Study Title: Effectiveness of supervised versus self-directed rehabilitation for people aged 50 years and over with ankle fractures: the AFTER trial

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AFTER – Ankle Fracture Treatment: Enhancing Rehabilitation trial

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Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

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1. KEY CONTACTS

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2. LAY SUMMARY

Around 1 in 10 of all people attending hospital with a broken bone have injured their ankle joint. Most of these injuries occur in people aged 50 years and over as a result of a fall from a standing height. After a broken ankle is treated with or without surgery, the ankle is kept still in a boot or cast for around six weeks. Keeping the ankle still protects it as it heals but causes stiffness and weakness. Putting weight through the ankle after the boot or cast is removed is difficult. People often feel unsteady and lack confidence. At this time, health care professionals are recommended to provide advice on early ankle exercises and on how to gradually return to daily life.

After this initial advice, there is no national guidance on whether further rehabilitation under the supervision of a physiotherapist should be provided. Previous research in younger adults found additional physiotherapy did not improve recovery, but it is not clear whether older adults would benefit. Extra sessions of physiotherapy can be difficult for patients to attend and are costly to the health service.

Our study will find out if referral for physiotherapy appointments after a person over 50 years has suffered a broken ankle helps them recover quicker and better when compared to good quality advice on self-management which includes booklets and videos.

To compare the two treatments properly 344 people will be recruited to take part. Participants will be placed by chance into one of two groups by a computer program, this will make sure that the groups are similar and the comparison is fair. Over a 6-month period participants will be asked about their health, walking ability and other daily activities, as well as any complications and specific costs.

A small version of this study was conducted to improve the design. We used feedback from health professionals and patients who took part. This project was developed by and will be run by a team of patient representatives, clinical experts in trauma rehabilitation and orthopaedic surgery, study management specialists, and experienced statisticians.

The Oxford Clinical Trials Research Unit, based within the University of Oxford, will support the study. Monitoring committees of patient representatives and independent experts will oversee the safety of participants and the progress and conduct of the study.

Findings of the research will be published so that it is free to access in scientific journals and shared at conferences. Our Patient and Public Involvement research team member will support development of lay summaries and will be actively involved in reaching patient networks.

3. SYNOPSIS

Study Title	Effectiveness of supervised versus self-directed rehabilitation for people aged 50 years and over with ankle fractures: the AFTER trial		
Internal ref. no. / short title	AFTER		
Study registration	The study has been registered with the current controlled trials database under reference number ISRCTNXXXXXX		
Sponsor	University of Oxford		
Funder	National Institute for Health Research		
Study Design	Multicentre randomised parallel-group superiority trial		
Study Participants	Adult patients aged 50 years and over with ankle fractures		
Sample Size	344		
Planned Study Period	September 2021 – July 2024		
Planned recruitment period	March 2022 – June 2023		
	Objectives	Outcome Measures	Timepoint(s)
Primary	Ankle Function	Olerud and Molander Ankle Scale (OMAS)	6 months post-randomisation
Secondary	Ankle Function	OMAS	Baseline, 2 and 4 months post-randomisation
	Health-related quality of life	EQ-5D-5L	Baseline, 2, 4 and 6 months post-randomisation
	Pain	Pain sub-scales of the EQ-5D-5L and OMAS	Baseline, 2, 4 and 6 months post-randomisation
	Physical Function	PROMIS Physical Function	Baseline, 4 and 6 months post-randomisation
	Self-efficacy	Self-Efficacy Exercise Score	Baseline, 4 and 6 months post-randomisation

	Exercise adherence	Self-reported exercise frequency	2, 4 and 6 months post-randomisation
	Complications	Complications Questionnaire and Case Report Form	2, 4 and 6 months post-randomisation
	Cost effectiveness	Health economics questionnaire	2 and 6 months post-randomisation
Intervention	Supervised rehabilitation		
Comparator	Self-directed rehabilitation		

4. ABBREVIATIONS

AE	Adverse Event
AFTER	Ankle Fracture Treatment: Enhancing Rehabilitation trial
CACE	Complier Average Causal Effect
CAT	Computer Adaptive Test
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DMP	Data Management Plan
EQ-5D-5L	EuroQol 5 Dimensions – quality of life questionnaire
GCP	Good Clinical Practice
HRA	Health Research Authority
HRQoL	Health Related Quality of Life
HTA	Health Technology Assessment
ICER	Incremental Cost-effectiveness Ratio
ICF	Informed Consent Form
ID	Identity
IP	Intellectual Property
IRAS	Integrated Research Application System
IRT	Item Response Theory
ISRCTN	International Standard Randomised Controlled Trial Number
ITT	Intention-to-treat
NDORMS	Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences
NHS	National Health Service
NIHR	National Institute for Health Research
NICE	The National Institute for Health and Care Excellence
OCTRU	Oxford Clinical Trials Research Unit

OMAS	Olerud and Molander Ankle Scale
PI	Principal Investigator
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
PROM	Patient Reported Outcome Measure
PROMIS	Patient-Reported Outcomes Measurement Information System
PSS	Personal Social Services
QALY	Quality Adjusted Life Year
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
REDCap	Research Electronic Data Capture
RfPB	Research for Patient Benefit
RGEA	Research Governance, Ethics & Assurance Team
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SEE	Exercise Self-efficacy
SFQ	Site Feasibility Questionnaire
SOPS	Standard Operating Procedures
TIDieR	Template for Intervention Description and Replication
TMG	Trial Management Group
TOC	Trial Oversight Committee
UK	United Kingdom
UKCRC	UK Clinical Research Centre
URL	Uniform Resource Locators
US	United States
VAS	Visual Analog Scale

5. BACKGROUND AND RATIONALE

What is the problem being addressed?

Ankle fractures are very common, accounting for 9% of all fractures managed in secondary care. (1) In the UK, incidence of these fractures is highest in people aged 50 years and over, peaking at 16 per 10,000 person-years in women aged 60 to 70. (2) As the population ages, a three-fold increase in these fractures is projected over the next two decades. (3) The mechanism of injury for people aged over 50 is usually a fall from standing height; the fracture is then defined as a fragility fracture. (4)

Treatments for ankle fractures range from conservative plaster casts or boots to surgical fixation. Our recent HTA-funded trial including adults aged 60 years and over found that, regardless of the initial fracture management, post-injury reduced ankle function and walking abnormalities remain at 6 months post-injury.(5, 6) Participants reported an average 30% loss of pre-injury ankle function. Function is poor due to pain, reduced joint motion,(7) lower limb muscle strength deficits,(8) gait abnormalities,(9) and resultant mobility limitations.(7, 10)

Weight bearing and ankle movement restrictions are usually lifted by the orthopaedic team six weeks after injury. At this stage, national guidance is that patients should be given advice on simple exercises and gradually resuming usual activities.(11) Advice is provided face-to-face in a fracture clinic and is sometimes supplemented by an information booklet.

