The TREADON Trial Protocol

Full title: Clinical and cost-effectiveness of individualised exercises and foot orthoses in the treatment of plantar heel pain: a randomised multi-arm multi-stage (MAMS) adaptive trial

Short title: TReatments of **E**xercise **A**n**D O**rthotics for pla**N**tar heel pain: TREADON

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Department of Health and Social Care disclaimer

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

SIGNATURE PAGE

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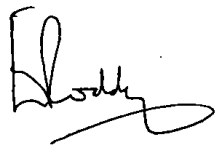
The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the research in compliance with the approved protocol, GCP guidelines, the Sponsor's SOPs, and other regulatory requirements as amended.

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

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

Chief Investigator:

Signature:



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

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LIST OF ABBREVIATIONS

Abbreviation	Description
CEAC	Cost Effectiveness Acceptability Curve
CI	Chief Investigator
CRF	Case Report Form
CRN	Clinical Research Network
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
FPI	Foot Posture Index
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GP	General Practitioner
IAU	Impact Accelerator Unit
ICER	Incremental Cost-effectiveness ratio
DMC	Data Monitoring Committee
DNA	Did Not Attend
HEAP	Health Economic Analysis Plan
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials Number
ITT	Intention-to-Treat
MAMS	Multi-Arm, Multi-Stage
MAR	Missing At Random
MCAR	Missing Completely At Random
MDC	Minimum Data Collection
MFPDI	Manchester Foot Pain and Disability Index
MNAR	Missing Not At Random
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRS	Numeric Rating Scale
PHP	Plantar Heel Pain
PI	Principal Investigator
PIL	Participant Information Leaflet
PPIE	Patient and Public Involvement and Engagement
PSS	Personal Social Services
QA	Quality Assurance
QALY	Quality Adjusted Life Year
RCT	Randomised Control Trial
REC	Research Ethics Committee

RUG	Research User Group
SAE	Serious Adverse Event
SMA	Self-Management Advice
SOP	Standard Operating Procedure
TMG	Trial Management Group
TSC	Trial Steering Committee
URL	Unique Resource Locator
UTA	Unable To Attend

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TRIAL SUMMARY

Trial Title	Clinical and cost-effectiveness of individualised exercises and foot orthoses in the treatment of plantar heel pain: a randomised multi-arm multi-stage (MAMS) adaptive trial	
Internal Ref. Number (or short title)	TReatments of Exercise AnD Orthotics for plaNtar heel pain: TREADON	
Trial Design	Interventional Allocation: randomised; Intervention model: four-arm two-stage adaptive parallel-group; Masking: trial administrator, data entry administrator, lead trial statisticians Primary purpose: Symptom control/reduction & reducing functional limitation Phase III	
Trial Intervention (where applicable)	Self-management advice (SMA) booklet (control arm) *versus* SMA booklet plus individualised exercises *or* SMA booklet plus prefabricated foot orthoses *or* SMA booklet plus individualised exercises and prefabricated foot orthoses	
Trial Participants	Adults aged 18 years or older with plantar heel pain (PHP)	
Planned Sample Size	Up to 696 (anticipated range based on adaptive trial design: 490-610)	
Treatment duration	12 weeks	
Follow up duration	12 months	
Planned Trial Period	01 January 2022 – 31 March 2026	
	Objectives	Outcome Measures
Primary	To determine, in adults with PHP, whether a SMA booklet combined with individualised exercises and/or prefabricated foot orthoses leads to greater improvement in pain in the medium term (average pain over 6-12 weeks of follow-up) than a SMA booklet alone.	Change in PHP intensity score 0-10 numeric rating scale (NRS) between baseline and average NRS score during weeks 6-12.
Secondary	To compare, in adults with PHP, the effect of an SMA booklet combined with individualised exercises and/or prefabricated foot orthoses compared with an SMA booklet alone on: i) short-term pain trajectories over weeks 1 to 12, including individual weekly comparisons	PHP severity score 0-10 numeric rating scale, first step pain on a 0-10 numeric rating scale; Foot Function Index; patient global rating of change; pain self-efficacy questionnaire; brief illness perceptions questionnaire; quality of life (EQ5D-5L); work loss and presenteeism; self-reported healthcare use for plantar heel pain (NHS

	ii) pain at 6 and 12 months, and monthly from 3 months to month 12 iii) first step pain, physical function, patient global rating of change, pain self-efficacy, illness perceptions, ability to work, and treatment satisfaction at 12 weeks, 6 and 12 months. iv) cost-effectiveness of an SMA booklet combined with individualised exercises and/or prefabricated foot orthoses with an SMA booklet alone.	and private); self-reported treatment adherence; satisfaction with care; treatment credibility; adverse events.

PLAIN ENGLISH SUMMARY

AIMS OF THE RESEARCH: To show whether exercises and/or foot orthoses (shoe insoles) provide more pain relief for adults with plantar heel pain than a self-management advice booklet alone, and whether this is good value for money for the NHS.

BACKGROUND: Pain under the heel (called plantar heel pain, PHP) is a common condition affecting 1 in 10 adults during their lifetime. It makes walking and completing everyday tasks, including going to work, difficult. Most patients who consult in general practice are given pain medication and advice, yet the problem often continues. In our successful pilot and feasibility trial, foot orthoses and exercises showed promise for improving pain and function, but a large, high-quality main trial is needed to confirm this.

DESIGN AND METHODS: In this randomised controlled trial, up to 696 adults with PHP will be given a self-management advice booklet and allocated by chance to one of four treatments: exercise, foot orthoses, combined exercises and foot orthoses, or no additional treatment. Participants will be sent a weekly text-message to collect pain scores for up to 12 weeks and then monthly from 3 to 12 months, as well as a questionnaire at 3, 6 and 12 months. Half-way through the trial, only treatments that appear to be reducing pain will continue to be offered and the trial will be stopped early if there is strong evidence that one treatment is better than the others, making the trial good value for money.

PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT: Patient representatives were involved in our pilot and feasibility trial and will support every stage of the main trial. Our lay co-investigator helped write this summary. Five patients with PHP took part in a workshop to help design the main trial. For example, they helped us decide how often pain should be measured. We will also involve patients to assist with our recruitment strategy and help us to interpret the trial findings, develop easily understandable messages to explain the findings and publicise the findings widely.

DISSEMINATION: We will present and publish the findings at healthcare conferences, in medical journals, on relevant websites, through social media, and in general practices and physiotherapy and podiatry services. A summary of the results will be provided to participants when the trial is completed. Articles about the trial will also be written for local magazines, newspapers, and radio.

Figure 1. Patient recruitment flow diagram Recruitment method 1a – General practice consultation – Clinical System Protocol (Preferred rolling monthly method)

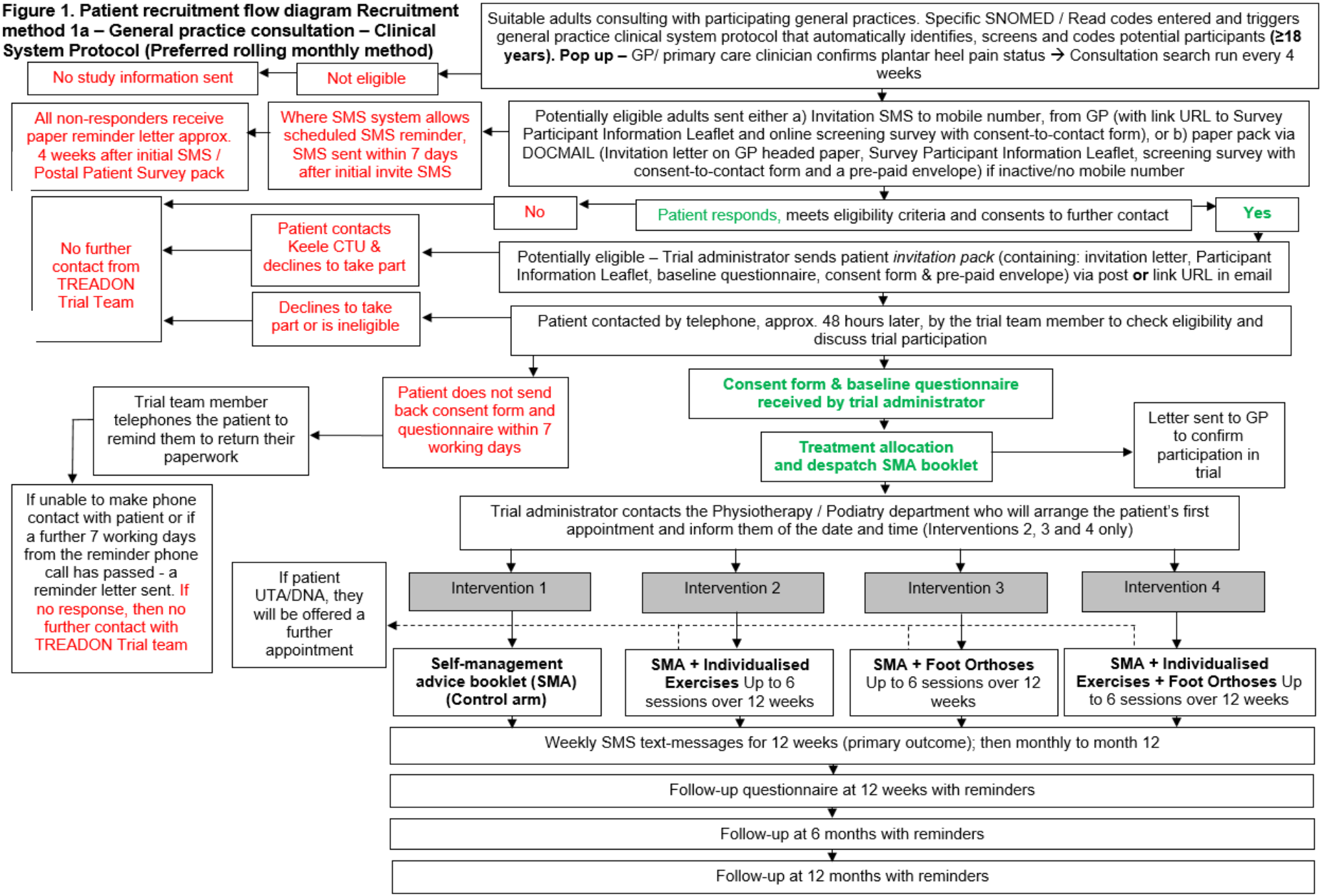


Figure 2. Patient recruitment flow diagram Recruitment method 1b – General practice consultation – Clinical System Search (Rolling monthly method)

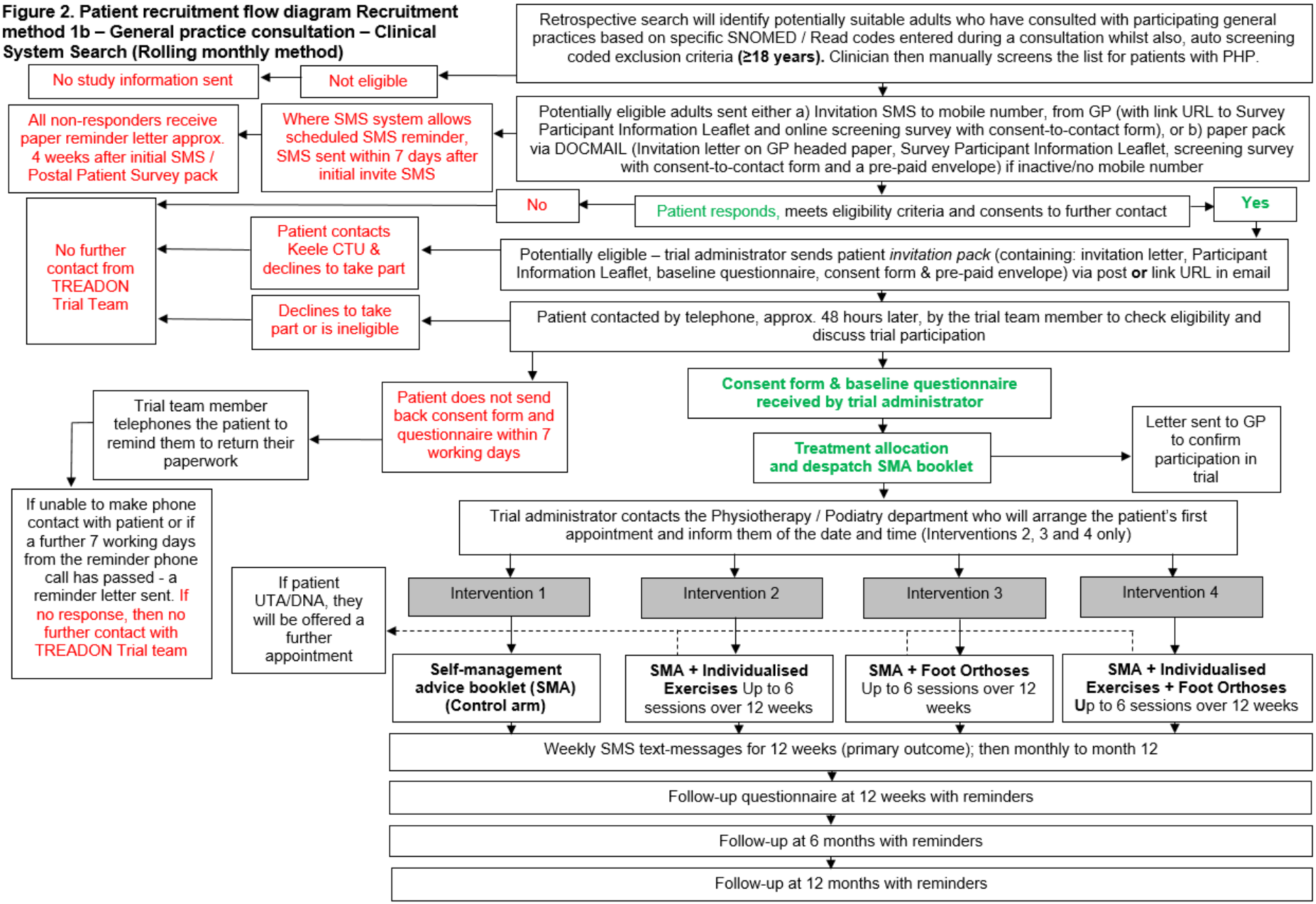


Figure 3. Patient recruitment flow diagram – Recruitment method 2
Retrospective (1 year) general practice search: Foot/ankle pain consulters

