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TRIAL PROTOCOL

Full title: Orthotics for Treatment of Symptomatic Flat Feet in Children (OSTRICH)

Authorised by
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Role: Chief Investigator

Signature: Date:

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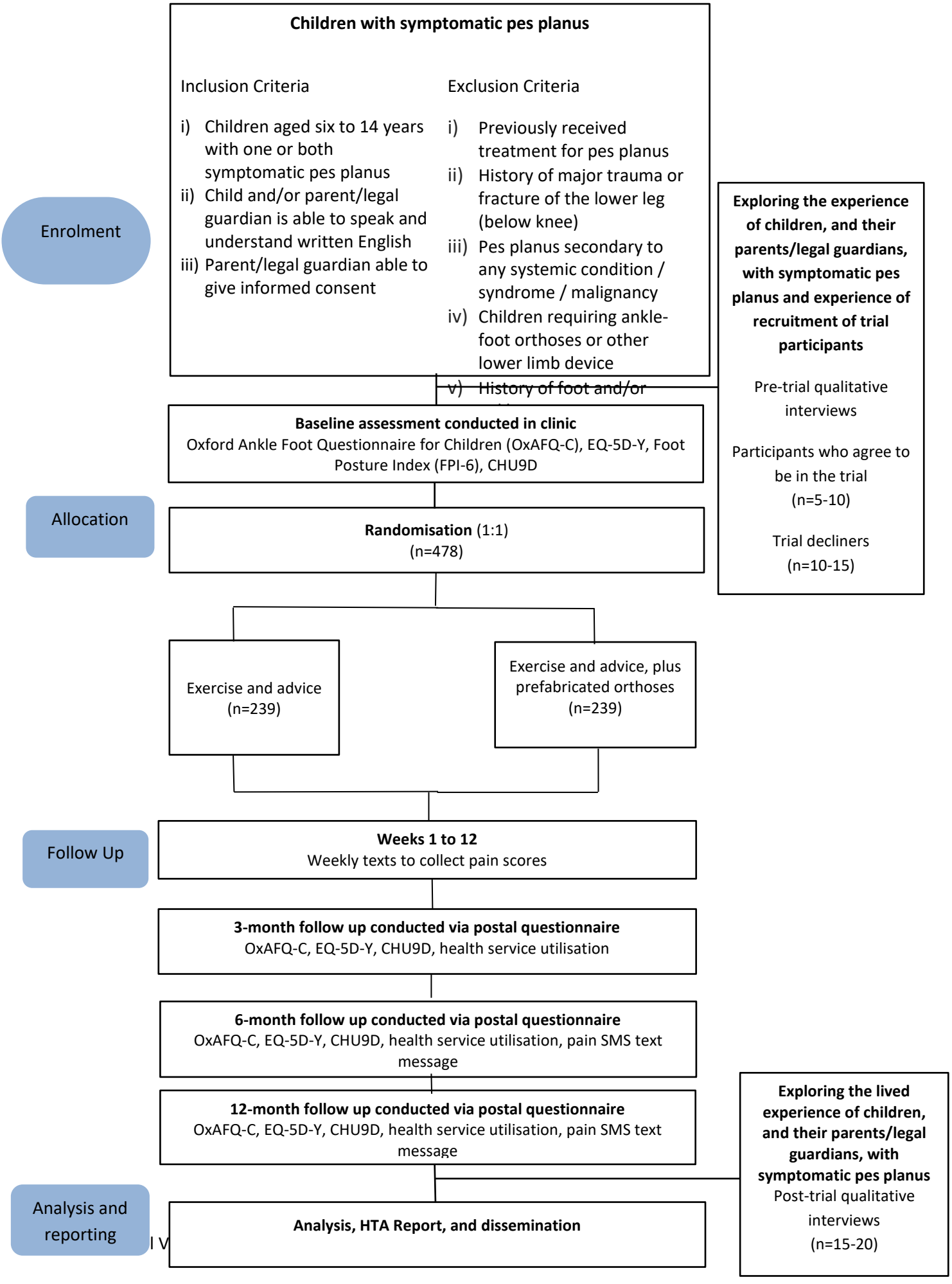
3. Trial summary

3.1 Trial summary table

Acronym	OSTRICH
Long title	Orthotics for Treatment of Symptomatic Flat Feet in Children
Study design	A multi-centre, two-armed, pragmatic, individually randomised controlled trial, with an internal pilot, economic evaluation, and qualitative study.
Setting	Any primary or secondary care outpatient clinic or Social Enterprises or Community Interest Companies providing care for children with symptomatic pes planus.
Target population	Children aged between six and 14 years who have symptomatic pes planus.
Interventions	i) Prefabricated orthoses plus exercise and advice ii) Exercise and advice, which will include a standardised exercise programme and advice regarding footwear
Primary outcome	Physical domain subscale of the Oxford Ankle Foot Questionnaire for Children (OxAFQ-C) over the 12-month follow-up period.
Secondary outcomes	*Clinical evaluation:* 'School and Play' and 'Emotional' subscales, and 'Footwear' item of the OxAFQ-C; pain score *Economic evaluation:* Healthcare resource use, EQ-5D-Y, CHU9D and costs *Qualitative study:* Parental/legal guardian and child experiences and management of pes planus
Estimated recruitment period and sites	May 2021 to March 2023 (subject to impact of Covid-19 pandemic). Approximately 18 sites
Duration per patient	12 months
Estimate total trial duration	42 months
Number of participants	478 in a ratio of 1:1 (239:239)