Data from 24 UK hospitals indicated that, in addition to this advice, about two thirds of patients were referred to see a physiotherapist in an outpatient clinic for supervised rehabilitation.(5) Referral patterns varied both within and between hospitals; at some centres few patients were referred, while at others the majority receive 4 to 6 sessions of physiotherapy over several months.(5) The variation reflects that referrals are currently being made based on local practice or clinical opinion due to a lack of robust evidence to inform national guidance.

A James Lind Priority Setting Partnership on lower limb fragility fractures ranked ‘What is the best physiotherapy and/or occupational therapy regime for adults during out-of-hospital recovery from a fragility fracture of the lower limb?’ as second in the top ten, highlighting the importance of this research to clinicians, patients and carers.(12) Ankle fractures have a substantial impact on people’s lives, resulting in mobility problems and reduced independence, and prognosis worsens with increasing age.(13) It is uncertain why people fare worse as they age but lower physiological reserves, comorbidities, reduced muscle mass and power (sarcopenia), and balance impairments are likely to contribute.(14) The resultant disability after injury has a significant associated socioeconomic burden, impacting on an individual’s capacity to work, care for others, and perform daily activities.(5)

Physiotherapy after ankle fracture aims to support patients during the recovery period and provide individualised progressive exercise to improve muscle strength, range of motion, gait and balance. However, as physiotherapy is not without patient and health service burden and costs, it is important that the clinical and cost-effectiveness of physiotherapy-supervised rehabilitation is compared with good quality self-management advice. If superiority of physiotherapy is not demonstrated, this would support disinvestment in routine physiotherapy in this population, and support widespread implementation of a standardised self-directed rehabilitation intervention.

A Cochrane review in 2012 of ankle fracture rehabilitation concluded that there was insufficient evidence regarding physiotherapy after ankle fracture.(15) Our updated searches identified just one new study, the EXACT trial (n=213), which reported no differences in lower limb function between supervised exercise and one-off advice for adults with ankle fractures.(16) While this trial certainly adds to the body of evidence in this area of research, the vast majority of patients (>70%) were younger than 50 years of age, and in the group allocated to basic advice, about 39% sought additional out-of-trial physiotherapy. In the proposed study we will focus on patients aged 50 years and over to allow clinical practice in this patient population to be informed by appropriate evidence. In adults aged 50 years and over, experience of losing confidence and fear of future injuries are common after ankle fracture.(5, 6) There is also good evidence that progressive exercise reduces risk of falls in other clinical populations.(17) A tailored progressive exercise intervention supervised by a physiotherapist therefore has the potential to improve recovery in this older group, where rehabilitation needs are often more complex.

We have conducted a feasibility RCT(18) that informed the design of this definitive trial. We have conducted a programme of research with stakeholders from clinical practice, research, and patient and public involvement representatives from the UK Musculoskeletal Trauma PPI Group to optimise a physiotherapist-supervised rehabilitation intervention and self-directed rehabilitation intervention.

6. OBJECTIVES AND OUTCOME MEASURES

The aim of this pragmatic, parallel-group, randomised controlled superiority trial is to evaluate the clinical and cost-effectiveness of supervised versus self-directed rehabilitation in improving ankle function for people aged 50 years and over with ankle fractures.

The primary objective is:
To quantify and draw inferences on differences in ankle function at 6 months post-randomisation between the trial intervention groups (supervised vs self-directed rehabilitation).

The secondary objectives are:

To quantify and draw inferences on differences in:

- ankle function at 2 and 4 months
- ankle pain at 2, 4 and 6 months
- health-related quality of life (HRQoL) at 2, 4 and 6 months
- physical function at 4 and 6 months
- self-efficacy to exercise at 4 and 6 months
- exercise adherence at 2, 4 and 6 months
- risk of related complications over the initial 6 months
- cost-effectiveness of the interventions at 2 and 6 months

Table 1: Assessments performed to enable delivery of objectives:

Outcomes	Objectives	Instruments	Timepoints
Primary	Ankle Function	Olerud and Molander Ankle Scale (OMAS)	6 months
Secondary	Ankle Function	OMAS	Baseline, 2 and 4 months
	Health-related quality of life	EQ-5D-5L	Baseline, 2, 4 and 6 months
	Pain	Pain sub-scales of the EQ-5D-5L and OMAS	Baseline, 2, 4 and 6 months
	Physical Function	PROMIS Physical Function	Baseline, 4 and 6 months
	Self-efficacy	Self-Efficacy Exercise Score	Baseline, 4 and 6 months
	Exercise adherence	Self-reported exercise frequency	2, 4 and 6 months
	Complications	Complications Questionnaire and Case Report Form	2, 4 and 6 months
	Cost effectiveness	Health economics questionnaire	2 and 6 months

6.1. **Outcome measures**

The primary outcome is patient-reported ankle-related symptoms and function at 6 months after randomisation measured by completion of the Olerud and Molander Ankle Score (OMAS).(19) The OMAS is a 9-item questionnaire which is completed directly by the participant (0-100, with higher scores indicating better function). The OMAS has been the primary outcome for a number of other ankle fracture trials, including NIHR HTA trials.(5, 20)

Secondary outcomes:

Health-related quality of life: assessed using the EuroQol 5 Dimensions (EQ-5D-5L) score.(21) The EQ-5D-5L is a validated, generalised and standardised instrument comprising a VAS measuring self-rated health and a health status instrument, consisting of a five-level response (no problems, some problems, moderate problems, severe problems and unable) for five domains related to daily activities; mobility, self-care, usual activities, pain and discomfort, and anxiety and depression. Responses to the health status classification system are converted into an overall score using a published utility algorithm for the UK population. The EQ-5D health status scale ranges from negative scores reflecting a patient's quality of life being worse than death, and 0 [death] to 1 [perfect health]. A respondent's EQ-VAS gives self-rated health on a scale where the endpoints are labelled 'best imaginable health state' (100) and 'worst imaginable health state' (0).

Pain: assessed using the sub-scales of the OMAS and EQ-5D-5L.