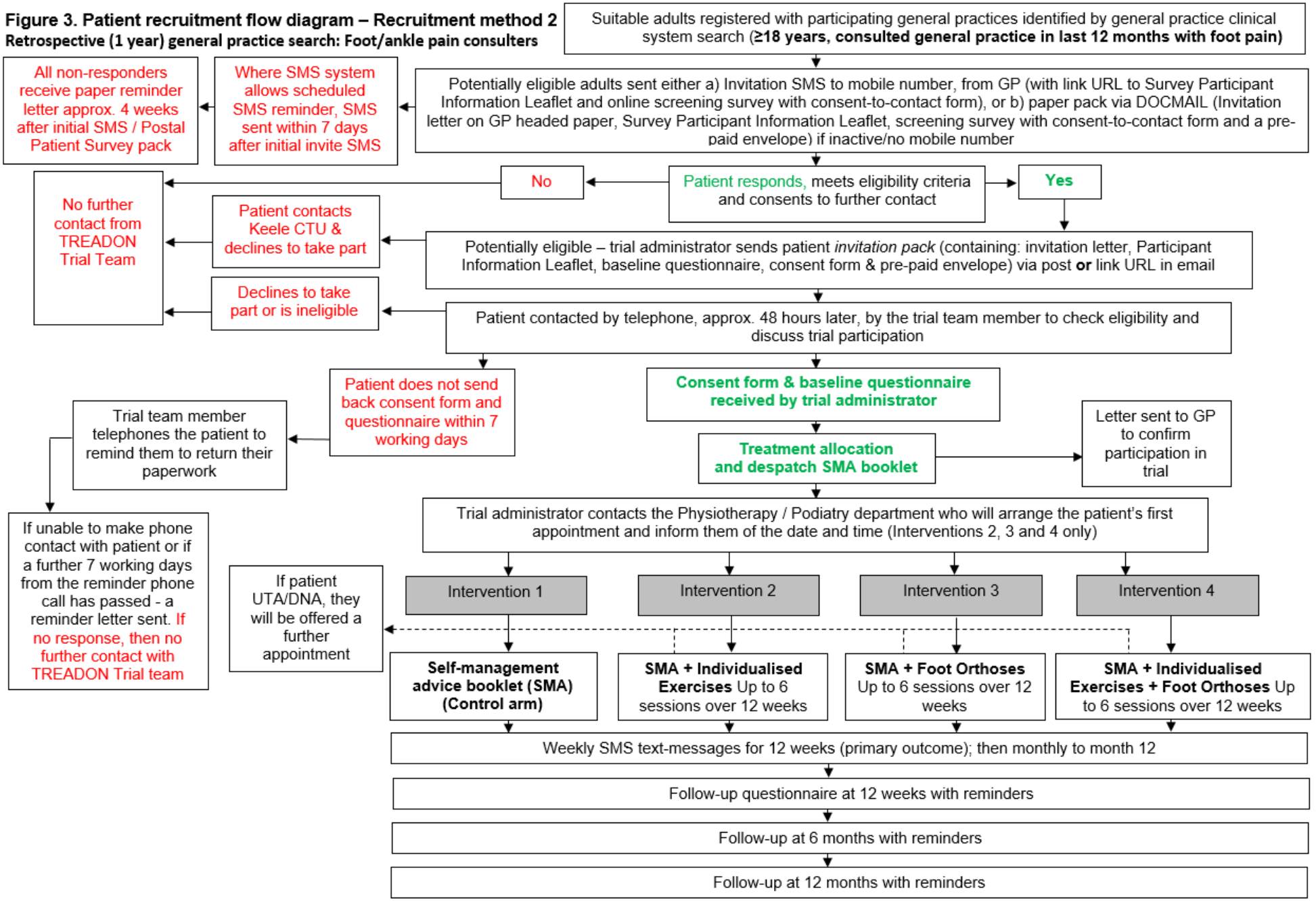


Figure 4. Patient recruitment flow diagram – Recruitment method 3 – General practice population survey

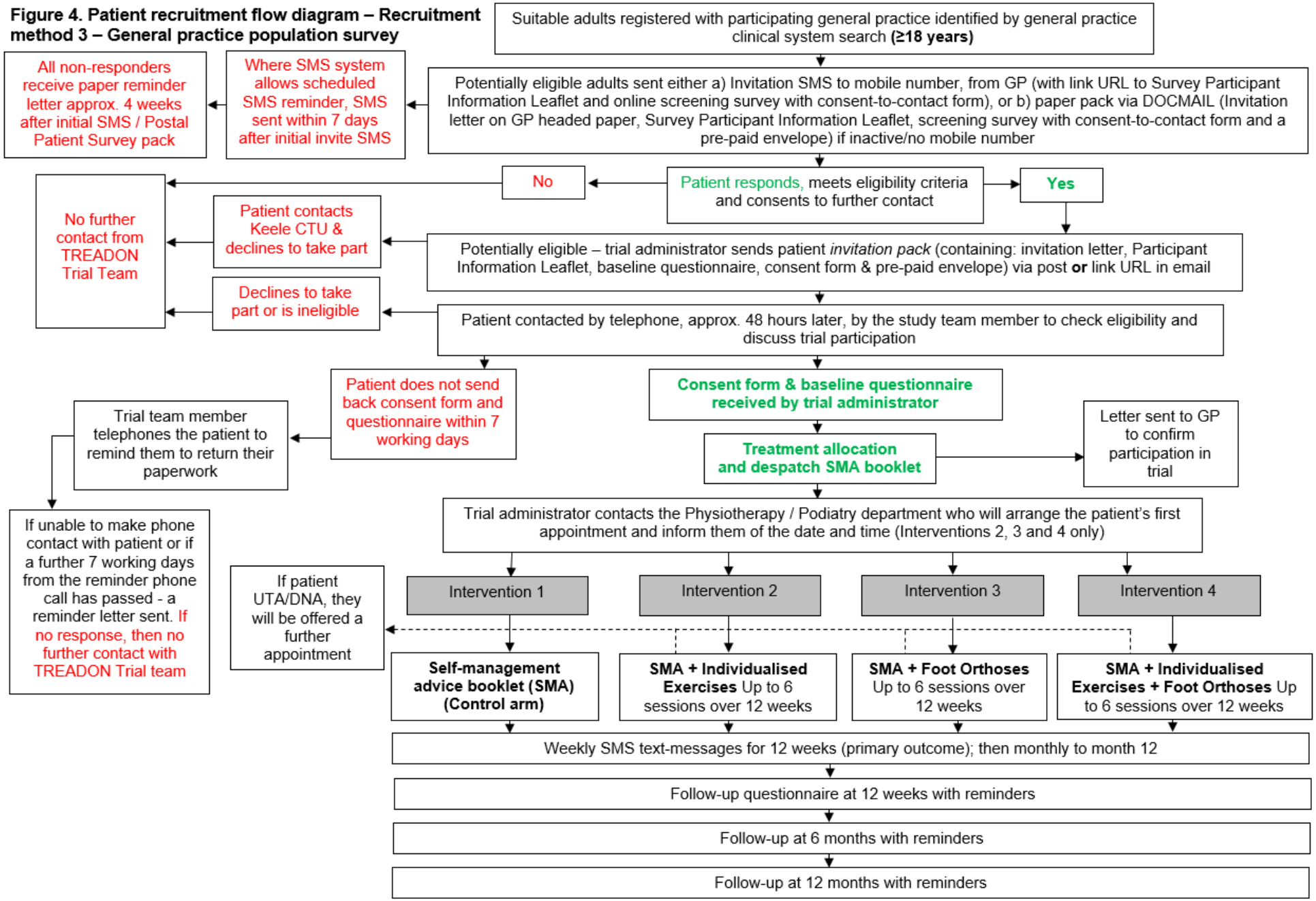


Figure 5. Patient recruitment flow diagram
Recruitment method 4 – Physio/ Podiatry Service Referral

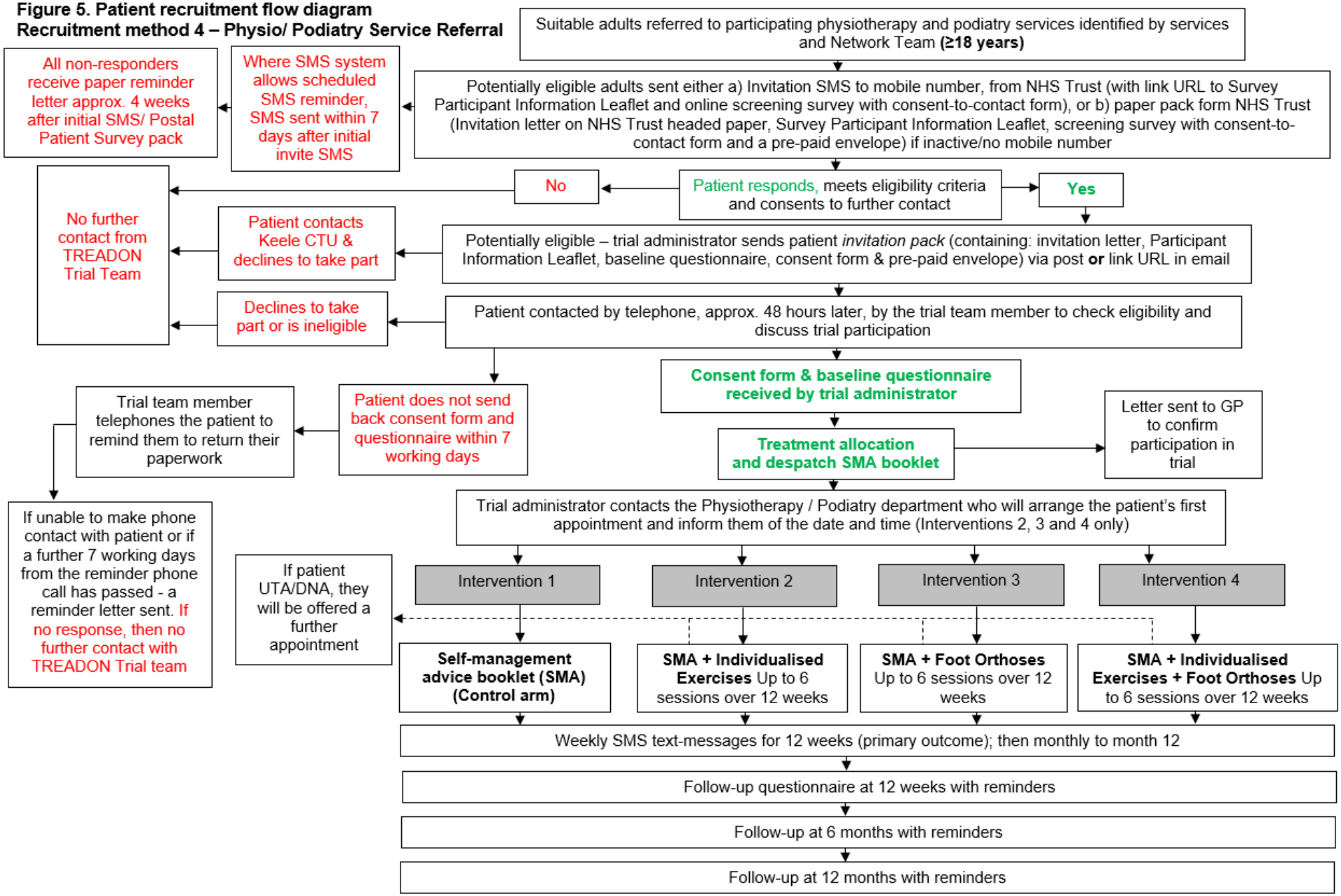
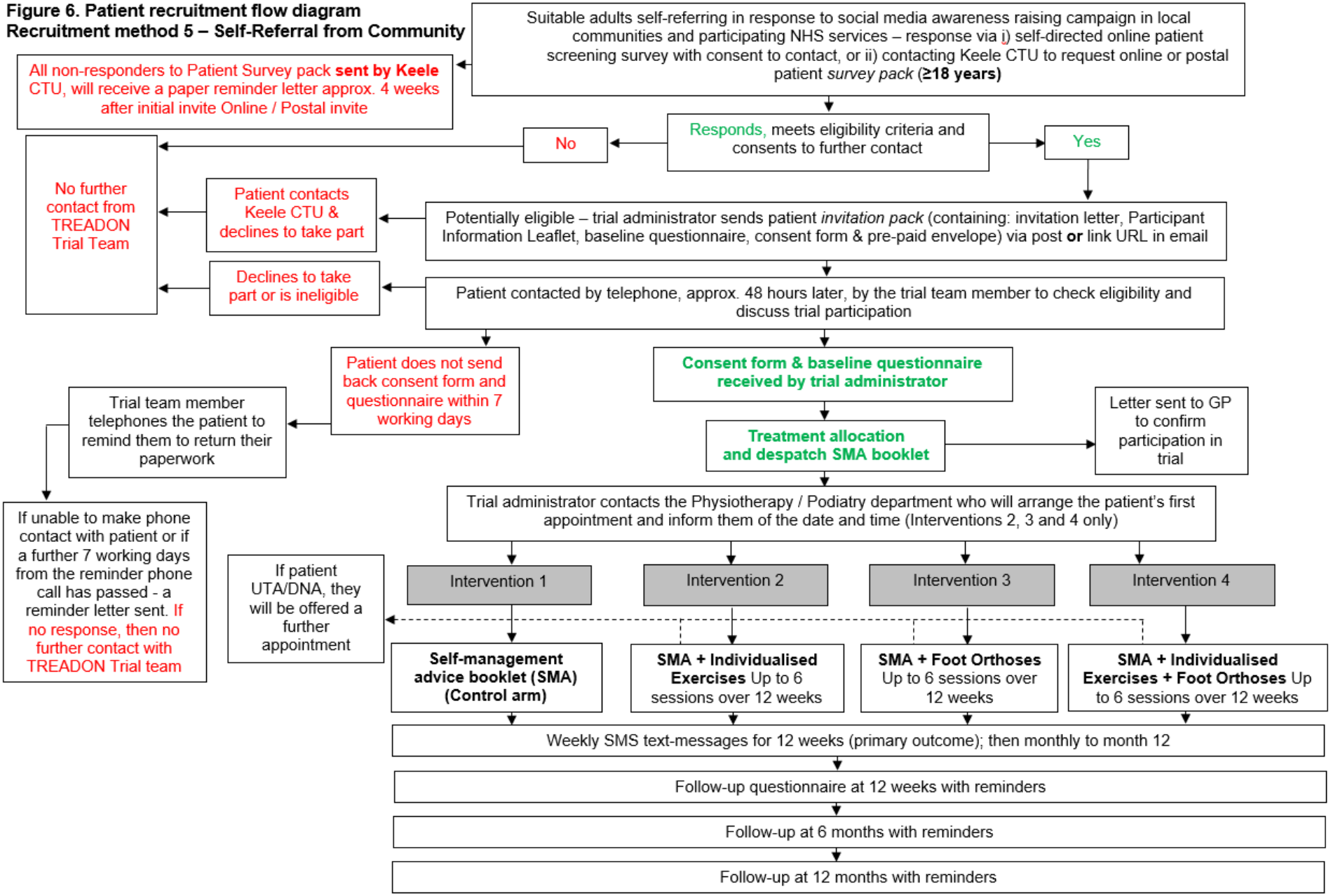


Figure 6. Patient recruitment flow diagram
Recruitment method 5 – Self-Referral from Community



1 BACKGROUND

Plantar heel pain (PHP) is a term describing several undifferentiated painful conditions affecting the plantar heel. It is now preferred to the label “plantar fasciitis”, which was used commonly in the past.[1] It is the most prevalent soft tissue foot complaint, affecting 10% of adults, and impairs mobility, foot and physical function, and ability to work, impacting negatively on quality of life.[2-4] Clinical features include pain under the heel, made worse by weight-bearing, particularly after prolonged rest. Its specific cause is uncertain although established risk factors include obesity; pronated foot posture; reduced ankle or first metatarsophalangeal joint range of motion; prolonged weight-bearing; and tightness in the gastrocnemius and soleus muscles, plantar fascia and Achilles tendon.[2,5] Weakness of the gastrocnemius, soleus, and intrinsic foot muscles has also been implicated.[6]

PHP is commonly thought to be a benign, self-limiting condition that, for most, resolves within 1 year.[7] However, symptoms can become chronic and persistent: almost half report persistent symptoms after 10 years, leading to impaired quality of life, physical inactivity and weight gain.[4,8] A NICE Clinical Knowledge Summary recommends initial treatment with analgesia and advice regarding rest, footwear, heel pads, weight loss and stretching exercises.[7] Referral to a podiatrist or physiotherapist is advised if mild symptoms persist beyond a few months despite conservative treatment or if symptoms are severe. In the Netherlands and Australia, the most frequent strategies employed by General Practitioners (GPs) to manage PHP are referral to a podiatrist (12-20%), watchful waiting (18-37%), NSAIDs (18-28%), and advice to wear insoles (16%).[9,10] In our population-based observational trial of 5,109 adults in the UK,[2,11] 80% of people with PHP did not improve significantly over 18 months and only 40% saw a podiatrist or physiotherapist in that time (unpublished data). Qualitative studies show that the expectations and needs of people with PHP are often unmet.[12]

Podiatrists and physiotherapists commonly use foot orthoses and/or lower limb exercises to treat patients with PHP.[13] Foot orthoses are insole devices designed to optimise foot loading distribution and adjust medial longitudinal arch function through control of specific foot motion.[14] They reduce rearfoot pronation in a dose-dependent manner, addressing planus foot posture (flat feet) and excessive foot pronation (eversion) associated with PHP, and increase foot-to-surface contact area, lowering plantar heel pressures and tensile stresses at the calcaneal-plantar fascia junction during loading to provide symptomatic relief from PHP.[14-18] Exercises, including stretching the Achilles tendon and plantar fascia and strengthening of the intrinsic muscles of the foot and lower limb muscles (e.g. hamstrings, quadriceps and triceps surae), aim to improve movement and restore normal foot loading.[19-21] Rearfoot eversion and tightness and weakness in the plantar fascia, Achilles tendon and foot muscles are therefore viable therapeutic targets for foot orthoses and individualised exercises respectively in the treatment of PHP. However, orthoses and exercises are infrequently used to treat this common and disabling condition despite many patients having persistent problems.