Inclusion criteria	Children aged between six and 14 years inclusive; Child and/or parent/legal guardian able to speak and understand written English; Have one or both symptomatic pes planus; Parent/legal guardian is able to give informed consent.
Exclusion criteria	Previously received any treatment for symptomatic pes planus (i.e any child who within the last three months, has been taking part in an exercise intervention or has used health professional prescribed insoles). History of major trauma or fracture of the lower leg (below knee); Pes planus secondary to any systemic condition/syndrome/malignancy; History of foot and ankle surgery; Children requiring ankle-foot orthoses or other lower limb device.
SWATs	One SWAT will evaluate the use of a multimedia interface to convey information to potential participants as part of the recruitment process. A second SWAT will evaluate a birthday card on response rates to postal questionnaires.

3.2 Study Flow Chart OSTRICH: Orthotics for children with symptomatic pes planus



3.3 Assessment schedule

	Pre-trial	Baseline	Weeks 1-12	3 months	6 months	12 months	Ad hoc
Qualitative interviews	x					x	
Eligibility screen		x					
Informed consent		x					
Demographic questions: e.g. date of birth, sex, ethnicity		x					
Personal details: name, address, parent's/legal guardian's mobile telephone number		x					
FPI, static single leg balance		x					
OxAFQ-C		x		x	x	x	
EQ-5D-Y		x		x	x	x	
CHU9D		x		x	x	x	
Health service resource use		x		x	x	x	
Randomisation		x					
Dispense foot orthoses		x					
Give advice and prescribe exercises		x					

	Pre-trial	Baseline	Weeks 1-12	3 months	6 months	12 months	Ad hoc
Weekly pain SMS text to parent/legal guardian			x		x		
Pain score				x	x	x	
Adherence				x	x	x	
Adverse events			x	x	x	x	x

3.4 Lay summary

As a child grows the shape of their foot changes and most develop an arch in their foot. For some, however, the arch does not fully form or it might be flat against the ground. When this happens, it is known as having flat feet which can cause pain in the feet, legs, or back. At the moment, we are not sure what the best treatment for flat feet is, so the purpose of this research is to conduct a trial to compare two of the most common treatments that are used today. The first is exercise and advice about things like which types of shoes might help. The second of the treatments we are going to test is a type of insole, which is put inside the shoe.

If a child or young person and their parent or guardian decide that they would like to take part in the trial, they will receive their treatment as part of their normal NHS care. We would like to find 478 children and young people aged between six and 14 years to take part in the study. Everyone will receive advice about the type of shoes to wear, exercises and foot health advice for children with painful flat feet. In addition to this, half of the participants will receive an insole. We will ask for their help for 12 months. During this time, we will track their progress by sending them three questionnaires in the post to fill in and we will send them weekly SMS text messages to find out how painful the children's feet are during the first few months. We also want to learn more about the problems that flat feet cause, and children's experiences of the treatments delivered as part of this clinical trial. We will explore this through in-depth conversations with children and their parent(s) or the person who looks after them. Once we have finished the trial, we will work with the people who took part in the trial, and clinicians, to make sure that our results can be used by as many people as possible.

4. Background

The main aim of this study is to undertake a large, pragmatic, two-armed, randomised controlled trial to assess the clinical and cost-effectiveness of therapeutic orthoses for children with symptomatic pes planus.

4.1 What is the problem being addressed?

In most children, pes planus (flat feet) are physiologically normal, asymptomatic, and part of the typical developmental trajectory of the feet (1, 2). However, a substantial number of children, estimated at 1%, develop symptoms associated with their foot posture (3). In addition to foot and ankle pain, children often report pain elsewhere in their legs and lower back, tiredness in their legs and being able to walk reduced distances in comparison to their peers; all of which can lead to reduced engagement with physical and childhood activities (4). Ensuring that the burden of foot and ankle pain in children with symptomatic pes planus is effectively managed is essential to keep children active and support their healthy physical, social and psychological development (5).

Pes planus have been described as one of the most common conditions seen in paediatric practice (6, 7) and the most common reason for attending paediatric orthopaedic clinics (8). There has long been debate about how children with symptomatic pes planus should be managed, or whether symptoms will resolve without intervention. A recent Delphi exercise suggests that the international consensus is that clinical intervention is warranted for

children presenting with symptomatic pes planus (9-11) despite repeated systematic reviews highlighting the lack of evidence informing this position or evaluating individual therapies (7, 11, 12). Currently, management options for symptomatic pes planus vary considerably across the country. Corrective surgery remains rare but exercise, foot orthoses, and advice regarding suitable footwear appear common in line with the international consensus, (12, 13) although important aspects of each treatment modality vary between and within centres. A recent update (12) to the existing systematic review for paediatric pes planus re-iterated the need for "robust, adequately powered randomised trials to inform current evidence" (7, 12). The aim of this study is to undertake a large, pragmatic, two-armed, randomised controlled trial to assess the clinical effectiveness and cost-effectiveness of therapeutic orthoses for children with symptomatic pes planus.