Physical function: assessed using PROMIS Physical Function.(22) Patient Reported Outcome Measurement Information System (PROMIS) questionnaires are administered electronically, via a Computer Adaptive Test (CAT), which are dynamic tests based on Item Response Theory (IRT). A mathematical model adapts the sequential questions asked based on a participant's previous response. A tailored set of questions is therefore asked from a large item pool. Participants are typically asked 4 to 6 questions. PROMIS instruments are scored from 0 to 100 with 50 points representing the mean score for the US general population, higher scores indicate better function. Participants who have not completed the online questionnaire or who have no internet access will be able to complete a paper-based version of the PROMIS questionnaire with 4-items (PROMIS Physical Function - Short Form 4a) via postal follow up. If a participant needs to be contacted directly by phone to complete their follow up they will be asked the PROMIS Physical Function CAT questionnaire as the central site team can directly enter patient responses on their behalf.

Self-efficacy: assessed using the Self-Efficacy Exercise Score (23). The score measures a participant's judgment of their confidence to carry out exercise. The questionnaire has 9-items specifically about the ability to continue to exercise despite barriers. The participant scores their confidence level from 0 (not confident) to 10 (very confident), if they were to exercise 3 times per week for 20 minutes during each of the nine situations presented. The overall scores range 0 to 90, with higher scores indicating greater confidence to exercise.

Exercise adherence: assessed using patient reported exercise frequency.

Complications: fracture and treatment complications will be recorded, but particular note will be made of complications related to the interventions. (see section 10.3)

Resource use: patient reported resource use and information on hospital treatments and appointments will be collected. This will include consultations with primary and secondary care, prescribed and over-the-counter pain medication use, additional physiotherapy and hospital admission, self-funded health and social care, out-of-pocket expenses and work absence.

7. STUDY DESIGN

AFTER is a multi-centre, parallel-group, superiority individually randomised controlled trial assessing the clinical effectiveness of supervised versus self-directed rehabilitation in improving ankle function for people aged 50 years and over after an ankle fracture. The trial will be conducted at secondary care trauma departments in a minimum of 20 NHS hospitals and their related physiotherapy services.

8. PARTICIPANT IDENTIFICATION

8.1. Study Participants

Adults aged 50 years and older with ankle fractures.

8.2. Inclusion Criteria

- Patient is aged 50 years and over with an ankle fracture undergoing surgical fixation or non-surgical management
- Patient has been provided with a cast or orthotic boot (non-removable or removable for non-weight bearing ankle movement) for at least 4 weeks and no longer than 10 weeks.
- Patient has capacity to consent to trial participation within 14 days of removal of the cast/boot.

8.3. Exclusion Criteria

The patient may not enter the study if ANY of the following apply:

- Patient is deemed unable to adhere to trial procedures or complete questionnaires
- Patient was not ambulatory before the injury
- Patient has contraindications to participation in an exercise programme

9. PROTOCOL PROCEDURES

9.1. Recruitment

Recruitment centres will be chosen from our existing network of over 100 research active sites based on track records with regards to efficiency of governance approvals, communication with central research teams, predicted recruitment numbers, and representation of diverse geographical regions, hospital sizes, and socio-demographic characteristics. An invitation pack which includes a Site Feasibility Questionnaire (SFQ) will be provided to potential sites. The SFQ may be completed by an individual with adequate, authoritative knowledge of the site (where a site is known to the study office through previous research enterprises the SFQ may be part-completed in advance). The PI or an appropriate deputy must confirm participation and the accuracy of any SFQ submitted to the central trial team in Oxford.

The central trial team will evaluate returned SFQs to ensure a site is equipped with appropriate resources to deliver the project and meet recruitment targets. Confirmation of collaboration will be provided in writing to the PI.

A conservative recruitment rate of 1.4 patients per centre per month has been based on screening and recruitment data collected during our feasibility trial as well as experience from other trials in the area of orthopaedic trauma.

9.2. **Screening and Eligibility Assessment**

Potentially eligible patients will be identified in the emergency department/minor injuries unit or via inpatient, virtual or outpatient trauma and orthopaedic clinics. A Participant Information Sheet (PIS) will be provided. The initial approach will be at any time point up to and including the clinic review when the cast/boot is no longer recommended when weight bearing. Experience from the AFTER feasibility study indicated that flexibility in when the first approach occurs to fit local clinical and research pathways is critical to successful recruitment. Patients that are happy to be consulted about participation in the study will be approached in the clinical setting. The local research team will approach the patient in person in a clinic or via telephone or video call to discuss the trial.

Eligibility will be confirmed at the timepoint where the cast/boot is being discontinued, prior to randomisation. This is usually 6 weeks (and a minimum of 4 weeks) after initial surgical/non-surgical fracture management. It is anticipated that most patients will be assessed at the fracture clinic appointment but as per the eligibility criteria, recruitment and randomisation can proceed if the patient has been informed by the orthopaedic team within the last 14 days that a cast/boot is no longer needed while weight bearing.

Screening logs recording the patients' age, sex at birth and initial fracture management (surgical or non-surgical), and if provided, the reasons for declining participation will be documented at each recruitment centre. This will determine the number of patients assessed for eligibility and reasons for exclusion. In addition, the number of patients eligible, approached, missed and recruited, and the number of patients who decline consent or withdraw will be recorded.

9.3. **Informed Consent**

As this is an intervention requiring active self-management, following advice and instructions, and use of written materials, all participants will be required to have capacity to consent to participation and sufficient cognitive function to manage a self-guided exercise programme.

A member of the responsible clinical team will briefly highlight the study to the patient and introduce a member of the local research team. They will approach the patient and explain the trial as described above. The local research team will also be able to answer any additional questions that the patient might have. In order to standardise the information provided to the patients, online and written recruitment materials will be made available to local research teams, including a short video detailing the study.

After eligibility has been confirmed at the clinical appointment where the cast/boot is removed, interested patients will then have a discussion with a member of the local research team. The informed consent discussion may either be in person or via telephone/video call, in accordance with the local recruitment centre policy. If happy to proceed, the patient will provide their consent using the latest approved version of the electronic Informed Consent Form (ICF) prior to any study related procedures or data being collected. Alternatively, if face to face consent is not feasible, consent will be recorded by a member of the local team on an online Verbal Informed Consent Form during the informed consent video/telephone call. A copy of the completed online or verbal ICF will be given to participants. When using verbal consent, sites will be requested as much as is feasible to have a witness available to view completion of the document, however in the trauma clinic context it will not always be possible and therefore not necessitated for consent to trial participation.

