# TReatments of Exercise AnD Orthotic devices for plaNtar heel pain

## **TREADON** pilot feasibility trial

## PROTOCOL

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Chief Investigator: Dr Edward Roddy

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## Funder

National Institute for Health Research (NIHR) RfPB study number PB-PG-0614-34021

# Signature Page

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 and will adhere to the principles of GCP guidelines, the Keele CTU and Sponsor's SOPs,.

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

**For and on behalf of the Study Sponsor:**

Signature: Date:
..... ...../...../.....

Name (please print):

.....

Position:
.....

In addition to the above, 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:
..... ...../...../.....

Name: (please print):

.....

# CONTENTS

## 1 TRIAL SUMMARY

**Title:** Treatments of exercise and orthotic devices for plantar heel pain: The **TREADON** feasibility and pilot trial

**Aims and Objectives**: The aims of this feasibility and pilot trial are to inform the robust design of a future, main, randomised controlled trial (RCT) of advice, exercise and foot orthoses as interventions for adults with plantar heel pain (PHP). The specific objectives are:

1) To compare the feasibility and success of three different patient invitation methods
2) To determine the number of arms and which treatments (from four in the feasibility trial) to test in the future main trial
3) To determine the primary outcome measure for the main trial by comparing feasibility of follow-up data collection between three possible primary outcome measures
4) To inform the sample size calculation for the main trial by providing estimates of data regarding changes in outcome measures and also to examine potential prognostic baseline factors and other outcomes that may need to be accounted for in the design and/or analysis of the main trial

**Study design:** four arm, parallel-group, multicentre, randomised pragmatic feasibility and pilot trial.

80 adults with PHP will be recruited from a general practice population over a 9-month period, and randomised to one of four treatment arms:

1. Self-management advice
2. Self-management advice and foot orthoses
3. Self-management advice and exercise
4. Self-management advice and a combination of both exercise and foot orthoses

**Randomisation** will be conducted by Keele CTU using block randomisation (block size of 4) to ensure parity in allocation from each of the three invitation methods and for each treating centre.

**Follow-up:** data will be collected weekly via text messaging, weekly patient self-report diaries and also by postal questionnaires at 12 weeks from the point of randomisation.

**Setting:** GP practices, physiotherapy and podiatry services drawn from Cheshire, Staffordshire and Stoke-on-Trent regions.

**Interventions:** All participants will be posted a high quality self-management advice booklet**.** Those receiving interventions of; exercise, foot orthoses, or a combination of these treatments will be offered up to 6 treatment contacts over 12 weeks, delivered by physiotherapists and podiatrists in local services who are trained in the trial protocol.

**Participants:** Males and females over 18 years of age with plantar heel pain.

**Trial supplies:** Participating treatment centres will use foot orthoses provided by Keele CTU.

**Process Outcomes:**

**i)** The three different patient identification methods will be assessed in terms of the number of participants identified, recruited and rate of recruitment over 9 months.

**ii)** The clinicians' evaluation of the feasibility of trial intervention delivery will be assessed by post-study evaluation workshops.

**iii)** The fidelity of intervention delivery and patient attendance for treatment will be assessed using case report forms.

**Clinical outcomes:**

**i)** The time to patients' report of plantar heel pain being 'significantly improved' (where this occurs) derived from a numerical pain rating scale (NRS 0-10) collected weekly via text message.

**ii)** Change in foot pain measured by the Foot Function Index pain subscale (FFI-PS) and the Manchester Foot Pain and Disability index pain subscale (MFPDI) from baseline to 12 weeks.

**iii)** Self-reported adherence, satisfaction with care, treatment credibility and self-report adverse events.

**iv)** Evaluation of completion rates of other outcome measures including; FFI disability (9 items) and activity limitation (5 items) subscales, MFPDI functional subscale (10 items) and personal appearance sub scale (2 items), first-step pain (NRS 0-10), quality of life (EuroQol EQ5D 5L), work loss (days absent and loss through reduced ability whilst at work); self-reported PHP healthcare use including contacts with primary and secondary healthcare professionals, use of prescribed and over-the-counter medication, hospital investigations and use of private healthcare.

**Statistical analysis and reporting:** The statistical analysis will focus on process measures and evaluative methods. There will be no emphasis on hypothesis-testing which is reserved for the future main trial. Analysis will include the following aspects:

(i) recruitment rate and effort required in recruiting by invitation method;
(ii) descriptive summary of baseline characteristics of participants;
(iii) number ineligible with reasons for ineligibility, and count of non-consenting population;
(iv) completion and performance of the measures of general foot pain and time to improvement in PHP in terms of the measurement properties;
(v) treatment adherence, treatment credibility and satisfaction with treatment;
(vi) descriptive and inferential (confidence interval) statistics around outcome performance by trial arm;
(vii) evaluation of parameters for informing a main study sample size calculation;
(viii) investigating potential prognostic indicators of outcome from baseline variables.

**Expected study duration:** 24 months in total. A recruitment period of 9 months is anticipated and follow-up will be for 12 weeks. The end of the feasibility and pilot trial is defined as the collection of the last data item for the last participant to be randomised.

## 2 GLOSSARY OF TERMS AND DEFINITIONS

| Abbreviation | Description |
|---|---|
| CI | Chief Investigator |
| CRF | Case Report Form |
| CRN | Clinical Research Network |
| CSG | Clinical Studies Group |
| CTU | Clinical Trials Unit |
| DNA | Did Not Attend |
| GCP | Good Clinical Practice |
| GP | General Practitioner |
| FFI | Foot Function Index |
| FPI | Foot Posture Index |
| ID | Identification Detail Number |
| ITT | Intention To Treat |
| REC | Research and Ethics Committee |
| MFPDI | Manchester Foot Pain and Disability Index |
| NHS | National Health Service |
| NICE | National institute for Health and Care Excellence |
| NIHR | National Institute for Health Research |
| NRS | Numerical Rating scale |
| PHP | Plantar Heel Pain |
| PI | Principal Investigator |
| PIL | Patient Information Leaflet |
| PPI | Patient and Public Involvement |
| PRO | Patient Reported Outcome |
| QoL | Quality of Life |
| RCT | Randomised Controlled Trial |
| RUG | Research User Group |
| SAE | Serious Adverse Event |
| SD | Standard Deviation |
| TREADON | TReatments of Exercise AnD Orthotic devices for plaNtar heel pain |
| TSC | Trial Steering Committee |

# 3 BACKGROUND AND RATIONALE

## 3.1 PLANTAR HEEL PAIN

Plantar heel pain (PHP) is a generalised term used to describe a range of undifferentiated conditions affecting the plantar aspect (sole) of the heel and hindfoot. The specific cause of PHP is uncertain although plantar fasciitis is often implicated and the terms are often used synonymously. [1-3] PHP reduces mobility, impairs foot and physical function and the capacity for work, all of which have a negative impact on health-related quality of life.[4-6]

### 3.1.1 Prevalence

PHP is the most prevalent soft tissue foot complaint affecting 10% of adults during their lifetime[4] and accounts for 25% of all foot disorders in athletes.[7] The age distribution of patients most commonly presenting with symptoms is 40-59 years. [8]

### 3.1.2 Clinical Features and Diagnosis

The cause of PHP is often unclear and may be multifactorial. Risk factors include obesity, pronated foot type, reduced ankle or big toe range of motion, and prolonged weight-bearing.[2,3,8]

The clinical presentation of PHP is characterised by insidious onset, localised pain in the plantar heel region (which may extend to the medial arch of the foot), which is most noticeable on the initial steps after a period of inactivity or after a period of prolonged weight-bearing. Severity can range from minor irritation to incapacitating pain.[4] Clinical history may show a recent change to an increased activity level. Diagnosis is usually straightforward and based on clinical signs. [9]

### 3.1.3 Prognosis

PHP is commonly thought to be a benign, self-limiting condition that resolves over 1 to 2 years, yet data from a population-based observational study of foot pain in 5,109 adults [10,11] show that only 20% of people with PHP experienced significant improvement over 18-month follow-up (unpublished data).[10] There are few longitudinal cohort studies of PHP and therefore little is known about the clinical course or about which factors predict recovery or persistence. [12-14]

### 3.1.4 Treatment Options

Guidance for clinicians managing patients with PHP recommend initial treatment with analgesia and advice regarding rest, footwear choice, heel pads and weight loss.[16,17] Onward referral to a podiatrist or physiotherapist is suggested if symptoms persist beyond several months. [15-16]

Physiotherapists and podiatrists commonly offer lower limb therapeutic exercise and foot orthoses for patients with PHP.[17-19] Available systematic reviews of these interventions [20-24] acknowledge that most trials conducted to date are of poor methodological quality with varied and often poor delivery of the treatments. However, the reviews collectively indicate that both exercise and foot orthoses are promising interventions for short and medium-term improvements in pain and function in patients with PHP.

Foot orthoses are non-invasive insole devices that are designed to optimise foot loading distributions and to correct medial longitudinal arch shape through control of specific foot joint rotations.[25] Research evidence suggests that there are two key mechanisms by which foot

orthoses are likely to impact upon the symptoms of PHP. Firstly, they address foot-specific factors that are associated with PHP which include, planus foot posture (flat feet) and excessive foot pronation (eversion).[26,27] Systematic review evidence of the effects of foot orthoses on foot function has demonstrated reductions in rearfoot pronation.[28] Moreover a linear dose-response effect can be achieved where rearfoot pronation is reduced incrementally with increasing levels of pronatory control from foot orthoses using rearfoot posts.[25] Secondly, foot orthoses increase foot-to-surface contact area and provide symptomatic relief for PHP through reductions in calcaneal-plantar fascia junction tensile stress and pressures when the foot is under a loading conditions.[29-32]

Risk factors for PHP have been shown to include tightness in the gastrocnemius and soleus muscles, the plantar fascia and Achilles tendon. Reduced dorsiflexion at the ankle, weakness of the gastrocnemius, soleus, and intrinsic foot muscles are also associated.[8] Stretching exercises that incorporate both the Achilles' tendon and the plantar fascia can be used to improve the movement within these structures and altered biomechanics across the connective tissues between them and is therefore a viable therapeutic target.[9] Equally, muscle strengthening exercises for the intrinsic muscles of the foot and triceps surae will assist with improving normal foot and lower limb function.[33] Exercises which target all muscle groups in the lower limb, such as the hamstrings and quadriceps, may also help to restore normal foot loading and movement patterns and are targeted by exercise intervention.[34]

Management approaches which use treatments of orthoses and/or exercise may be viewed as challenging by patients as achieving good clinical outcomes will require a level of adherence to these treatment regimens, usually over a period of weeks or months. Educating patients about the condition and highlighting the importance of adherence is therefore an important component of treatment.

### 3.2 RATIONALE FOR THE TREADON FEASIBILITY AND PILOT TRIAL

PHP is a common cause of foot pain and patients are usually managed in primary care.[15,16] PHP commonly affects those of working age, and often leads to pain, reduced mobility and difficulties with everyday activities including work. PHP is associated with reduced quality of life and potentially poor long-term health.[4-8] Currently the evidence-base to inform clinical decisions about treatments is limited and generally of poor quality.

Evidence suggests that foot orthoses and exercises offer potential benefits in terms of; reduced pain, improved function and more rapid treatment response than usual GP care which frequently involves a watchful waiting approach. These interventions may also provide cost-effective treatment options by reducing further healthcare use and facilitating earlier return to everyday activities, including work. However, there is a lack of high-quality evidence to support their use either alone or in combination and there is currently no evidence of cost-effectiveness for these PHP treatments. Therefore it is currently unclear if the NHS should be offering these interventions.

Our patient advisory group has highlighted the importance of access to effective interventions which result in a rapid reduction in symptoms. Their experiences of GP management are mostly based on a 'watch and wait' approach, resulting in on-going and considerable pain alongside functional limitation.

In view of the often prolonged duration of symptoms and the substantial impact of PHP on physical function and ability to work, access to exercise and/or orthotic devices may be

justified to help patients achieve faster recovery, improve function and ability to work and reduce future healthcare use.

A large multicentre NHS-based trial with long-term follow-up is required to examine the clinical and cost-effectiveness of individualised exercise and foot orthoses in addition to good self-management advice for adults with PHP. However, such a trial will require a large sample and will be a significant undertaking in terms of time and cost. Consequently, there are a number of design aspects which we need to consider carefully in order to be confident that a main trial is feasible.

This feasibility and pilot trial will provide important information on which to optimise the plans for a future main RCT in the NHS which will investigate the additional benefit, in terms of clinical and cost-effectiveness, of individualised exercise and foot orthoses to good self-management advice for adults with PHP. The future main trial will inform NHS policy and commissioning decisions about treatments for this patient group.

A comprehensive search of PHP research literature and the trials registers has been undertaken and no directly comparable trials have been identified.

# 4 AIMS AND OBJECTIVES

The overall aim of this feasibility and pilot trial is to establish important parameters and to test several processes and outcomes that will inform the design of a future, main RCT of advice, exercise and foot orthoses as interventions for adults with plantar heel pain.

## 4.1 OBJECTIVES

The specific objectives include both process and clinical outcome evaluation and are detailed as follows:

### 4.1.1 Process evaluation objectives:

**i. To compare the feasibility, success and cost of three different patient identification methods;**

- patients who consult with heel pain at participating general practices during the study period
- retrospective review of electronic medical records to identify patients who have consulted their GP with heel pain in the last 12 months
- population survey posted to adults registered at selected participating general practices to identify those who have heel pain but have not consulted their GP in the last 12 months.