4.2 Primary objective

The primary objective of this study is to compare the clinical effectiveness of prefabricated orthoses in addition to exercise and advice with exercise and advice alone on the physical functioning of children with symptomatic pes planus, as measured by the physical domain of the OxAFQ-C.

4.3 Secondary objectives

- To undertake a development phase to (i) develop a healthcare professional training package; and (ii) compile a menu of acceptable orthoses and exercises to be used in the trial.
- Conduct an internal feasibility phase to review recruitment and retention, and if necessary modify trial practices.
- Compare the effectiveness of prefabricated orthoses in addition to exercise and advice, with exercise and advice alone on:
    a) physical domain of the OxAFQ-C
    b) the other domains of the OxAFQ-C
    c) the EQ-5D-Y
    d) child-reported foot pain as measured by Wong-Baker FACES Pain Rating Scale (0 to 10) for both the left and right foot
    e) parent/carer-reported child foot pain via the question "On average, how would you rate your child's foot pain in relation to their left/right foot over the past week?" on a scale of 0=no pain to 9=worst pain imaginable
    f) foot pain as measured by 12 weekly SMS text messages sent to/from the child/young person's parent/legal guardian with an NRS scale from 0 to 9 (no pain to worst pain imaginable) and a single text at six and 12 months
    g) CHU9D.

- Estimate the cost-effectiveness of the prefabricated orthoses compared with exercise and advice.
- Use qualitative approaches to (i) understand the experiences of children and young people with symptomatic pes planus and their parents/legal guardians, explore common strategies to manage the condition, impact on child and family behaviours/choices such as social participation, and experience of using the interventions in the trial; and (ii) explore with clinicians the barriers and facilitators

to delivering the trial, conducting future trials in this population and implementing the trial's results in clinical practice.

- To undertake an assessment of fidelity and acceptability of the intervention using qualitative interviews, direct observations, and an intervention delivery case report form.
- Undertake two SWATs to aid recruitment and retention to the trial.

5. Study design

5.1 Study design

OSTRICH is a multi-centre, two-armed, pragmatic, individually randomised, controlled trial. It includes an internal feasibility phase, economic evaluation, and qualitative study.

5.2 The OSTRICH development phase

During the first 12 months of the study, prior to the start of recruitment, we will undertake the following activities in preparation for the trial:

5.2.1 Clinician survey

We will undertake a survey of podiatrists, orthotists, physiotherapists and paediatric orthopaedic and podiatric surgeons from participating sites, to ascertain, for children with symptomatic pes planus, (1) the most frequently prescribed orthoses (prefabricated and custom) and types of orthoses previously used, (2) the type of exercises prescribed, and (3) the type of footwear advice given. The survey will be designed by the research team and will be piloted in the same professions we plan to survey. Invitations to participate in the survey will be sent to sites that have expressed an interest in taking part in the study. To be eligible to complete the survey, participants should be working within an NHS setting, registered with a professional body and be able to access the online survey. The survey will consist of a mixture of closed and open-ended questions and will be developed by the OSTRICH clinicians, who are experienced in treating children with symptomatic pes planus. A definition of what a prefabricated and custom-made orthoses is will be provided. Demographic data such as sex, profession, training and experience and average number of children with pes planus seen per month, will be collected from the respondents. Consent to take part in the survey will be implied by completion of the survey. If survey participants request, we will send them a summary of the survey's findings.

5.2.2 Consensus development phase

We will hold two consensus group meetings using a modified nominal group technique methodology. The group will consist of orthotists, podiatrists, physiotherapists, and paediatric orthopaedic and podiatric surgeons who are involved in the management of symptomatic pes planus at participating sites as well as patient representatives. The group will be informed of the results of the survey and will be shown samples of orthoses in order to help them reach an informed agreement on the recommended 'menu' of orthotics, exercises and footwear advice to be used in the trial.

5.3 Identification of sites

We will conduct the study in NHS outpatient clinics, in either primary or secondary care within the United Kingdom (UK), or Social Enterprises or Community Interest Companies

(who provide services for NHS patients), which treat children with symptomatic pes planus and are able to provide the trial interventions. We will aim to recruit sites covering a range of clinical professions (podiatrists, orthotists, physiotherapists and orthopaedic surgeons). Thirty NHS Trusts expressed an interest in the study at the grant application stage, which is more than the 18 we anticipate we will require. However, if additional sites are required, we will ask the local Clinical Research Network (CRN) for assistance or members of the study team will use their contacts to approach potential sites. A Principal Investigator (PI) will be identified for each site. The PI will then invite suitably qualified health professionals to be part of the local research delivery team. This may occur in consultation with the local Research and Innovation team. Being part of the local research delivery team will be voluntary and health professionals can decline the invitation if they wish.