Patients will be given as much time as possible to consider the information and discuss it with relatives/carers. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal. The person who obtained the consent must be suitably qualified and experienced and have been delegated to do so by the Principal Investigator and listed to take consent on the study delegation log. Permission from the participants will also be obtained to inform their GP of their inclusion in the study. If the participant has an email address, an electronic version of the signed ICF will be automatically emailed to them. If the participant does not have access to an email address the local team will be able to print a copy of the signed ICF and provide this to the participant. The local research team will also store a further copy in the participants' medical notes.

9.4. **Randomisation**

Participants will be randomised by the local research team using a web-based service. Participants will be randomised at the stage they have weight bearing and movement restrictions outside of a cast or boot lifted at approximately 6 weeks (and no earlier than 4

weeks) after injury/surgery, and eligibility has been confirmed, consent received, and baseline data completed.

The randomisation will be on a 1:1 basis to supervised versus self-directed rehabilitation, using a validated computer randomisation program managed through a secure (encrypted) web-based service by the Oxford Clinical Trials Research Unit (OCTRU). Randomisation will use a minimisation algorithm to ensure balanced allocation across the two treatment groups, stratified by centre and initial fracture management (surgical vs non-surgical).The first few participants will be randomised by simple randomisation to seed the minimisation algorithm and a probabilistic element introduced to the algorithm to ensure the unpredictability of intervention allocation.

On randomisation of a participant the central trial office, main site contact and local study team will be notified. This will take place via an automated email as part of the randomisation process.

9.5. **Blinding and code-breaking**

The patient-reported outcome data will be collected from participants remotely via self-reported questionnaires. It will not be possible to blind participants or those delivering the interventions.

The local research team reviewing hospital records will also not be blind to the treatment allocation.

9.6. **Description of study intervention, comparators and study procedures (clinical)**

After randomisation, the trial interventions will be delivered from the timepoint when the participant's weight bearing and ankle movement restrictions outside of a cast or boot are lifted by the orthopaedic team, typically 6 weeks (and no earlier than 4 weeks) after injury/surgery regardless of the initial treatment of the fracture (surgical/non-surgical).

Both of the interventions fit within the range of care pathways currently offered but there is hospital-to-hospital variation. The intervention content has been refined and standardised during the feasibility RCT to enable evaluation and implementation across the NHS. This study will assess which of these approaches is most clinically and cost-effective for patients and the NHS.

Self-directed rehabilitation:

Self-directed rehabilitation is the provision of standardised high-quality detailed advice on self-management and a set of exercises that can be progressed independently by the participant in

the following months of recovery. The advice materials will be provided by a healthcare professional during the fracture clinic appointment. The advice will be accessible in paper format as well as online with additional instruction videos. Commonly used simple methods to support exercise adherence will be used, including goal setting and provision of an exercise diary. (24)

Supervised rehabilitation:

Participants randomised to supervised rehabilitation will also receive a study advice booklet available in paper or online format from the fracture clinic, it will contain key information on early recovery after removal of the cast/boot and basic initial exercises that they can start ahead of seeing a physiotherapist. They will be referred to see a physiotherapist, which is the most common current standard of care. Participants will have 4 to 6 one-to-one sessions with a physiotherapist, spread over 3 months from the initial session. This period allows sufficient time for neuromuscular adaptation to exercise.(25) The first session will be as soon as possible after the referral, and no later than three weeks from randomisation. This volume of physiotherapy can be delivered within NHS commissioning paradigms of 4 to 6 sessions in an outpatient physiotherapy department. We have previously used similar intensity of physiotherapy to enhance implementation into the NHS to good effect in other trials.(26, 27) Sessions will be delivered via face-to-face or telephone/videoconference, whichever mode of physiotherapy delivery would usually be provided for the patient.

Therapists will support participants with a progressive exercise programme focusing on recovery of movement, muscle strength, balance and gait training, and ensure access to exercise programme supporting materials. The exercise programme, refined during our feasibility work, is highly structured but permits tailoring to enable the physiotherapist to build a programme with the participant that targets their recovery goals and increases physical activity.(28) The programme uses contemporary evidence-based guidelines on exercise volume and load to optimise the physiological response. (29) Based on the participant's functional goals, exercises are progressed to make them task-specific, for example walking on uneven surfaces or slopes, climbing stairs, or jogging. Exercise progression will be individualised by progressing and regressing the volume and load in line with each participant's capabilities and preferences.

As adherence to physiotherapy advice and exercises can be poor,(30) the supervised rehabilitation intervention includes evidence-based exercise adherence strategies used successfully in previous rehabilitation trials.(26, 27, 31) These are integrated into exercise planning with the participant. Participants will be asked to identify their goals and, with the physiotherapist's help, write an action plan for where and when they will perform their home exercises and a contingency plan for managing difficulties. Participants receive a personal exercise guide and diary. Therapists will be trained to focus on helping participants identify barriers to exercise and becoming more physically active post-injury, and facilitating problem-

solving. The therapists will offer education on how exercise and physical activity can help participants to achieve their goals and will reassure participants about their capacity to exercise and increase their physical activity.(32) The intervention will give participants individualised feedback on their rehabilitation progress and reinforcement over the sessions, and will facilitate identification of barriers to doing the home exercise programme, which all have a strong evidence base to support their use.(28)

All physiotherapists will have online (or face to face if COVID-19 restrictions allow) training in the exercise protocols and equipment requirements. All physiotherapists delivering the supervised rehabilitation programme will be provided with a manual with full details of the exercise protocols and equipment requirements. Any materials (workbook, website access, exercise planner and diary) required by the participants will be provided to the local physiotherapy teams by the central study team.

If hospital sites are unable to reach participants to book their supervised rehabilitation session, then the central trial team may send a letter, SMS text message or email to request participants to either get in touch with their treating hospital or the central trial team to arrange.

Concomitant care:

Other aspects of health and social care will continue as normal. Records will be made of additional treatments related to their ankle fracture received by the participant. The manualised intervention delivered by physiotherapists will not be available outside of those allocated to the intervention in the trial, although usual physiotherapy care would be available for those requiring it. The use of out-of-trial physiotherapy will be captured in follow-up questionnaires and will be carefully monitored and reported. The participant's GP will be notified that they need to be aware their patient is taking part in the study as they can also make physiotherapy referrals.

Intervention quality assurance and fidelity:

All clinical staff delivering the interventions will be trained to enhance standardisation of the study procedures. Sites will identify physiotherapists that will deliver the AFTER supervised rehabilitation intervention and receive the training. We will ask that the AFTER trained physiotherapists are not involved in the rehabilitation of participants in the self-management group as far as it is practical to do so. Also, physiotherapists not trained in the AFTER supervised rehabilitation will be asked not to deliver the intervention. Although this has been feasible in other rehabilitation trials to limit potential contamination, we appreciate this can be challenging so we will ask staff to record where this occurs so issues can be identified and addressed during the trial.