**ii. To determine both the number of arms and which treatments to test in the future main trial;**

This will be achieved by collecting data regarding:

- engagement and adherence by patients with the treatment in each arm
- patient-reported satisfaction with each treatment packages
- patient-reported credibility of each treatment package
- practitioner views of the feasibility and acceptability of the trial intervention training and the feasibility of delivering the trial interventions within their clinical service.

### 4.1.2 Clinical outcome elevation objectives

**iii. To determine the primary outcome measure for the main trial;**

This will be achieved by comparing the feasibility of follow-up data collection between three self-report outcome measures. Comparisons will include; follow-up rates, missing data and properties such as floor and ceiling effects and change over time in outcome values.

**iv. To inform the sample size calculation for the main trial**

- by providing estimates of data completion, mean (and standard deviation) scores, variability in data, proportion of participants who are significantly better across time, including median 'event' times in the time-to-event evaluation, correlation of repeated measures, estimates of completion for the Foot Function Index Pain Scale (FFI-PS) [35,36,63] and Manchester Foot Pain and Disability Index [37] (MFPDI) pain subscale estimate the minimum clinically important differences.

v. **To examine potential prognostic baseline factors that may need to be accounted for in the design and/or analysis of the main trial**.

# 5 RESEARCH PLAN

## 5.1 DESIGN AND SETTING

The TREADON feasibility and pilot trial is a four arm, parallel-group, multicentre, randomised pragmatic trial. Participants will be identified from participating general practices drawn from Cheshire, Staffordshire and Stoke-on-Trent areas.

## 5.2 STUDY POPULATION AND ELIGIBILITY

The study population will consist of community dwelling adults with PHP. The eligibility criteria are designed to select a relatively homogeneous group of patients with idiopathic PHP, which is suitable for treatments of exercise and foot orthoses and who do not require immediate onward referral for surgery. 80 participants (20 in each arm) will be recruited over a nine-month period.

### 5.2.1 Inclusion criteria

1. Male or female aged ≥ 18 years
2. Self-reported localised pain under the heel which is aggravated by weight bearing activities, worst when first standing or after a period of rest, especially on getting out of bed in the morning, or following periods of prolonged sitting [12]
3. Symptom duration of episode of at least 4 weeks with a minimum pain score of 2 on a Numerical Rating Scale (NRS 0-10)
4. Owns or has access to a mobile phone that receives text messages or a landline telephone
5. Able and willing to participate and provide written informed consent

### 5.2.2 Exclusion criteria

1. Inflammatory arthritis (e.g. rheumatoid arthritis, ankylosing spondylitis, reactive arthritis, systemic lupus erythematosus, gout, psoriatic arthritis), fibromyalgia
2. Serious pathologies or serious suspected pathologies (e.g. malignancy, trauma, infection)
3. Current treatment for PHP or treatment in the last 3 months by a physiotherapist or podiatrist
4. Previous surgery or on waiting list for surgery on the affected foot
5. Corticosteroid injection into the affected foot in last 3 months
6. Unwilling or unable to participate with the interventions or unable to attend clinics for treatment
7. Unable (even with telephone support) to complete follow-up questionnaires written in English or unable to receive text messages or phone calls

8. Known skin allergies to common orthotic device materials (e.g. adhesives, latex, sock dyes, certain shoe types)

## 5.3 RECRUITMENT PROCESSES

### 5.3.1 Participant identification

Potentially eligible adults with PHP will be identified in one of three ways, which will proceed in parallel; and are described below. In addition the trial will be advertised in the waiting rooms of participating general practices, providing information to potentially eligible patients, who may then ask their GP about the trial. See Appendix 1 for summary flowcharts of the three methods.

1. During a patient consultation and on entering a relevant diagnostic or symptom Read code into electronic medical records, GPs will be prompted about the trial and patient eligibility by an automatic 'pop-up' screen. GPs will screen for eligibility (using the inclusion/exclusion criteria listed) and patients identified as suitable and interested in trial participation will be asked for written consent to further contact by the research team. The GP will then fax or email the consent to contact form to Keele CTU. Patients who are interested and provide consent to contact will continue to receive advice from the GP who will be asked to avoid providing interventions other than pain relief medication. The patients will be advised by the GP that providing consent to contact does not oblige them to take part in the trial. On receipt of the consent to contact form a member of the study team will post patients a full TREADON trial information pack.
2. Patients who have already consulted their GP in the participating practices for foot or ankle pain in the last 12 months, will be identified by medical record review. Practice staff supported by members of the NIHR Clinical Research Networks (CRN) of West Midlands and North West Coast and informatics teams who are contracted to work in the participating GP practices, will screen records to identify adults aged 18 years and over who have consulted with foot/ankle pain in the last 12 months at the practice. We have previously shown that 38% of foot/ankle GP consultations are not coded with a specific diagnostic label such as PHP, hence the need to search the medical records using broader symptom codes.[39] The electronic screening protocol will exclude those patients with potentially serious pathology (e.g. inflammatory arthritis, malignancy as listed in the exclusion criteria) and those in nursing home accommodation. GPs will also be invited to screen the sample list for patients whom they consider should be excluded from the invitation mailing. Practice staff, supported by CRN staff, will then mail to those names remaining on the list, a covering letter and a patient information sheet and a screening survey for foot pain, which will include questions regarding demographic details (gender, age, employment and health status, height and weight, ethnicity), questions to assess eligibility criteria (location and duration of pain, access to a mobile/telephone) and quantify the nature and burden of foot pain/problems. A request to consent to further contact and a pre-paid return envelope will also be included. Within the screening survey, respondents will be asked to indicate the location of pain on a foot manikin () and complete the MFPDI (pain and function subscales). PHP will be identified by overlaying a reliable coding

template previously used in our foot pain research when the completed manikin is returned. [40] Non-responders will be sent a reminder postcard at two weeks following mailing of the screening survey pack. A second screening pack containing a reminder letter and repeat documentation will be sent to those non-responders after a further two weeks.

3. A population survey posted to adults registered at selected participating general practices to identify those who have heel pain but have not consulted their GP in the previous 12 months. Our data indicate that only 60% of people with PHP consult their GP.[11] Practice staff supported by members of the CRN West Midlands who are contracted to work in the participating GP Practices, will screen records to identify all registered adults (≥18 years of age). These records will then be further screened by GPs for patients whom they consider should be excluded from the invitation mailing. Patients will be mailed a covering letter and study pack as outlined in method 2 above. Non-responders will also be followed up as described in method 2 above. The mailout for this survey will be performed by Docmail, which is a standards-compliant hybrid mail service, providing document management and ISO 27001 secure mailings.

All communications to the patients will be on GP practice letter-headed paper. Repeat mailings to the same person, which may result from different identification methods of recruitment at the same practice, will be avoided by conducting duplicate searches of the lists of potentially eligible participants and ensuring pop ups are not activated in route 1 for patients who have responded to the mailing from methods 2 and 3.

Participating GP practices will have a formal agreement with CRN West Midlands/North West Coast whereby staff in the CRN are contracted to work for the practice to undertake data quality and training functions associated with GPs' use of their computerised clinical systems and to undertake administration tasks and functions associated with identifying and inviting patients to take part in research.

### 5.3.2 Participant invitation and recruitment

All patients who provide consent to contact via identification route 1 and return their screening questionnaires and consent to further contact to Keele CTU via routes 2 and 3, and who appear eligible will be posted a full information pack about the TREADON feasibility and pilot trial.

The full trial information pack (which will be pre-coded with a participant trial ID number) will include:

- a cover letter and invitation to consider participation in the trial
- participant information leaflet (PIL)
- consent form
- baseline questionnaire (pre-treatment questionnaire)
- pre-paid return envelope.

This will allow potentially eligible participants to consider the trial in detail in their own time.

**Telephone eligibility screen**

Patients who have been sent a full TREADON information pack will be contacted by a research nurse by telephone, within 2-5 working days, after posting the pack. Up to five attempts will be made to contact the patient, including at different times of the day. Where no contact is made this will be recorded.

During this telephone contact the research nurse will check and confirm all eligibility criteria in order to ensure that only those who meet these criteria are recruited to the trial. An Eligibility Screening Form for all patients considered for inclusion will be completed. Anonymised information regarding age and gender will be retained from the Eligibility Screening Forms. Documented reasons for ineligibility or declining participation will be monitored by the Keele CTU as part of a regular review of recruitment progress. Screened patients who are not randomised either because they are ineligible or because they decline participation will also have the following information recorded:

- the reason why the patient is not eligible for study participation, OR
- the reason for declining if eligible. Patients are not required to give a reason, but if a reason is ascertained it will be recorded.

If the individual has agreed to further contact by the research team but has not provided a contact telephone number, an adapted invitation letter will be sent stating that the research team do not have their contact number and if they are interested in participating to either contact the trial team using the information provided or return their telephone contact details on the form and free post envelope provided. If no contact is made within 10 working days from the date the letter was sent then the study team will not contact them again. Where patients provided consent to contact via their GP (identification method 1) a similar process will be followed but the letter will state that if the research team have not heard from them within 10 days the patient should return to their GP for their heel problem should ongoing care be required.

## 5.4 INFORMED CONSENT

Prior to obtaining verbal and subsequently written informed consent to trial participation, the research nurse must have established the patient's eligibility for inclusion (see section 5.2). A full verbal explanation of the trial as per the patient information leaflet will then be given over the telephone for the patient to consider. This will include information about the rationale, design, treatment packages and follow-up requirements of the trial. The research nurse will address any concerns or questions. Prior to receiving this telephone call, the patient will have received a copy of the patient information leaflet for them to read in their own time and consider.

**Written Consent to Full Trial Participation**

A research nurse will gain verbal informed consent from willing eligible patients by reading through each section of the consent form explicitly and clarifying each point the individual needs to confirm.

Those who wish to take part in the trial will be asked to sign and date the consent form included in their information pack and return to the research team in the pre-paid envelope. Patients who return an incomplete consent form will be sent a letter asking them to complete the consent form, a copy of their consent form with the incomplete section(s) highlighted and a pre-paid return envelope. Recruitment will be complete when the signed consent form is received at Keele CTU. This recruitment method is identical to a recent successful trial. [42]

Patients who decline to participate at this point will be thanked for their time and advised that they should contact their GP regarding further care if required. The reason for declining (if given) will be recorded for anonymous reporting purposes and personal details will be cleared from the contact database in accordance with Keele CTU procedures.

Research nurses taking part in the informed consent process will have received appropriate training and will be authorised in the trial delegation log and permitted to take informed consent. The right of the participant to refuse consent without giving reasons will be respected. Further, the participant will remain free to withdraw from the trial at any time without giving reasons and without prejudicing any further treatment.

The signed and dated trial consent form will be retained by Keele CTU along with a record of the consent process detailing the date of verbal consent and will be separated from any research clinical data. A copy of the signed and dated consent form will be made and returned to the participant.

**Follow-up of people for whom the consent form is not signed and returned:**

Individuals who are eligible and have verbally provided consent by phone will be contacted by phone if they do not return their consent form and/or baseline questionnaire after seven working days of the original consent phone call date, to remind them to return their paperwork. Where phone contact is not made or if after a further seven days from the reminder phone call, the patient still has not returned their paperwork, a letter will be sent to remind them to return their paperwork.

**Informed Consent Responsibilities**

The CI retains overall responsibility for the informed consent of participants through Keele CTU. The CI will also ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent to participate according to the ethically approved protocol, principles of GCP and Declaration of Helsinki 1996. Such delegated responsibilities will be recorded in a trial delegation log. Informed consent will be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study and are out-with standard routine care at the participating site (including the collection of identifiable participant data). The right of a participant to refuse participation without giving reasons will be respected.

Where a participant is required to re-consent or new information is required to be provided to a participant, it is the responsibility of the CI to ensure this is done in a timely manner and according to any timelines requested by Keele CTU.

**Loss of Capacity Following Informed Consent**

Where valid, informed consent is provided by the participant and the participant subsequently becomes unable to give on-going informed consent by virtue of physical or mental incapacity, the initial consent provided remains legally valid and endures. Participants who lose capacity

after informed consent has been obtained and are unable to continue with protocol treatment or questionnaires will be withdrawn from further active trial participation.

## 5.5 BASELINE DATA COLLECTION

Those patients who have verbally consented to take part in the trial will be asked to complete the baseline questionnaire included in the study pack and return it to the research team along with a signed and dated consent form in the pre-paid envelope provided. On receipt at Keele CTU the authorised study administrator will check it for completeness before the participant proceeds to the randomisation stage.

. Participants who are eligible and have returned their consent form will be contacted by phone if they do not return their baseline questionnaire after seven working days of the original consent phone call date, to remind them to return their paperwork. As described in section 5.4, where phone contact is not made or if after a further 7 days from the reminder phone call, the patient still has not returned their paperwork, a letter will be sent to remind them to return their questionnaire.

## 5.6 RANDOMISATION

Following confirmation of eligibility, receipt of a correctly completed and signed consent form and completed baseline questionnaire, the authorised study administrator will randomise participants to one of the four interventions via an in-house Keele CTU secure randomisation system. The randomisation will be performed using random permuted blocks and will be blocked by treatment site (block size of 4) to ensure parity in allocation via each of the three identification methods and to ensure that patients at each treating site have an equal chance of receiving any of the interventions.

The following information will be required for randomisation:

- Participant details, including initials, gender and date of birth
- Participant trial ID
- Name of person undertaking randomisation
- Confirmation of eligibility
- Confirmation of written informed consent and date

Authorised access codes and passwords will be required to access the randomisation system. On successful access to the system the study administrator will be notified of the participant's treatment allocation.