5.4 Identification of participants to receive an invitation mail out

Potential participants will be identified by searching either electronic or paper patient medical notes or from on-going referrals for the treatment of flat feet to the NHS outpatient clinics taking part in this study. Patients will be eligible for an invitation mailing if they are aged between six and 14 years and have been referred for the treatment of symptomatic pes planus. Patients who have previously received any treatment for symptomatic pes planus will be ineligible for this mail out. Patient identification sites may be used if required.

All patients who are identified by the recruiting site as eligible for an invitation mailing will be sent an invitation pack (letter of invitation, participant information sheet(s), consent form, and baseline questionnaire) by the sites asking if they would like to take part in the OSTRICH study. The letter will invite potential participants to a clinic appointment, where participation in the study will be discussed and consent sought. This appointment forms part of the usual treatment pathway following a referral, and so will take place regardless of whether the participant is interested in the trial or not. Age appropriate participant information sheets will be sent; for example, one for the parent/legal guardian, and one for those aged 6-10 or aged 11-14. All identifiable information will be held solely in the NHS until written consent has been obtained from participants and/or parent/legal guardian. Members of the research team may, if they wish telephone the potential participant to check if they have received the invitation pack and answer any provisional questions they have.

Alternatively, if a patient presents in clinic, and they are found to have symptomatic flat feet, and they have not been sent information in the post, the clinician may give them the documents in the recruitment pack in the clinic. If having read the study documentation, they are willing to take part in the study, they may be recruited and randomised on the same day. Alternatively they may take the documentation home with them to consider trial participation, and if willing to take part a further clinic appointment made to enrol them in the study.

5.5 Declining participation in the study

Participation in the OSTRICH study is voluntary. Patients who do not wish to take part in the study can decline. They will inform the treating clinician about their decision not to take part in the study at their clinic appointment. Reasons for non-participation will be recorded where these are provided, but the patient does not have to provide a reason. Patients who

decline will not have to return any forms to the York Trials Unit (YTU). However, where possible, we will collect screening data for these patients. They will also be given the opportunity to take part in a qualitative interview to explore the reasons for non-consent into the trial and treatment preferences.

5.6 People who wish to take part in the study

When the patient and their parent/legal guardian attend the clinic appointment, the treating clinician, who has experience of working with children/young people, will explain the study and answer any questions they may have. The individual trial activities will be explained to the child/young person in a suitable language. If the child or young person does not wish to take part, they will not be enrolled into the study. If the patient and their parent/legal guardian is willing to take part in the trial, then the treating clinician, research nurse or trial associate will obtain written informed consent and the participant and their parent/legal guardian will complete a questionnaire. YTU will inform the participant's General Practitioner (GP) of their participation in the study. This is standard practice and is undertaken to ensure that the GP: (i) is fully aware that the patient is taking part in the trial; (ii) is provided with a description of the trial including the care the patient may receive; (iii) provides an extra point of contact should the patient have any further questions; and (iv) continues to be able to provide coordinated care for participants.

5.6.1 Informed consent and completion of the consent and assent form

Consent will be sought from the child/young person's parent/legal guardian. Clinicians will be encouraged to seek written assent from children and young people who want to participate in the trial.

Qualitative interviews: The qualitative researcher will obtain written informed consent for the qualitative interviews, from the parent/legal guardian and will be encouraged to seek written assent from children and young people who want to participate in the interview. Interviewers will be sensitive to the issues that may arise from the interviews and will adapt their interview technique accordingly to children of all ages.

Clinician focus groups: The researcher conducting the focus group will obtain written informed consent from members of the focus group. At the start of the focus groups, participants will be reminded that their contributions are voluntary and that they have the right to withdraw at any time without giving a reason. However, it will be made clear to the participant that any data collected up to the point of withdrawal, would be used in the study as their data is merged with those of the other participants.

Studies within trials (SWATs): Due to the nature of the embedded SWATs, it will not be possible to ask participants to give their informed consent to enter these studies. Please see section 12.1 for further details.

Notwithstanding the above, personal and special category data will be processed in connection with this study under the legal bases of Article 6(1) (e) and Article 9(2) (j) of the General Data Protection Regulation (GDPR), respectively for processing for the performance of a task carried out in the public interest, and as necessary for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes, with Article

9(2) j operating in conjunction with the safeguard requirements set out in Article 89(1) of the GDPR.

The participant will ideally complete their baseline questionnaire during this appointment, or they may have completed it at home prior to attending, and will give it to the treating clinician who will return it to the YTU.

6. Eligibility criteria for the OSTRICH trial

6.1 Assessment of eligibility

The treating clinician at site will assess eligibility for the trial using the eligibility criteria in sections 6.2 and 6.3 of this protocol. If a patient is deemed to be ineligible for the study, the treating clinician will thank the patient for their interest in the study but inform them verbally that they are not able to take part. They will then continue with their usual care.

6.2 Inclusion criteria

Potential participants will be included in the trial if they fulfil all of the following criteria:

- Are aged between six and 14 years, inclusive
- Have one or both symptomatic pes planus*
- The child and/or parent/legal guardian is able to speak, write and understand English
- The parent/legal guardian is able to give informed consent

*Symptomatic pes planus is described as the manifestation of foot and lower limb symptoms, secondary to altered foot alignment (reduced medial longitudinal arch, everted rearfoot and abducted forefoot). The diagnosis will be made pragmatically, by treating clinicians in line with current practice.