A rigorous process of fidelity checks will be conducted to ensure fidelity of intervention delivery.(33) Treatment case report forms will be used to monitor intervention fidelity. Data will be collected with regards the health professional delivering the intervention (profession, grade), the intervention content delivery and the number of treatment sessions attended, to facilitate monitoring and reporting. If deemed necessary, site visits and/or audio/video recording of interventions will be conducted. Permission will be sought, and verbal consent recorded, from the trial participants to observe or record treatment sessions. The sites will regularly receive feedback from quality assurance activities to help maintain and improve fidelity.

9.7. **Baseline Assessments**

Baseline sociodemographic, injury, mobility, height, weight, smoking status, diabetes diagnosis and alcohol consumption data will be collected in the baseline CRF. Participants will also be asked to complete the validated questionnaires outlined in section 6.

9.8. **Treatment logs**

After the usual care or intervention (in addition to usual care) sessions the date, duration, session content, clinician profession and experience details, setting, mode of delivery, and the material and resources issued will be recorded on treatment logs.
For the supervised rehabilitation arm any advice given outside of the AFTER exercise programme and early discharge from the intervention will also be recorded here.

9.9. **Remote Follow-up at 2, 4 and 6 Months**

Participants will receive an electronic/paper invite (according to the participant's preference) to complete questionnaires which include the OMAS, PROMIS Physical Function, EQ-5D-5L, Self-Efficacy Exercise Score, exercise adherence, complications and resources use (see section 6). Reminders will be sent by email, post and/or text message. A secure online link will be included in the email or text message so that participants can complete the questionnaires online. Participants who do not complete the questionnaires within a specified timeframe will receive reminder emails and/or text message and if this does not elicit a response, an SMS message may be sent to inform participants they be contacted by phone by the trial team within a specified time frame. Participants will then be followed up with a telephone call from the central study office, and questionnaires completed verbally. A postal CRF will be sent to participants that don't respond to an electronic invite and the central trial team are unable to reach participants by telephone. A schedule of email and SMS reminders, follow-up phone calls and postal reminders for those participants failing to complete the questionnaires will be outlined in the trial data management plan and approved by the CI and trial statistician.

Should data queries arise from participant-completed questionnaires, the central study office will attempt to contact the participant by telephone, email or text message to resolve the query if it is not appropriate to be clarified with the clinical site team.

Further communication will be sent to participants as a letter in the post three weeks after joining the trial in the form of a Welcome Pack. This pack will prepare them for future questionnaire invitations, explain the process of accessing the trial website, and will ensure those in the supervised rehabilitation arm have been booked into their initial intervention appointment by site. All participants will also be thanked for their participation. A small gift of a keyring will be sent to all participants alongside this information.

9.10. Early Discontinuation/Withdrawal of Participants

During the course of the trial a participant may choose to withdraw early from the study at any time, without giving reasons, and without prejudicing their clinical care.

Participants will not have the option to withdraw the data collected up until the point of withdrawal, as the data will be required for the intention-to-treat (ITT) main analysis and analysis of safety. The options for withdrawal will be explained clearly in the PIS. The type of withdrawal and reason for withdrawal, if the participant is willing to provide one, will be recorded in the withdrawal CRF.

In addition, the Investigator may discontinue a participant from the study treatment at any time if the Investigator considers it necessary to safeguard the safety or wellbeing of the participant, including but not limited to ineligibility (either arising during the study or retrospectively having been overlooked at screening).

Withdrawn participants will not be replaced.

9.11. Definition of End of Study

The end of the study is defined as the last follow up of the last participant and once all queries have been resolved.

10. SAFETY REPORTING

Safety reporting for each participant will begin from randomisation and will end when the participant has reached their final main follow-up time point, at 6 months post-randomisation.

10.1. Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

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

10.2. Reporting Procedures for Serious Adverse Events

If an SAE arises in the period between randomisation and the final follow-up visit, that is deemed related to the trial interventions, the site will complete an SAE form and record the description, date of onset, end date, severity and assessment of relatedness to trial intervention.

For the purpose of safety recording for this trial, only unforeseeable SAEs potentially related to the intervention will be reported immediately to the central trial team. When the local research team becomes aware of an SAE in a trial participant, the PI will review the SAE locally and make a decision about the causality (i.e. likelihood of the event to be related/attributed to the intervention). Further details on the grades of causality are available in the *SAE Reporting Guidelines* document in the Investigator Site File. Following the assessment of causality the PI will assess any related events for expectedness. For any SAEs assessed as unexpected and potentially related, the details of the event will be entered on an SAE reporting form on the database, and the local research team will notify the central trial team via email or telephone within 24 hours of the PI becoming aware of the event. Once received, causality and expectedness will be confirmed by the Chief Investigator (CI) or delegate (Nominated Person). In the event that consensus is not reached between the PI and Nominated Person about assessment of causality and expectedness, this will be escalated to the CI for further discussion. However, if no consensus decision is reached about expectedness after further discussion within one working day, and the SAE is judged to be unexpected by any one of either the PI, Nominated Person or CI, the event will be classified as an unexpected event.

A serious adverse event (SAE) occurring to a participant should be reported to the REC that gave a favourable opinion of the study where in the opinion of the Chief Investigator the event was 'related' (resulted from administration of any of the research procedures) and 'unexpected' in

relation to those procedures. Reports of related and unexpected SAEs should be submitted within 15 working days of the Chief Investigator becoming aware of the event, using the HRA report of serious adverse event form (see HRA website). All such events will also be reported to the Trial Management Group (TMG) at their next meeting.

Adverse events (AEs) that are unrelated to the injury, intervention or treatment will not be reported.

10.3. Reporting Procedures for Foreseeable Serious Adverse Events and Adverse Events Not Defined as Serious

Foreseeable SAEs and adverse events not defined as serious that are related to the interventions will be recorded by participants (through a bespoke patient-reported complications questionnaire) or recruitment centre staff (on a site complication CRF) but will not need to be reported immediately.. These events will be verified with the participant and/or by the site investigators to ensure accurate recording and avoidance of duplicate reports over the follow-up timepoints.