2 RATIONALE

PHP is the most common musculoskeletal cause of foot pain and is mostly managed in primary care.[2] It commonly affects people of working age, and leads to pain, reduced mobility, impaired quality of life and difficulties with everyday activities including work.[2-4] People with plantar heel pain commonly feel their problem is ignored and not taken seriously by health professionals.[12]

The evidence-base to inform clinical decisions about treatments is limited and often of poor quality.[22-24] Despite the plausibility of foot orthoses and exercises as interventions for PHP, recent systematic reviews highlight limitations of the existing evidence about their effectiveness. Many published randomised controlled trials (RCTs) are limited by small sample sizes, short-term follow-up and poor methodological quality, illustrating the need for larger trials incorporating longer follow-up, more robust methods, and higher reporting standards.[22-24] Two systematic reviews of foot orthoses compared with sham orthoses for PHP published in 2018 reached different conclusions despite pooling data from the same three trials: one found moderate-quality evidence that foot orthoses are effective at reducing pain in the medium term (7-12 weeks) but had no effect in the short term or on function,[22] whereas the other found that foot orthoses were ineffective.[23] This difference has been attributed to the reviews extracting outcome data for different measures of foot pain.[25] Our recent network meta-analysis found

that exercises alone did not reduce pain or improve function in patients with PHP in the short or medium term, but improved function at 12 months compared with placebo/sham interventions based on only two small RCTs (<50 participants each).[24] No treatments commonly used for the management of PHP (including orthoses and exercises) were significantly better than any other for pain and function. Placebo/sham interventions and NSAIDs were the least effective, suggesting that current recommendations to manage PHP first-line with analgesics, NSAIDs and watchful waiting may be suboptimal. We found only one RCT which examined the effectiveness of combining orthoses and exercises.[26] Prefabricated orthoses plus stretching exercises were more effective than stretching exercises alone although the trial was small (42-51 participants per arm), follow-up was short (8 weeks) and risk of bias was high.

Subsequently, one small RCT (n=95) reported greater improvement in pain with usual podiatry care plus physical therapy than with usual podiatry care alone at 1 year, but there was no difference in physical function.[27] A larger RCT (n=185) concluded that referral to a podiatrist for custom-made insoles does not lead to better outcomes compared with usual GP care.[28] However, usual GP care within the trial was more intensive than in routine practice with 41% of participants receiving biomechanical interventions such as heel cups and 15% corticosteroid injection.[10,29] Key differences from our trial are the type of orthosis (prefabricated, not custom-made), shorter follow-up (6 months versus 12 months), and lack of standardisation of the orthosis intervention. We found a small ongoing pilot RCT (48 participants with PHP) which compares radial shockwave therapy plus exercises versus exercises alone and a small ongoing feasibility study (n=20) for a RCT of foot exercises plus education versus brief advice.[30,31] We did not find any large pragmatic RCTs comparing the clinical and cost effectiveness of a combination of exercises and orthoses against usual care for PHP.

Treatments such as foot orthoses, individualised exercises or a combination of both show promise for improving pain and function in people with PHP and have potential to be cost-effective by reducing further healthcare use and facilitating earlier return to everyday activities including work. There is currently no evidence of cost-effectiveness of exercise programmes for PHP, with evidence for orthoses limited to one study which showed that prefabricated orthoses were similarly effective to customised orthoses but significantly less expensive.[32] High-quality evidence to support their clinical and cost-effectiveness for PHP either alone or in combination in a primary care population is needed to guide patients, clinicians and commissioners whether these treatments should be more routinely offered. Informed by our successful feasibility and pilot trial[33], this definitive trial will investigate the clinical and cost-effectiveness of individualised exercises and/or pre-fabricated foot orthoses plus good self-management advice compared with good self-management advice alone for adults with PHP in primary care over the medium and long term. Such a trial is needed to support clinical decision-making and inform NHS policy and commissioning pathways for this patient group who experience considerable pain and functional limitation but are often overlooked in terms of treatment options that are available but only accessed by a few.[9,10]

2.1 The TREADON pilot and feasibility trial

We completed the TReatments of Exercise AnD Orthotics for plaNtar heel pain (TREADON) pilot and feasibility trial.[33]

Eighty-two participants with PHP were randomised to one of four intervention arms:

(1) a self-management advice (SMA) booklet providing advice about exercises, pain relief, footwear, and weight loss (as per NICE Clinical Knowledge Summary [7])
(2) SMA booklet and individualised exercises
(3) SMA booklet and prefabricated foot orthoses
(4) SMA booklet, individualised exercises and prefabricated foot orthoses.

The trial demonstrated feasibility in terms of participant identification and recruitment methods; intervention fidelity; intervention delivery by both physiotherapists and podiatrists; adherence satisfaction, and credibility of the three clinician-supported interventions; and retention over 12 weeks. Important information to inform the choice of primary outcome and sample size was obtained. We successfully demonstrated the feasibility and acceptability of conducting this large RCT investigating

the costs and long-term clinical effectiveness of individualised exercises and/or prefabricated foot orthoses on pain and function for PHP that will inform clinical practice.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

The overall aim of the trial is to compare the additional benefit of individualised exercises and/or prefabricated foot orthoses versus a self-management advice (SMA) booklet alone to treat adults with plantar heel pain (PHP) in primary care.

3.1 Primary objective/Research question

In adults with PHP, does a SMA booklet combined with individualised exercises and/or prefabricated foot orthoses lead to greater improvement in pain in the medium term (average pain over 6-12 weeks of follow-up) than a SMA booklet alone?

3.2 Secondary objectives

To compare, in adults with PHP:

3.2.1 The effect of an SMA booklet combined with individualised exercises and/or prefabricated foot orthoses with a SMA booklet alone on;

i) short-term pain trajectories over weeks 1 to 12, including individual weekly comparisons,

ii) pain at 6 and 12 months, and monthly from 3 months to month 12,

iii) first step pain, physical function, patient global rating of change, pain self-efficacy, illness perceptions, ability to work, and treatment satisfaction at 12 weeks, 6 and 12 months.

3.2.2 The cost-effectiveness of an SMA booklet combined with individualised exercises and/or prefabricated foot orthoses with an SMA booklet alone.

3.3 Outcome measures/endpoints

To determine the primary outcome measure for the main trial, three outcomes were evaluated as part of the TREADON pilot and feasibility trial.[33] These included:

i) pain intensity change score using a 0-10 numeric rating scale (NRS),
ii) change in foot pain measured using the Foot Function Index pain subscale[34],
iii) change in foot pain measured using the Manchester Foot Pain and Disability Index (MFPDI) pain subscale.[35]

Due to limited responsiveness to change over time, reported in previous studies[36,37], the MFPDI was considered unsuitable for the main trial.[33] In the TREADON feasibility and pilot trial, both the pain intensity NRS and Foot Function Index pain subscales completion rates, responsiveness to change, and correlation with other change scores supported their use in a future main trial.[33] The NRS pain score has a more versatile application as part of weekly data collection using SMS text-message and was therefore selected as the primary outcome[33], with the Foot Function Index being retained as an important secondary outcome.

The end points are defined as:

- Primary end point at 6-12 weeks for clinical effectiveness and at 12 months for cost-effectiveness analysis.

3.4 Primary endpoint/outcome

The primary outcome for clinical effectiveness is change in PHP intensity (0-10 NRS) between the baseline and the average rating over weeks 6 to 12. Outcome data are patient-reported and will be collected by SMS text-message (weekly between weeks 1-12, monthly thereafter until 12 months) and questionnaires at 12 weeks and 6 and 12 months.

3.5 Secondary endpoints/outcomes

Secondary outcomes will comprise PHP severity score (0-10 NRS), first step pain (0-10 NRS), Foot Function Index,[34] (pain, disability, activity restriction subscales, and overall), patient global rating of change, pain self-efficacy questionnaire,[38] brief illness perceptions questionnaire,[39] quality of life (EQ5D-5L),[40] work loss and presenteeism,[41] self-reported healthcare use for PHP (NHS and private), self-reported treatment adherence, treatment credibility, satisfaction with care, and adverse events.

Adverse events: Trial-related adverse events (for example skin irritation from orthoses, muscle soreness from exercise) will be captured through case report forms (CRF) completed by TREADON physiotherapists/podiatrists, and direct contact between the CTU and the participant, their TREADON physiotherapist/podiatrist, GP or site PI. Participants randomised to the clinician-supported intervention arms will record adverse events in a weekly diary for the 12-week intervention period.

Trial safety reporting procedures will ensure any unexpected serious adverse events which are deemed related to the trial will be reported to the Research Ethics Committee and Sponsor.
All SAEs either confirmed or suspected to be related to the trial procedures will be reviewed by the Data Monitoring Committee and reported to the Trial Steering Committee.

4 TRIAL DESIGN

Multi-centre, primary care-based, randomised, parallel group, four-arm two-stage adaptive trial, with 6-month internal pilot.

4.1 Interventions/Treatments

The duration of the intervention regardless of group allocation will be 12 weeks. Participants will be asked not to use other types of treatments, other than medication that their GP has provided, during the intervention period if possible; however any additional healthcare and self-care use will be recorded in the 12-week follow-up questionnaire, 6 month follow-up questionnaire and 12 month follow-up questionnaire.

4.1.1 Self-management advice (SMA) booklet (control arm)

Participants randomised to receive SMA only will be mailed a SMA booklet, based on the Versus Arthritis leaflets on plantar fasciitis[42] and foot and ankle pain,[43] supplemented with specific advice and information including a small number of stretching exercises and self-help messages about pain relief, footwear, rest and weight loss. This will be consistent with best practice guidance.[44] The booklet describes five stretching exercises for the plantar fascia and Achilles tendon to be performed twice per day[42], without instructions for individualisation, progression or supervision of exercises.

4.1.2 SMA booklet plus individualised exercises (SMA-exercises)

Participants randomised to SMA-exercises will be given the SMA booklet at the initial treatment appointment. The treating clinician (a physiotherapist or podiatrist) will assess foot posture and function to determine the exercise type and dose. At the discretion of the clinician, a more generic lower limb assessment of alignment and function can also be undertaken, 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 (Figure 7). Exercise dose will be individualised and progressed, based on assessment findings and informed by current exercise guidelines.[45] The exercises are drawn from best available evidence[5,19-21,46-47] and discussion with clinicians during workshops prior to our pilot and feasibility trial. Exercises will include foot-specific stretches/exercises targeting the plantar fascia, intrinsic foot muscles, Achilles tendon, key ankle related muscle groups such as soleus and gastrocnemius, and other muscle groups in the lower limb identified as targets within the assessment. Participants will be taught how to perform and progress these exercises and

given an individualised and detailed exercise sheet (online or paper) describing the regimen and showing photographs of the exercises. The exercise sheets provided will be trial-specific exercises selected by the clinician and comprising photographs and written instruction completed by the clinician. Participants will be followed up for up to 6 treatment appointments over 12 weeks at the discretion of the treating clinician (face-to-face appointments prioritised if possible, or virtual, telephone, if required). We will aim for appointment lengths of 1 hour for the initial appointment and 30 minutes for follow-up appointments.

Exercise programme 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.

The exercise programme will be supervised during each treatment appointment and may be progressed at subsequent treatment appointments according to observed changes in presentation, modelled on successful exercise interventions in our earlier trials.[48,49] A record of the exercise prescription will be recorded on the Intervention Details CRF for each treatment appointment. Adherence will be encouraged by provision of written individualised exercise sheets (online or paper) and use of a paper-based diary to discuss with the clinician during subsequent treatment appointments. The diary will be collected at 12 weeks.

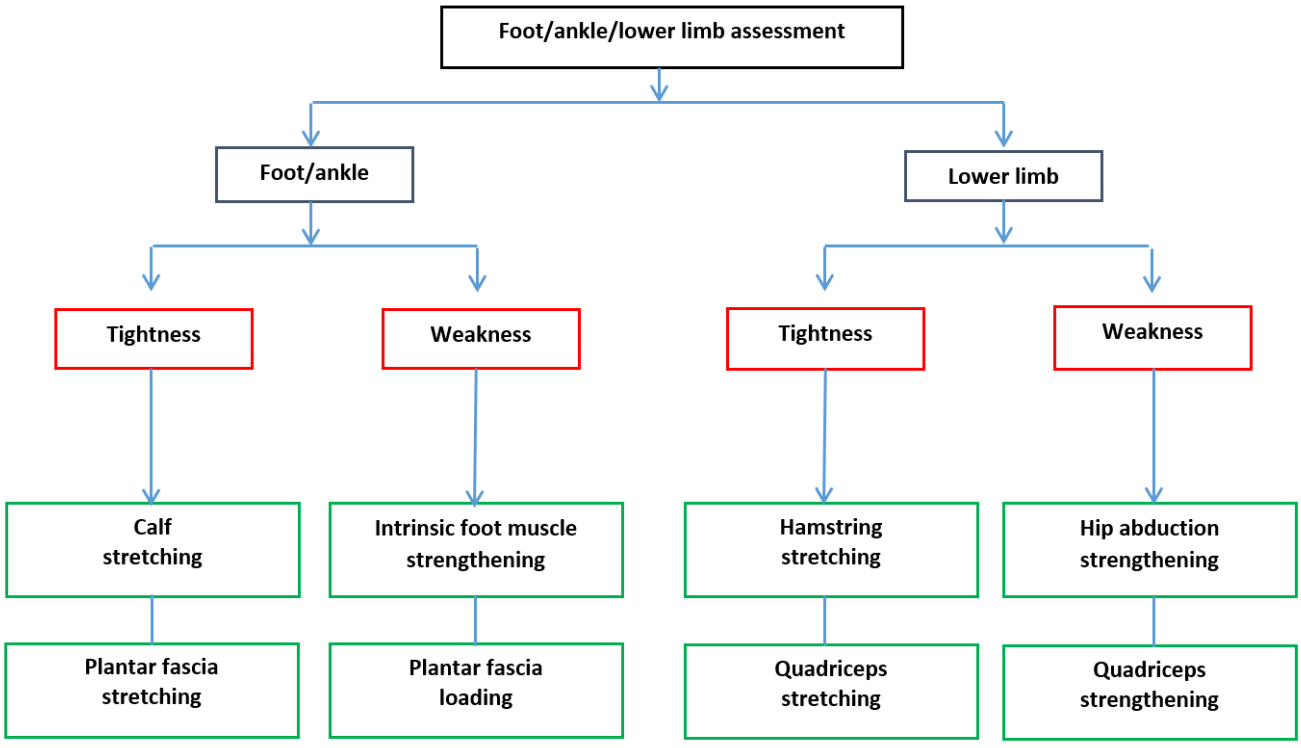


Figure 7: Summary flow chart of exercise prescription

4.1.3 SMA booklet plus prefabricated foot orthoses (SMA-orthoses)

Participants randomised to SMA-orthoses will be given the SMA booklet at the initial treatment appointment. The treating clinician (a physiotherapist or podiatrist) will assess foot posture using the Foot Posture Index-6 (FPI-6)[50] and select the appropriate orthotic device according to the degree of static rearfoot eversion and body weight (see Figure 8 for the foot orthoses and body weight

algorithm). These data will be recorded on the CRF by the treating clinician. If deemed clinically relevant to PHP, this can include assessment of hip position (anteversion/retroversion) and knee position (genu varus/valgus).