6.3 Exclusion criteria

Potential participants will be excluded from the study if they fulfil any of the following criteria:

- Have a history of major trauma or fracture of the lower leg (below knee)
- Have pes planus secondary to any systematic condition/syndrome** /malignancy
- Have a history of foot and/or ankle surgery
- Require an ankle-foot orthoses or other lower limb device
- Have previously received treatment for pes planus (i.e any child who within the last 3 months, has taken part in an exercise intervention or has used health professional prescribed insoles).
- Has or had a sibling that participated in the OSTRICH trial.

** This does not exclude children with hypermobility spectrum disorder (HSD) where the manifestation is non-syndromic and isolated (L-HSD), peripheral (P-HSD) or generalised hypermobility (G-HSD)(14).

6.4 Primary outcome

The primary outcome in this study is the physical domain subscale score of the Oxford Ankle Foot Questionnaire for Children (OxAFQ-C) over the 12-month follow-up period. The OxAFQ-C (15) is a 15-item questionnaire used to measure subjective well-being for child patients aged five to 15 years who are affected by foot and ankle conditions. Fourteen of the items are used to calculate domain scores. Six of these items relate to the 'Physical'

subscale. The remainder of the measure comprises of four 'School and Play' items, four 'Emotional' items, and a final question that asks whether their foot or ankle has stopped the child from wearing any shoes they wanted to wear.

There is both a child-reported and proxy (parent/legal guardian)-reported version of the OxAFQ-C. The validation study for this instrument used both versions administered to the parent-child pairing simultaneously (16). The authors state that they did not supervise the completion of the questionnaires, and parents were free to help their children complete the instrument. We propose to have, at each timepoint, a Case Report Form (CRF) for the child and one for the parent/legal guardian, and the information sheet will explain that parents/legal guardians may assist their child to complete the questions.

The primary outcome will be the child-reported response.

6.5 Data collection for the primary outcome for the trial

Participants (children and parents/legal guardian) will be asked to complete paper/online/ telephone questionnaires at baseline, and at three, six and 12 months post-randomisation to collect the physical domain subscale of the OxAFQ-C.

6.6 Secondary outcomes and other important data

The secondary outcomes in this study are the 'School and Play' and 'Emotional' subscales and the 'Footwear' item of the OxAFQ-C (see section 6.4); and pain scores. Healthcare resource use data and the EQ-5D-Y and CHU9D will be collected for the economic evaluation. Adherence to wearing insoles and undertaking exercises will be recorded. Age, sex, ethnicity, Foot Posture Index (FPI-6), and static, single-leg balance with eyes open and eyes closed (will be recorded only if undertaken as part of routine practice) will be collected at baseline. Adverse events and expected side effects of treatment such as pain, discomfort, blisters, calluses, or skin irritation will be collected.

6.7 Data collection for secondary outcomes

The OxAFQ-C, CHU9D, EQ-5D-Y, healthcare resource use data, and adherence to undertaking exercises and wearing orthoses (intervention group only), will be collected via paper/online/telephone questionnaires at baseline and at three, six and 12 months post-randomisation. The CHU9D and EQ-5D-Y are recommended for completion by the child from the age of 7 and 8 years respectively, with a proxy version for younger children. For simplicity, we propose to include the child and proxy versions in the child and parent/legal guardian CRFs, respectively, regardless of the age of the child. Parents/legal guardians will be able to assist their child to complete their questionnaires if necessary and, for these two instruments, will be instructed that the questions can be omitted if they feel their child is too young to provide an answer to them.

Pain scores will be collected via:

a) Text messages sent to the participant's parent/legal guardian.
The participants' parent/legal guardian will be sent a welcome text message, followed by weekly text messages (one per week for 12 weeks then at the 6 month and 12 month timepoints), with the following content (or similar): *"OSTRICH study: Welcome to the OSTRICH study. Thank you for agreeing to take part. You will*

receive weekly text messages asking how much pain your child has had in their feet over the past week. The texts will come from this number and begin with the word OSTRICH so that you can recognise them. Thank you."

and

"*OSTRICH study: On a scale of 0 to 9, with 9 being the worst pain they could have, please tell us how much pain your child has had in their feet over the past week? Thank you."*

b) Foot pain, over the past week, for both the left and right foot, as measured by Wong-Baker FACES Pain Rating Scale (0 to 10, in increments of 2) in the child-completed questionnaires at three, six and 12 months, and via the question "On average, how would you rate your child's foot pain in relation to their left/right foot over the past week?" on a scale of 0=no pain to 9=worst pain imaginable, on the parent/carer questionnaire at three, six and 12 months.

6.8 Participant withdrawal

Participants can withdraw from the trial at any point during the course of the study by directly contacting the study team at the YTU. If a participant indicates that they wish to withdraw from the trial, they will be asked whether they wish to withdraw from the intervention only (i.e. withdrawal from wearing the insole and undertaking the exercises) or withdraw fully from the trial. Where withdrawal is only from the intervention then follow-up data will continue to be collected. Participants will be informed that they do not have to give a reason for their decision to withdraw from the study. However, if the participant indicates the reason this will be recorded. Data provided by participants who withdraw will be retained for analysis.