Foreseeable adverse events include:

- pain increase after exercises that required an increase in analgesia or medical doctor consultation
- treatment-related exacerbations of other medical conditions after exercise that require medical treatment, which also do not meet the definition of serious (for example angina after exertion)
- Falls and injurious falls during performance of exercise that do not meet the definition of serious

Fracture management complications will be collected from participants in the 2, 4 and 6 month questionnaires but will not be reported as adverse events, these include:

- Deep Vein Thrombosis/Pulmonary Embolus
- Wound infection treated with antibiotics
- Heel or ankle pressure sore (grade II or above)
- Surgery/further surgery to the injured ankle (unless an adverse event directly related to the exercise intervention, in which case this would be an SAE)

11. STATISTICS AND ANALYSIS

11.1. Statistical Analysis Plan (SAP)

The statistical aspects of the study are summarised here with full details of all analyses to be fully described in a separate statistical analysis plan. The SAP will be drafted early in the trial and finalised prior to the primary outcome analysis. The SAP will be reviewed by the TOC. Interim analyses of the efficacy outcomes are not planned and will be performed only if requested by the TOC. It is anticipated that all analysis will be undertaken using Stata (StataCorp LP, www.stata.com) or another well validated statistical package.

11.2. Sample Size Determination

292 (146 per arm) participants providing primary outcome data at 6 months are required to detect a difference of 8 points on the OMAS score with an estimated standard deviation of 21 with 90% power and 5% (2-sided) significance. The minimum clinically important difference for the OMAS selected in surgical trials has usually been 10 points but for this trial of physiotherapy we have chosen a smaller difference of 8 points, which is likely to be clinically important and was supported by our patient advisory group. The chosen standard deviation of 21 is based on the AIM trial (6) (SD 21.7) and the feasibility study data (SD 20.5 based on 32 participants having reached the 6 month time-point - unpublished). This equates to a standardised effect size of 0.38, a small to moderate effect. In the AFTER feasibility study there was 11% loss to follow-up (those not providing the primary outcome data). In order to allow for potential loss to follow-up of participants in the definitive trial we have inflated the sample size by 15% to 344 participants (172 per arm).

11.3. Analysis populations

11.4. Primary analysis population will be the intention-to-treat population (ITT), that is participants will be analysed in the group in which they were randomised regardless of what treatment they received. The analyses will be repeated for the per protocol population, which will be finalised using blinded data prior to the final datalock. Description of the Statistical Methods

All available data from both treatment arms will be used in data analysis based on the intention-to-treat population. Reporting of the results will be in accordance with the CONSORT statement (34) using the extensions for non-pharmacological treatment interventions and patient-reported outcomes. Standard descriptive statistics will be used to describe the demographics between the treatment groups reporting means and standard deviations or medians and interquartile ranges as appropriate for continuous variables and numbers and percentages for binary and categorical variables. Standard statistical summaries and graphical plots will be presented for the primary outcome measure and all secondary outcome measures.

The OMAS score at 6 months is the primary outcome in this study and will be compared between treatment groups as the dependent variable in a mixed-effects linear regression model including outcome information at intermediate time-points. This model will adjust for stratification factors

(recruitment centre and initial fracture management; operative or non-operative) and baseline OMAS score. A random effect will be included to account for heterogeneity due to recruitment centres. The treatment effect will be based on adjusted mean differences at 6 months and will be reported together with their 95% confidence intervals.

We will also undertake a Complier Average Causal Effect (CACE) analysis which essentially compares the "compliers" in each group. Full compliance in the intervention group is defined as receiving a minimum of 4 physiotherapy sessions and partial compliance is receiving at least one physiotherapy session (i.e. starting the treatment). This will provide supporting evidence to any findings from the principal analysis. Subgroup analysis by surgical vs non-surgical treatment of the fracture, and by self-perceived self-efficacy at baseline will be undertaken using the same methodology incorporating a treatment by subgroup interaction term and presented using forest plots.

Similar methods to the primary outcome will be used to analyse continuous secondary clinical outcomes and patient reported outcomes. Complications will be reported by type for each intervention group, and, if appropriate, compared between the two groups using logistic regression models.

11.5. The Level of Statistical Significance

All outcomes will be assessed with 5% level of significance and will be presented with effect sizes and 95% confidence intervals. P-values will be reported with up to 3 decimal places.

11.6. Procedure for Accounting for Missing, Unused, and Spurious Data.

Missing data will be minimised by careful data management. Missing data will be described with reasons given where available; the number and percentage of individuals in the missing category will be presented by treatment arm. All data collected on data collection forms will be used, since only essential data items will be collected. No data will be considered spurious in the analysis since all data will be checked and cleaned before analysis. The nature and mechanism for missing variables and outcomes will be investigated, and if appropriate multiple imputation will be used. However, the analysis method proposed is reasonably robust to missing at random (MAR) data. Sensitivity analyses will be undertaken to assess potential departures from the missing at random assumption. Any imputation techniques will be fully described in the Statistical Analysis Plan.

11.7. Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any changes or deviations from the original SAP will be described and justified in the protocol, updated SAP, final report and publications as applicable, depending on the timing of the changes.

11.8. Health Economics Analysis

A within-trial cost-effectiveness analysis will be conducted from a NHS and Personal Social Services (PSS) perspective using the multiple imputed trial data over a period of 6 months for the base case (or primary) analysis. Trial data would consist of resource use extracted from the trial report forms and questionnaires. Unit costs for resource inputs will be drawn from a range of primary and secondary sources. Completion rates for values for each resource use and cost category will be computed by trial arm at each time-point. Utilisation of resources will be summarised by trial arm and follow-up period and differences between arms will be analysed using t-tests for continuous variables and chi-squared test for categorical variables. Means and standard errors for values of each cost category will be estimated by treatment allocation and follow-up period. Differences in mean costs will be assessed using t-tests and the bootstrap 95% confidence intervals will be computed based on 10,000 replications. The cost-effectiveness analysis will adopt an intention-to-treat ("as randomised" with imputation of missing data) approach and an incremental cost-effectiveness ratio (ICER) will be calculated as the difference in mean costs divided by the difference in mean QALYs between the trial comparators. The NICE cost-effectiveness threshold of £20,000-£30,000 per additional QALY will be used to determine the cost-effectiveness of supervised progressive exercise compared to best practice advice. Sensitivity analysis will be performed to explore the effects of (i) extending the study perspective (i.e. societal perspective where the out-of-pocket expenses and productivity loss will be included), (ii) assessing the impact of missing data (i.e. using complete case analysis) on the ICERs, and (iii) including an additional £15,000 per QALY threshold to reflect recent trends in healthcare decision-making. Findings of this economic evaluation will be reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement (https://www.ispor.org).

12. DATA MANAGEMENT

The data management aspects of the study are summarised here with full details described in the Data Management Plan (DMP).

