates	Numbers of participants continuing in allocated treatment Follow-up response rates to questionnaires at three and six months post-randomisation (including Oxford Shoulder Score and EQ-5D-5L)
Zone of clinical equipoise	Data from screening logs, including reasons for not approaching potentially eligible patients Qualitative data; audio recording and individual interviews
Proportion and reasons for treatment cross-over	Numbers of participants receiving treatment (surgery or PT-led exercise) other than that which was allocated to determine proportion of participants who cross-over Qualitative data; individual interviews
Number of potential and willing sites for the future main trial.	Number of recruiting participating sites and numbers of additional sites who are interested in participating in the main trial
Barriers and facilitators to recruitment and retention	Data from screening logs Qualitative data; audio recording and individual interviews
Patient participant satisfaction with the interventions	Participant satisfaction with intervention using a questionnaire with 5-point ordinal satisfaction question

7.8 Follow-up assessments

To meet the pre-specified objectives, the following data will be collected:

Measure	Description	3 months	3 months MDC	6 months	6 months MDC
Clinical status					
Shoulder Pain	Oxford Shoulder Score (OSS); 12 items, 5 discrete responses per item	✓	✓	✓	✓
Shoulder Function	Oxford Shoulder Score (OSS); 12 items, 5 discrete responses per item	✓	✓	✓	✓
Health related quality of life	EuroQol:EQ-5D-5L	✓	✓	✓	✓
Global change measure	Via questionnaire	✓	✓	✓	✓
Time taken to return to work (if applicable)	Via questionnaire	✓		✓	
Time taken to return to driving (if applicable)	Via questionnaire	✓		✓	
Adverse events	Via questionnaire and clinician report	✓	✓	✓	✓
Trial assessments/ Process Outcomes					
Patient participant satisfaction with the interventions	Participant satisfaction with intervention using a questionnaire with 5-point ordinal satisfaction question; very satisfied/satisfied/neutral/dissatisfied/very dissatisfied	✓		✓	
Health Care Utilisation					
Health Care Resource Use (including medication use)	Health Care Resource Use Questionnaire	✓		✓	
Days lost from work (if applicable)	Days lost from work due to the shoulder problem as a component question of Health Care Resource Use Questionnaire	✓		✓	
Date treatment commenced (surgery or physiotherapist-led exercise)	Via on-site Research Health Care Practitioner				

MDC = Minimum Data Collection over the telephone

7.9 Integrated studies

Quintet Recruitment Intervention (QRI)

Surgical RCTs can be challenging to recruit to with clear obstacles including a lack of time and strong patient preferences but also hidden challenges including tensions for clinicians and challenges around assuming a position of equipoise [35,36]. However, without formal evaluation, the recruitment challenges remain unknown and opportunities to change RCT processes, for example study training and documentation, are lost to the potential detriment to the RCT. In recognition of this the QRI will be integrated with the SPeEDy RCT to understand the challenges associated with recruitment and develop action plans to address these challenges rapidly while recruitment is underway.

The QRI is a mixed-methods approach that includes data collection and analysis of screening and eligibility logs, audio-recordings of recruitment consultations (i.e. consultations during which recruitment to the RCT is discussed), individual interviews with patients and clinicians involved in recruitment, and review of study documentation as a basis for developing action plans to address identified difficulties while recruitment to the RCT is underway [36,37]. It has been shown to facilitate recruitment to the most challenging RCTs, including orthopaedic RCTs [36,38]. A targeted QRI, investigating recruiter information provision, patient responses to this information and recruitment performance across recruiters/sites, will be integrated within the recruitment period of the SPeEDy RCT over the first nine months to enable barriers to recruitment to be identified and any changes to the recruitment process to be made and re-evaluated.