All participants who are randomised will be posted a high quality self-management advice booklet and informed of their allocation in writing. Where participants have been allocated to a treatment package which includes exercise and/ or orthotic device intervention, the trial coordinator will then liaise with the appropriate service and a first appointment for each trial participant will be made. It is anticipated that the service will be responsible for notifying the patient of the date, time and location of their first appointment, which is to be within two weeks following randomisation. It is also anticipated that subsequent appointments will be managed through the normal service channels. Patients who do not attend appointments (DNAs) should be reappointed for the duration of the trial. The GP of each trial participant will be sent a letter

to confirm that their patient is taking part in the research study. Participants allocated to the self-management advice and information arm will not be required to attend for any study specific clinical intervention.

To date (version 2.0) we have gained sufficient data to evaluate the 'participant identification methods' process outcome objective of this feasibility trial. Recruitment has been achieved in line with expectations for recruitment method 3 (Population survey), whilst participant identification methods 1 (Consultation identification) and 2 (Medical Record Review) have not identified the number of participants estimated from our consultation Read code databases. Overall recruitment remains below anticipated numbers. In order to test process outcome other objectives of adherence and fidelity of the clinical interventions, sufficient numbers are still required within each of the treatment arms that require clinical attendance, (these being; self-management advice plus foot orthoses; self-management advice plus exercise; and self-management advice plus exercise and foot orthoses). In order to address this issue, and in accordance with version 2.0 of the protocol, an adaptation to the randomisation will be performed once n=10 is reached in the Self-management advice: control arm. From that point forward participants will no longer be randomised to the control arm and all further recruitment and randomisation will be to the three treatment arms requiring clinical attendance. This will be performed using random permuted blocks and will be blocked by treatment site (block size of 3; 1:1:1 ratio) to ensure parity in allocation via each of the three identification methods and to ensure that patients at each treating site have an equal chance of receiving any of the interventions.

### 5.6.1 Protecting against sources of bias at recruitment

Selection bias at recruitment will be avoided by the use of the following methods; all patients will receive identical study information and questionnaires minimising the threat to participation bias from the different identification routes. The same research nurses will contact patients to discuss eligibility regardless of identification route and will not take part in treatment allocation. Allocation concealment will be achieved by separating the processes and individuals involved in determining treatment allocation and treatment delivery and through the use of random permuted blocks.

## 6 TRIAL INTERVENTIONS

### 6.1 SETTING

Participants randomised to the self-management advice and information arm will receive a high-quality self-management advice booklet posted to their home address. Treatment packages for those participants randomised to interventions which include exercise or foot orthoses treatments, will be delivered by participating physiotherapy and podiatry services selected from Cheshire, Staffordshire and Stoke-on-Trent areas. Participating services will be those who have agreed to participate, have local management approval, have been trained in study specific interventions and procedures and are accessible to the GP practices participating in the trial.

### 6.2 TRAINING FOR PARTICIPATING CLINICIANS

Up to 25 clinicians will participate in training workshops with the research team prior to the start of recruitment and treatment. The focus of the training will be on carrying out the standardised assessment and delivery of the interventions in line with the agreed protocol. The training will include completion of all study paperwork requirements, good clinical practice as applicable to research and the maintenance of the site file and study records. Reporting of

serious adverse events, serious breaches and adverse events will also be covered. The training will be supplemented by a comprehensive manual, providing clear treatment protocols and study paperwork guidance for the clinicians.

## 6.3 INTERVENTIONS

The duration of the intervention regardless of group allocation will be considered to be 12 weeks from randomisation. Participants will be advised not to use other types of treatments, other than medication that their GP has provided, during the 12 week period if possible; however any additional healthcare and self-care use will be recorded in the 12 week follow-up questionnaire and weekly self-report patient diary.

All participants will receive a self-management advice and information booklet. Exercise and foot orthoses interventions will be delivered in up to 6 treatment sessions (which can include clinical attendance, telephone or email consultations) over 12 weeks by physiotherapists and podiatrists trained in the trial treatment protocols. DNA patients should be reappointed for the duration of the trial and Case Report Forms (CRF) should be completed to note the DNA. Clinicians will be trained to deliver both interventions and will be notified which arm the participant has been randomised to in advance of their clinic appointment. Clinicians will be required to complete a treatment CRF for each patient appointment.

To inform decisions about inclusion criteria for the main trial, participants randomised to exercise and foot orthoses interventions will undergo an assessment by the treating clinician of the point tenderness under the heel initiated by pressing the thumb into the underside of the heel (medial calcaneal tubercle specifically) [12] and also the medial longitudinal arch. Other potential causes of heel pain (e.g. neurologic cause; sciatica, tarsal tunnel, entrapment neuropathy, radiculopathy, heel/inferior midfoot pain of other soft tissue origin e.g. posterior tibial tendon dysfunction, trauma) will also be assessed as part of routine clinical practice.

### 6.3.1 Self-management advice: control arm

Participants will be posted a high-quality self-management advice booklet containing information and advice about PHP. This will be based on the Arthritis Research UK patient exercise leaflets on plantar fasciitis and foot pain, and supplemented with additional study-specific advice and education information. It will include a small number of stretching exercises and self-help messages about; pain relief, appropriate footwear, rest and weight loss.

### 6.3.2 Self-management advice plus pre-fabricated foot orthoses

In addition to the Self-management advice booklet, participants will undergo an assessment of their foot posture and function using the Foot Posture Index-6 (FPI-6)[43] to determine the orthoses type and level of control required.

The results of the FPI-6 assessment will be recorded on the Intervention Details CRF. If deemed clinically relevant to PHP this can include assessment of hip position (anteversion/retroversion) and knee position (genu varus/valgus).

Selection of the appropriate orthotic device will be based on the level of observed static rearfoot eversion according to an adapted version of the Foot Posture Index (FPI-6).[43] See figure 1.

Participants will be taught how to correctly fit the device into their shoe, and be instructed to use it for a minimum of 4 hours/day after an acclimatisation period. During the acclimatisation period participants will be advised to gradually increase the wearing time of their foot orthoses starting from a total of one hour and increasing by an hour each day until they are wearing the orthoses for at least 4 hours/day. Initial consultations will take place face-to-face in the clinic. Participants will be followed up for 12 weeks, in up to 6 consultations at the discretion of the treating clinician in agreement with the participant.

Adherence will be encouraged by a paper diary to capture use and facilitate discussion with the clinician. The foot orthosis may be changed or altered during subsequent clinical consultations according to participants self-report of tolerance or clinical presentation.

**Protocol for prescription of pre-fabricated foot orthoses**

The assessment protocol for the prescription of foot orthoses includes two key components to guide the podiatrist/physiotherapist towards the most appropriate foot orthosis prescription.

1. The main driver in influencing the rearfoot posting component of the foot orthosis prescription will be rearfoot posture component of the FPI-6. This will be assessed by the podiatrist/physiotherapist when the participant is in a relaxed stance position. The podiatrist/physiotherapist will observe whether or not the calcaneus is either inverted, vertical, everted, or highly everted (see figure 1). The remaining factor will be assessment of body weight which will influence the selection of the appropriate orthotic device.
2. Each foot orthotic device will be fitted according to the size of the participant's foot using the orthotic device shells of various sizes.
3. Clinicians will select the appropriate first choice device with appropriate rearfoot medial posting dose (see selection flowchart figure) in place and assess the participant for correct size of orthotic device (weight-bearing and non-weight-bearing fit-to-foot).
4. Clinicians will then check the fit of the orthotic device to the shoe (fit-to-shoe).
5. Tolerance will be evaluated by asking the participant if they are happy with the comfort and fit of their orthotic device (tolerance). If the participant is not happy with comfort or fit, the clinician may choose to taper the shell density and/or the dose of rearfoot posting.
6. Foot orthoses should be prescribed for both feet according to the intervention protocol which is driven by participants' foot posture and bodyweight, regardless of whether or not the heel pain presentation is unilateral or bilateral.

**Foot Orthoses Choice:** Our advisory group identified desirable characteristics of an orthotic device intervention protocol including as follows:

- an element of patient choice between different device based on comfort and fit
- scope for device adjustment/tailoring by the clinician to provide the desirable level of pronatory control for individual symptoms.

As a result we developed a pragmatic foot orthoses intervention algorithm which includes devices that are prefabricated and modifiable with the use of 'click-in' or adhesive additions (medial rearfoot posts) which can be used to change the level of pronatory control, as well as permitting adjustment according to patient comfort and therefore potentially impacting on levels of adherence. Moreover, a range of orthotic shell material densities allows for a more supportive orthotic device for participants with a higher bodyweight. [44] At present there is little

evidence to suggest that one brand/type of foot orthoses is more effective than another for the management of PHP. [45]

**Foot Orthoses details**

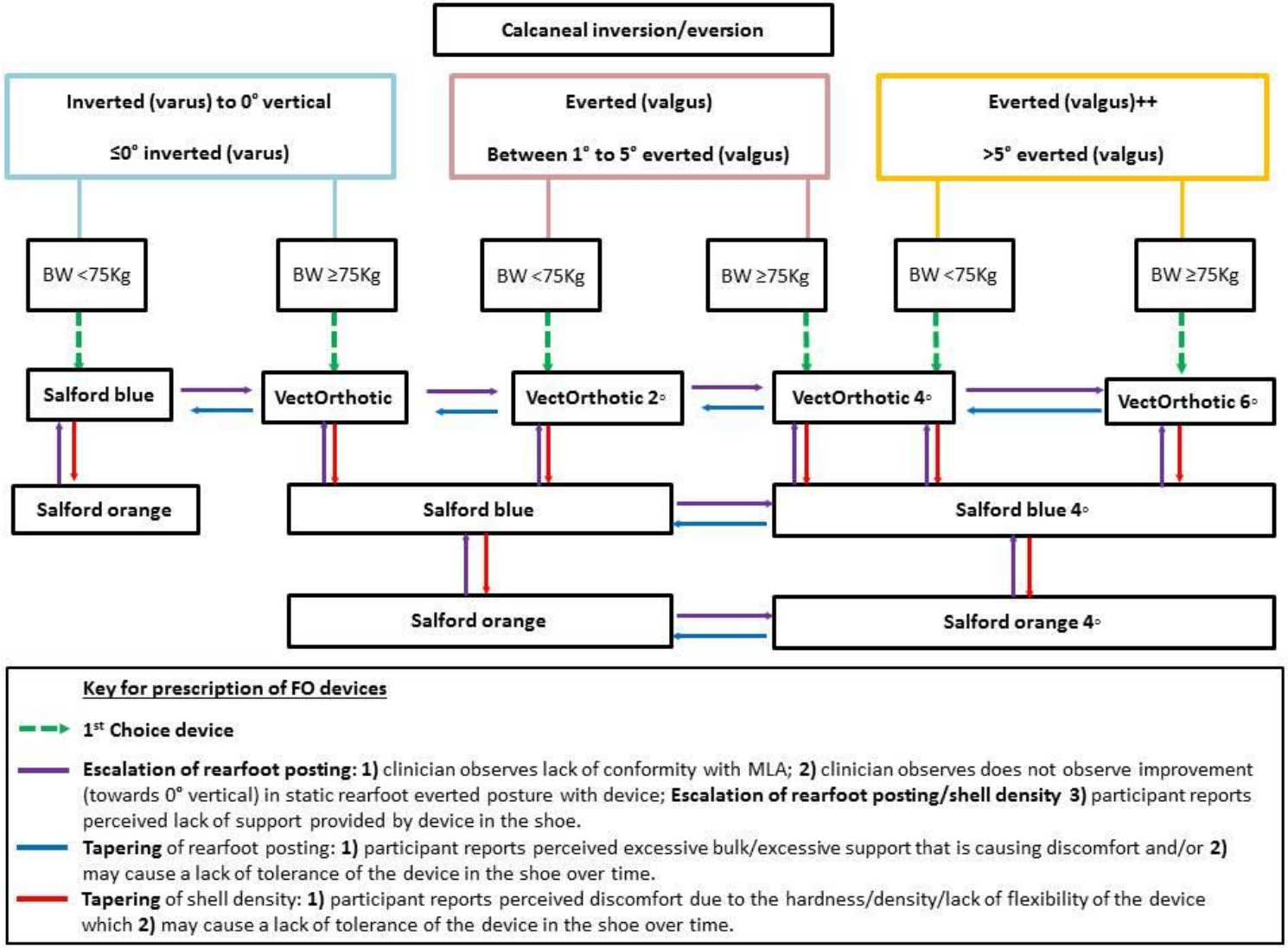
Vectorthotic devices® (firm density shell), Salfordinsole™ Firm (medium to-firm density shell) and Salfordinsole™ Flex (low-medium density shell)

Materials**:** Vectorthotic devices® - semi-rigid polypropylene shell with a closed cell polyethylene cover and polypropylene 2°, 4° and 6° rearfoot posts, Salfordinsole™ shells and 4° rearfoot posts both Sure Step-Control™ thermoplastic elastomer material.

Supplier Details**:** Participants randomised to receive foot orthoses should receive a trial orthotic device. These will be supplied free of charge by Keele CTU in accordance with the Supply Instructions provided in the Investigator Site File.

Storage: Orthotic devices should be stored in accordance with manufacturer's recommendations and as outlined in the supply instructions provided in the study information.

**Figure 1: Summary Flow chart of foot orthoses prescription**



### 6.3.3 Self-management advice plus individualised exercise

In addition to the self-management advice booklet, participants randomised to this group will undergo an assessment of their foot posture and function to determine the exercise type and dose that will be provided. The assessment will include a multidimensional examination of static foot posture using the Foot Posture Index (FPI-6).[43] At the discretion of the clinician a more generic lower limb assessment of alignment and function can also be performed enabling strengthening and stretching for hip abductors, quadriceps and hamstrings to be prescribed if deemed to be important as part of the overall PHP treatment.