6.9 Randomisation

Participants who fulfil the eligibility criteria, provide written consent/assent to take part in the study and complete a baseline questionnaire will be eligible for randomisation. Participants will be randomised by a member of the site study team at the clinic appointment using the YTU's secure web-based randomisation system. An independent statistician at the YTU, who is not involved in the recruitment of participants, will generate the allocation sequence. Block randomisation stratified by Trust will be used with randomly varying block sizes. Participants will be randomly allocated 1:1 to either (a) the prefabricated orthoses plus exercise and advice regarding footwear, or (b) exercise and advice regarding footwear. Participants will be notified verbally of their group allocation by the treating clinician.

6.10 Blinding

This is an open study. Due to the nature of the treatment groups, it will not be possible to blind participants to their allocation, nor the trial team, Trial Management Group or Trial Steering Committee/Data Monitoring and Ethics Committee.

6.11 Exercise and advice group

Participants allocated to the exercise and advice group will be offered an exercise programme and advice regarding footwear. The treating clinician will be able to prescribe appropriate exercises from a menu of exercises (which will be compiled following the consensus meetings). However, where local treatment pathways require onward referral to

other healthcare professionals such as physiotherapists additional appointments are permitted in order to prescribe exercises. Sites may use the Physiotec app (which is currently used within the NHS,) to prescribe exercises. In order to maximise response rates to the final 12-month questionnaire, participants will be sent a study newsletter two weeks before the questionnaire is due to be sent out. Participants will also be sent an unconditional £5 with the 12-month questionnaire in recognition of their commitment to the study and to cover any expenses incurred in completing the questionnaires and £10 towards travel costs to attend appointments.

6.12 Intervention group

In addition to the exercise and advice, detailed in section 6.11, participants allocated to the intervention group will be offered a pair of prefabricated orthoses (i.e. mass produced to a generic shape but can be adapted by a clinician). The prefabricated orthoses will be CE marked and used for their intended purpose. It is anticipated that only one appointment will be required to assess, diagnose and recruit the participant as well as prescribe and fit the orthoses in line with standard practice. However, where local treatment pathways require additional appointments to provide and fit the orthoses, additional appointments are permitted.

Participants will be advised how to fit the device into their shoe, and instructed how to acclimatise to wearing the device. During the acclimatisation period participants will be advised to gradually increase the time they wear their foot orthoses.

Upon completion of the trial, participants will revert to standard care as provided in their locality. Details of ongoing care, beyond the trial, will be decided in collaboration between the child/young person, their parent/legal guardian, and their treating clinicians.

As with the exercise and advice group, participants will be sent a study newsletter two weeks before their 12-month questionnaire is due to be sent out and will receive an unconditional £5 with the questionnaire and £10 towards travel costs to attend appointments.

6.13 Training for clinicians delivering the trial treatment

A training package will be developed during the development phase of the study and provided to the clinicians delivering the trial treatments during the site initiation visit (SIV). The SIVs will be conducted either face-to-face, or by tele- or videoconference according to the site's preference. The focus of the training will be on delivering the intervention in line with the agreed protocol. Relevant training in day-to-day trial management related activities such as completion of trial paperwork, good clinical practice as applicable to the research and the maintenance of the site file and study records, will also be provided. Reporting of adverse events and serious breaches will also be covered. The training will be supplemented by a comprehensive manual, providing clear treatment protocols and study paperwork guidance for the clinicians.

In addition, if treating clinicians have any clinical trial queries, they will be able to discuss these with the other clinicians and the research team, at any time, via email, videoconference or telephone. They will also be invited to attend the Trial Management

Group Meetings and will be encouraged to raise any issues that have occurred at their site at the meeting.

7. Data collection

If data generated from the trial needs to be shared between the University of York and the other co-applicant's institutions, appropriate data sharing agreements will be put in place.

7.1 Quantitative data collection

Participants and their parent/legal guardian will complete a paper/online/telephone baseline questionnaire and three follow-up paper/online/telephone questionnaires, which will be sent in the post with the information pack and at three, six and 12 months post-randomisation, respectively. Participants who provide an email address or a mobile phone number, and consent to be contacted by these methods, will be sent either a prompt email or text on the day their follow-up questionnaire is due, to alert participants to its impending arrival and encourage response. Participants who do not return their follow-up questionnaire within two weeks will be sent up to two reminders by post followed by a telephone call two weeks later. Members of the research team may contact participants or their delegated contact as documented on the consent form, by telephone, post, email or text regarding any queries they may have in relation to the follow-up questionnaires. Data on pain scores will be collected for the first 12 weeks post randomisation, via weekly texts from participants' parent/legal guardian who have a mobile phone and consent to provide text data and once at 6 and 12 months post randomisation.

Cost data, such as time off work for the parent/legal guardian to take the child to clinic appointments, and child healthcare resource use, will be collected through a combination of questionnaires (parent/legal guardian reported at baseline, three, six and 12 months) and review of child participants' medical records.