Recruitment

Prior to commencement of the relevant hospital clinic, the clinician or RHCP will screen the clinic list of all clinicians at study sites who have consented to audio-recording of their clinic appointments with potentially eligible patients. Information about the QRI will be presented to the clinicians and RHCPs during the initial study site training where the purpose and process of audio recording will be explained. Clinicians will be provided with written health care professional (HCP) participant information sheets during site training visits and will be given the opportunity to consent to audio-recording of clinic and recruitment appointments and/or consent to take part in an individual interview. If clinicians consent to participate in the audio-recording aspect of the QRI, this will be recorded at site. Although we aim to collect as many audio-recordings as possible, participation in the QRI (either consent to audio recordings or interviews) is not a pre-requisite for participation in the SPeEDy RCT.

The initial screen of the clinic list will identify, as far as possible, adult patients (≥18 years) suspected of presenting with a traumatic tear of the rotator cuff (shoulder pain +/- weakness following a traumatic incident, e.g. a fall. This initial screen will be reviewed by the attending clinician (surgeon or physiotherapist) to confirm potential eligibility based on available details, as required.

On arrival at the orthopaedic department, prior to the clinic appointment, the clinician or RHCP will meet the patient and discuss the QRI (referred to as the 'communication study') the purpose of which is to investigate how clinicians discuss trial participation with patients. Consent to contact regarding a future interview to explore reasons for participating or not participating in the SPeEDy RCT, if eligible, will also be requested at this point. A brief Participant Information Sheet (PIS) describing the QRI will be appended to a full PIS and will be provided along with a consent form relating to consent to audio-recording and consent to contact for a future qualitative interview, if relevant. The patient will be given time to consider the brief PIS prior to their clinic appointments.

If informed consent is gained, the clinician will be informed and the patient's clinic appointments will continue with audio-recording. Audio files will be removed from the recorder at the earliest opportunity by the clinician or RHCP at site and audio files uploaded and held on NHS computers (in accordance with NHS information governance and security arrangements) and deleted from the recorder. For consenting participants (clinicians and patients), a two working day cooling off period will be offered. This will enable participants time to read the full PIS after the clinic appointment. Participants will be provided with contact details of the clinical site Principal Investigator or nominated person whom they can contact to withdraw consent and hence request that the audio recordings be deleted rather than securely sent to the research team for analysis.

If consent remains in place (for both clinician and patient participant) after the two-working day cooling off period, only then will audio files will be securely transferred via nhs.net to Keele University and saved on Keele's Secure Network.

If informed consent is not gained, clinic appointments will continue without audio-recording.

During clinic, if a diagnosis of traumatic rotator cuff tear is confirmed and the patient is eligible for surgery, then the clinician will introduce the SPeEDy RCT or record reasons for not discussing the RCT (e.g. not fit for surgery, size and/ or location of tear implies clear need for surgery in clinician's opinion, tear deemed irreparable and not surgical candidate) and routine care will continue. If the patient has been invited to join the RCT but has declined participation, routine care will continue but, where written consent has been given (described above), the patient will be invited by the clinician or RHCP to confirm consent to contact by the research team to discuss participating in an interview to explore reasons for declining. Purposive sampling will be used to include a wide range of experience, e.g. patients from different sites, patients approached by different clinicians. Interviews will explore the perspectives of the interviewees in relation to the recruitment process to identify facilitators and barriers[36].

Where participants consent to audio-recording and also are interested in participating in the SPeEDy RCT, these recruitment appointments with the clinicians and/ or RHCP will be audio-recorded where

prior consent is provided. The two working day cooling off period will also apply, for both RHCPs and patients.

Data Collection

In line with the SEAR (Screening, Eligibility, Approached, Randomised) framework [39], screening and eligibility logs will detail: patients who were screened (by RHCP and attending clinician); those eligible or ineligible along with reasons; those approached about participation, including reasons why not approached; and whether they accepted randomisation within the RCT, and if not, why not. Logs will also record which arm patients accepting randomisation are allocated to and whether they accept this allocation. These will be completed at the clinical site.