Exercise selection will be informed by the level of clinically-observed muscle tightness, weakness and functional limitation. The exercises will be drawn from best available evidence and clinical consensus and will include foot-specific stretches / exercises targeting the plantar fascia and intrinsic foot muscles, key ankle-related muscle groups such as soleus and gastrocnemius, and other muscle groups in the lower limb identified as treatment targets within the assessment.

Participants will be taught how to perform and progress these exercises and will be given an individualised and detailed exercise sheet describing the regimen and showing pictures of the exercises. The exercise sheets provided will be study-specific exercises selected by the clinician and comprising photographs and written instruction completed by the clinician. The exercise regimen should be progressed at subsequent clinical consultations (up to 5 further sessions as required) according to observed changes in participant clinical presentation modelled on a previously successful exercise intervention from one of our earlier trials.[42,46] A record of the exercise prescription will be recorded on the Intervention Details CRF for each consultation.

Initial consultations will take place face-to-face in the clinic. Participants will be followed up for 12 weeks, in up to 6 consultations at the discretion of the treating clinician in agreement with the participant.

Exercise treatment modification will be based on a subjective and/or objective re-assessment and include either:

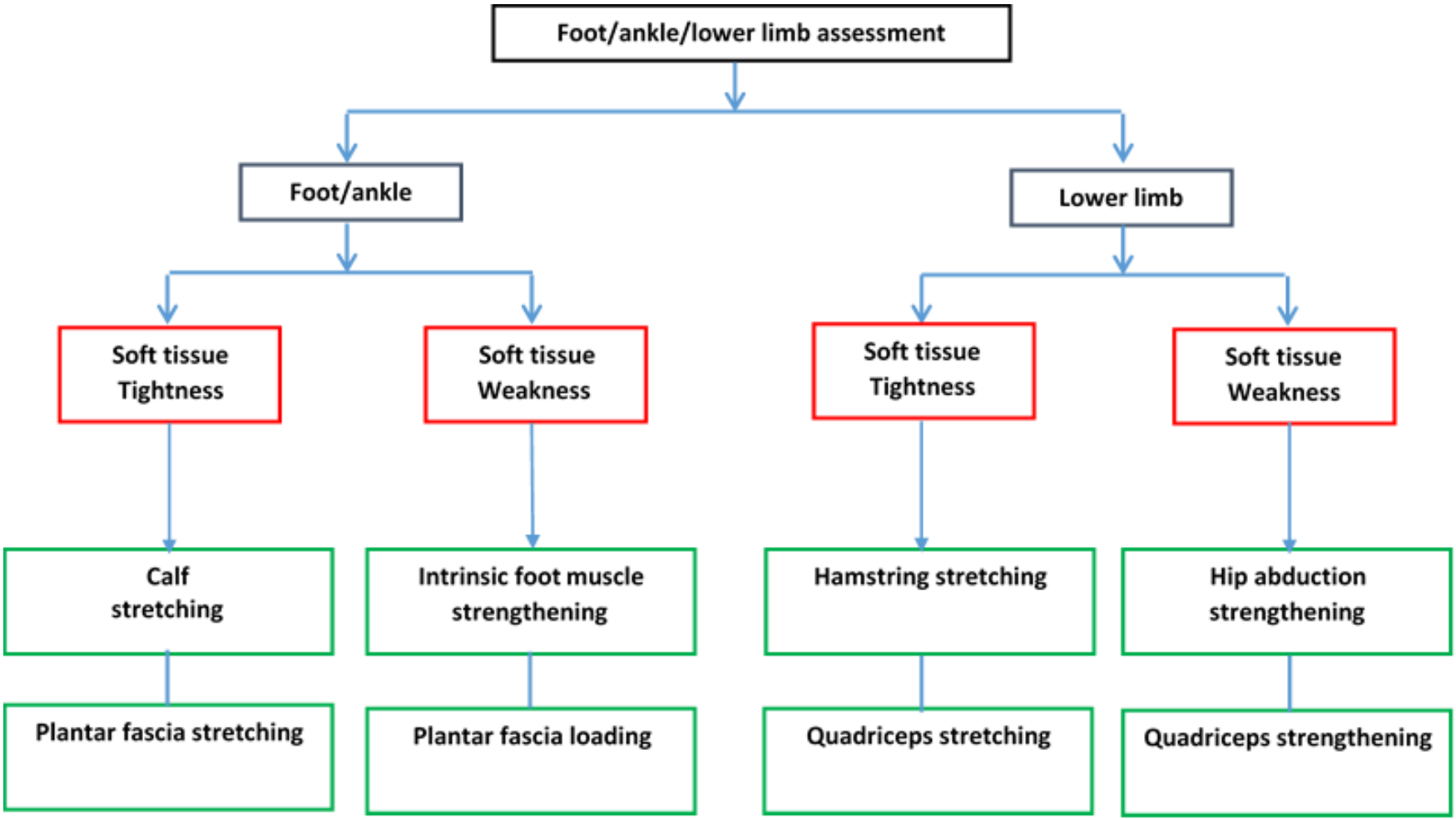
i) progression of prescribed exercises if tolerated with minimal pain and discomfort,

ii) maintenance if tolerated but some moderate pain and discomfort, or

iii) reduction in frequency, duration, intensity or modification of exercise type if not tolerated or adhered to.

Participants will be provided with a study-specific paper diary to capture adherence during the course of treatment. This will be collected at 12 weeks.

**Figure 2: Summary flow of exercise prescription**




Individual features targeted as required based on clinical assessment

### 6.3.4 Self-management advice plus a combination of individualised exercise and pre-fabricated foot orthoses

In addition to the self-management advice booklet, participants will receive both exercise and foot orthoses interventions as described above in sections 6.3.2 and 6.3.3. Additional clinical appointment time will be arranged to support this.

Participating physiotherapy and podiatry services responsible for delivering the interventions will be expected to maintain a file of essential trial documentation (Investigator Site File), which will be provided by Keele CTU, and keep carbon copies of all completed CRFs for the trial in accordance with the Sponsor-Site Agreement.

Clinical trial data will be recorded by clinicians who are taking part in the trial and have been trained in accordance with the protocol on trial-specific paper CRFs. CRFs will be collected by a study team member, posted, faxed or emailed to Keele CTU as agreed with the site. Only the participant's trial number plus date of birth, initials and gender will be included on CRFs. Where CRFs are sent to Keele CTU the trial participating services are responsible for redacting all other personal identifiable data prior to sending. Following receipt of CRFs that are sent, Keele CTU will contact trial sites to resolve any missing or discrepant data queries relating to clinical data in accordance with Keele CTU procedures.

### 6.3.5 Summary table of interventions

| Self-management advice | Self-management advice plus pre-fabricated orthotic devices | Self-management advice plus individualised exercise | Self-management plus combination of pre-fabricated orthotic devices and individualised exercise |
|---|---|---|---|
| Advice and information booklet | Advice and information booklet<br><br>Up to 6 sessions over 12 week treatment period<br><br>Individually tailored pre-fabricated foot orthotic device<br><br>Device adjustment/tailoring as required<br><br>Clinical supervision of orthotic device use /tolerance | Advice and information booklet<br><br>Up to 6 sessions over 12 week treatment period<br><br>Individually tailored and written exercise programme<br><br>Focus on foot/ankle specific stretching and strengthening +/- lower limb muscle groups<br><br>Individualised exercise programme that is progressed<br><br>Clinical supervision of exercise programme | Advice and information booklet<br><br>Up to 6 sessions over 12 week treatment period<br><br>Individually tailored pre-fabricated foot orthotic device<br><br>Device adjustment/tailoring as required<br><br>Individually tailored and written exercise programme<br><br>Focus on foot/ankle specific stretching and strengthening +/- lower limb muscle groups<br><br>Individualised progression<br><br>Clinical supervision |

# 7 OUTCOMES

To meet the specified objectives, both process and clinical outcomes will be collected (See table 7.4).

## 7.1 OUTCOME COLLECTION METHODS AND TIME POINTS

### 7.1.1 Weekly text messages for 12 weeks

All participants will be asked to respond to weekly mobile phone SMS text messages which will be automatically sent each week for 12 weeks to collect pain scores. Patients who do not wish to use text-messaging will be offered the option of brief telephone calls at the consent stage.

The research nurse will explain this process over the telephone, when gaining informed consent at the start of the participation. Non-responders to the initial text-message will be sent a further automated text message reminder 24 hours later, those receiving phone calls will receive another call the next working day. Non-response to this phone call will be recorded and no further contact at this attempt made.

94% of UK adults have a mobile phone (http://media.ofcom.org.uk/faPHP/) and previous research shows that weekly text messages (followed by a telephone call for the first text that is not answered) had an 83% mean response rate. [46,47]

### 7.1.2 Weekly adherence Patient Diary for 12 weeks

All patients randomised to an exercise or foot orthoses intervention will be asked to keep a simple weekly paper diary over the 12 weeks of the intervention. This will capture aspects of adherence, general patient engagement with the intervention and any self–reported adverse events. The diary can also be used by patients to aid discussions with their treating clinicians but is not considered to form part of the intervention. Patients will be asked to return the diary to the Keele CTU using the pre-paid envelope at 12 weeks.

### 7.1.3 Postal Questionnaire at 12 Weeks

All participants will be asked to complete a self-report questionnaire 12 weeks after randomisation. The questionnaire will be sent to participants by Keele CTU approximately 11 weeks post randomisation to ensure questionnaires are received in time. Where a questionnaire has not been returned to Keele CTU within 10 days from mail despatch, a reminder text message or post card will be sent. Where a questionnaire is still not returned following this, a second questionnaire will be mailed 5 working days after the text message (or postcard). For non-responders, minimum data collection (MDC) to capture the primary outcome measures will be undertaken by a Keele study team member by telephone approximately 3 weeks after the initial mailing, during this phone call if participants decline to provide MDC over the phone they can be offered the choice to receive a postal MDC questionnaire. Where a participant is not able to be contacted by telephone, a postal MDC questionnaire will be sent. Participants will be asked to return the completed questionnaire with the patient diary to the Keele CTU using the pre-paid envelope.

## 7.2 PROCESS OUTCOMES

**The feasibility of the three patient identification methods will be assessed in terms of the following outcomes**;

- The number of patients identified, eligible and recruited over a period of nine months by each method.
- The rate of recruitment (number of consenting/randomised participants per month) and retention rate (returned questionnaire at 12 weeks and number of weekly texts answered over 12 weeks) in total and per identification method.
- The cost and effort of each method will also be evaluated.

**The number of arms and interventions to test in the main RCT will be determined by the following process outcomes**;

- Patient reported engagement and adherence with the treatment in each arm will be collected in the 12 week questionnaire (all arms) and weekly patient diary (exercise and orthoses arms only) including; a global intervention adherence scale (5 point scale adapted from previous research) [42,46] for each different intervention, number of weeks adherence, the duration and frequency of completing exercises and/or wearing the foot orthoses, reasons for non-adherence in all arms.
- Patient reported satisfaction with each treatment package (3 x 5 point Likert-scale).[42]
- Patient reported credibility of each treatment package (5 x Likert-scales, adapted from previous research).[,48 61]
- A free text box in the 12 week questionnaire will also allow participants to comment on their allocated intervention.
- The fidelity of intervention delivery and clinician reported patient attendance to treatment assessed using case report forms.
- Clinicians' (physiotherapists and podiatrists) evaluations of the trial intervention delivery, assessed by end of trial clinicians' workshops. Practical issues including the clinicians' acceptability of the FPI-6 assessment, the number and duration of treatment sessions, ease of use of the orthotic devices, practicality of generating individualised exercise regimen sheets and general patient engagement with the treatments and clinical attendance will be discussed.

## 7.3 CLINICAL OUTCOMES

**To determine the primary outcome measures for a future main trial the following three outcomes will be evaluated**

i) the time to patients' report of significantly better plantar heel pain over the last seven days (where this occurs) derived from a numerical pain rating scale (NRS 0-10) with 0 denoting 'no pain' and 10 denoting 'worst pain imaginable' describing average pain over the last week collected weekly via text message (or brief telephone call), for 12 weeks. Scores will be dichotomised into 'significantly better' or not, where significantly better is defined as scores of either 0 or 1 recorded over two consecutive weeks within the 12 week period.

In addition, the original numerical scale will also be used to assess the change of score over time. Specifically, participants will be asked to rate their level of average PHP pain over the last seven days on a 0-10 Likert scale (where 0 indicates no pain, and 10 indicates maximum pain).

ii) a change in foot pain measured by the Foot Function Index pain subscale (FFI-PS) [40,63] from baseline to 12 weeks. The FFI-PS is a nine item self-administered questionnaire.[35] A 0-10 point Likert scale with anchors of 'no pain' and 'worst pain imaginable' are used.[36,63]. The sum of the score is expressed as a percentage of the maximum possible score. The scale FFI-PS has been widely used and evaluated with good reliability and validity reported.'[36]

iii) a change in foot pain measured by the Manchester Foot Pain and Disability Index (MFPDI) pain subscale [37] from baseline to 12 weeks. The MFPDI pain subscale is a 7 item Patient Reported Outcome (PRO) measure developed and validated to measure pain specifically related to a foot disability. Items are recorded on a three point scale responses are recorded on a three point scale; none of the time, on some days, on most /every day(s). The MFPDI has been validated for assessing the impact of painful foot conditions in community and clinical populations. [37]

**The analysis and sample size calculation for the main trial will be informed by completion rates and data from the following outcome measures:**

Global impression of change score (modified 6 point scale), [49] the presence of pain in the heel (yes/no), first step pain (NRS 0-10), pain elsewhere in the foot (foot manikin), [40] patient reported adverse events, FFI disability (9 items) and activity limitation (5 items) subscales, [36,63] MFPDI functional subscale (10 items) and personal appearance (2 items). [37] Quality of life (EuroQol EQ5D 5L), [50] work loss (days absent and loss through reduced ability whilst at work),[51, -53] self-reported PHP healthcare use including contacts with primary and secondary healthcare professionals, use of prescribed or over-the-counter medications or interventions (e.g. foot orthoses, heel pads, hospital investigations and use of private healthcare).