At enrolment, participants will be asked to indicate their preference for the delivery and completion of follow-up questionnaires – electronic, postal or telephone follow-up at 2, 4 and 6 months. Data collected in electronic format will be done by direct entry onto the trial database, including the collection of documentary evidence of consent. Electronic data collection has the major advantage of building “data logic” into forms, minimising missing data, data input errors and ensuring completeness. All data entered will be encrypted in transit between the

participants/recruitment centre and server. All electronic patient-identifiable information will be held on a server located in an access-controlled server room at the University of Oxford. The data will be entered into a Good Clinical Practice (GCP) compliant data collection system and stored in a database on the secure server, accessible only to the research team based on their role within the study. The database and server are backed up to a secure location on a regular basis.

Identifiable data will be limited to contact details (including name, address including postcode, and email addresses), NHS/ CHI number, sex at birth, DOB and telephone numbers and will be accessed separately from the outcome data obtained from/about the participants and managed within the rules of the clinical database system. In all other data, participants will be identified by a trial ID only. Direct access to source data/documents will be required for trial-related monitoring and/or audit by the Sponsor, NHS Trust or regulatory authorities as required. Contact details will be retained for 12 months after the last data collection. Electronic de-identified trial data will be retained for three years after publication of the trial.

12.1. Source Data

Source documents are where data are first recorded, and from which participants' CRF data are obtained. These include, but are not limited to, hospital records (from which medical history and previous and concurrent medication may be summarised into the CRF), clinical and office charts, laboratory records, diaries, microfiches, radiographs, audio recordings and patient-reported outcome measures that are submitted directly to the sponsor and correspondence.

CRF entries will be considered source data if the CRF is the site of the original recording (e.g. there is no other written or electronic record of data). All documents will be stored safely in confidential conditions. On all study specific documents, other than the signed consent and contact details form, the participant will be referred to by their study ID, not by name.

12.2. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations. Site staff will have access to the centrally collected patient-reported outcome data for participants that they recruit at their site on REDCap, to ensure that they can download a complete dataset for their patients at the end of the trial.

12.3. Data Recording and Record Keeping

Trial data will be collected and managed using REDCap electronic data capture tools hosted at OCTRU, University of Oxford.

REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Wherever possible, trial data will be entered directly into the trial database by site staff or participants. Data on paper forms or captured during phone calls to participants will be entered into the trial database by suitably trained central office staff. Full details will be recorded in the DMP. The participants will be identified by a unique trial specific number in any data extract. Identifiable data will only be accessible by members of the study team with a demonstrated need (managed via access controls within the application) and only used to communicate with the participant (e.g. sending follow-up reminders for online form completion or telephone follow-up).

Audio recordings of intervention sessions will be made digitally on password protected devices. They will be stored on secure servers at the University of Oxford, identified by a trial ID and/or initials only and will only be accessible to the CI and those members of the Oxford research team who have been authorised to do so by the CI. Any audio recordings will be retained for 12 months after intervention delivery checks and then deleted. It is necessary to retain the recordings for this period as they are the source data and help us to interpret treatment delivery. Access to them is required in case these are needed to refer back to these during analysis and reporting.

13. QUALITY ASSURANCE PROCEDURES

This study will be coordinated by the UKCRC registered Oxford Clinical Trials Research Unit (OCTRU) at the University of Oxford. A rigorous programme of quality control will be implemented to ensure compliance to the current approved protocol, GCP, relevant regulations and OCTRU Standard Operating Procedures (SOPs). Quality assurance checks will be undertaken by the trial management team to ensure integrity of randomisation, study entry procedures and data collection. Inspections of the Trial Master File will be carried out by the OCTRU Quality Assurance team (at least once in the lifetime of the study, more if deemed necessary). Furthermore, the processes of consent taking, randomisation, registration, provision of information and provision of treatment will be monitored centrally.

Intervention delivery will be monitored periodically to ensure fidelity. Site visits and/or audio/video recording of interventions will be conducted. Permission will be sought from the trial participants to observe or record treatment sessions. Verbal consent will be provided and recorded on site visit checklists or on the audio-recording as appropriate.

CRFs will also be used to monitor intervention fidelity. Data will be collected on intervention content delivery and number of treatment sessions attended to facilitate monitoring and

reporting. The sites will regularly receive feedback from quality activities to help maintain and improve fidelity.

Additionally, the study may be monitored, or audited by sponsor or host sites in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

13.1. Risk assessment

A risk assessment will be prepared before the study opens and will be reviewed as necessary over the course of the study to reflect significant changes to the protocol or outcomes of monitoring activities.

13.2. Study monitoring

The monitoring activities will be based on the outcome of the risk assessment. Quality control procedures will be undertaken during the recruitment and data collection phases of the study to ensure research is conducted, generated, recorded and reported in compliance with the protocol, GCP and ethics committee recommendations. The CI and the Trial manager will develop data management and monitoring plans.

13.3. Trial Oversight

The trial will be conducted in accordance with the principles of GCP and guidelines, the Declaration of Helsinki, OCTRU SOPs, relevant UK legislation and this Protocol. GCP-trained personnel will conduct the trial.

13.4. Trial Management Group

The day-to-day management of the trial will be the responsibility of the Trial Manager, supported by a Senior Trial Manager. This will be overseen by the Trial Management Group (TMG), who will meet monthly to assess progress. A Patient and Public Involvement (PPI) representative will be an integral member of the TMG. It will also be the responsibility of the Trial Manager to undertake training of the research staff at each of the trial centres. The trial statistician, health economist and the information specialist will be closely involved in setting up data capture systems, design of databases and clinical reporting forms.

13.5. Trial Oversight Committee

The Trial Oversight Committee (TOC), which includes independent members, provides overall supervision of the trial on behalf of the funder. Its terms of reference will be drawn up in a TOC charter which will outline its roles and responsibilities. Meetings of the TOC will take place at least once a year during the recruitment period. An outline of the remit of the TOC is to:

- Monitor and supervise the progress of the trial towards its interim and overall objectives.
- Review accruing data, completeness and blinded summaries if required and will assess the screening algorithm against the eligibility criteria
- Consider emerging evidence from other related trials or research
- Review any safety issues
- Inform the funding body on the progress of the trial.

The TOC will include at least one PPI representative as an independent member. Full details including names will be included in the TOC Charter.

14. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from GCP or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file, the TMG will decide on a case-by-case basis if a protocol deviation is considered important. All protocol deviations will be evaluated in accordance with OCTU SOP GEN-032

15. SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of GCP which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the trial subjects; or

(b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the CI, the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

16. ETHICAL AND REGULATORY CONSIDERATIONS

16.1. Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

16.2. Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and in compliance with the principles of Good Clinical Practice.