Clinic and recruitment appointments will be audio-recorded and then subjected to targeted data extraction and transcription, focusing on issues relevant to recruitment to the SPeEDy RCT. Such a targeted approach recognises that much of the recorded discussion will not primarily relate to issues around recruitment to the SPeEDy RCT and hence are unlikely to be relevant to the aim of the QRI. Audio files of these appointments will be securely transferred from Keele CTU to a professional transcription company, who are contracted under strict terms of confidentiality, via a secure portal. Transcripts will be password encrypted when being returned by email by the transcription company to Keele University. These will then be securely uploaded back onto Keele's Secure Network and the email version deleted.

In-depth, semi-structured interviews will be conducted, guided by topic guides with a purposive sample of patients, clinicians involved in identifying patients and RHCPs, (responsible for explaining the trial and obtaining informed consent) from selected sites. Selection of sites will be determined by willingness to participate in the QRI and relative recruitment performance, i.e. high and low-recruiting sites. On receipt of consent to contact, contact to discuss an interview will be made by telephone initially. Subsequently, upon receipt of written consent, the interviews will be undertaken at a time and place convenient to the interviewee and could include interviews at home, either face-to-face or telephone, or at the hospital.

Given the responsive and iterative nature of the QRI, it is not realistic to pre-specify a required number of participants. But, we will sample data from at least four out of the eight hospital sites and data collection will be limited to the pre-specified maximum nine-month period. However, data collection will cease if no new themes emerge from the ongoing analysis prior to this time point.

Data Analysis

Data from the screening and eligibility logs will be analysed descriptively to identify differences between sites and points in the recruitment pathway where patients at particular sites are ‘lost’ to recruitment.

Findings from this analysis will guide sampling for audio-recording of recruitment discussions and interviews.

Audio-recordings of clinic and recruitment appointments will be analysed using thematic, content and targeted conversation analysis techniques with the aim of understanding the challenges to recruitment [40]. In tandem with this, data from individual interviews will be analysed using constant comparison techniques which involves detailed coding followed by comparison of emerging themes and codes within transcripts and across the dataset looking for shared or disparate views. Findings will be presented anonymously.

Further analysis of the study documentation, including PIS and consent forms and Trial Management Group (TMG)/Trial Steering Committee (TSC) meeting minutes, will be reviewed with reference to the findings from the interviews and recruitment appointments. Data from screening logs, audio recordings, interviews and study documentation will be triangulated to identify where findings are confirmed across data sources.

Upon completion of this analysis an action plan will be generated to address the factors that appear to be hindering recruitment. Previous reports of the outcome of the QRI have identified generic and study specific barriers to recruitment which can be addressed through bespoke action plans [36]. Also in some instances the QRI has provided clear reasons why recruitment to the RCT might not be achievable [36]. Once the action-plan is agreed, where relevant, study documentation will be amended and further training offered to recruiters across all of the hospital sites. Post implementation of the plan, a further evaluation of the recruitment process will be undertaken using feasibility outcome data described in this protocol.

Further qualitative interviews

Recruitment

Following the six-month follow-up point, a further sample of patient participants will be purposively sampled from both treatment arms and interviewed to explore reasons for initial participation, treatment acceptability, reasons for non-completion of treatment, where relevant, and any reasons for treatment cross-over.

Information relating to the qualitative interviews will be included in the initial PIS for the SPeEDy RCT and consent to further contact will be included. Where consent to contact is indicated, the researcher will telephone the patient to discuss involvement in the qualitative interviews. If the patient expresses interest, then a PIS describing the qualitative interviews and a consent form will be posted to them. On receipt of a signed consent form, a mutually convenient time to undertake the interview will be agreed.

Patients will be purposefully sampled with respect to allocated group, change in pain and disability status according to the OSS, whether the allocated treatment was completed or not and in relation to treatment cross-over. Patients will be able to decline participation in the interviews yet still be involved in the RCT.