## 7.4 Table summary of outcome measures by follow up time point and method.

| Measure | Description | Baseline Day 0 | weekly text follow-up for 12 weeks | Weekly Diary/Text | 12 week follow-up |
|---|---|---|---|---|---|
| **Patient descriptors** | | | | | |
| Demographics | Gender, date of birth | ✓ | | | ✓ |
| Previous PHP episodes | Number of episodes | ✓ | | | |
| Previous treatments received | Type and number of orthotic devices/exercise treatments: 2 questions | ✓ | | | |
| Current PHP episode description | Location and duration : 2 questions | ✓ | | | |
| | Laterality | ✓ | | | ✓ |
| Preference for treatment intervention | Patient self-report: 2 questions | ✓ | | | |
| **Process Outcomes** | | | | | |
| Adherence with treatment | Adherence with interventions (variable number according to intervention) adapted from previous research [53-55] | | | ✓ | ✓ |
| Satisfaction with treatment | 3 x Likert scale adapted from previous research | | | | ✓ |
| Credibility of treatment: | 5 x Likert scale adapted from previous research | | | | ✓ |
| Adverse events | Patient self-report | | | ✓ | ✓ |
| Patient comments on treatment adherence, satisfaction and credibility | Free text box | | | | ✓ |
| **Clinical outcome** | | | | | |
| Plantar Heel Pain | Average plantar heel pain over the last 7 days using Numerical rating scale (0-10) '0' denoting no pain and 10 worst pain imaginable | ✓ | ✓ | ✓ | ✓ |
| | Presence of pain in the heel; yes or no | ✓ | ✓ | | ✓ |
| | First step pain (NRS 0-10) | ✓ | | | ✓ |
| | | | | | ✓ |

| | | | | | |
|---|---|---|---|---|---|
| | Global Impression of change score (6 point scale) | | | | |
| Foot pain | Foot Function Index pain subscale, 9 items, 10 point likert scale<br>Manchester Foot Pain and Disability Index pain sub scale 7 items | ✓<br>✓ | | | ✓<br>✓ |
| Presence of pain elsewhere in the foot | Foot Manikin (© The University of Manchester 2000. All rights reserved) | ✓ | | | ✓ |
| Foot Function | Foot Function Index disability (9 items) and activity limitation subscale (5 items) ,10 point likert scale<br>Manchester Foot Pain and Disability Index functional subscale (10 items) and personal appearance (2 items). | ✓<br>✓ | | | ✓<br>✓ |
| Health related quality of life | EuroQuol:EQ5D-5L | ✓ | | | ✓ |
| **Healthcare costs** | | | | | |
| Employment | Current employment status | ✓ | | | ✓ |
| Performance at work | How performance at work is affected NRS 0-10 | ✓ | | | ✓ |
| Work loss (absenteeism) | Number of days lost | ✓ | | | ✓ |
| PHP Healthcare utilisation | Use of prescribed or over-the-counter medications or interventions e.g foot orthoses, heel pads | | | | ✓ |
| | Hospital investigations and use of private healthcare | | | | ✓ |

## 7.5 SAFETY REPORTING AND SERIOUS 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.

An SAE occurring to a research participant must be reported to the Research Ethics Committee (REC) where in the opinion of the Chief Investigator the event was: "Related" that is, it resulted from administration of any of the research procedures, and "Unexpected" that is, the type of event is not an expected occurrence as a result of the intervention provided.

The treatments being utilised in the TREADON Trial are those already used in routine clinical practice and adverse events are uncommon and generally minor. The following expected adverse events will not be collected; transient post exercise soreness from a new exercise regimen, some initial discomfort from wearing new foot orthoses and development of pain in other body regions (as a result of altered biomechanics). Some patients may also undergo planned surgical procedures that require hospitalisation for foot /heel related pain. We will ask clinicians to report blisters and falls resulting from orthotic device use. We will also ask study clinicians including GPs to report unexpected adverse events and SAEs they become aware of during the trial, with the exception of planned hospitalisations. Reporting procedures will be made clear during the protocol study training and will be contained in site files for all clinicians and GPs involved in the study. We will also ask patients to report any adverse events they have experienced in their 12 week questionnaire and diaries.

Where a study clinician or the participant's GP becomes aware that an SAE has occurred, this must be reported to a member of the trial team at Keele CTU. This information is to be passed to the Trial Manager who will ensure that the necessary paperwork is completed and inform the CI. In line with Keele CTU Standard Operating Procedures (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, according to the process laid out in Keele CTU's SOP. Any SAE considered to be related to the trial procedures will be reported to the Research Ethics Committee and the TSC Chair by the CI within 15 days of becoming aware of the event. All events will also be reported to the trial sponsor and Trial Steering Committee (TSC). SAEs occurring later than 12 weeks post randomisation do not need reporting. This is deemed a low risk trial as we are utilising interventions already in common use by podiatrists and physiotherapists.

## 7.6 BLINDING

Blinding of patients and clinicians is not possible, therefore a study team member blind to treatment allocation will oversee the collection of baseline and follow-up outcome data which because they are in the form of patient self-reported measures should not be influenced by the treating clinicians. Use of validated outcome measures will reduce measurement error. One statistician will remain blind to group until analysis of clinical estimates are performed. The TSC will be blinded to group unless it becomes necessary to reveal allocation due to safety concerns.

# 8 STATISTICAL CONSIDERATIONS

## 8.1 SAMPLE SIZE

A sample size of 55-70 (10 per arm – control; 15-20 per arm in the three active treatment arms) is large enough to obtain sufficiently precise estimates around key process measures and outcome parameters required for calculation of the sample size for the future main trial. 55 patients will allow us to:

(i) derive a sufficiently precise 90% one-sided lower-bound confidence level estimate around the observed follow-up rate. Assuming an 85% follow-up in the feasibility trial we can be 80%-90% confident that the follow-up in the main trial will be at least 80%, since the standard error for calculating the interval width is 0.05;

(ii) derive a sufficiently precise 90% one-sided lower-bound confidence level estimate around the overall adherence to intervention protocols. Assuming around 50% adherence overall in the feasibility trial, we can be over 90% confident that the overall adherence in the main trial will be at least 40% (since the standard error for calculating the interval width is 0.07);

(iii) derive a sufficiently precise estimate of the SD for the FFI /MFPDI (at the level of an inflation factor of 1.1 in the point estimate of the feasibility SD) such that we can be approximately 80% confident in attaining the nominal power of the main trial if this adjusted SD is utilised in the sample size calculation. [57]

## 8.2 RECRUITMENT RATE

Based on previous research, [11,39,42] we estimate the number of potential participants that could be recruited to the trial is as follows:

- We estimate that from a population of 60,000 general practice patients, 162 patients over 9 months will consult with PHP and have a recorded foot/ankle Read code. Of these we anticipate that 45% (n=73) will be eligible and provide consent to trial participation.
- From a primary care general practice population totalling 60,000 patients, the 12 month retrospective record review will identify 1,800 foot/ankle consulters, of which 720 (40%) will respond to the survey and 12% will have PHP. Assuming 25% still have pain, will be eligible and consent, up to 21 participants could be recruited to the trial via this second method.
- Surveying 5,000 adults registered at 1 practice will yield 100 people (5%) with PHP. Assuming 25% are eligible and consent, up to 25 participants could be recruited to the trial via this method.

Therefore in total we conservatively estimate 119 eligible and consenting participants could be randomised from a total population of 60,000 patients. Therefore approximately 12 GP practices of average size (or equivalent non average size) will need to be recruited to identify sufficient patients to meet the target of n=80 randomised patients.

## 8.3 CLINICAL APPOINTMENT COMPLIANCE AND INTERVENTION ADHERENCE

Estimates of clinical appointment compliance are based on previous trials we have conducted with similar recruitment methods. In the BEEP trial [42] 39 of 514 (7.6%) participants received

no physiotherapy sessions despite several attempts at contact to offer an appointment, and in the SUPPORT trial [46] 11 out of 128 (8.5%) participants did not receive any physiotherapy sessions. In the APEX trial [61] less than 5% of participants recruited failed to attend for any physiotherapy intervention and approximately 85% of participants had 3 or more treatment sessions. Therefore, data from our previous trials suggest that clinical appointment attendance will be high.

Estimates for intervention adherence are similarly based on previous research; 75% of participants in the SUPPORT trial [64] randomised to physiotherapist-led exercise reported adherence to recommended regimens at 6 months with 50% reporting adherence across all groups.

### 8.4 PATIENT SATISFACTION / CREDIBILITY

Estimates for success criteria of satisfaction levels and participant reported intervention adherence are based on previous research where 82% of participants in the SUPPORT trial [46] randomised to a physiotherapist-led exercise programme reported being satisfied with their care at 6 months and 49% reported satisfaction at 12 months. The BEEP study [42] showed 75% were satisfied with their care at 3 months and 71% believed the treatments they received were credible in terms of their clinical condition.

### 8.5 STATISTICAL ANALYSIS

Statistical analysis is the responsibility of Keele CTU biostatisticians. The analysis plan outlined in this section will be reviewed and a final statistical analysis plan (SAP) written before any analysis is undertaken. The SAP will be written in accordance with current Keele CTU standard operating procedures and will be finalised and agreed by the biostatisticians, the CI, the trial management team and the relevant independent members of the TSC. Any changes to the finalised analysis plan, and reasons for changes, will be documented.

The statistical analysis will focus on process measures and evaluative methods described below. There will be no emphasis on hypothesis-testing which is reserved for the future main trial.

(i) recruitment rate and effort required in identifying and recruiting participants, stratified by method of identification;

(ii) summary baseline characteristics of the study population (demographic and self-report clinical characteristics) and comparison to ineligible and non-consenting patients, to ascertain adequacy of inclusion/exclusion criteria and likely generalisability of the sample to the required targeted population (this evaluation will draw on the total sample as well as scrutinising those recruited from each of the three recruitment methods);

(iii) attainment and performance of the three potential primary outcomes measures for the future main trial, in relation to response and item completion rates, floor/ceiling effects, and responsiveness;

(iv) adherence (including confidence interval estimation around the overall treatment adherence and point estimates for levels of adherence stratified by treatment arm), credibility and satisfaction with treatment;

(v) descriptive statistics around outcome performance by trial arm. These will be presented in terms of mean pain scores (±standard deviation), and life table and

Kaplan-Meier survival plots with emphasis on mean survival times for the time-to-event data, and (%) who meet minimal clinically important difference threshold of 12 points on the FFI–P subscale;

(vi) parameters for informing a main study sample size calculation such as likely effect size, standard deviation (SD), inter-correlation of scores (for repeated measures) and dropout. The focus will be on point and interval estimates of effect; but not on statistical significance as the feasibility trial is not powered to formally conduct tests of statistical significance;

**(vii)** prognostic indicators of outcome. Associations between baseline variables (e.g. bilateral PHP, older age, duration of PHP at baseline, pain elsewhere) and the three clinical outcomes will inform whether variables should be included as baseline covariates in regression-based adjustment within the main trial.

## 8.6 HEALTH ECONOMICS

We will look to assess the feasibility of collecting health resource use data and quality of life assessment (that would be used for formal economic evaluation in a main trial) through the 12 week follow up questionnaires. Clinical CRFs will also provide information required for the cost review of the interventions. Costs will be derived by linking intervention costs and other healthcare resource use costs obtained from self-reported data with available unit costs of the resources. Costs will be summarised in aggregated and disaggregated form and descriptively compared between treatment groups. No formal cost-effectiveness analysis is planned as this would be one of the key objectives of a main trial – the main purpose in this pilot is to check the adequacy of our processes of data derivation of costs and measures of effect needed to undertake a full cost-effectiveness evaluation in a main trial.

Costs will be collected within the trial to determine the cost of the interventions along with other healthcare utilisation due to the plantar heel pain. Self-reported resource use information will be obtained on primary care consultations (general practitioners and practice nurses), secondary care consultations (e.g. hospital consultants, physiotherapists), prescriptions, hospital based procedures (diagnostic tests, injections, and investigations) nature and length of inpatient stays, and surgery. Patients will be asked to distinguish between UK NHS and private provision. Unit costs will be obtained from standard sources and healthcare providers including the British National Formulary (BNF) and Unit Costs of Health and Social Care and NHS Reference costs (PSSRU). [57] Information will also be collected from participants on occupation status and reduced work performance (presenteeism) and time off (absenteeism). This enables the calculation of productivity costs, allowing descriptive assessment of from a societal cost perspective. The average wage for each respondent will be identified by linking responses to employment questions with UK Standard Occupational Classification coding and annual earnings data for each job type. [58-60] The EQ5D-5L will be used in order to derive a descriptive summary of quality-adjusted-life-year values (QALYs – the key economic effect measure) over 12 weeks for each of the four treatment groups.