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

1. A main driver in influencing the rearfoot posting component of the foot orthosis prescription will be the rearfoot posture component of the FPI-6[50]. This will be assessed by the podiatrist/physiotherapist when the participant is in a relaxed stance position. The podiatrist/physiotherapist will observe whether the calcaneus is inverted, vertical, everted, or highly everted (see Figure 8).

2. Assessment of body weight will also influence the selection of the appropriate orthotic device (greater body weight resulting in selection of a device with a higher material density).

3. Each foot orthotic device will be fitted according to the size of the participant's foot using the orthotic device shells of various sizes.

4. Clinicians will select the appropriate first choice device with appropriate rearfoot medial posting dose (see Figure 8) in place and assess the participant for correct size of orthotic device (weight-bearing and non-weight-bearing fit-to-foot).

5. Clinicians will then check the fit of the orthotic device to the shoe (fit-to-shoe).

6. 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.

7. 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 the heel pain presentation is unilateral or bilateral.

Foot orthoses choice
In the development of our pilot and feasibility trial[33], our patient and clinician advisory group identified desirable characteristics of an orthotic intervention protocol including:

(1) an element of patient choice between different devices based on comfort and fit

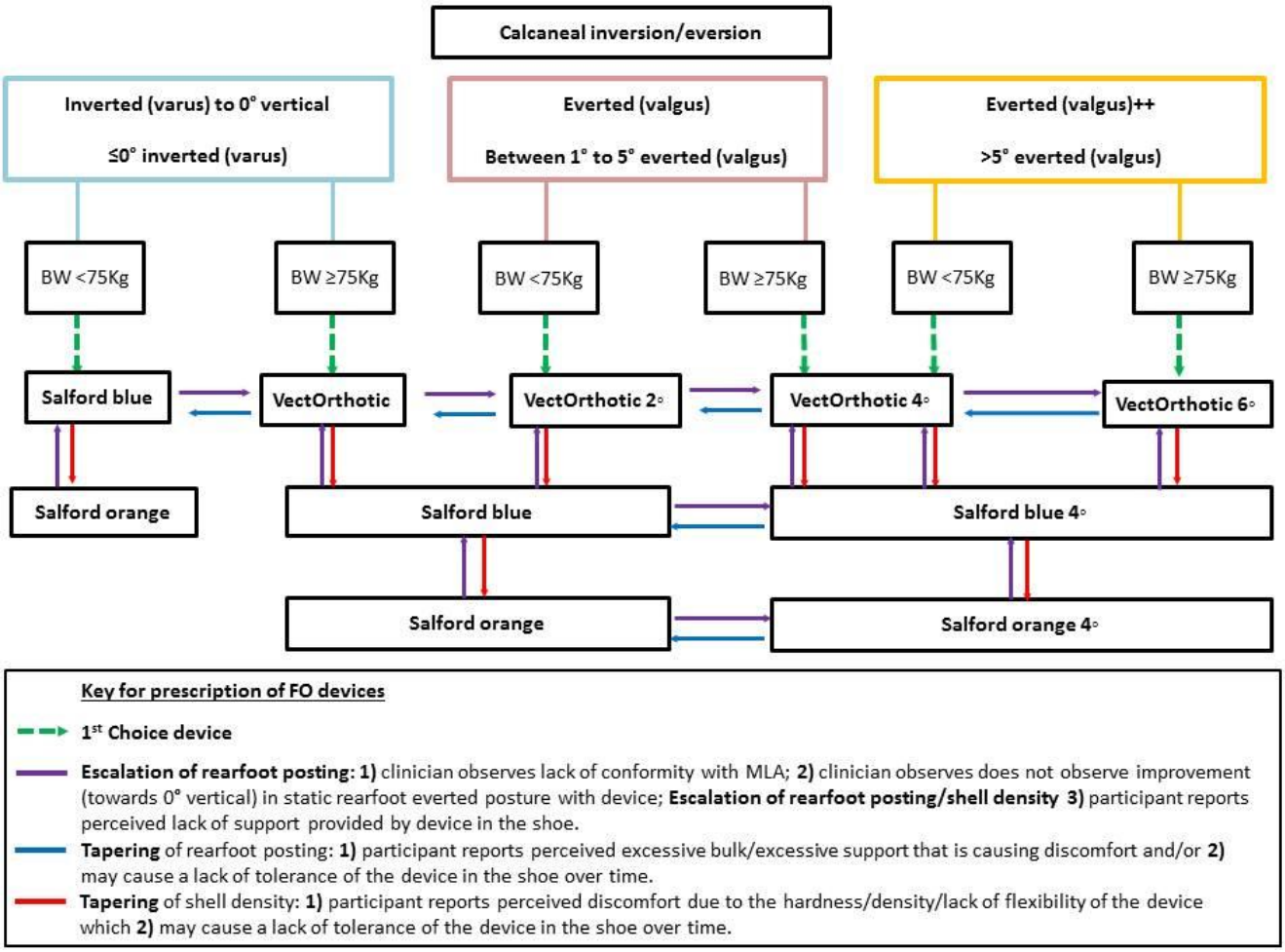
(2) scope for device adjustment/tailoring by the clinician to provide the desirable level of rearfoot posture/functional control for individual symptoms.

As a result, we developed a pragmatic foot orthosis intervention algorithm, which includes the following devices:

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

These devices 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 patient comfort and therefore potentially influence adherence. A range of shell material densities allows for a more supportive orthotic for participants with a higher bodyweight.[51] 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.[22,52] Participants will be instructed how to fit the device and advised to wear it for one hour per

day, gradually increasing by one hour per day up to at least four hours per day, and given an individualised and detailed orthosis information sheet. Participants will be followed up for up to 6 treatment appointments over 12 weeks at the discretion of the treating clinician (face-to-face appointments prioritised if possible, or virtual, telephone, if required). The orthosis can be altered during subsequent consultations according to participants' self-reported tolerance or clinical presentation. Adherence will be encouraged by a diary to capture use and facilitate discussion with the clinician. The diary will be collected at week 12. The foot orthosis may be changed or altered during subsequent clinical treatment appointments according to participants' self-report of tolerance or clinical presentation.



BW: Body weight.

Figure 8: Summary flow chart of orthoses prescription

Foot orthoses details
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 (ISF).

Storage and consignment stock: Orthotic devices should be stored in accordance with manufacturer's recommendations and as outlined in the supply instructions provided in the trial information. A consignment stock of orthoses will be sourced and purchased by a member of the research team and delivered to each site. This will ensure that participants can be provided with the appropriate orthoses, as required. The Principal Investigator at each site is responsible for consignment stock monitoring and replenishment. At the end of the trial, any leftover stock will be returned to Keele CTU.

4.1.4 SMA booklet plus individualised exercises and prefabricated foot orthoses (SMA-combined)
In addition to the SMA booklet provided at the initial treatment appointment, participants randomised to SMA-combined will receive both individualised exercises and prefabricated foot orthoses interventions as described above and delivered over up to 6 treatment appointments, over 12 weeks, by a physiotherapist or podiatrist. Duration of appointments will be the same as in the SMA-exercises and SMA-orthoses arms.

4.2 Interventions/Treatments general treatment appointment procedures
Participating physiotherapy and podiatry services responsible for delivering the interventions will be expected to maintain an ISF of essential trial documentation, which will be provided by Keele CTU, and keep 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. All clinicians will be trained in accordance with the protocol on how to record trial-specific data. Data will be collected on either paper CRFs or electronic CRFs depending on site capability. Paper CRFs will be collected by a trial team member, posted, faxed or emailed to Keele CTU as agreed with the site. Electronic CRFs will be entered directly onto the REDCap trial database by the clinician. Only the participant's trial number plus date of birth, initials and sex at birth will be included on CRFs. Where paper 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 paper 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.

For all three clinician-supported intervention arms (SMA-exercises; SMA-orthoses; SMA-combined), participants who do not attend (DNA), or who are unable to attend (UTA) their physiotherapist/podiatrist appointment should be reappointed for the duration of the trial and CRFs should be completed to note the DNA/cancellation. This will take place flexibly in conjunction with participating services. Clinicians will be trained to deliver both exercise and orthosis interventions and will be notified which arm the participant has been randomised to in advance of their first treatment appointment. Clinicians will be required to complete a treatment CRF for each patient appointment. Table 1 summarises each intervention arm.

Table 1: Summary table of interventions

Self-management advice	**Self-management advice *plus* individualised exercises**	**Self-management advice *plus* prefabricated foot orthoses**	**Self-management *plus* individualised exercises and prefabricated foot orthoses**
Advice and information booklet	Advice and information booklet	Advice and information booklet	Advice and information booklet
	Up to 6 sessions over 12-week treatment period	Up to 6 sessions over 12-week treatment period	Up to 6 sessions over 12-week treatment period
	Individually tailored and written exercise programme	Individually tailored pre-fabricated foot orthotic device	Individually tailored and written exercise programme
	Focus on foot/ankle specific stretching and strengthening +/- lower limb muscle groups	Device adjustment/ tailoring as required	Focus on foot/ankle specific stretching and strengthening +/- lower limb muscle groups
	Individualised exercise programme that is progressed	Clinical supervision of orthotic device use/ tolerance	Individualised exercise programme that is progressed
	Clinical supervision of exercise programme	Orthosis diary	Clinical supervision of exercise programme
	Exercise diary		Individually tailored pre-fabricated foot orthotic device
			Device adjustment/ tailoring as required
			Clinical supervision of orthotic device use/ tolerance
			Exercise & orthosis diary

4.3 Trial Training

Treatment packages for those participants randomised to interventions which include exercises or foot orthoses treatments, will be delivered by participating physiotherapy and podiatry sites. Participating services will be those who have agreed to participate, have local management approval, have been trained in trial specific interventions and procedures, and are accessible to patients registered at the

GP practices participating in the trial. A research clinician (e.g. physiotherapist, podiatrist, nurse) will be trained to perform telephone screening of potential participants, confirm eligibility and obtain consent. Trial administrators will also be trained to support site processes (e.g. booking participants into treatment appointments) as required.

Physiotherapists and podiatrists: Treating physiotherapists and podiatrists (at least NHS Agenda for Change Band 5) will participate in training workshops (2- 3 days) with the research team prior to the start of recruitment and treatment (hybrid remote and face-to-face delivery or remote delivery only if the covid-19 pandemic requires). The workshop(s) will be based on the training provided in our pilot and feasibility trial. The focus of the training will be on carrying out standardised assessment, delivery of the exercises and orthosis interventions in line with the agreed protocols (including remote delivery if the covid-19 pandemic requires) and supporting participants to adhere to the interventions. The training also will cover completion of all trial paperwork requirements including case report forms to assess intervention fidelity, Good Clinical Practice as applicable to research, maintenance of the site file and trial records, and reporting of serious adverse events, serious breaches, adverse events and protocol non-compliance.

In the pilot and feasibility trial, participants in the three clinician-supported intervention arms attended a mean of 2.3 consultations whereas the protocol permitted up to 6 sessions and adherence to exercises in the SMA-exercises arm was lower than adherence to orthoses in the SMA-orthoses arm (and adherence to exercises and orthoses in the SMA-combined arm). In the clinician training programme, we will therefore emphasise the importance of supervision and progression of exercises by utilising the available number of treatment sessions and strategies to improve adherence to exercises such as encouraging completion and review of exercise diaries. Throughout the training programme, we will emphasise the key characteristics of the therapeutic alliance that facilitate exercise adherence, including agreement on goals and tasks (goal setting), clear communication, a sense of connectedness, positive feedback, genuine interest, individualised care plans (including exploring specific barriers to exercise adherence), trust in the clinician and feeling empowered.[53,54]

The training will be supplemented by a comprehensive manual, providing clear treatment protocols and guidance for completing trial paperwork. Case Report Forms completed by clinicians to capture data on intervention delivery will be regularly audited against the treatment protocol to examine if the interventions are being delivered in accordance with the protocol. Individual feedback will be given to clinicians if required. Refresher training will be offered where needed. Additional training on remote delivery of interventions will also be provided if the covid-19 pandemic requires.

5 TRIAL SETTING

Participants will be recruited from NHS general practice, physiotherapy and podiatry services and from self-referral from within the community following an awareness raising campaign, within England and Scotland. Interventions will be delivered in TREADON treatment appointments that will be integrated into routine NHS physiotherapy and podiatry services. This will ensure sampling from a heterogeneous population spanning a range of area-level deprivation/affluence and a mix of urban, semi-rural and rural areas.

6 ELIGIBILITY CRITERIA

The target population is adults aged 18 years and over with PHP. Our inclusion/exclusion criteria are broad, and thus representative of a primary care population (Table 2). Only participants who have symptoms unlikely to be attributable to PHP, current/recent experience of the interventions, or for whom the interventions would be contraindicated/inappropriate will be excluded. There are no exclusions based on language and we will utilise local interpreter services (e.g. NHS, local authority) at all stages of data collection to ensure the trial is accessible to non-English speaking populations.

Eligibility for the trial has been informed by our pilot and feasibility trial.[33]

Table 2. Eligibility criteria (assessed by telephone eligibility screening)

Inclusion criteria
Adults aged 18 years and over
Self-reported localised pain under the heel which is worst when standing after rest and after prolonged weight-bearing
Symptom duration at least 4 weeks with pain ≥2 (0-10 Numeric Rating Scale [NRS])
Access to a mobile phone that can send/receive SMS text-messages or a landline telephone
Able and willing to participate and provide informed consent
Exclusion criteria
Inflammatory arthritis, systemic lupus erythematosus, gout, fibromyalgia
Heel pain of neurologic cause e.g. tarsal tunnel, entrapment neuropathy, radiculopathy
Serious pathologies requiring urgent medical attention (e.g. trauma, tumour, infection)
Current treatment or treatment in the last 3 months by a physiotherapist or podiatrist for PHP, or currently using a contoured foot orthosis
Previous surgery or awaiting surgery on the affected foot
Corticosteroid injection into the affected foot in the last 3 months
Extracorporeal shockwave therapy to the affected foot in the last 3 months
Unlikely to tolerate the interventions (e.g. allergies to common orthotic device materials) or unable to attend for treatment

7 TRIAL PROCEDURES

7.1 Recruitment

Patient identification

Potential participants will be identified based on the three methods that were employed successfully in our pilot and feasibility trial: 1) general practice consultation, 2) retrospective review of general practice medical records, 3) population survey.[33] In addition, and to further optimise recruitment, we will 4) screen referrals to NHS physiotherapy and podiatry services and, on the advice of our PPIE group, 5) identify participants through community advertising and self-referral. All recruitment arms will proceed in parallel until the required sample size is reached. See Figures 1-6 above for summary flowcharts of the five methods.

For recruitment methods 1-4, participating sites will either upload to REDCap or send a file, via secure transfer, to the Keele CTU team for upload upon sending survey invites. This will be on a regular basis (approximately weekly) for methods 1 & 4. Methods 2 & 3 will be sent when the search and mail out has been completed. These files are to include the Organisational Code, invite date and method of invitation for each patient sent an invitation to take part in the trial, plus NHS number, anonymised identifier, age, and sex where IT systems allow.. When screening questionnaires are received into the CTU (online or paper) the information from their consent to take part in the trial will be matched to the NHS number from the import to ensure that the correct patient is taking part in the trial and allows reminders to be sent from the sites to the correct patients (non-responders only). NHS numbers of those that do not respond to the trial invitation will be deleted.