Qualitative Data Collection

The interviews will be based on semi-structured topic guides developed in relation to the pre-specified aims but also with PPIE (approximately 30-minute telephone interview).

It is expected that approximately 20 patients will be sufficient to attain rich data. Telephone interviews will be conducted, audio-recorded and transcribed ad verbatim.

Qualitative Data Analysis

Interviews will be analysed both thematically and as narratives (capturing the 'patient journey' for each participant). This analytical approach ensures that the context of individual patient journeys is preserved while undertaking a broader thematic analysis [41,42]. NVivo software will be used, enabling development of an appropriate coding strategy and coding framework in a manner which facilitates data retrieval and comparative analysis [43].

7.10 Withdrawal criteria

Participants are free to withdraw from the study at any time during participant follow-up. The local site PI, study CI and Keele CTU will make every effort to ensure that the specific wishes of any participant who wishes to withdraw consent for further involvement in the trial are defined and documented.

Participants who wish to withdraw from the treatments will have the option to still receive follow-up questionnaires, if they are willing.

7.11 End of study

The end of the RCT is defined as completion of all data are collected, including MDC and case report forms.

8 STATISTICS AND DATA ANALYSIS

8.1 Sample size calculation

Randomising 76 participants will enable the 1-sided lower 90% confidence limit for the follow up rate to be estimated within about 6% of the anticipated 80% level at six months. Further, a sample size of about 76, allowing for dropout, will be sufficient to allow precise calculation of estimates of standard deviation around the OSS for the main trial [44].

Additionally, with reference to treatment crossover of less than 25% (principal concern relates to those randomised to the physiotherapist-led exercise programme crossing over to surgery), randomising 38

participants to the physiotherapist-led exercise programme enables precise 1-sided upper confidence limits (e.g. around 8% above the desired upper level of around 15% for a 90% upper confidence limit).

8.2 Planned recruitment rate

Data from NHS Hospital sites suggests there are one to two potentially eligible patients per month per surgeon equating to four to six potentially eligible patients per month at a medium-sized sites (four surgeons). Hence, working with eight sites means that it is reasonable to expect to identify 32 potentially eligible patients per month (eight x four) and the recruitment target is six to seven participants per month across approximately eight sites; this equates to a conservative 20% participation rate. The recruitment period for the RCT will be 15 months in total to enable staged recruitment of approximately eight sites over the first three months. This will enable the last site to be open for a 12 month recruitment period.

8.3 Data analysis plan

As this is a pilot and feasibility RCT, the main analysis will focus on process outcomes, for example consent rate, retention rate, and follow-up rates. Means and confidence intervals of the OSS will be calculated in order to inform the sample size calculation for the main trial. A detailed data analysis plan will be developed and agreed by the TSC.

At the end of the study, we will review the findings and in discussion with the TSC make a recommendation about proceeding to a future main trial. The following success criteria will be used to decide on whether to proceed to developing a main trial funding application:

i) Identification of eight recruiting sites during the pilot phase with expressions of interest from at least a further eight sites; this criterion recognises that a future main trial would likely require greater than 400 participants and thus a minimum of 20 sites recruiting over a two-year period

ii) Recruitment rates: Consent and randomisation of 20% or more of eligible patients

iii) Treatment cross-over less than 25% at six months in each of the two treatment arms. In a future main trial, if treatment cross-over is less than 50% at 12-months this would suggest that significant financial saving could be made while offering useful data to inform decision-making. Hence, if treatment cross-over is less than 25% at six months, with accepted limitations, this will be regarded as acceptable in the context of the upper limit of longer-term cross-over

iv) Follow-up rates for the OSS greater than 70% at six months.

8.3.1 Primary outcome analysis

Not applicable to this pilot and feasibility RCT.

8.3.2 Secondary outcome analysis

Not applicable to this pilot and feasibility RCT.

8.4 Subgroup analyses

There are no planned subgroup analyses in this pilot and feasibility RCT.