16.3. Approvals

Following sponsor approval, the protocol, informed consent form, participant information sheet and all patient facing study materials will be submitted to an appropriate Research Ethics Committee (REC), and Health Regulatory Authority (HRA) for written approval.

The CI will submit and obtain approval from the above parties for all substantial amendments to the original approved documents.

16.4. Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation, Sponsor and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties. The CI will submit progress reports to the funder according to their reporting requirements.

16.5. Transparency in Research

Prior to recruitment of the first participant, the trial will have been registered on a publicly accessible database [ISRCTN].

The trial team undertakes to keep trial data up to date and to make the results publicly available.

16.6. Participant Confidentiality

The participants will be identified only by a trial ID number on all study documents and any electronic database, with the exception of the randomisation CRF, where participant initials may be added. The authorisation functionality within the data collection system will be utilised to ensure that identifiable data can only be accessed by appropriate members of the trial team. All documents will be stored securely and only be accessible to study staff and authorised personnel. The study will comply with the General Data Protection Regulation and the Data Protection Act (2018), which requires data to be de-identified as soon as it is practical to do so.

16.7. Expenses and Benefits

Participants will not undergo any hospital visits in addition to normal care, therefore no expenses will be payable. Participants will have remote sessions via video/telephone call, or

face to face sessions at their local hospital, in order to receive the exercise interventions. As this is part of delivering the intervention treatment no expenses will be payable to them.

17. FINANCE AND INSURANCE

17.1. Funding

This study is funded by the National Institute for Health Research, Research for Patient Benefit (NIHR201950).

17.2. Insurance

The Sponsor has a specialist insurance policy in place – Newline Underwriting Management Ltd, at Lloyd's of London – which would operate in the event of any participant suffering harm as a result of their involvement in the research. Standard NHS cover for negligent harm is in place for NHS procedures.

17.3. Contractual arrangements

A contract will be drawn up between the Department of Health and the University of Oxford. Appropriate contractual arrangements will be put in place with all third parties.

18. PUBLICATION POLICY

The core aim of our dissemination and communication strategies are to translate our research findings into clinical practice for the benefit of patients and the NHS.

To achieve this impact there is a requirement to report our study open-access and to a high standard in accordance with guidelines. The next stage is to ensure these findings, and the intervention indicated for implementation, reach the patients and clinicians within the NHS.

The study protocol and results will be published in open-access journals in accordance with CONSORT statement(35) and related extensions, and the template for intervention description and replication (TIDieR)(36) complex intervention reporting guidance. We will work with networks to disseminate findings, for example through annual meetings and newsletters of the Association of Trauma and Orthopaedic Chartered Physiotherapists, Orthopaedic Trauma Society, and the Fragility Fracture Network. The findings will also be shared with patients and the public more widely through local and national charity newsletters and other media channels.

19. DEVELOPMENT OF A NEW PRODUCT/PROCESS OR THE GENERATION OF INTELEECTUAL PROPERTY

Ownership of IP generated by employees of the University vests in the University. The University will ensure appropriate arrangements are in place as regards any new IP arising from the trial. The materials used for the intervention were developed at Oxford University and therefore background IP is held by the University.

20. ARCHIVING

Documents and electronic systems will be archived as per the appropriate SOPs as prepared by OCTRU.

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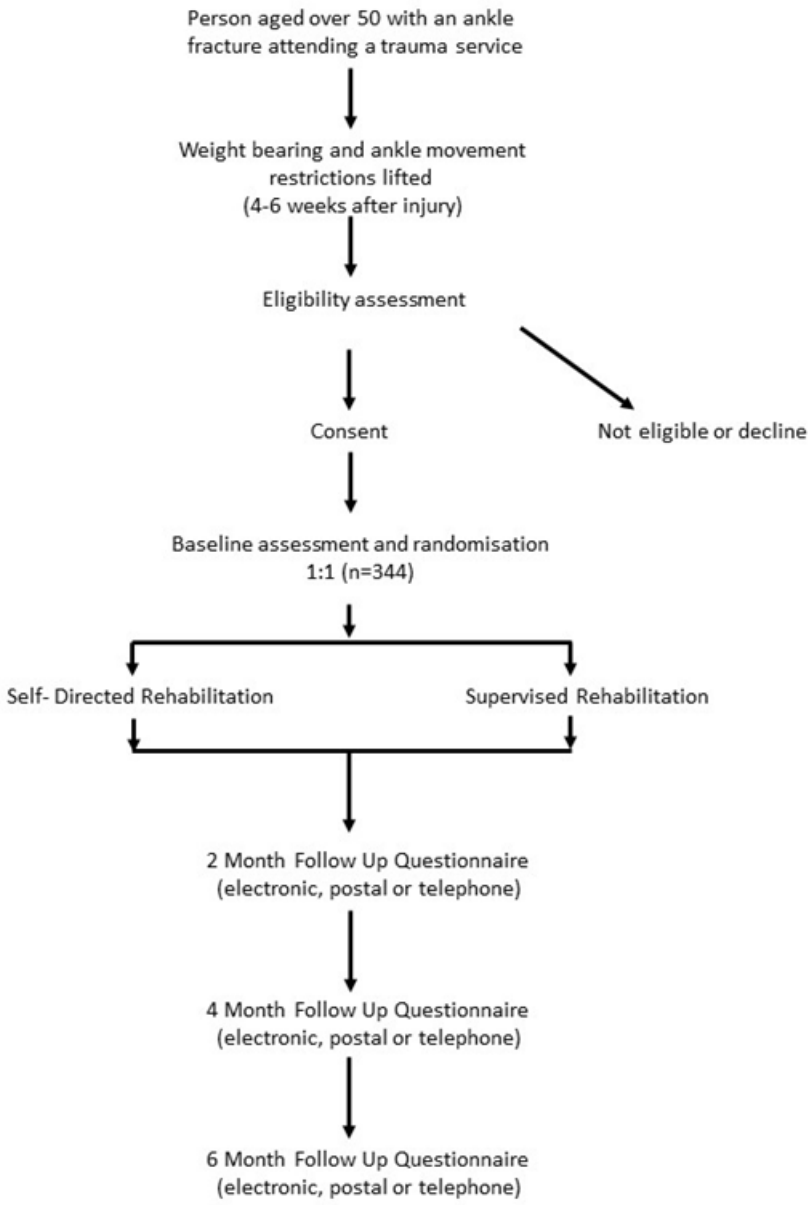
22. APPENDIX A: STUDY FLOW CHART



23. APPENDIX B: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
N/A – 1st Version	V1.0	XXMon2021		