## 8.7 FREQUENCY AND TIMING OF ANALYSES

No formal interim statistical analyses of the outcome measures are planned. Reports will be made to the TSC on regular basis throughout recruitment and follow-up for independent review of interim safety, recruitment and retention. At any point in the trial, the TSC may request, unblinded outcome analysis if the interim safety data suggest issues with any of the

treatments. Based on this unblinded analysis, the TSC can stipulate an early termination of the trial.

The main analysis will be completed after the final 12 week follow-up questionnaire has been received. The treatment allocation will be unblinded once this analysis has been completed in accordance with the agreed analysis plan.

## 9 PILOT TRIAL EVALUATION CRITERIA AND INDICATORS OF SUCCESS

The following criteria will be considered when determining the success of this feasibility and pilot trial and will provide indicators for procedures or improvement in procedures to carry forward to a main trial:

I. Target recruitment of ~80% (~n=64) of the anticipated total number of participants over 9 months (n=80), accepting a shortfall in sample size affects the precision of our standard deviation estimate for the main trial but still allows identification of the optimal and most efficient recruitment strategy/strategies

II. clinicians' evaluation that trial intervention delivery is feasible within available services or can be modified as such

III. the research team can successfully deliver the training and fidelity of intervention delivery is demonstrated

IV. adequate attendance to the first clinical appointment

V. adherence levels across all interventions is demonstrated

VI. treatment packages have acceptable levels of patient reported satisfaction

VII. treatment packages have acceptable levels of patient reported credibility

VIII. a comparison of the 3 potential primary outcome measures for a future main trial, in terms of (i) the spread of data, completion rates (where the lower 1-sided 90% confidence interval for the overall response rate is ~ 80%) and effort required in obtaining responses to underpin the decision for the most appropriate measure to be carried forward as primary outcome for the main trial

IX. reliable data estimates to inform the sample size calculation

## 10 QUALITY ASSURANCE AND ETHICAL CONSIDERATIONS

### 10.1 QUALITY ASSURANCE

The trial will be conducted in accordance with the principles of Good Clinical Practice (GCP) in clinical trials, the NHS Research Governance Framework. Keele CTU have a quality management system in place and standard operating procedures which must be followed in the conduct of the trial. Studies run by Keele CTU may be subject to an audit by the Keele Quality assurance office.

## 10.2 NON-COMPLIANCE: DEVIATIONS AND SERIOUS BREACHES OF GCP AND/OR THE TRIAL PROTOCOL

Non-compliance may be identified through any trial activity, but in particular through:

- Central monitoring procedures such as consent form review or data management
- Site visits
- Self-reporting by a trial site or participant

Deviations from clinical trial protocols and GCP occur commonly in clinical trials. The majority of these instances are technical non-compliances that do not result in harm to the trial participants, do not compromise data integrity, or significantly affect the scientific value of the reported results of the trial. These technical deviations must be documented, and appropriate corrective and preventative actions must be taken. In addition, these deviations should be included and considered when producing the final CONSORT diagram, which describes how such deviations have been handled during analysis, and their impact on patient safety and the conduct of the analysis reported in the applicable Study Report.

Healthcare professionals involved in the trial are required to notify Keele CTU immediately of a serious breach. A "serious breach" is a breach which is likely to affect to a significant degree:

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

In the event of doubt, or for further information or guidance, the healthcare professional should contact the Trial manager or PI at Keele CTU.

## 10.3 ETHICAL CONSIDERATIONS

Potential participants will be informed about the trial in writing and only those expressing an interest will be contacted by a study team member. Written informed consent will be gained from all participants, prior to their entering the trial. Completion of the consent form will be discussed over the telephone by a research nurse who will fully explain the trial procedures and what taking part means for the patient. Patients who consent to participate will be randomised to one of four interventions. All patients will receive an intervention of a high quality self-management advice booklet and will continue to have access to usual GP care. Participants randomised to receive physiotherapy or foot orthoses interventions will receive treatment from clinicians trained in the protocol and treatment packages that are already in use in clinical care. No new treatments are being developed or tested in this pilot trial. The interventions are considered to be of very low clinical risk with well documented safety profiles and adverse events are usually of minor and transient nature. All serious and unexpected adverse events will be recorded and monitored in accordance with Keele CTU SOPs.

The standard research governance and operation procedures applicable within the NHS sites and in Keele CTU will be employed to protect participant confidentiality and anonymity.

The trial will be submitted for approval by the HRA through which REC approval will be gained. Keele CTU will provide the REC with a copy of the final protocol, patient information sheets, consent forms and all other relevant study documentation as part of the HRA approval process.

### 10.4 EXPERTISE IN THE TEAM

Our multidisciplinary team has wide clinical and methodological experience in carrying out large scale primary care based studies. Keele CTU are supporting the operationalisation of this trial and have a vast amount of experience in the delivery of trials with complex interventions within primary care settings. We work closely with our local CRN which is embedded within local NHS services to strengthen the NHS infrastructure to host support delivery of the research from within clinical settings. The CRNs have robust administrative infrastructure to support partnership arrangements with GP practices and dedicated health informatics teams who work within GP research Network practices and are trained in refining GP practice computerised clinical systems to support recruitment to clinical research studies. All NHS clinical research network staff involved in identifying patients operate within strict protocols that meet strict ethical and confidentiality requirements.

Previous studies have demonstrated our expertise in training primary care clinicians to deliver interventions according to pre-defined protocols.

## 11 MONITORING AND MANAGEMENT

### 11.1 STUDY ORGANISATIONAL STRUCTURE

**Trial Sponsor:** The Sponsor is responsible for trial initiation, management and financing of the trial. These functions are devolved to the Keele CTU as detailed in the Delegation of Sponsorship Functions agreement.

**Chief Investigator (CI):** The CI leads the design, conduct, co-ordination and management of the trial. The CI has overall responsibility for the scientific quality and delivery of the trial and will provide senior support to the Keele PI.

**Principal Investigator (PI):** The Keele PI is responsible for the conduct and leadership of the trial and ensuring the trial is run in accordance with the Research Governance Framework and GCP guidance. This includes (but is not limited to) informed consent of trial participants, eligibility, collection of initial questionnaires, randomisation, delivery of interventions, and safety reporting.

**Keele CTU:** The Trial Sponsor, Keele University, delegates the conduct of the trial to Keele CTU. Keele CTU will provide set-up and monitoring of trial conduct to Keele CTU SOPs, and the GCP Conditions and Principles as detailed in GCP standards, randomisation design and service, database development and provision, protocol development, CRF design, trial design, monitoring schedule and statistical analysis for the trial. In addition Keele CTU will support obtaining research ethics and governance approvals and clinical set-up, ongoing management including training, monitoring reports and promotion of the trial. Keele CTU will be responsible for the day-to-day running of the trial including trial administration, database administrative functions, data management, safety reporting and all statistical analyses. Regular Monitoring of study recruitment will be performed and intervention CRFs will be audited against the clinical records by Physiotherapy Research Facilitators, for completion accuracy.

**NIHR Clinical Research Networks**: The North West Coast and West Midlands CRNs will coordinate the patient identification process in participating GP practices and co-ordinate local implementation and study set up into physiotherapy/podiatry sites or services and report progress to the study team. The CRN will provide funding or staff resource to secure the

additional clinical time associated with service support to embed the study into primary care sites to allow identification of suitable and potentially eligible participants.

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

### 11.2 TRIAL MANAGEMENT GROUP

The CI is responsible for the conduct of the trial and will convene a TMG. The TMG, will comprise members of the research team and Keele CTU and will have responsibility for the clinical set-up, ongoing management and monitoring, promotion of the trial, and for the interpretation of results. Specifically, the CI is responsible for and will chair the TMG to oversee; (i) the protocol completion, (ii) CRF development, (iii) obtaining approval from the HRA and agreements with sites, (v) completing cost estimates and project initiation, (vi) nominating members for, and facilitating, the TSC, (vii) reporting of related and unexpected serious adverse events to the REC, TSC and sponsor, (viii) monitoring of screening, recruitment, treatment and follow-up procedures, (ix) data collection, and database development, (x) reporting annually to the REC. The TMG will meet on a regular basis throughout the trial.

### 11.3 TRIAL STEERING COMMITTEE

An independent Trial Steering Committee (TSC) has been appointed in line with Keele CTU SOPs (see list of members under key contacts Page 3) and will provide overall supervision of the trial, in particular trial progress, adherence to protocol, participant safety and consideration of new information relevant to the trial question or design. It will include an Independent Chair and not less than two other independent members including a statistician. The CI, PI, lead biostatistician and other members of the TMG may attend the TSC meetings and present and report progress. The TSC will meet initially to approve the protocol prior to submission for ethical approval and then at agreed time points for the duration of the trial. Since this is a pilot trial with no planned interim statistical analysis a data monitoring committee has not been formed and the TSC has agreed to take responsibility for reviewing the safety of the trial. Detailed reports focusing on recruitment, retention and safety will be prepared for the TSC after the first 3 months of participant recruitment and then at agreed intervals.

### 11.4 PATIENT AND PUBLIC INVOLVEMENT

We have adopted the approach advocated by INVOLVE (2012) and PPI has been central to the development of the research question and the TREADON feasibility trial design.

Within an advisory workshop which included 4 patients with plantar heel pain and 15 physiotherapists / podiatrists, patients discussed their experiences of PHP and their concerns about the need for effective treatment options that would give good symptom relief and rapidly lead to pain-free walking. These priorities form the basis of the agreed research question. Clinicians identified prescribed exercise and foot orthoses as interventions likely to meet the objective of pain free walking and achieve good long term clinical outcomes.

Two further workshops included the patient representatives from the advisory group and members from the Arthritis Research UK Primary Care Centre Public and Patient (PPI) group

(who have a range of pain conditions including foot pain). These workshops further developed the interventions, in particular; (i) the choice of foot orthoses, taking account of; the requirement to modify the orthoses to patient needs, the differing requirements of male and female footwear and expectations surrounding adherence to daily orthotic device use (ii) the exercise programme, including realistic expectations of adherence to regimens and (iii) the information and advice to be provided within the self-management intervention which members were keen to ensure was of high quality without unduly comprising the intended 'usual care' nature of the intervention. The suitability of three different outcome measures selected to reflect the patient stated priority of a rapid response to treatment were also discussed. In particular patients provided feedback on the principle and practicality of a proposal to collect participants' pain scores weekly via text message to allow a 'time to response' outcome to be measured which patients identified as important

Eleven clinicians and all four patients who participated in the workshop have agreed to continuing involvement with the feasibility and pilot trial through membership of an advisory group. Via this advisory group, patients and clinicians will continue to be actively involved with the trial development particularly in relation to; honing the patient journey through the three different methods of recruitment, advice on patient documentation and information leaflets and also the content of questionnaires and text messages. This involvement will contribute to optimising recruitment and retention in the trial. Adherence to wearing foot orthoses and to following the exercise recommendations is likely to be key to the outcome of these interventions so we will seek further input into this aspect in three areas; (i) refining the clinical protocols to maximise adherence (ii) discussing methods to maximise completion of adherence questions in the follow up process (iii) review of the definitions of adherence for purposes of analysis. This will help to underpin fidelity of intervention protocols. Patient input to maximising follow up through mobile phone text messaging (or telephone call where preferred) has already been sought.

For trial monitoring purposes patients will be involved in the Trial Steering Committee (TSC) and discussion regarding use and dissemination of the findings. The Arthritis Research UK Primary Care Centre has a User Support Worker and PPI co-ordinator who help to co-ordinate the continued PPI 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 PPI groups to ensure that they will be involved with the interpretation of the results of the feasibility trial and any considerations for the future main randomised controlled trial design. Where appropriate dissemination of findings beyond the traditional academic routes will be discussed.

### 11.5 STUDY TIMELINE

The TSC approved protocol will be submitted for HRA approval during May 2016. General practices and physiotherapy/podiatry services will be recruited to take part in the study from January 2016 through June 2016. Most Clinicians will be trained in the period from February to June 2016. We anticipate the trial will commence participant recruitment in June 2016 and will continue for 9 months until March 2017. A 12 week follow-up period will continue until June

2017 with reminders posted through to July 2017. Analysis will be completed by October 2017 and we anticipate dissemination will begin November 2017.

In accordance with version 2.0 of the protocol, the timelines have been adjusted to reflect HRA approval received in September 2017. Participant recruitment began in November 2017 and will continue for 9 months until July 2017. A 12 week follow-up period will continue until October 2017 with reminders posted through until November 2017. Analysis will be completed by February 2018 and we anticipate dissemination will begin March 2018. See Appendix 2 for a Gantt chart timeline.

### 11.6 END OF TRIAL

The end of the trial is defined as the collection of the last data item for the last participant to be randomised.

### 11.7 DATA MONITORING

Trial data will be monitored for quality and completeness by Keele CTU. Where CRFs are returned by post, study clinicians will be contacted to provide any missing clinical data which will be followed up until it is received, or confirmed as not available, or the trial is in the analysis stage. All participants must have a completed Baseline / Pre-treatment Questionnaire before they can be randomised to treatment and missing participant follow-up questionnaires will be followed up in accordance with the protocol. The Keele CTU/Sponsor will reserve the right to conduct source data verification exercises on a sample of participants, which will be carried out by staff authorised by Keele CTU/Sponsor. This review may involve direct access to participant healthcare records at the participating centres and the on-going central collection of copies of consent forms and other relevant investigation reports. A Trial Monitoring Plan will be defined and agreed by the Trial Management Group.