8.5 Interim analysis and criteria for the premature termination of the trial

Not applicable to this pilot and feasibility RCT

8.6 Procedure(s) to account for missing or spurious data

As this is an external pilot and feasibility RCT we will report the amount of missing/spurious data across all outcome measures and CRF items. Missing data within individual items of composite tools will be dealt with according to validated-scoring recommendations for those measures if indicated (or otherwise, dealt with using reasonable Keele CTU rules which will be outlined in the data analysis plan). A statistical review will be undertaken to assess the relationship between missingness at follow up (the most likely source of missing data) and baseline variables: in the event of strong associations being observed that indicate a missing at random pattern this will usefully inform the data analysis plan for a main trial.

8.7 Economic evaluation

A formal economic analysis will not be undertaken in this pilot and feasibility RCT. Health Care Resource Use data will be collected within the three and six month questionnaires and completion and response rates analysed to assess the feasibility of undertaking a full economic evaluation in a future main trial.

9 DATA HANDLING

9.1 Data collection tools and source document identification

Self-report questionnaires and clinical data collected on study specific CRFs and audio-recordings and screening logs will form the basis of the data collection. All data collected during the course of the study will be kept strictly confidential and will be handled and stored in line with the local NHS and Keele CTU Data Security procedures and Keele University's Health and Social Care Quality Management System's Standard Operating Procedures (HSCR QMS SOPs), which are in accordance with the relevant Data Protection regulations and good practice guidelines.

Study data will be recorded by clinicians or local research staff who are taking part in the study and will be trained in accordance with the protocol on completing CRFs. Originals will be retained at site and copies securely sent to Keele CTU at Keele University. Other than the Participant Contact CRF and consent form, which will contain the participant's details to allow contact for follow-up by Keele CTU, only the participant's pseudo-anonymised data will be included on CRFs. Questionnaires will include

the participant's Study ID plus date of birth and gender. The study site is responsible for redacting all other personal identifiable data prior to CRFs and any other reports being sent to Keele CTU. Following receipt, Keele CTU will contact the site to resolve any missing or discrepant data queries relating to clinical data in accordance with Keele CTU procedures

9.2 Data handling and record keeping

Data management is by Keele CTU. Audit of data entry is undertaken for questionnaires and CRFs by Keele CTU following HSCR QMS SOPs and the verification checks supported by the research team. For details on data protection systems, see Section 11.5.

9.3 Access to Data

The research team will receive anonymised datasets for purpose of data reporting to the TMG and TSC and at the end of follow up for final data cleaning/checking and end-of-study analysis. All identifiable data will be retained within the Keele CTU-secure network drives and at local sites in line with NHS information Governance policies.

9.4 Data Sharing Agreements

Prior to the start of recruitment, a signed Organisation Information Document and model non-commercial trials agreement (mNCA) will be in place between each hospital site, and Keele University to ensure the safe and lawful process of data sharing across organisations. A service level agreement, including data sharing agreement, will be in place between Derby CTU and Keele University to ensure the safe and lawful process of service provision and data sharing across the organisations. Derby CTU will not have access to personally identifiable data for the purpose of randomisation. Audio files containing qualitative data will be securely shared with a professional UK based transcription company under the terms of a confidentiality and data sharing agreement.

The EQ-5D-5L will be used with permission from EuroQol under the terms of its Non-Commercial Research Licence. Similarly, the OSS will be used with permission from the developers.

9.5 Archiving

At the end of the trial, data will be securely archived in line with the Sponsor's procedures for 10 years after submission of the End of Study Declaration. Data held by Keele CTU will be archived in the designated Keele CTU archive facility and site data and documents will be archived at the participating sites. Following a retention review, if the archived material is agreed to be destroyed, arrangements for confidential destruction will then be made.