The YTU will manage the CRF questionnaire and text data. Paper CRFs will be scanned and processed in accordance with YTU standard operating procedures (SOPs) by data management staff. This will include cross-checking data against the hard copy of the CRF. Text messages will be validated, using YTU SOPs. Quality Control will be applied at each stage of data handling to ensure that all data are reliable and have been processed correctly. A data validation plan for the CRFs will be written by the data manager, trial statistician and trial manager. A management system will be developed and used to track participant recruitment, study status and CRF/postal questionnaires/text returns.

7.2 Mixed methods process evaluation

During the first six months of recruitment, there will be a qualitative component to highlight any barriers or facilitators to recruitment of trial participants. This will inform any improvements that can be made to the recruitment process and how the trial is communicated to potential participants as the trial progresses. There will be two components:

(i) Brief interviews will be conducted with children and parents who agree to take part in the trial (n=5-10) and who decline participation (n=10-15). These will be purposefully sampled to ensure maximum variation based on age, gender and

responses to quantitative questions on reasons for consent/non-consent into the trial, treatment preferences and recruitment processes.

(ii) Brief interviews with participating clinicians and trial recruiters regarding their preferences/views on the trial and any issues with recruitment (n=10-15). A purposive sample will ensure that a mixture of type of clinician, years of experience are included in the study.

Rapid analysis will be conducted using a Framework approach on an ongoing basis to specifically address recruitment issues, which will be implemented as appropriate. Recruitment to the sub studies within the process evaluation will be separate to the main trial.

(a) Children and their parents or guardians will initially be approached through the clinical team, and interest in taking part in the qualitative study will be recorded on the main trial consent form the parent/legal guardian completes. The qualitative researcher will send the approved invitation letter, and age appropriate information sheets and consent/assent forms to the potential participants. Written informed consent and assent will be obtained prior to the interview. For face-to-face interviews, the consent/assent form(s) will be completed just prior to the interview. For interviews completed remotely, for example over the telephone or via skype, after discussing the study with the participant(s) over the phone, and answering any questions they may have, the participant(s) will be asked to complete the consent/assent form prior to the interview. This/these will then be emailed/posted (freepost envelope provided) to the qualitative researcher. Just prior to the start of the interview, the qualitative researcher will answer any further questions the participants have, and confirm they are willing for the interview to go ahead. The qualitative researcher will sign the consent/assent form. After the interview, the qualitative researcher will send a copy of the completed consent/assent form in the post to the participant(s) for their records.

(b) Our initial approach to individual clinicians/trial recruiters to participate in the process evaluation will be in writing, through the approved invitation letter. The Principal Investigator at the site will send the clinician/trial recruiter the invitation letter along with the information sheet and consent form, via either secure NHS email or the University of York DrofOff system (in accordance with the trust's preference). The information sheet will contain the qualitative researcher's details, so that they can contact them if they have any queries about the qualitative study. The qualitative researcher will telephone the participant to see if the clinician is willing to take part in the study. If they are willing, then they will obtain written informed consent prior to the start of any of the qualitative work. If they decide to decline, they will not have to provide a reason, but if one is provided it will be recorded. For face-to-face interviews, the consent form will be completed just prior to the interview. For interviews completed remotely, for example over the telephone or via skype, after discussing the study with participant over the phone, and answering any questions they may have, the clinician will be asked to complete the consent form prior to the interview. This will then be emailed/posted (freepost envelope provided) to the qualitative researcher. Just prior to the start of the interview, the qualitative researcher will answer any further questions the clinician has about the qualitative aspect of the study and confirm they are willing for the interview to go ahead. The qualitative researcher will sign the consent form.

After the interview, the qualitative researcher will send a copy of the completed consent form (again in accordance with the trust's policy) to the participant for their records.

7.2.1 Fidelity and acceptability of interventions:

In order to record whether each arm of the intervention is being delivered as intended, the following procedures will be in place:

(i) A sample of participating clinicians (n=18) will be observed (by an expert podiatrist within the team) delivering two trial arms using a checklist developed specifically to record aspects of intervention delivery. A purposive sample will ensure that a mixture of type of clinician, site, training received, and those who have undertaken many or only a few trial appointments have been included.

(ii) An intervention delivery inventory (Clinical Case Report Form) will be completed for all trial participants detailing exact elements of the intervention (including any advice and/or exercise components).

(iii) Outcome questionnaires (at three, six and 12 months) will include information on adherence with the intervention or any cross-over.

(iv) Interviews with trial participants (and parents where appropriate), following primary outcome data collection (n=15-20) will be conducted. Participants will be purposively sampled (based on age, gender, study arm and site) and will ascertain the acceptability of the interventions and how they adapted these into their everyday lives. Interviews will be conducted face-to-face, telephone or via Skype according to the preferences of each interviewee.

Two elements of the fidelity and acceptability review require additional recruitment, which is separate from the main trial: the clinical observations; and the post-trial interviews.