### 11.8 CLINICAL GOVERNANCE ISSUES

NHS organisations are responsible and accountable for the overall quality of care received by participants during the study period as stated in the service level agreements, clinical governance issues pertaining to the study intervention delivery will be the responsibility of the NHS Trusts, individual participating GPs or Physiotherapy/Podiatry centres but will be brought to the attention of the Trial Steering Committee and, where applicable, to the sponsor and the ethical committee.

## 12 CONFIDENTIALITY

All information collected during the course of the trial will be kept strictly confidential. Information will be held securely on paper and managed electronically by Keele University through Keele CTU. Keele CTU comply with all aspects of the 1998 Data Protection Act and operationally this includes:

- Consent from participants to record personal details including name, date of birth, address, telephone number.
- Appropriate storage, restricted access and disposal arrangements for participant personal and clinical details.

- All data collection forms that are transferred to and from Keele CTU will be coded with a trial number and will include three further participant identifiers, usually the participants' gender, initials and date of birth.
- Where pseudo-anonymisation of documentation is required, participating centres are responsible for ensuring only the instructed identifiers are present if the documentation is to be sent to Keele CTU. All research data will be anonymised as quickly as possible.

The trial data will be held on a secure database hosted on a secure server at the UK CRC registered Keele CTU. Provision of appropriate client server links / permissions will be given to authorised members of the trial team at Keele CTU.

If a participant withdraws consent from further trial intervention and/or further collection of data their data will remain on file and will be included in the final study analysis, unless requested otherwise.

## 13 ARCHIVING

Archiving will be completed as soon as possible after study closure, analysis and dissemination and will be in accordance with Keele CTU SOPs. At the end of the trial, data will be securely archived in line with the Sponsor's procedures for a minimum of 5 years after publication of the main findings and until the sponsor authorises destruction. Data held by Keele CTU will be archived in the designated Keele CTU archive facility and site data and documents will be archived by the participating sites in line with local protocols. Following authorisation from the Sponsor, arrangements for confidential destruction will then be made.

## 14 STATEMENT OF INDEMNITY

This trial is sponsored by Keele University and Keele University will be liable for negligent harm caused by the design or management of the trial.

The NHS has a duty of care to patients treated, whether or not the patient is taking part in a clinical trial, and the NHS organisation remains liable for clinical negligence and other negligent harm to patients under this duty of care.

As this is an investigator-led trial, there are no arrangements for no-fault compensation.

## 15 PUBLICATION POLICY

We recognise that the findings of this feasibility and pilot trial cannot provide evidence about the clinical and cost-effectiveness of exercise and foot orthoses for PHP.

Dissemination will focus upon results addressing each of the four identified objectives. In addition to descriptive findings relating to these objectives, reporting will include the implications of the findings of the feasibility trial for a future main trial, how the main trial might best be designed, and how that will differ from the design of the feasibility and pilot trial. Publication will be in an open-access peer-reviewed journal.

Results will also be presented at relevant national conferences (British Society for Rheumatology, Podiatry, Physiotherapy UK, National Conference of the Institute of

Chiropodists and Podiatrists). Findings will be disseminated to randomised participants, participating clinicians (GPs, treating physiotherapists and podiatrists) and members of the Keele CTU RUG and the trial Advisory Group via a dedicated dissemination events and newsletters.

### 15.1 NIHR RfPB REQUIREMENTS

The NIHR require notification of first and last participants recruited. Yearly Progress Review Reports must also be submitted to the NIHR Progress Review Committee (PRC) in accordance with the requirements of the Special Conditions- Clinical Study of the Grant Award.

On acceptance for publication, a copy of the final manuscript of all peer reviewed research papers must be deposited in an open access archive such as PubMed Central (PMC) or UK PubMed Central (UKPMC), to be made freely available within six months of publication.

All publications, presentations, correspondence and advertisements arising or related to the grant must acknowledge NIHR as the study's funding source. When acknowledging NIHR UK support, the grant reference number must be quoted.

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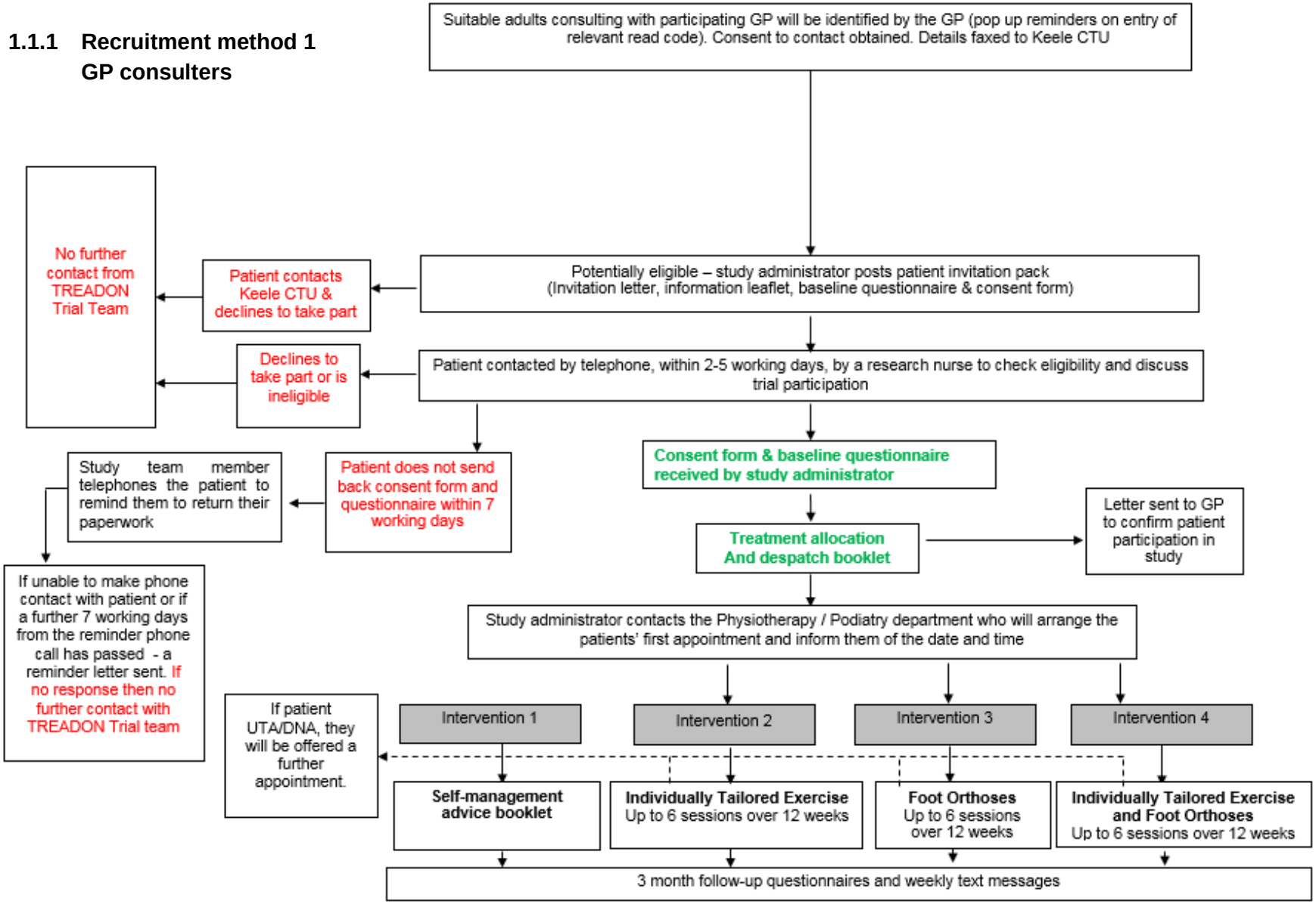
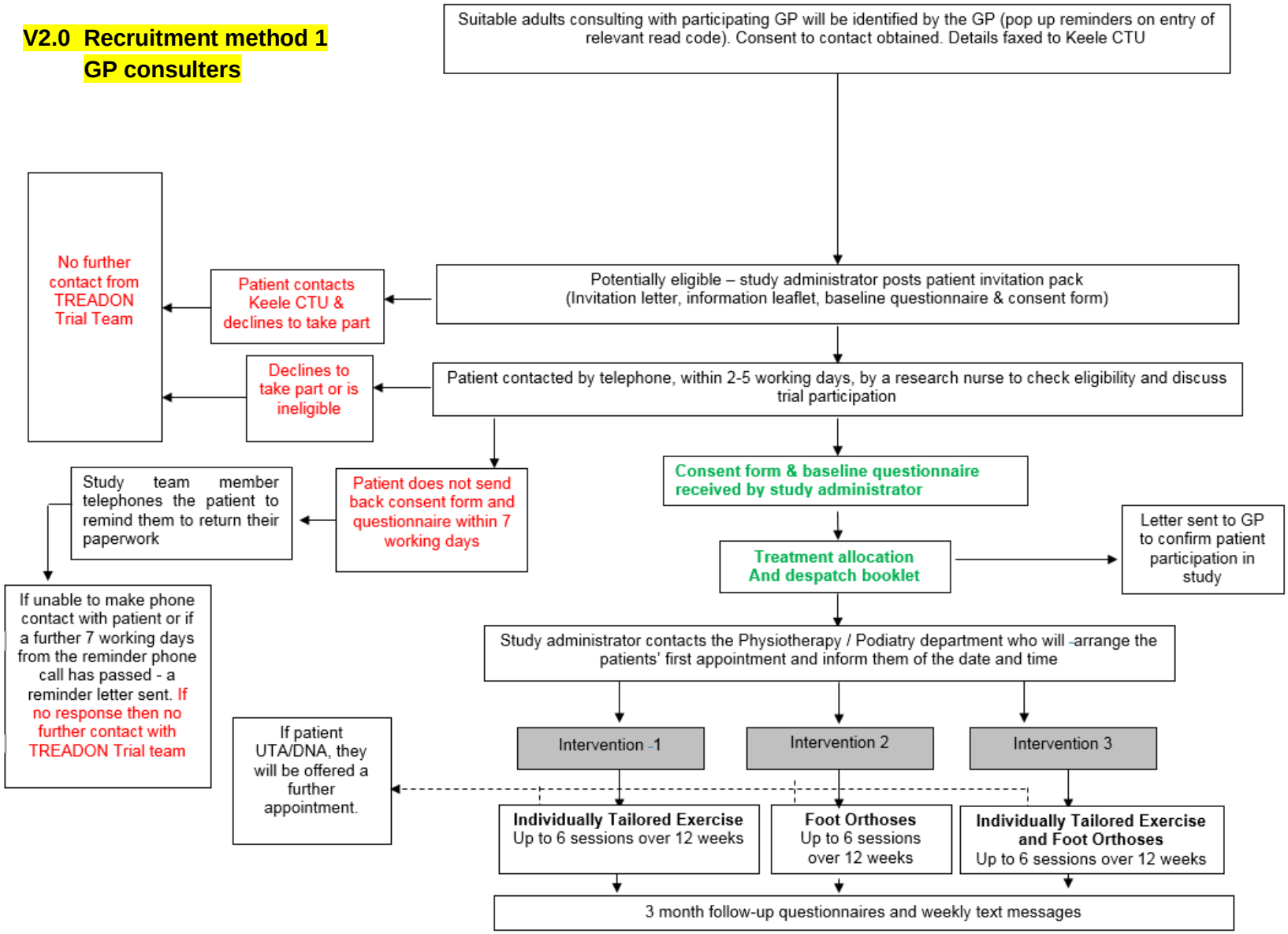
# 17 Appendices

## 17.1 Appendix 1 – Participant Journey Flow Charts

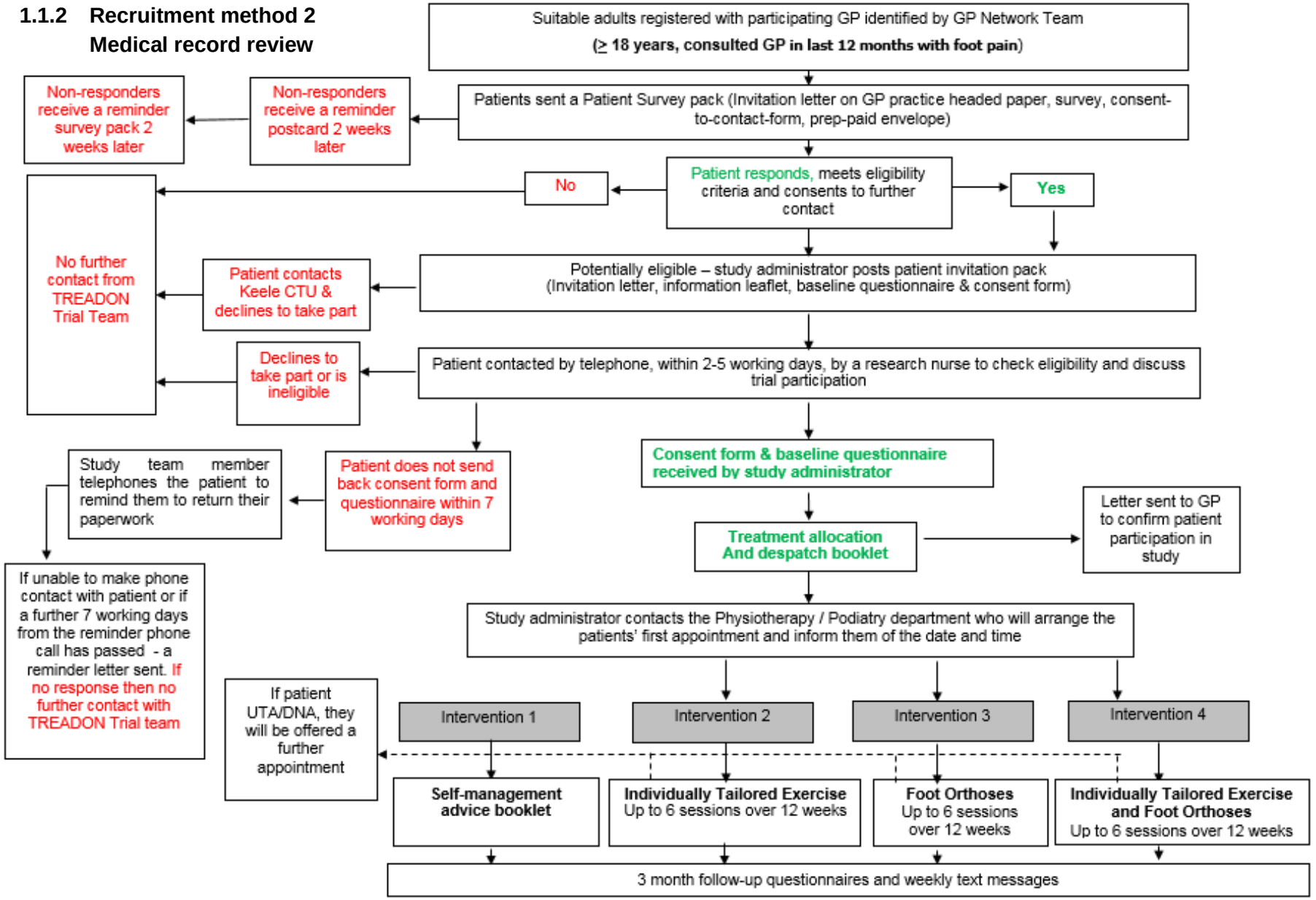
### 1.1.1 Recruitment method 1 GP consulters