10 MONITORING & AUDIT

10.1 Study Management

Trial Sponsor: Keele University as the sponsor is responsible for trial initiation, management and financial management of the trial. These functions are devolved to Keele CTU as will be detailed in the Delegation of Sponsorship Functions agreement, as follows:

Chief Investigator (CI): The CI (CL) is also the NIHR Post-Doctoral Fellowship holder and will lead the design, conduct, co-ordination and management of the study. The CI has overall responsibility for the scientific quality and delivery of the study. The CI will also be responsible for safety reporting and escalation of reportable adverse events.

CTU: The Trial Sponsor delegates the management of the trial to Keele CTU. Keele CTU will provide set-up and monitoring of trial conduct to Keele University's HSCR QMS SOPs, and the GCP Conditions and Principles as detailed in GCP standards. In addition, Keele CTU will provide support in obtaining research ethics and governance approvals and clinical site set-up, ongoing management including training, monitoring reports and promotion of the trial. In association with the CI, Keele CTU will support the day-to-day running of the trial including some help with trial management and administration, data management, and safety reporting. Regular monitoring of study recruitment will be performed and intervention CRFs will be audited against the clinical records by clinical site PI's or their designate, for completion accuracy.

Derby CTU will provide and manage the randomisation system for the SPeEDy RCT.

NIHR Clinical Research Networks: The West Midlands CRN will co-ordinate CRN support across the recruiting sites and together with other CRNs will provide funding or staff resource to secure the additional clinical time associated with service support to embed the study into the sites to allow identification and recruitment of eligible participants.

Clinical Site PIs: The clinical site PIs will be responsible for the conduct of the trial at their site as detailed in the applicable Sponsor-Site Agreement available in the Study Site File and ensuring the trial is run at their site in accordance with the GCP Conditions. This includes (but is not limited to), ensuring GCP training for those undertaking consent, completion of relevant CRFs, delivery of intervention, care of the patients and safety reporting.

Trial Management Group (TMG): The CI is responsible for the conduct of the trial and will convene the TMG. The TMG will comprise members of the research team and Keele CTU and will have overall responsibility for the clinical set-up, ongoing management and monitoring, promotion of the trial, and for analysis and interpretation of results. The CI will chair the TMG to oversee; (i) the protocol delivery, (ii) CRF development, (iii) obtaining approval from the HRA and agreements with sites, (iv) completing cost estimates and project initiation, (v) nominating members for, and facilitating, the TSC, (vi) monitoring of screening, recruitment, treatment and follow-up procedures, (vii) data collection, and database

development, (viii) reporting annually to the REC. The TMG will meet on a regular basis throughout the study.

10.1.1 Trial Steering Committee (TSC) members

An independent TSC has been appointed in line with Keele University's HSCR QMS SOPs (see list of members under key contacts Page 6) and will provide overall supervision of the study, in particular study progress, adherence to protocol, participant safety and consideration of new information relevant to the research question(s) or design. It includes an Independent Chair and four other independent members, including a statistician (1), lay representatives (2) and clinical representatives (2). The CI, senior statistician and Trial Manager will attend the TSC meetings and present and report progress. The TSC will meet initially to approve the protocol prior to submission for Health Research Authority approval and then at agreed time points over the duration of the trial. Since this is a pilot trial with no planned interim statistical analysis, a Data Monitoring Committee will not be formed and the TSC will take responsibility for reviewing the safety of the trial including advice regarding progression to a main RCT with reference to the pre-specified progression criteria.

10.2 Monitoring arrangements

Monitoring will be conducted by the TMG based on the trial risk assessment and in accordance with Keele University's HSCR QMS SOPs, and agreed by the TSC. Monitoring will also be undertaken by the approving Research Ethics Committee (REC) in the format of annual progress reports and the funder in the format of progress reports as required by the NIHR Post-Doctoral Fellowship scheme.

10.3 Auditing procedures

Completeness of consent forms and baseline questionnaires will be audited by the research team and Keele CTU. Clinical case notes will be audited by the clinical site PI, or delegate, with reference to the trial interventions as a means of contributing to the assessment of intervention fidelity.