Method 1 – Rolling monthly identification - General practice consultation: Foot/ankle pain consulters

Clinical System Protocol (Preferred method)

Potential participants will be identified through routine primary care consultation (face-to-face or telephone) about PHP at their general practice. Where possible, a study designed general practice clinical system protocol will automatically identify, screen and code potential participants aged 18 years and over. The protocol will trigger when specific SNOMED or Read codes are entered into a consultation, these codes are based on foot/ankle pain related diagnostic or symptomatic Read or SNOMED codes that were successfully used to identify adults with PHP in our pilot and feasibility trial.[33] As in our pilot and feasibility trial, a broad range of symptom codes will be used because foot/ankle consultations are often not coded with specific diagnostic labels such as PHP.[55] The protocol will automatically exclude those patients with potentially serious pathology (e.g. inflammatory arthritis, as listed in the exclusion criteria), potentially vulnerable patients. The clinician triggering the protocol will be asked to confirm if the patient is suffering from plantar heel pain and therefore eligible to receive further information. A clinical system search will be manually run approximately every 4 weeks to identify these eligible patients.

Clinical System Search

In practices where using a Clinical System protocol is not possible, a study designed clinical system search will be run to identify patients who have had a qualifying foot/ankle consultation in the last 4 weeks. For consistency, the search will utilise the exact same SNOMED/Read code lists that the protocol uses to identify (trigger) and for the automated exclusions. A practice clinician will then perform a manual screen of this list to confirm if plantar heel pain present.

Patient contact

Approximately every 4 weeks, the GP practice will send potentially eligible patients identified in the last 4 weeks, identified as above, an SMS text-message containing a link URL to the online screening survey pack(including the survey participant information leaflet, online consent to contact reply form and the screening survey), with a reminder SMS text-message to be sent within 7 days after the initial message.

Patients who do not have an active mobile number, or who have opted out of SMS contact from their GP practice, will be sent the screening survey pack by post (an invitation letter from their GP, survey participant information leaflet, postal consent to contact reply form and screening survey with a pre-paid return envelope) via Docmail, which is a standards-compliant hybrid mail service, providing document management and ISO 27001 secure mailings.

The screening survey will ask respondents to indicate the location of pain on a validated foot manikin[56,57] (© The University of Manchester 2000. All rights reserved) and complete questions regarding foot pain, demographic details and eligibility. For those completing the foot manikin online, the participant will select the location of pain on the foot manikin. For those completing a paper survey, the participant will shade directly the location of pain on the manikin, which will be read by overlaying a reliable coding template previously used in our foot pain research to identify PHP.[57]

Non-responders will be sent a reminder approximately four weeks after the initial invite. Pilot and feasibility trial recruitment rate: 6/10,000 practice population.[33]

Method 2 – Retrospective (1 year) general practice search: Foot/ankle pain consulters

The GP practice will run a study designed clinical system search to identify adults aged 18 years and over and have a SNOMED/Read coded consultation for foot/ankle pain in the preceding year. The clinical criteria of the search for inclusion and exclusion will utilise the same code lists used in Method 1.

The GP practice will then contact eligible screened patients via the SMS and Docmail methods outlined in method 1 above.

Non-responders will be sent a reminder approximately four weeks after the initial invite. Potential participants who appear eligible and who consent to contact will be sent a full trial information pack either online or postally. Pilot and feasibility trial recruitment rate: 2.6/10,000 practice population.[33]

Method 3 – General practice population survey

All adults registered at selected general practices will be contacted to identify those who had heel pain but had not consulted in the preceding year. Our data indicate that only 43% of people with PHP consult their GP[2]. The GP practice will run a clinical system study designed search to identify all registered adults (≥18 years of age and exclude potentially vulnerable patients), and GPs / primary care clinicians will screen lists to exclude potentially vulnerable patients. Patients will be contacted, and non-responders followed up, as described in Method 1 above. Pilot and feasibility trial recruitment rate: 27/10,000 practice population.[33]

Method 4 - Physiotherapy and podiatry referrals

To capture potential participants who have either been referred from primary care or self-referred to physiotherapy/podiatry, the NHS trust/Health Board will screen referrals against eligibility criteria to identify adults with PHP. Where IT systems allow, identified patients will be sent an SMS text-message from the physiotherapy/podiatry service providing a link URL to the online screening survey pack (including the survey participant information leaflet, online consent to contact reply form and the screening survey). Patients who are unable or unwilling to complete this online will be able to opt for postal completion. Where IT systems do not have SMS function, patients who do not have an active mobile number will be sent the screening survey pack by post from the physiotherapy/podiatry service or via Docmail. Non-responders will be sent a reminder approximately four weeks after the initial invite.

Method 5 – Self-referral from the community

Our PPIE group told us that not all individuals with PHP will consult about it. Therefore, to capture non-consulters, adults with PHP will be able to self-refer for consideration for the trial. Local communities around each participating NHS service will be provided with information about the trial via an awareness raising campaign. Informed by our previously successful awareness raising campaign in the HTA-funded EASE Back feasibility and pilot trial[58] and PROP OA trial[59] and PPIE feedback, information directing individuals to the research team's online/telephone contact details will be shared via social media (Facebook and Twitter), a trial website, local radio and newspapers, and flyers, posters in general practices, physiotherapy and podiatry practices, and community settings. Where possible, automated check-in screens for patients attending general practices, and waiting room display screens, will display information about the trial. Potential participants who register their interest via the trial website will be directed to the online screening survey pack (including the survey participant information leaflet, online consent to contact reply form and the screening survey).
Those contacting Keele CTU directly will be given the option to complete the screening survey either online or via post. Those wishing to complete online will be provided with a link URL to the online screening survey pack. Patients who are unable or unwilling to complete this online will be able to opt for postal completion. Non-responders will be sent a reminder approximately four weeks after the initial survey invite.

Duplicate invitations
All communications to the patients identified via methods 1-4 will be from the GP practice or NHS trust/Health Board. Whereby a patient is identified by their general practice via methods 1, 2 or 3, systematic searches will be conducted to ensure that potentially eligible participants will not receive duplicate invitations if identified via any of these methods. Invitation correspondence with potential participants will include a statement that we cannot completely eliminate the possibility of duplicate invitation.

Full trial information pack
Participants will be asked to indicate their preferred method of contact (for trial information and questionnaires), either as post or electronically, on their 'consent-to-contact' form. To facilitate online methods, email address and mobile number will be requested from those who prefer electronic contact.

The full trial information pack (which will be pre-coded with a participant trial ID number) will be sent to participants through a link URL or by post, depending on their preference, from Keele CTU and will include:

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

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

Telephone screening
Potential participants sent a full trial information pack by any of the five recruitment methods will be called by a clinical researcher, within 2-5 working days after sending the full trial information pack, to explain the trial, confirm eligibility and facilitate consent to participate. 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.
The completed trial consent form and baseline questionnaire will be returned to Keele CTU online or by post.

During this telephone contact the clinical researcher will check and confirm all eligibility criteria in order to ensure that only those who meet these criteria are recruited to the trial. A Telephone Eligibility Screening Form for all patients considered for inclusion will be completed. Information regarding age and sex at birth will be retained as unidentifiable variables 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 trial 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 by postal mailing, 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 trial team will not contact them again.

Prior to receiving verbal and subsequently written informed consent to trial participation, the clinical researcher must have established the patient's eligibility for inclusion (see section 6). The trial will be explained, as per the PIL, 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 clinical researcher will address any concerns or questions. Prior to receiving this telephone call, the patient will have received a copy of the PIL for them to read in their own time and consider.

Those patients who have verbally consented to take part in the trial will be asked to complete the baseline questionnaire included in the trial pack and return it to the research team along with a signed and dated consent form in the pre-paid envelope provided (or equivalent online correspondence). On receipt at Keele CTU, the authorised trial administrator will check it for completeness before the participant proceeds to the randomisation stage. Online correspondence checking will be performed by automated processes. 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 required correspondence. As described above in this section, 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 required correspondence, a letter, through a link URL or by postal mailing, will be sent to remind them to return their questionnaire.

7.2 Consent

Consent to full trial participation
A research team member 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 baseline pack and return to the research team either in electronic-consent online format or in the pre-paid envelope provided to those who opt for paper-based involvement. Patients who return an incomplete paper 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,[60] and the TREADON pilot and feasibility trial[33], with additional modification to incorporate an online correspondence option.

Patients who decline to participate during the telephone call will be thanked for their time and advised that they should contact their GP or referring physiotherapy/podiatry service 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.

The clinical researcher 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. Furthermore, the participant will remain free to withdraw from the trial at any time without giving reasons and without prejudicing any further treatment.

The signed (online authorised by patient) 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.

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 online or offline 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, through a link URL or by postal mailing, to remind them to return their online/offline paperwork.

Informed Consent Responsibilities
The Chief Investigator (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 trial and are out-with standard routine care at the participating site. 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.

7.3 Randomisation

Following confirmation of eligibility, receipt of a correctly completed and signed consent form and completed baseline questionnaire, participants will be randomly allocated to an intervention. Randomisation will be conducted by an authorised administrator (at site or CTU, depending on service preference) via REDCap. This is a secure web-based data collection system that uses a randomisation module; the randomisation sequence will be computer-generated (random block randomisation, stratified by identification method and geographical region). Emergency telephone backup will also be available. Allocation will be concealed from the blinded researchers, as outlined in section 7.4. Participants will be randomised on an equal 1:1:1:1 basis to one of the following interventions:

(i) Self-management advice (SMA) booklet (control arm)
(ii) SMA booklet plus individualised exercises (SMA-exercises)
(iii) SMA booklet plus pre-fabricated foot orthoses (SMA-orthoses)
(iv) SMA booklet plus individualised exercises and pre-fabricated foot orthoses (SMA-combined).

The following information will be required for randomisation:

- Participant details, including initials, sex at birth and date of birth
- Participant trial ID
- Name of person undertaking randomisation
- Confirmation of eligibility
- Confirmation of written informed consent and date
- Completed baseline questionnaire including participant recorded pain score
- Identification method and geographical region (stratification variables).

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

All participants who are randomised will be informed of their allocation through a link URL or in writing by postal mailing and receive a high quality SMA booklet. Participants in the SMA control arm will be posted an SMA booklet. Participants in the three treatment arms will be given an SMA booklet at their first treatment appointment. Where participants have been allocated to a treatment package which includes exercise and/ or orthotic device intervention, a coordinator member of the trial team will then liaise with the appropriate service and a first appointment for each trial participant will be made. This will take place through normal routine service channels. It is anticipated that the service will be responsible for notifying the participant of the date, time and location of their first appointment. We aim

to agree a maximum wait for treatment start of no more than 2 weeks following randomisation with participating sites. It is also anticipated that subsequent appointments will be managed through the normal routine service channels. Patients who DNA/UTA appointments will be offered further appointments as needed as part 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 trial. Participants allocated to the SMA booklet control arm will not be required to attend for any trial-specific clinical intervention.

Selection bias at recruitment will be avoided by the use of the following methods; all patients will receive identical trial information and questionnaires minimising the threat to participation bias from the different identification routes. A clinical researcher 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.

7.4 Blinding

It will not be possible to blind participants and treating clinicians (physiotherapists and podiatrists) to treatment allocation. Research staff involved in data collection and analyses (including the trial administrator overseeing collection of SMS text-messages, follow-up questionnaires and minimal data collection; data entry administrator; and a blinded lead statistician) will remain blind to treatment allocation until all data collection up to 12-month follow-up has been completed and the main intention-to-treat analyses of clinical effectiveness at 12 months performed. Statistical analysis of the primary outcome including interim analysis will be carried out by an (unblinded) trial statistician and separately by the (blinded) lead statistician with consensus agreement, and independently verified by a (blind) external statistician collaborator (with expertise in adaptive trials) to ensure the integrity of the trial evaluation. To ensure these research staff remain blind to treatment allocation, treatment arms in relevant databases will always be stored as a unique code and code break will be held within the REDCap database and a paper copy stored securely (only accessible to the Software Development Team; hidden from others who have access to the REDCap database).

7.5 Baseline data

The following forms will be completed prior to treatment:

- Informed consent form
- Eligibility Screening CRF
- Informed consent form for randomisation and intervention
- Participant baseline questionnaire.

7.6 Trial assessments

Table 3. Schedule of enrolment, interventions and assessments

		Enrolment		Randomisation		Post-randomisation					
Measure	**Description**	**Screening survey**	**Enrolment**	**Baseline pre-treatment**	**Random allocation and initial treatment**	**weekly text/call follow-up for 12 weeks/then monthly**	**Up to 6 clinician follow-ups**	**Weekly Diary**	**12 week follow-up**	**6 month follow-up**	**12 month follow-up**
Enrolment											
	Telephone screening		✓								
	Informed consent	✓	✓	✓							
	Random allocation				✓						
	Initial treatment visit				✓						
Participant descriptors											
Demographics	Date of birth, sex at birth	✓		✓					✓	✓	✓
Ethnicity	Ethnic origin			✓							
Body mass index	Height and weight			✓							
Typical activity, last week	Time on feet, hours per day			✓							
Previous PHP episodes	Number of episodes			✓							
Previous treatments received	Type and number, including exercise/orthotic device treatments: 2 questions			✓							
Current PHP episode description	Duration and severity: 2 questions	✓		✓							
	Laterality	✓		✓					✓	✓	✓

Preference for treatment intervention	Patient self-report: 2 questions	✓						
Clinical assessment								
Foot Posture Index-6	Foot posture		✓					
Interventions								
Self-management advice (SMA)			✓					
Self-management advice booklet plus individualised exercises (SMA-exercise)			✓	✓				
Self-management advice booklet plus prefabricated orthoses (SMA-orthoses)			✓	✓				
Self-management advice booklet plus individualised exercises and prefabricated orthoses (SMA-combined)			✓	✓				
Intervention adherence								
					✓	✓	✓	✓
Intervention credibility and satisfaction								
						✓	✓	✓
Adverse events related to interventions								
					✓	✓	✓	✓
Clinical outcome								
Plantar Heel Pain	Average plantar heel pain over the last 7 days using numeric rating scale (0-10 NRS) '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				✓	✓	✓
	Pain self-efficacy questionnaire, 10 items, 6 point scale		✓		✓	✓	✓
	Brief illness perception questionnaire, 8 items, 10 point scale		✓		✓	✓	✓
Foot pain	Foot Function Index pain subscale, 9 items, 10 point Likert scale		✓		✓	✓	✓
Presence and location of pain 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		✓		✓	✓	✓
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/presenteeism)	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, treatments and use of private healthcare				✓	✓	✓

7.7 Follow-up assessments

Outcome collection methods and time points

Text-messages weekly for 12 weeks, then monthly to month 12
All participants will be asked to respond to mobile phone SMS text-messages which will be automatically sent each week for 12 weeks, and monthly thereafter to month 12, to collect pain severity 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 team member 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 text/phone call will be recorded and no further contact at this attempt made.

96% of UK adults have a mobile phone (https://cybercrew.uk/blog/smartphone-usage-statistics-uk/) and previous research shows that weekly text-messages (followed by a telephone call for the first text-message that is not answered) had an 83% mean response rate.[49,61]

Weekly adherence Patient Diary for 12 weeks
All patients randomised to one of the three clinician-supported intervention arms will be asked to keep a weekly paper-based 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. Patients will be asked to return the diary to Keele CTU at 12 weeks, using a pre-paid envelope provided. If after 13 weeks, the patient still has not returned their diary a reminder will be sent by SMS text-message or by postal mailing.