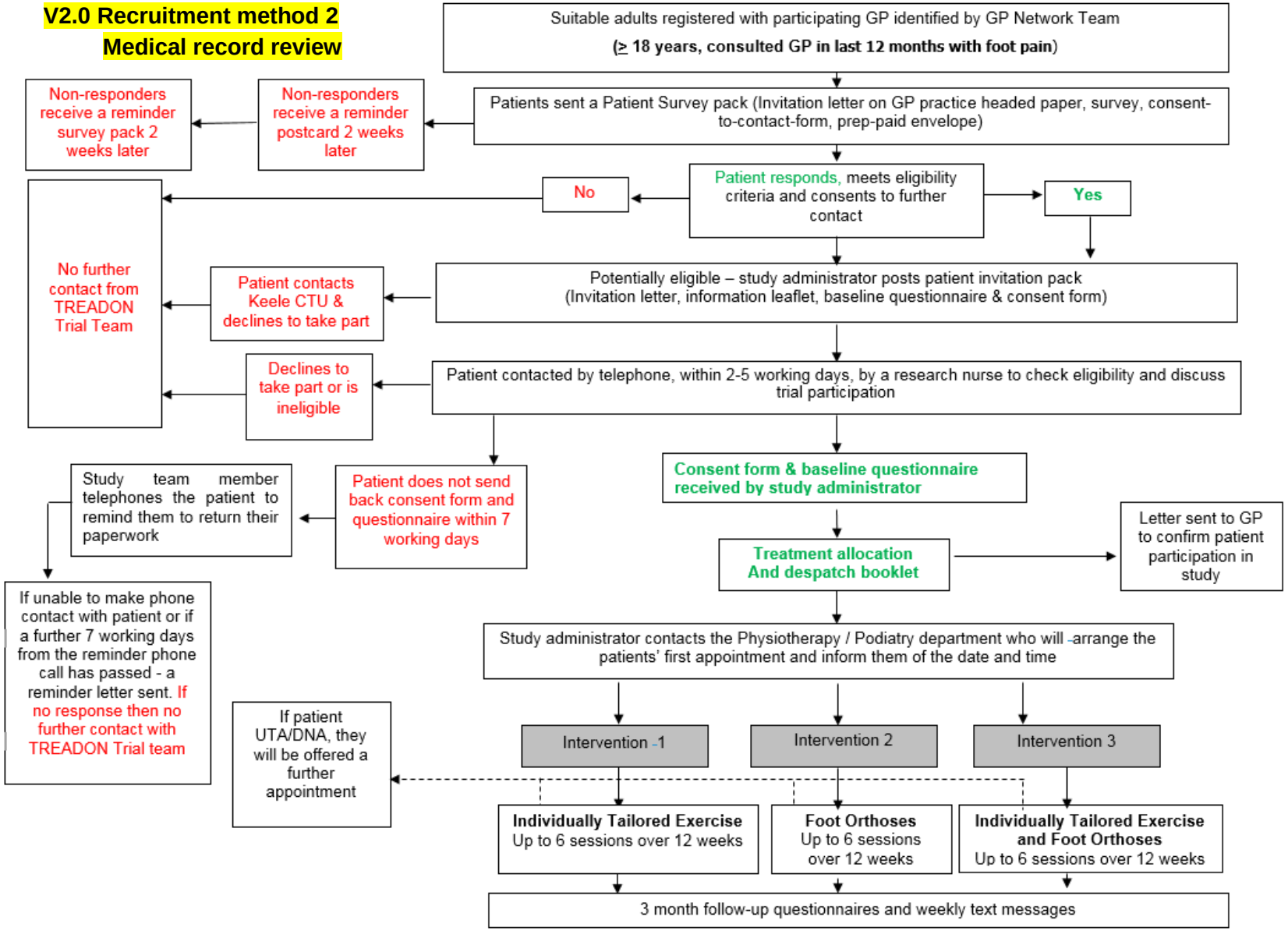
**V2.0 Recruitment method 1**
**GP consulters**



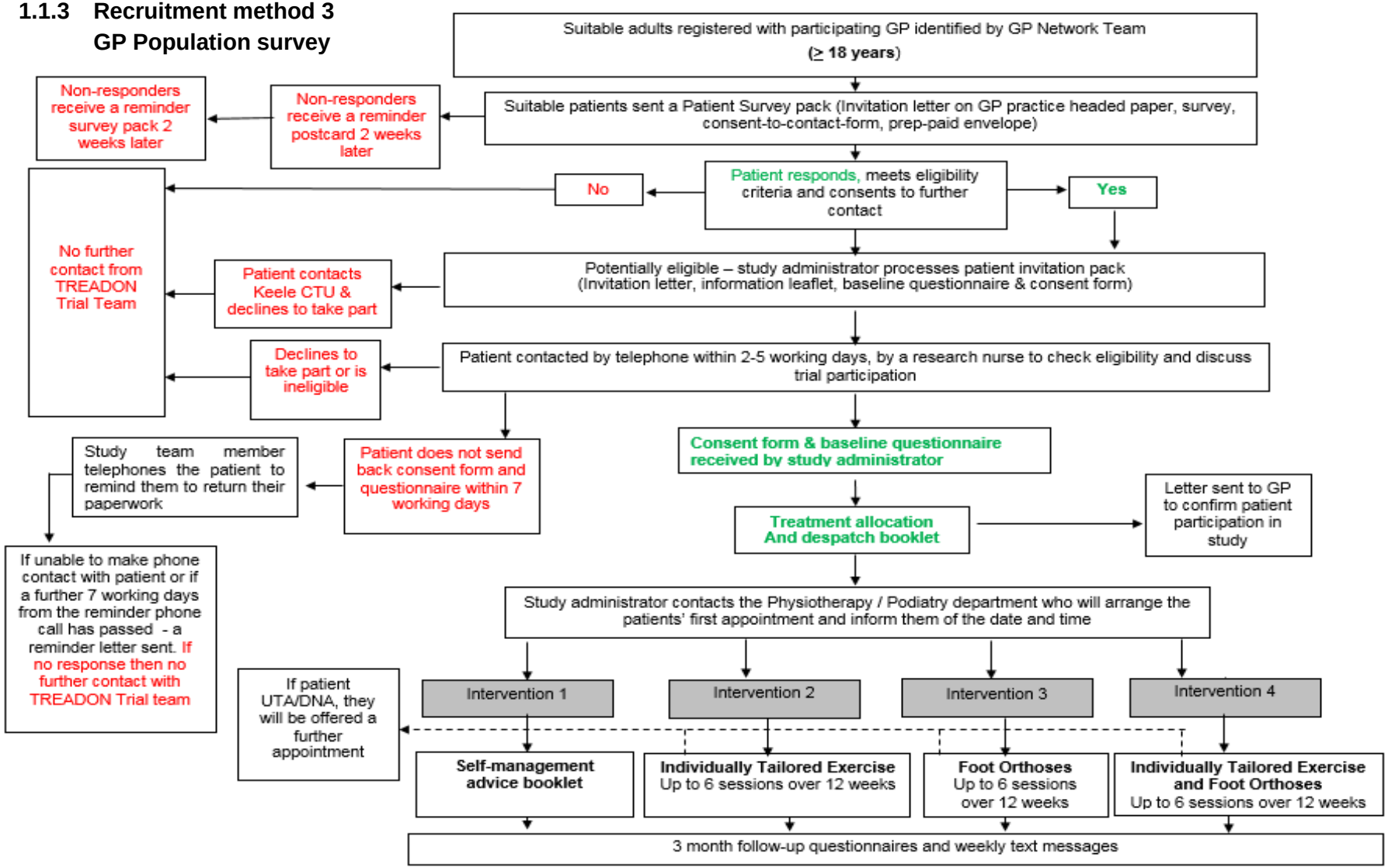
### 1.1.2 Recruitment method 2
### Medical record review



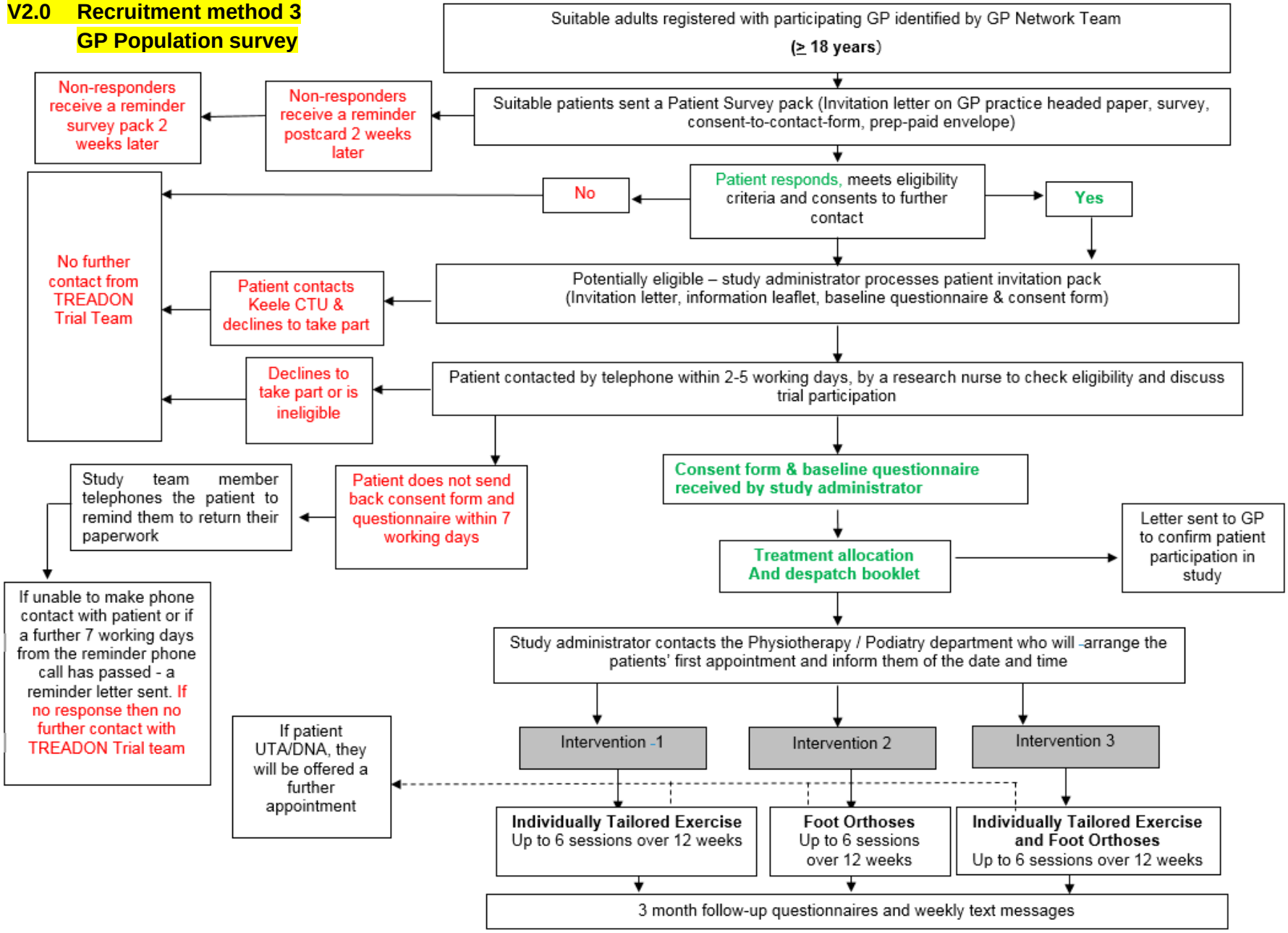
**V2.0 Recruitment method 2**
**Medical record review**



### 1.1.3 Recruitment method 3
### GP Population survey



**V2.0 Recruitment method 3**
**GP Population survey**



## 17.2 Appendix 2 – Gantt Chart Timeline