10.4 Safety Reporting

Adverse events

A Serious Adverse Event (SAE) is defined by the Health Research Authority (HRA) as an untoward occurrence that: (a) results in death; (b) is life-threatening; (c) requires hospitalisation or prolongation of existing hospitalisation; (d) results in persistent or significant disability or incapacity; (e) consists of a congenital anomaly or birth defect; or (f) is otherwise considered medically significant by the investigator.

In the context of the SPeEDy study, expected SAEs include re-rupture or failure to heal of the repaired rotator cuff tendon(s), and participants allocated to physiotherapist-led exercise subsequently undergoing surgery to repair their rotator cuff.

A SAE occurring to a research participant must be reported to the REC where in the opinion of the CI the event was: “Related” that is, it resulted from administration of any of the research procedures, and/ or “Unexpected” that is, the type of event that is not an expected occurrence as a result of the intervention provided.

In addition to participant self-report, we will ask study clinicians including orthopaedic surgeons and physiotherapists to report all related and/or unexpected adverse events and SAEs if they become aware of them during the trial, with the exception of non-trial related prolongation of the existing hospital stay or planned hospitalisations. Similarly, if the participant’s GP becomes aware that a SAE has occurred we will request that this is reported, as detailed in the letter informing them that their patient is participating in the study. Reporting procedures will be made clear during the protocol study training and will be contained in site files for all clinicians involved in the study. We will also ask participants to report any adverse events they have experienced due to their participation in the trial in their three and six month questionnaires.

Once a SAE is identified and reported, this information will be passed to the Trial Manager who will ensure that the necessary paperwork is completed and inform the CI. In line with Keele University’s HSCR QMS SOPs the reporting clinician is to give their assessment and the CI will assess whether the event is related to or resulted from any of the trial procedures or interventions and expectedness, according to the process laid out in Keele University’s HSCR QMS SOPs. Any SAE considered to be related to the trial procedures and/ or unexpected will be reported to the Sponsor, REC and the TSC Chair by the CI within 15 days of becoming aware of the event. SAEs occurring later than six months post randomisation do not need reporting.

10.5 Trial timeline

Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
Protocol finalisation																																				
TMG meetings																																				
PPIE meetings																																				
TSC meetings																																				
Approvals																																				
Site preparation																																				
Recruitment (RCT)																																				
QRI																																				
Follow-up (RCT)																																				
Qualitative data collection & analysis																																				
Data analysis (RCT)																																				
Study close down																																				

TMG = Trial Management Group/ PPIE = Patient & Public Involvement & Engagement/ TSC = Trial Steering Committee/ QRI = Quintet Recruitment Intervention/ Follow-up (RCT) includes time lag to intervention

Months 1 to 9: Study set-up period including Health Research Authority approval, commencement of site initiation and trial-specific training. Initial TSC meeting.
Months 10 to 12: Complete site set-up and commence participant recruitment (15 months' recruitment in total), and commence QRI.
Months 13 to 24: Commence outcome data collection, including qualitative interviews, complete QRI and make recommendations to TMG, and complete recruitment for RCT.
Months 25 to 32: Complete outcome data collection and initiate data analysis.
Months 33 to 36: Final PPIE group and TSC meetings with assessment of RCT success according to agreed criteria.
Months 37 to 48 (beyond study period but within fellowship period of CI): Final report writing, main trial application if applicable, initiate dissemination plan and archiving.

11 ETHICAL AND REGULATORY CONSIDERATIONS

11.1 Research Ethics Committee (REC) review & reports

The study will be submitted to and approved by the HRA (which includes REC) to gain the appropriate NHS Permissions prior to recruiting participants into the study. Keele CTU will provide the final protocol, participant information sheets, consent forms and all other relevant study documentation as part of the ethical approval process.

Following initial approval from the REC, they will continually be informed of all substantial changes to the management of trial. Routine reporting will take place in line with REC requirements.