Questionnaire at 12 Weeks, 6 months and 12 months
All participants will be asked to complete a self-report questionnaire 12 weeks, 6 months and 12 months after randomisation. The questionnaire (online or paper) will be sent to participants by Keele CTU at 12 weeks, 6 months and 12 months' post randomisation. Where a questionnaire has not been returned to Keele CTU within 10 days from link URL in SMS text-message/mail despatch, a reminder text-message, or postcard will be sent. Where a questionnaire is still not returned following this, a second questionnaire will be sent 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 trial team member by telephone approximately 3 weeks after the initial SMS text-message invite/mailing, during this phone call if participants decline to provide MDC over the phone they can be offered the choice to receive an online or postal MDC questionnaire. Where a participant is not able to be contacted by telephone, a MDC questionnaire will be sent through a link URL in an SMS text-message or by post. Participants will be asked to return the completed questionnaire (together with the patient diary at 12 weeks) to the Keele CTU, either online or using the pre-paid envelope.

7.8 Withdrawal criteria

Participants may withdraw from the trial at any time without giving reasons and without prejudicing any further treatment. Any information provided up to the point the participant withdraws will be included in the dataset and used unless the participant asks for their data to be destroyed.

Any discontinuation of exercise or orthoses interventions for any reason is not a reason for withdrawal from the trial.

7.9 Storage and analysis of samples

All data will be stored and anonymised in line with Keele CTU Quality Management Systems.

7.10 End of trial

The trial end is at the point at which the trial database is locked. CRF data will have been received by the data management team at Keele CTU and any data queries will have been resolved. Copies of CRFs will remain at each participating site. The Chief Investigator will notify the REC of the end of the trial within 90 days of trial completion.

8 STATISTICS AND DATA ANALYSIS

8.1 Sample size calculation

Up to 696 participants will be required to detect a small-to-moderate standardised between-group effect-size of 0.3 (equating to a minimum clinically important difference of 0.8 in average pain NRS over 6-12 weeks follow-up with anticipated standard deviation 2.7) in at least one clinician-supported intervention arm against the control arm (SMA booklet) with 90% probability, while controlling the probability of the overall type I error at 5% (one-sided).[62,63] The maximum sample size is based on equal allocation of participants, on the assumed, repeated measures correlation of 0.7, baseline-outcome correlation of 0.5[64], 20% loss to follow-up, and 70% response to SMS text-messages (informed by our pilot trial and previous trials). This accounts for multiple comparisons of each of the intervention arms to the control and **one formal interim analysis upon the primary outcome being observed for 348 participants** (87 per arm).[65] The total sample size of 696 also represents the maximum possible sample size under the 2-stage MAMS adaptive trial design; the minimum sample size being half of this if the trial is stopped (all three clinician-supported intervention-control interim evaluations yield between-group differences below the futility bound or at least one beyond the superiority bound) after the interim analysis; hence, the actual sample size will be in the range of 348 to 696. Extensive (>100,000) simulations indicate that the expected sample size varies between 415 and 532 participants. For logistical reasons, recruitment will not be suspended whilst the formal interim analysis is undertaken; to maintain momentum with recruitment, the trial will carry on recruiting and hence we anticipate, due to the expected lag of around 4 months (12-week data follow-up plus 4 weeks for data transfer, checking and interim analysis), approximately 100 further participants will have been recruited by the time of the interim decision-making. Hence, taking this lag into account, the revised minimum sample size would be about 448 and the expected sample size range would be about 490-610. If the efficacy boundary is crossed at the time of the interim analysis and the trial is stopped earlier, the conclusion on the efficacy of this treatment will be based on the test statistic (and the corresponding efficacy boundary value given in Section 8.3.2 below) at the time of the interim analysis and will not be affected by the data from the participants recruited after the interim analysis. The data from the stage-2 participants, however, in this case, will be included in the primary and secondary analysis to obtain more accurate treatment effect estimates.

8.2 Planned recruitment rate

Estimated recruitment rates: Based on our pilot and feasibility trial[33], we anticipate needing 45,000 adults to complete the screening survey, of whom a third will respond to express their interest (N=15,000). Approximately 10% of these will be potentially eligible (N=1500) and sent the full trial information pack, along with an additional 390 people identified by the general practice consultation method. After telephone eligibility screening, 696 people (37%) will be eligible and consent to participate. We will phase in recruitment over the first 4 months (with recruitment targets of 16, 22 and 28 participants respectively, then 30 per month). We anticipate identifying the required 1,900 potentially eligible patients from across up to 60 general practices (denominator adult population 420,000). This estimate is based on the three participant identification and recruitment methods used in our pilot and feasibility trial. However, the pool of potential participants will be increased by using

the additional recruitment methods (screening of physiotherapy/podiatry referrals and self-referral following community awareness-raising).

8.3 Statistical analysis plan

A comprehensive analysis plan will be developed and describe all trial analyses. It will be kept as a separate document to this protocol and represents the *a priori* analysis plan. It will be written using standard operating procedures for Keele CTU and an approved version 1.0 will be signed off by the TSC and DMC committees prior to the start of trial recruitment. Consequently, only a brief outline of the analysis plan is below.

8.3.1 Summary of baseline data and flow of patients

A CONSORT flow diagram, together with appropriate adaptive trial design extensions, will be produced to document the flow of participants through the trial and will include reasons for withdrawal if given. Serious or trial-related adverse events and protocol violations will be reported throughout the trial by treatment arm. Descriptive statistics will be used to describe the key baseline characteristics of participants included at each stage of recruitment and follow-up. The DMC will receive these data and serious or trial-related adverse events and protocol violations disaggregated by trial arm, prepared by the unblinded trial statistician.

8.3.2 Primary outcome analysis and decisions about adaptations to the trial

The main between-group evaluation for the primary outcome will be undertaken using linear mixed modelling adjusted for geographical region treatment site, identification method, age, sex at birth and baseline pain score, by ITT, analysing participants according to their randomised allocation. At stage 1, 87 participants will be recruited to each arm: if a clinician-supported intervention arm is shown to be inferior to control it will be dropped for futility i.e. if it is below the futility bound of t=0.000 (if all clinician-supported interventions are inferior [below the futility bound] the trial will be stopped); if one or more clinician-supported interventions are shown to be superior to control the trial will be stopped for efficacy (i.e. standardised mean group comparison test statistic is above 2.352 for at least one of the intervention arms (versus control), then the trial will be stopped and the arm with the highest test statistics will be recommended). If the trial continues, an additional 87 patients will be recruited to each remaining clinician-supported intervention arm and control. At the end of stage 2, the focus of the pain NRS evaluation will be on superiority testing against an efficacy boundary of t=2.218, and ensuring an overall one-sided 5% type 1 error; hence, if the standardised treatment effect statistic is above 2.218, then the corresponding treatment arm will be recommended. The testing boundaries are constructed under a generalised Dunnett testing procedure using a triangular efficacy boundary and binding futility boundary (i.e. if a test statistic for the corresponding treatment is crossing lower futility boundary, the treatment must be dropped at the interim analysis). If the test statistic for at least one of the treatments crosses the upper efficacy boundary at the time of the interim analysis, the trial will be stopped earlier. If the test statistics for more than one treatment cross the upper efficacy boundary (either at the time of interim or final analyses), all corresponding treatments will be concluded to be superior to the control. Interim and final analysis of the primary pain outcome will be carried out blind to treatment arm allocation and independently by two statisticians to support scientific integrity. As well as the primary endpoint evaluation of the 6-12 week between-group difference in pain severity, we will also evaluate as secondary analyses the between-group differences at individual time-points between weeks 1 to 12 through inclusion of a time x group interaction term. Follow-up pain NRS trajectories will be presented graphically to show the comparative summary data between treatment arms. Further to the primary endpoint (average 6-12 weeks pain NRS), sensitivity analysis of the final primary outcome comparison will include a comparison of complier average causal effect (to ascertain an unbiased estimate of explanatory treatment effect) and analysis of therapist random effects.

8.3.3 Secondary outcome analysis

Between-group evaluation of secondary outcomes will only be undertaken at the end of the trial. Analysis will be through linear and generalised mixed models with aligned link function appropriate to

the outcome data being analysed. Analysis will take into account patient-level clustering (repeated measures data) through patient-level random effect and the following fixed effects: geographical region, identification method, age, sex at birth, baseline pain score and corresponding baseline value (as appropriate). Reporting of numbers analysed at each follow-up stage will be given and summary descriptive statistics will be presented per treatment arm that align to the type of data e.g. mean (SD) and/or median (interquartile range) for numeric outcomes; frequency counts and percent per category per treatment arm for categorical outcome variables.

For all primary and secondary analyses, the main between-group estimates will be given along with 95% two-sided confidence intervals and p-values.

8.3.4 Subgroup analyses

Exploratory subgroup analyses of the primary pain outcome will also be carried out (including baseline symptom duration as a potential modifier of treatment effect); the full and exact specification of subgroup variables will be decided upon discussion with the TSC. These will be agreed *a priori* with the TSC and included in the Statistical Analysis Plan. In each case, subgroup variables will be represented in categorical form and exploratory statistical modelling of the subgroup effect will be through statistical interaction of the dummy treatment variable x subgroup variable.

8.3.5 Adjusted analysis

Analyses will take into account patient-level clustering (repeated measures data) through patient-level random effect and the following fixed effects: geographical region, identification method, age, sex at birth, baseline pain score and corresponding baseline value (as appropriate).

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

At stage 1, 87 participants will be recruited to each arm: if a clinician-supported intervention arm is shown to be inferior to control it will be dropped for futility i.e. if it is below the futility bound of t=0.000 (if all clinician-supported interventions are inferior [below the futility bound] the trial will be stopped); if one or more clinician-supported interventions are shown to be superior to control the trial will be stopped for efficacy (i.e. standardised mean group comparison test statistic is above 2.352 for at least one of the intervention arms (versus control), and the arm with the highest test statistics will be recommended). Any potential requirement to stop any trial arms for safety reasons will be closely monitored by the Data Monitoring Committee.

8.3.7 Participant population

All randomised participants will be analysed according to an ITT approach (analysed as randomised). For any outcome, participants will be included in an analysis if baseline and at least one follow-up measurement is available for that outcome.

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

The linear and generalised mixed models specified in sections 8.3.3 and 8.3.4 analyse all available data and assume that missingness is ‘missing at random’ (MAR) rather than ‘missing completely at random’ (MCAR). Patterns of missing primary outcome data will be explored to check the possibility of the data being ‘not missing at random’ (NMAR) to which a pattern-mixture model may be applied.

8.4 Economic evaluation

Health Economics Outcomes

Resource use information will comprise participant-specific costs for the type of intervention received including sessions attended and any other resources incurred as part of the intervention. PHP-related resource data will be collected for primary care consultations (e.g. GPs, practice nurses, First Contact Practitioner), visits to other professionals (e.g. hospital consultants, physiotherapists), private healthcare, prescribed medications and hospital-based tests and investigations and procedures, non-

drug treatments (e.g. injections) and inpatient stays. All costs will be collected via participant questionnaires at 6 and 12 months. Unit cost data will be derived from nationally represented sources such as the British National Formulary (BNF), the National Schedule for Reference Costs and the Unit Costs of Health and Social Care. Given the nature of the condition, broader costs related to both out of pocket costs (e.g., over the counter medications) and productivity losses (e.g., time-off work related to PHP and reduced work performance (presenteeism) will be collected. Information on time off work, occupation, typical work activities and the nature of their employment (full time or part time) will be requested, and the Single-Item Presenteeism Question from the Work Productivity and Activity Impairment Questionnaire will be used to estimate productivity losses relating to presenteeism. The average wage for each respondent will be identified using UK Standard Occupational Classification coding and annual earnings data for each job type.

Health Economic Analysis

A full health economics analysis plan (HEAP) will be written in parallel with the Statistical Analysis Plan, prior to the analyses. The plan will be agreed by the trial health economists, and other members of the trial and TSC/DMC prior to the analysis. Consequently, a brief outline of the data analysis plan is included in this protocol. An economic analysis will be undertaken alongside the trial to estimate the cost-effectiveness of the interventions in the final analysis and will adhere to the recommendations of the NICE Reference Case and these will be calculated using EQ-5D-5L responses.

The evaluation will take the form of an incremental cost-utility analysis to estimate the cost per quality adjusted life year (QALY) over 12 months follow-up using data from the trial. The base-case analysis will be from an NHS/personal social services (PSS) perspective, with an additional analysis from a wider societal perspective taking into account costs of productivity loss. The outcome of interest for the economic analysis is the quality-adjusted life years (QALYs), and utility data will be estimated using participant responses obtained from the EQ5D-5L questionnaire administered at all follow-up time points using the “area under the curve” approach. The crosswalk value set will be applied to patient responses to obtain utility scores, in line with current NICE recommendations. A cost-consequence analysis will initially be reported, describing all the important results relating to costs and consequences (across the full range of clinical and cost outcomes). Subsequently, incremental cost-utility analysis will be undertaken to estimate the incremental cost per QALY gained, adjusting for baseline covariates in line with the primary clinical evaluation. The robustness of the results will be explored using sensitivity analysis.

Final outcomes adjusting for the adaptive design of the trial will be expressed as incremental cost-effectiveness ratios (ICERs) using ICER plots and cost-effectiveness acceptability curves (CEACs) to represent the probability of being cost-effective at different willingness to pay thresholds. Given the limited consensus in analysing economic evaluations alongside adaptive multi-arm platform trials,[66,67] decision modelling will also be undertaken as a means of adjusting for the adaptive nature of the trial. The model will be updated as the trial progresses using the interim trial data, literature review of previous relevant models, and stakeholder consultations. The model will be subject to deterministic sensitivity and probabilistic sensitivity analyses in the final analysis. Cost-effectiveness planes and cost-effectiveness acceptability curves will be presented to show the probability the intervention is cost-effective at different cost/QALY thresholds. Full details of the model approach will be described in the HEAP.

9 DATA HANDLING

9.1 Data collection tools and source document identification

Self-report questionnaires (online and paper-based), treatment diaries, SMS text-messages and CRFs will form the basis of data collection.

9.2 Data handling and record keeping

Data management will be carried out in accordance with a Data Management Plan, in accordance with Keele University Health and Social Care Research (HSCR) Standard Operating Procedures (SOPs). The trial data will be stored on Keele University storage services within the UK and protected by industry standard security tools. All confidentiality arrangements adhere to relevant data protection regulations and guidelines (General Data Protection Regulation (GDPR), Caldicott, General Medical Council (GMC), Medical Research Council (MRC) UK Policy) and the Chief Investigator and the Data Custodian has responsibility for the use, security and management of all data generated by the study.

Questionnaires completed electronically will be date stamped electronically on receipt at Keele CTU. Paper-based questionnaires will be sent to the Keele CTU data management team in pre-paid envelopes provided to participants. Paper-based questionnaires will be date stamped on receipt at Keele CTU. Questionnaires will then be logged as returned on a management database and the participant's responses entered into the trial database; the database will be tested *a priori* for reliability. The trial statistician will determine coding of questionnaire items, in accordance with standardised coding procedures of Keele CTU, to facilitate data entry. Members of the research team will enter data and cross checks (a minimum of 1 in 10) will be carried out by other team members to ensure reliability and quality assessment of data entry.

The trial is designed so that all participant personal data (e.g. names, addresses, email addresses prior to de-identification) are located on a Keele REDCap database hosted by Amazon Web Services (AWS) secure web servers, restricted to authorised personnel. Furthermore, all data used for analysis will be kept separate from participant personal data to ensure anonymity to meet the necessary standards of the Keele CTU data security policy. Similarly, all hard copy information (e.g. signed consent forms, questionnaires) will be stored securely within the Keele CTU in accordance with Standard Operating Procedures (SOPs).

SMS text-messages will operate using a third party text service provider which adheres to the Data Protection Act 2018 as well as the EC Directive "Private and Electronic Communications Regulations 2003". Communication between Keele CTU's secure server and the text-message service provider is both encrypted and authenticated using a unique ID and password.