All correspondence with the REC will be retained in the Trial Master File (TMF). Study Site Files including details of the original REC approval will be updated with any REC approval letters acknowledging a substantial change.

11.2 Peer review

This trial has been subject to internal peer review, and external peer review by the funding body (NIHR Post-Doctoral Fellowship scheme).

11.3 Public and Patient Involvement

We have adopted the approach advocated by INVOLVE (2012) and PPIE has been central to the development of this study protocol.

We have held PPIE meetings to inform the design of the study and these suggestions have been incorporated into this protocol and the patient facing materials.

For trial monitoring purposes, two PPIE representatives will also be involved in the TSC and discussion regarding use and dissemination of the findings. The Research Institute for Primary Care and Health Sciences has a PPIE co-ordinator who will continue to help to co-ordinate the PPIE work. They will also provide support such as explaining research methodology, where necessary, to the patient members of both the advisory group and TSC. We also provide users with a glossary of terms used in research and offer access to a training session designed to meet the needs of research users.

We plan to hold meetings with the advisory group and PPIE groups to ensure that they will be involved with the interpretation of the results of this pilot and feasibility RCT and any considerations for the future main RCT. Where appropriate dissemination of findings beyond the traditional academic routes will be discussed.

11.4 Notification of Serious Breaches to GCP and/or the protocol

Keele CTU has systems in place to ensure serious breaches of GCP of the study protocol are identified and reported. A “serious breach” is a breach which is likely to effect to a significant degree;

- the safety or physical or mental integrity of the study participants; or
- the scientific value of the study.

In the event of doubt, or for further information or guidance, the investigator should contact the Trials Manager or CI at Keele CTU. All protocol deviations and breaches of GCP will be recorded and reported to the Sponsor, REC and TSC according to the applicable HSCR QMS SOP.

11.5 Data protection and patient confidentiality

Each participant will be allocated a unique Study ID, so that only anonymised data are used for analysis. At the end of the trial, the database will follow HSCR QMS SOP to ensure that database anonymisation and locking is undertaken.

All identifiable data will be housed in Keele CTU infrastructure which is a secure virtual network requiring two factor authentication (2FA) in order to access the data stored within. Permissions are applied to users within the network to restrict access to study data as required. The CTU secure infrastructure has been independently audited and achieved level one of the government backed Cyber Essentials Scheme.

All hard copy information will be stored anonymously and securely following HSCR QMS SOPs which are in accordance with relevant regulatory requirements including the UK Policy Framework for Health and Social Care Research, Data Protection Act 2018, GDPR and good clinical practice (GCP). Consent forms containing personal identifiable information will also be kept securely but separately to any data.

All confidentiality arrangements adhere to relevant regulations and guidelines and the CI and study statisticians (Data Custodian) have responsibility to ensure the integrity of the data and that all confidentiality procedures are followed.

11.6 Indemnity

This trial is sponsored by Keele University and Keele University provides compensation for negligent and non-negligent harm caused by the design and/or management of the trial by Keele.

For harm to participants arising from the conduct of the research indemnity is provided through the NHS schemes or professional indemnity of NHS staff.

11.7 Amendments

The detailed protocol will be updated in response to approved amendments, as required.

11.8 Access to the final trial dataset

The anonymised datasets generated during and/or analysed during the current study are/will be available upon request from primarycare.datasharing@keele.ac.uk. Core data will be available immediately after publication of the trial results. A data request form is required to be completed and must outline the type of data to be obtained, the reason for obtaining this data (research question / objective), the timing for when the data is required to be available (start date/end date). Checks will be performed by a Data Custodian and Academic Proposals (DCAP) committee at Keele to ensure that the data set requested is appropriately suited to answer the research question/objective and that the request fits with the original ethical approval and participant consent and adheres to funder and legal restrictions. Only de-identified data are available for request in aggregated format or at the level of the individual participant.

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