All protocol deviations are expected to be reported to Keele CTU as soon as the Investigator has become aware of the event. These will be reported accordingly to Keele University's SOPs.

The Data Management Team based at the Keele CTU will oversee all responsibilities delegated to the CTU for data management and data entered to the trial database.

9.3 Access to Data

Direct access to trial-specific data only will be given to authorised representatives of the Sponsor to permit trial monitoring and audit.

9.4 Data Sharing Agreements

Keele CTU is committed to sharing access to our anonymised research data derived from our population, consultation, clinical and RCT cohorts. Requests for access to the anonymised data from anyone outside of the trial team (e.g. collaboration, joint publication, data sharing requests from publishers) will be reviewed. All information will be held securely and in strict confidence. Each person in the trial will be given a unique trial ID so that data will not have any identifiable information, such as names and addresses. On this basis, these anonymised data will be kept electronically and may be used in other research studies.

9.5 Archiving

At the end of the trial, data will be securely archived in line with the Sponsor's procedures for 10 years after end of the trial declaration and until the sponsor authorises destruction. Archiving will be carried out in accordance with Keele University SOPs.

10 MONITORING & AUDIT

10.1 Trial Management

The TREADON trial is fully supported by Keele CTU, a UKCRC registered CTU. An experienced Trials Manager at Keele CTU will be responsible for day-to-day trial management, supported by a CTU Senior Trials Manager. The Trial Manager will support a Trial Coordinator at each of the collaborating academic sites who will liaise with general practices, physiotherapy and podiatry services, and research networks (CRNs and NHS Research Scotland Primary Care Network). The trial is sponsored by Keele University, and will be conducted in line with applicable Keele University Health and Social Care Research and Keele CTU SOPs. Keele CTU will provide trial services for: eligibility screening, consent, data collection and response management, data entry, follow-up administration and minimal data collection; IT to include database development, health informatics, data management, randomisation, and SMS text-message system; statistical design and analysis.

The Chief Investigator (Roddy) will be responsible for financial management of the trial, supported by Keele's Associate Investigator (Thomas), the Senior Trials Manager, Keele CTU and the School of Medicine Finance and Business Manager. Contracts will be developed and in place between the academic institutions and the NHS sites, to clearly articulate roles and responsibilities.

The Trial will be overseen by the Trial Management Group (TMG) chaired by the Chief Investigator (Roddy) or Keele's Associate Investigator (Thomas) and consist of representatives of all key groups involved in the design, operation and management of the trial. This group will meet monthly and will monitor progress along the planned timetable, discussing any issues as they arise and troubleshooting as required. Remote conferencing (e.g. Microsoft Teams) will be utilised for all TMG meetings, as required, to facilitate participation of co-investigators from all institutions.

The lead NIHR Clinical Research Network (CRN) for the delivery of the trial will be West Midlands (WM), with whom we have an excellent relationship. Their remit will involve the identification of sites and associated activities involved in site set-up and the recruitment of eligible participants. York/Humber CRN and the NHS Research Scotland Primary Care Network will work with the clinical teams within their local participating NHS services and local R&D teams. Our experience of working with other networks, includes receiving valuable advice and feedback on the feasibility of planned recruitment methods, and on efficient ways of securing Network infrastructure and service support to secure timely delivery of research. In addition, we engage with resources of West Midlands CRN Physiotherapy Research Facilitators who also provide targeted support for partnering NHS services, site set up and participating physiotherapists and podiatrists. This collaborative approach has been successful in a number of previous trials supported by Keele CTU (e.g. HTA-funded SCOPiC trial[68] and PROP OA trial[59]). We also support the NIHR CRN West Midlands to achieve 'time to target' and 'first patient in' targets contributing to the highest accrual of NHS patients involved in research nationally. CRN representatives will attend relevant TMG meetings.

An independent TSC that includes two patient representatives, and a DMC will be established and provide independent oversight of the trial. The TSC and DMC will meet initially at the start of the trial to approve the trial protocol and subsequently at regular intervals as agreed by the TSC/DMC.

10.1.1 Trial Steering Committee (TSC) members

See under Key Trial Contacts.

10.1.2 Data Monitoring Committee (DMC) members

See under Key Trial Contacts. The DMC may request to review overall unblinded safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

10.2 Monitoring arrangements

A trial Risk Assessment will inform a Trial Monitoring Plan. The Keele CTU data management team will perform data quality checks of CRF data. Data queries will be entered to a log which will be sent to the Trial Manager, who will work with each site to resolve data queries in a timely fashion and provide further training as required. This, along with safety reports, will inform a risk-based approach towards assessing a need for any onsite monitoring visits. Trial monitoring reports will be reviewed by the TMG, DMC and TSC.

10.3 Auditing procedures

Keele CTU will conduct internal audits across their research studies in line with the Keele CTU Quality Management System, following a risk-proportionate approach as appropriate.

10.4 Safety Reporting

Collaborating centres should record events or concerns about the safety of subjects that arise as a result of the trial, even if these events or concerns do not meet the definition of a Serious Adverse Event requiring notification to the regulatory authorities.

Adverse Events

The occurrence of adverse events considered to be related to the trial interventions for each intervention will be monitored and assessed using case report forms, contact with the trial team, physiotherapist/podiatrist report, and follow-up questionnaire. Expected adverse events from prefabricated orthoses include: blisters, skin irritation and transient lower limb discomfort during the initial ‘wear-in’ process. An expected adverse event from unaccustomed exercise and physical activity is temporary, mild muscle soreness. Physiotherapists and Podiatrists delivering the interventions will advise participants about how to manage such symptoms.

Serious Adverse Events (SAE)

An SAE is an untoward event that:

(a) results in death;
(b) is life threatening;
(c) requires hospitalisation or prolongation of existing hospitalisation;
(d) results in persistent or significant disability/incapacity;
(e) consists of a congenital anomaly/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), and to the Sponsor where, in the opinion of the Chief Investigator, the event was *related*, i.e. it resulted from administration of any of the research procedures, and was *unexpected*, i.e. the type of event is not an expected occurrence as a result of the intervention provided. There are no expected SAEs in this trial.

All SAEs considered to be potentially related to the trial procedures and occurring from the point when participants are registered on the trial will be notified to Keele CTU via telephone within 24 hours of the research staff at the site becoming aware of the event. Keele CTU will then provide the appropriate CRF and inform the CI. The CRF must be completed and returned to Keele CTU (via

secure transfer) within one week of receipt, and ideally within 24 hours. Clinicians will be asked to assess whether they considered the SAE was due to the trial procedures. Any follow-up information should be sent to Keele CTU as it is available. Events will be followed up until the event has been resolved or a final outcome has been reached. GPs will be asked in the letter that informs them of their patient's participation in the trial to report to Keele CTU any SAEs that they judge to be potentially related to TREADON trial procedures.

All SAEs either confirmed or suspected to be related to the trial procedures will be reviewed by the DMC and reported to the TSC.

Responsibilities for safety reporting

Investigator (PI) at site

- Using clinical judgement in assigning seriousness, causality.
- Ensuring that SAEs are recorded and reported to Keele CTU in line with requirements of the protocol.

Chief Investigator (CI)

- Clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk/benefit.
- Assessing seriousness and causality where it has not been possible to obtain local clinical assessment.
- Review of all related SAEs as detailed in the trial monitoring plan.

Keele CTU

- Central data collection and verification of related SAEs.
- Ensuring related SAEs are reported to the TSC and DMC.
- Preparing annual reports to the REC in collaboration with appropriate members of the TMG, and reports required by the sponsor.

10.5 Death notification form

All deaths occurring during the 12 week intervention period must be recorded on the Notification of Participant Death CRF. The trial team will respond to this upon notification, for example if death occurrence is reported by the treating physiotherapist/podiatrist or by a participant's family member contacting Keele CTU.

10.6 Trial timeline

The trial will be delivered over 51 months between January 2022 and March 2026.

10.7 Internal pilot phase

Our pilot and feasibility trial demonstrated feasibility of participant identification and recruitment, intervention fidelity, adherence, and retention at general practices and physiotherapy and podiatry services in the West Midlands.[33] We will undertake an internal pilot phase to test participant identification and recruitment, intervention fidelity, adherence to orthoses and exercises, and response to SMS text-messages across all geographical regions in England and Scotland.

Objectives: Specific objectives of the internal pilot phase of the trial are to:

1. check the numbers of recruited participants overall, per month and per region per month
2. explore intervention fidelity and participant adherence to exercises and orthoses
3. determine response to SMS text-messages.

Methods: The internal pilot will last for 6 months, commencing from the start of recruitment (month 10 of the trial timeline). All regions will participate in the internal pilot. Data collection methods will be as described above.

Outcomes: Outcomes of interest for the internal pilot include:

1. numbers of adults with plantar heel pain recruited (overall; per month; per region per month)
2. intervention fidelity measured by percentage of participants who received the allocated intervention
3. self-reported adherence to orthoses and exercises measured by the percentage reporting performing exercises and/or wearing orthoses as advised
4. response to SMS text-messages collecting primary outcome pain NRS data during weeks 6-12.

Sample size: Sixty participants are required across the three clinician-supported intervention arms to be able to estimate the proportion of patients adhering to exercises/orthoses with at least 80% confidence (lower limit 1-sided alpha 0.2) with a 5% margin of error, assuming adherence of 80%.

Progression criteria: A success criteria traffic-light system relating to the internal pilot trial objectives will be used to inform whether we stop at the stage of the internal pilot phase, proceed to the main trial (including the planned interim analyses) or proceed but with protocol amendments (Table 4).

Table 4. Internal pilot progression criteria

	Do not proceed to main trial	Proceed to main trial with protocol amendments	Proceed to main trial
Participant recruitment:			
Overall by month 6 of internal pilot recruitment	<78 (<50%)	79-155 (50-99%)	≥156 (≥100%)
Number recruited per month*	<15	15-29	≥30
Number recruited per region per month*	<5	5-9	≥10
Intervention fidelity:			
Received allocated treatment	<80%	81-99%	100%
Adherence to intervention:			
Performing exercises/wearing orthoses as advised	<60%	61-79%	≥80%
Follow-up:			
6-12 week SMS text-message response	<50%	51-69%	70%

*in months 4-6 of internal pilot allow for phased in recruitment over months 1-4.

11 ETHICAL AND TRIAL ADMINISTRATION

This clinical trial has been designed, and will be run, in accordance with the Principles of Good Clinical Practice. The lead Chief Investigator (Roddy) will ensure there is clear delegation of responsibilities within the trial team and will be supported by the lead academic representative (Thomas) and lead representatives from collaborating academic institutions (Hendry, Jaki, Keenan, Kigozi, Menz, Foster). The prefabricated orthoses used in the trial are CE-marked medical devices being used for their intended purpose.

We do not anticipate any major ethical concerns with this trial. All participants will receive at least self-management advice which accords with recommendations in a NICE Clinical Knowledge Summary for PHP[7]. In addition, some participants will also be randomised to receive individualised exercises and/or prefabricated orthoses which are already available within NHS clinical care. All interventions are deemed safe, with only minor expected adverse events (for example skin irritation from orthoses, muscle soreness from exercise) seen in our pilot and feasibility trial. Trial safety reporting procedures will ensure any unexpected serious adverse events which are deemed related to the trial will be reported to the Research Ethics Committee, Sponsor, TSC and DMC.

The trial requires the recruitment of patients identified within the NHS to an individually randomised trial involving the collection of primary patient-based data. The CTU will operate this activity in accordance with the Data Protection Act 2018, General Data Protection Regulation (GDPR), other relevant regulations and GCP guidelines. The CTU Secure Infrastructure has been independently audited and achieved level one of the Government backed Cyber Essentials Scheme. Keele University as the Sponsor has a quality management system in place containing standard operating procedures which will be adhered to in the conduct of the trial.

Potentially eligible patients will receive information about the trial and will have time to consider this prior to undertaking telephone screening and prior to providing written informed consent. Participants will be assured of confidentiality and participant identification details will not be made available to anyone outside the trial team. GPs, physiotherapists and podiatrists will be informed of their patients' willingness to be part of the trial (depending on the initial source of participant identification). Those who do not consent to be part of the trial or are ineligible will be asked for their consent to use the information already provided for the trial and given advice to consult their GP (or physiotherapist/podiatrist if identified from physiotherapy/podiatry referral screen) if their PHP continues to be troublesome.

All data collected during the course of the trial will be handled and stored in line with Keele CTU's Data Security procedures and SOPs, which are in accordance with the Data Protection Act 2018, GDPR, other relevant regulations and GCP guidelines. We will anonymise and archive the data for 10 years on a secure server at Keele University. Lead statistician, Lewis, will be the data custodian. We will make the data accessible to other researchers, in line with Keele CTU procedures.

11.1 Research Ethics Committee (REC) review & reports

Before the start of the trial, approval will be sought from a REC for the trial protocol, informed consent forms and patient self-report questionnaires.

- Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the trial (note that amendments may also need to be reviewed by NHS R&D departments before they can be implemented in practice at sites).
- All correspondence with the REC will be retained in the Sponsor Trial Management/local Investigator Site File.
- An annual progress report will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended.
- It is the Chief Investigator's responsibility to produce the annual reports as required.
- The Chief Investigator will notify the REC of the end of the trial.
- If the trial is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.
- Within one year after the end of the trial, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC.

11.2 Peer review

The trial has been funded by the NIHR HTA Programme through open competition and hence has undergone external peer review by appropriate patient and healthcare professional representatives.

11.3 Public and Patient Involvement

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

TREADON pilot and feasibility trial

Prior to the pilot and feasibility trial, we held an advisory workshop, which included four 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 Primary Care Centre Versus Arthritis (then Arthritis Research UK Primary Care Centre) PPIE 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 males and females regarding 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 advice booklet 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.

Patients/service users with PHP advised us about participant identification methods; design and content of patient-facing documentation including participant information leaflets, questionnaires and text-messages; and design of the exercise, foot orthoses and self-management advice treatments to maximise adherence.

Eleven clinicians and all four patients who participated in the workshop agreed to continuing involvement with the feasibility and pilot trial through membership of an advisory group. Via this advisory group, patients and clinicians have continued 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 contributed to optimising recruitment and retention in the feasibility and pilot 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 invited 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 helped to underpin fidelity of intervention protocols. Patient input to maximising follow up through mobile phone text messaging (or telephone call where preferred) was also sought.

For trial monitoring purposes, a patient was involved in the Trial Steering Committee (TSC) and discussion regarding use and dissemination of the findings. The Primary Care Centre Versus Arthritis (then Arthritis Research UK Primary Care Centre) has a User Support Worker and PPIE co-ordinator who helped to co-ordinate previous and continued PPIE work. They 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 held meetings with the advisory group and PPIE groups to ensure that they were involved with the interpretation of the results of the pilot and feasibility trial and any considerations for the future main randomised controlled trial design. Where appropriate dissemination of findings beyond the traditional academic routes was discussed.

TREADON main trial
We held a further advisory workshop in March 2020 in which members of our Research User Group with experience of plantar heel pain advised on the development of the funding application for this main trial. They told us about the substantial and often prolonged impact of plantar heel pain on their daily activities and work. They reported receiving little treatment from their GP: “I just got told to go away and put my foot up. Now I don’t even bother going to the GP”. The group shared their concerns about the need for effective treatment options that would give good pain relief. These observations form the basis of our agreed research question.

The group recognised the success of the three methods employed in our pilot and feasibility trial to identify potential participants through general practices. However, they told us that people do not necessarily seek health care for plantar heel pain and, following their advice, we have added community advertising, for example using social media, and self-referral as a route into the trial.

They also advised us about the trial’s outcome measures. They viewed pain reduction, but not necessarily pain resolution, as the most important outcome: “I just want to reduce the intensity of pain a bit, that’s the main thing because it affects life, what you do, where you go. I can’t even go out with the dog”. Whilst going to work was considered important, they advised us to examine whether people with plantar heel pain can do their job fully (work presenteeism) as they felt that plantar heel pain sufferers might attend work but have difficulty performing their job. They reviewed the wording of the SMS text-message which will be used to collect pain scores and agreed this was appropriate and acceptable. We also asked them how often the SMS text-message should be sent during the primary outcome phase (first 12 weeks of follow-up). They felt that weekly was best, as participants might forget how they had been if text-messages were sent less often.

The group reviewed the self-management advice booklet and the foot orthoses which they felt were acceptable and appropriate and did not recommend any changes. We discussed strategies to improve adherence to exercise. The group felt that communication about the importance of adherence was the key to optimising adherence and as a result we will modify the training programme to stress the importance of communication and the therapeutic alliance between participants and therapists to improve adherence (as well as other measures outlined in the research plan).

Lay co-investigator Brammar advised on the Plain English Summary.

11.4 Regulatory Compliance

The trial will be conducted in accordance with the principles of Good Clinical Practice (GCP) in research studies and the UK Policy Framework for Health and Social Care Research. Keele CTU have a quality management system in place containing standard operating procedures which will be adhered to in the conduct of the trial. Studies run by Keele CTU may be subject to an audit by Keele University as the Sponsor.

11.5 Protocol compliance

Non-compliance may be identified through any trial activity but in particular through the use of central monitoring procedures such as consent form review or data management, CRF review, site visits and self-reporting by the trial site or participants. Deviations from protocols and GCP may occur in research studies. 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 will be documented, and appropriate corrective and preventative actions will be taken by the research team with responsibility being taken by the CI and where needed with agreement from the TSC.

11.6 Notification of Serious Breaches to GCP and/or the trial protocol

Participating sites are expected to notify Keele CTU as soon as they become aware 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.

These will be reported accordingly to Keele University’s SOPs.

11.7 Data protection and patient 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 complies with data protection regulations:

- Appropriate storage, restricted access to disposal arrangements for participants personal and clinical details
- Consent from participants for access to their healthcare records by responsible individuals from the research staff or regulatory authorities, where it is relevant to trial participation
- Consent from participants for the data collected from the trial to be used to evaluate safety and develop new research
- All data collection forms that are transferred to and from Keele CTU will be coded with a trial number and will include up to three further participant identifiers: the participant’s sex at birth, initials and date of birth
- Where anonymisation (and/or appropriate pseudo-anonymised) of documentation is required, participating centres are responsible for ensuring only the instructed identifiers are present before sending to Keele CTU.

All data will be housed in the CTU infrastructure, which is a secure virtual network requiring two factor authentication in order to access the data stored within. Roles and permissions are applied to users within the network as well as within an application to restrict what data a user can access and operations they can perform. All research staff/CTU operational staff involved in this trial adhere to robust data security procedures and have explicit duties of confidentiality. These practices are written into their employment contracts and are equivalent to the duty placed on NHS staff.

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 trial analysis.

11.8 Financial and other competing interests for the Chief Investigator, PIs at each site and committee members for the overall trial management

Edward Roddy, Martin Thomas, Gordon Hendry and Anne-Marie Keenan have no financial or other competing interests to declare. The members of the TSC and DMC also have no financial or other competing interests to declare.

11.9 Indemnity

The trial is sponsored by Keele University and therefore Keele University will be liable for negligent harm caused by the design of the trial.

The NHS has a duty of care to patients treated, whether or not the patient is taking part in a trial, and the NHS organisation remains liable for clinical negligence and other negligent harm to patients under this duty of care.
Agreements between the Sponsor and participating NHS organisations detailing trial conduct and the responsibilities to be honoured by each party will be fully executed before the trial can start at the local NHS Trust/Health Board.

11.10 Amendments

The detailed protocol will be updated in response to approved amendments, as required. All amendments will be reviewed and authorised by the Sponsor and submitted for review or information to REC/HRA, as appropriate.

11.11 Post trial care

Participants allocated to intervention arms including prefabricated orthoses will be allowed to keep their orthoses after the end of the trial intervention period. The assessments and treatments by the physiotherapist or podiatrist will stop once the participant has completed the 12-week intervention period. Participants will not be offered further healthcare as part of their trial involvement once they have been discharged by their treating physiotherapist/podiatrist following their episode of care within the trial. The participants randomised to either exercise or foot orthoses will have the opportunity to continue with the advice and exercises given and/or continue to use the orthoses.

11.12 Access to the final trial dataset

At the end of the trial, archiving of essential trial documents at Keele University will be authorised by the Sponsor following submission of end of trial reports, which will be for ten years after the end of the trial. Destruction of essential documents will be carried out in accordance with Keele University SOPs.

All data will be held by Keele CTU and will be archived in the designated Keele CTU archive facility. Arrangements for the destruction of all confidential data will be carried out in accordance with Keele University SOPs.

Any subsequent requests for access to the data from anyone outside of Keele CTU (e.g. collaboration, joint publication, data sharing requests from publishers) will be carried out in accordance with Keele University SOPs.

12 DISSEMINATION POLICY

12.1 Dissemination policy

The findings of this randomised trial will be of direct relevance to patients with PHP and the GPs, physiotherapists and podiatrists in primary care who care for them.

Key outputs will be:

- new evidence regarding the clinical and cost-effectiveness of self-management advice (SMA), individualised exercises and prefabricated orthoses for the management of PHP in primary care which will directly inform treatment decisions
- a high-quality SMA booklet that can be used to provide information to people with PHP alongside other treatments
- training materials and treatment protocols to enhance the skills of physiotherapists and podiatrists to prescribe individualised exercises and prefabricated orthoses in the treatment of people with PHP
- dissemination of results as they become available via our website
- open-access publications in high quality peer-reviewed journals
- presentations at conferences attended by the most relevant stakeholders including GPs (e.g. Royal College of General Practitioners (RCGP) conference, Society for Academic Primary Care), podiatry (College of Podiatrists), physiotherapists (Physiotherapy UK) and rheumatology (e.g. British Society for Rheumatology (BSR))

- the team's strong links with patient, professional, third sector and NHS organisations will allow the evidence generated to influence national and international clinical guidelines
- working with our Research User Group (RUG), we will disseminate our findings in ways that will allow patients to better understand the effectiveness of pre-fabricated orthoses and individualised exercises for PHP.

Informing and engaging patients/service users, carers, NHS, Social Care organisations and the wider population

We will make all outputs from this work widely and freely available to all stakeholders, in ways that are easy to access at no cost. In addition to publication in open-access journals, we will use our website and social media, via our dedicated and widely followed Twitter and Facebook feeds, to support dissemination of our findings. Our lay co-investigator and RUG will advise on how to translate the findings into easily understandable messages and on how best to disseminate the results to the wider public. We have strong links with Versus Arthritis (formerly Arthritis Research UK), which will allow us to support patient and clinician education initiatives and promote best practice in the management of musculoskeletal disorders. The team has strong links with patients, NHS organisations and into the key professional networks needed to engage patient, clinical and professional partners, facilitating dissemination to all stakeholders and allowing us to influence national and international clinical guidelines. The trial investigators include members of national (e.g. NICE) guideline groups and work closely with the RCGP, College of Podiatry, Chartered Society of Physiotherapy, Primary Care Rheumatology and Musculoskeletal Medicine Society, and British Society for Rheumatology. The TMG also includes international team members who will facilitate dissemination internationally.

Informing the health and care system and society as a whole

Informed by NIHR 'Push the Pace' guidance, dissemination of the outputs arising from this research will be supported by the Impact Accelerator Unit (IAU) within Keele University's School of Medicine. The IAU, led by Dziedzic, NICE Fellow and NIHR Knowledge Mobilisation Fellow and Senior Investigator, has a strong multidisciplinary team of experts in implementation and knowledge mobilisation and works with local, regional, national and international bodies to support proactive translation of research into clinical practice. Previous projects include STarT Back and JIGSAW-E implementation (https://www.keele.ac.uk/pcsc/research/impactacceleratorunit/projects/) which have been adopted into national and international guidelines and widely taken up into clinical practice. We are committed to ensuring our research influences clinical practice and guidelines. With the support of the IAU, we will seek to optimise dissemination to facilitate translation into clinical practice. Existing strong NHS partnerships will ensure that the research findings are made readily available to general practitioners, physiotherapists, podiatrists, rheumatologists and Integrated Care Systems (ICSs). We will work closely with the NIHR Applied Research Collaborations (co-investigator Mallen is West Midlands long-term conditions theme lead), Academic Health Science Network (AHSN), RCGP, College of Podiatry, Chartered Society of Physiotherapy and British Society for Rheumatology to support uptake of the findings. We have very strong links, formalised through our NHS Consortium, ICSs (via our former links with CCGs), NHS Trusts (including community Trusts with experience of recruiting to RCTs), Public Health England and the Sustainability and Transformation Partnership. A shared research strategy ensures relevant research findings are 'pulled' into our key partnerships and established as routine practice.

Further funding/support options

Our extensive networks, described above, will allow us to rapidly disseminate findings and maximise impact. The team includes opinion leaders capable of driving dissemination and, by working with the AHSN, IAU, Versus Arthritis and professional bodies (e.g. Royal College of Podiatry, Chartered Society of Physiotherapy) we can draw on additional expert resource to pump prime rapid adoption into clinical and guidelines. Depending on the trial findings, we will apply to the AHSN to support wider roll out and to develop educational initiatives to support implementation. We have an established track record in this area, influencing national and international clinical and commissioning guidance through our research.

Potential barriers to future research, development, adoption and implementation
All background intellectual property (IP) relating to this trial is held by Keele University. All foreground IP will be managed by Keele University. Keele University is involved in building a research framework into the Integrated Care System model, and chair a Staffordshire and Shropshire Health Economy Research Partnership (SSHERPA) to deliver a joint research strategy. Keele University will ensure that all outputs from the proposed trial are clearly identified, disseminated broadly and made freely available to policymakers, the public and health care professionals. Early identification of potential IP is supported by Keele's Partnership Development team who are responsible for identifying and supporting knowledge transfer opportunities, IP protection, dissemination and NHS partnerships. The aim of our joint free and open-access IP policy is to actively facilitate rapid translation of research into clinical practice for the benefit of patients, clinicians and NHS services. We do not anticipate any regulatory hurdles to dissemination or adoption of the research outputs into clinical practice. However, we recognise that achieving behaviour change in clinicians is challenging. The questions we will answer are of direct interest to our wider stakeholder group. Harnessing the combined strengths of our collaborating academic institutions and working with key professional bodies and organisations committed to getting research into practice (e.g. AHSN, NIHR Applied Research Collaborations) will facilitate translation of our findings into changes in clinical practice and minimise barriers to uptake.

Potential impact of research
This work will impact on a broad range of stakeholders including patients, clinicians, and healthcare commissioners. It was co-designed with patients to ensure relevance and to maximise potential future impact. Current recommendations for primary care management of PHP advocate initial treatment with analgesia and advice, with referral to a physiotherapist or podiatrist only recommended if symptoms persist beyond a few months. Patients often experience chronic symptoms and inability to work, yet few are referred to a physiotherapist or podiatrist. However, evidence regarding the effectiveness of SMA, individualised exercises and prefabricated orthoses, alone or in combination, is limited. By addressing this evidence gap, we will help patients and clinicians better understand the effectiveness of these interventions for PHP and allow them to make more informed treatment decisions. Healthcare commissioners will be provided with evidence of the clinical and cost-effectiveness of these interventions on which to base the commissioning of services, increasing the availability of these treatments for people with PHP. At the end of the trial, training materials and treatment protocols will be readily and immediately available and we will be well placed to support scale-up of the training programme to enable physiotherapists and podiatrists to deliver evidence-based treatment for PHP.

Sharing trial progress and results with trial participants
We will share our trial findings with participants via our website, dedicated social media feeds (Facebook, Twitter) and posters in participating general practices and physiotherapy and podiatry services. Our lay co-investigator and RUG will advise us on how best to disseminate the results to participants and the wider public and will help us to translate the findings into easily understandable messages. We will provide a summary to all trial participants describing the trial findings.

12.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship will be available to those who fulfil the International Committee of Medical Journal Editors (ICMJE) criteria (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html) and in accordance with the requirements and guidance for authors from the NIHR Journals Library (https://www.journalslibrary.nihr.ac.uk/information-for-authors/).

Staff heavily involved in the practicalities of trial operationalisation and delivery, including dedicated study co-ordinators, will be considered for co-authorship of protocol papers on the condition they can contribute to critical revision of drafts, approve the final version, and be accountable for the content. Professional writers will not be used.

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14. APPENDICIES

14.1 Appendix 1 - Trial management / responsibilities

We are a multi-disciplinary team with representation from general practice, rheumatology, physiotherapy, podiatry, biostatistics, health economics, adaptive trial design, and PPIE. We have internationally-recognised expertise in PHP, exercise interventions, foot orthoses, and RCT design and delivery. We have an experienced lay co-investigator with strong institutional PPIE support. Keele CTU has expertise in delivering large RCTs in primary care.

The trial requires considerable understanding of PHP, exercise interventions, and orthoses in the context of primary care and NHS physiotherapy and podiatry services and the co-investigator team and collaborators have this relevant expertise. Roddy, Keenan, Hendry, and Menz are international leaders in the fields of musculoskeletal foot problems including PHP. We have extensive clinical and research expertise in exercise interventions (Foster, Holden, Thomas) and foot orthoses (Keenan, Hendry, Menz) for musculoskeletal problems, and extensive expertise in primary care and musculoskeletal health (Mallen, Foster, Roddy, Keenan, Menz).

The team also has extensive experience and expertise in trial methodology (Lewis, Foster, Menz, Roddy, Keenan, Mallen), adaptive trial design (Jaki, Mozgunov, Burnett), biostatistics (Lewis), and health economics (Kigozi). Our PPIE co-investigator (Brammar) will ensure the patient perspective is heard throughout the whole research process.

We have a strong track record of successful delivery of trials with high recruitment and follow-up rates, including in musculoskeletal and foot problems in primary care and trials using adaptive designs.[48,49,68-74] Our research is published in the top medical journals (e.g. Lancet, BMJ). Keele CTU has extensive experience in delivering trials in this field and has established NHS and University links. Recent trials in this field supported by Keele CTU recruited to target demonstrating our ability to deliver this trial in successful partnership with NHS clinicians and services and CRNs.

Roddy (Chief Investigator (CI)) will have overall responsibility for the trial. Thomas has completed a NIHR Development and Skills Enhancement Award in Clinical Trials (2020-2021), a stated goal of which was to be Academic Principal Investigator of the TREADON trial, if funded, under the supervision of Roddy. He will work closely with Keele CTU and the PIs for Glasgow (Hendry) and Leeds (Keenan) to provide day-to-day trial oversight. Foster, Hendry, Holden, Keenan, Thomas, and Menz will design and deliver the training programme for trial physiotherapists and podiatrists, building on the programme used in our pilot and feasibility trial.

Lewis (statistical lead) will be responsible for generating the statistical analysis plan, TSC/DMC reports, conducting data analysis, and supervising the junior statistician. Mozgunov, Jaki and Burnett will provide expertise in adaptive trial design and analysis and will support Lewis and junior statistician to undertake the interim and final analyses. Kigozi will undertake the economic evaluation. Brammar, our PPIE representative, will ensure the patient view actively informs the whole of the trial, supported by Thomas (PPIE lead).

Contribution of collaborators: Dr Thomas Burnett (University of Bath) will provide further expertise in adaptive trial design and analysis and will support co-investigator Mozgunov and Jaki. Professor Hylton Menz (La Trobe University, Melbourne, Australia) is an international leader in podiatry and will contribute considerable expertise and experience in plantar heel pain, randomised trials and foot orthoses.