The clinical observations require additional consent from both the clinician and child/young person and their parent/guardian. Clinicians will be approached in writing and provided with an information sheet, with a follow up phone call arranged for those who are willing to participate. Then, the researcher will attend a clinic with the participant, and written informed consent will be obtained for each consultation that is observed to ensure they consider that observation is suitable for each patient. Children and young people and their parent/ guardians will be provided with the approved letter and information sheet by their clinician. The researcher will then take written informed consent from the parent or guardian, and assent from the child/young person. Participants can decline to have their consultation observed, without their care being affected.

The qualitative researcher will approach participants who have indicated on their main trial consent form that they would be interested in taking part in the qualitative research. The initial approach to the post trial interviews will be in writing using the approved invitation letter, and will include the age appropriate information leaflets. Written informed consent and assent will be obtained prior to recruitment to the interviews using the same process as detailed above.

7.2.2 Implementation

To inform any potential implementation strategy (if the trial shows an effective/cost effective result) we will conduct two focus groups of participating clinicians in order to discuss barriers and facilitators to use of the interventions in routine practice. Approximately six clinicians will be included in each focus group (purposively sampled according to professional background, site, and number of interventions delivered). A brief summary of study findings will be presented at each focus group to stimulate discussion (including effectiveness outcomes, findings from fidelity work and patient experiences). We will ascertain information on barriers and facilitators to implementation into practice, taking a normalisation process theory approach to the development of the topic guide and data analysis (17).

Our initial approach to individual clinicians to participate in the post-trial focus groups will be in writing through the approved invitation letter sent to them via the site's PI. They will also provide with a written information sheet, and written informed consent will be obtained prior to recruiting them to the focus group.

We will use NVivo software to assist our organisation of the qualitative analysis. To achieve a systematic approach to data analysis we will conduct Framework analysis (18) engaging in: detailed familiarisation; identification and indexing of key themes; contextualising these themes in relation to the broader dataset; and interpreting them with a focus on addressing the specific questions in each phase of the research.

7.3 Studies within a Trial (SWATs)

The YTU is a Trial Forge 'Studies Within a Trial' Centre (19). Randomised controlled trials are the gold standard method for evaluating healthcare treatments. However, there is little evidence about how to effectively design and deliver these trials. Undertaking SWATs will increase the evidence base for trial methodology and will help improve trial efficiency and reduce waste in research. We will therefore take this opportunity to undertake the following SWATs.

7.3.1 Birthday card SWAT

We will undertake an embedded RCT to evaluate the effectiveness of sending a birthday card to participants on questionnaire response rates. All participants recruited into the host trial will be eligible to take part in this SWAT. Participants will be randomly allocated 1:1 to one of two groups to receive (i) a birthday card on or shortly before their birthday, or (ii) no birthday card. Block randomisation stratified by the main trial allocation using randomly permuted block sizes will be used. Allocation will take place at the time of allocation to the main trial so as not to miss any participants whose birthdays are shortly after their randomisation date. The allocation sequence will be generated by the trial statistician who is not involved in the follow-up of participants.

The primary outcome of this SWAT is the response rate to the participant follow-up questionnaire at the first time point following receipt of the birthday card. Secondary outcomes include: response rate to the participant follow-up questionnaire at the 12-month follow-up; time to response[a]; completeness of host-trial primary outcome measure (defined

as providing sufficient data to produce a valid summary score) [a]; need for a postal reminder[a] and cost per participant retained[a]. [a] these will all be considered for the questionnaire sent at the first time point following receipt of the birthday card.

Analysis of dichotomous outcomes will be via mixed-effect logistic regression adjusting for main trial allocation, and site as a random effect. Time to response will be analysed using a Cox proportional hazard model with a shared centre frailty and adjusting for main trial allocation. Subgroup analyses for age and gender will be undertaken for the primary outcome to see if the effect differs between the groups. This will be undertaken by including an interaction between the factor (age/gender) and embedded trial allocation in the logistic regression model.

The sample size for this embedded trial will be constrained to the number of participants recruited into the host trial. The host trial aims to recruit 478 participants. With this sample size, we would have 90% power to detect a 10 percentage point increase in response rate between the no birthday card (control) group and the birthday card group assuming a response rate of 80% in the no birthday card group, using a two-sided alpha of 0.05.

7.3.2 Multimedia Interface (MMI) SWAT

We will undertake an embedded SWAT to evaluate the effectiveness of providing a multimedia interface (MMI), consisting of a graphical webpage and an animation, to convey the study information to potential participants to improve trial recruitment. This will be conducted as a cluster RCT, with recruiting site as the unit of randomisation. Sites will be allocated 1:1 such that all potential trial participants from that site will receive either (i) a standard printed patient information sheet (PIS) with a QR code/ link to the MMI, or (ii) the standard printed PIS only (which does not contain a QR code/ link to the MMI), when approached to take part in the trial. Minimisation will be used to allocate sites, using geographical area and size of site (determined by patient list size) as minimisation factors.

The primary outcome of this SWAT is recruitment rate, defined as the proportion of potential participants in each SWAT group randomised into the OSTRICH trial. Cost-effectiveness of the MMI will be evaluated as a secondary outcome.

The likelihood of potential participants being recruited into the trial will be compared between the two groups using logistic regression, with site as a random effect. The cost per additional recruited participant associated with receiving the MMI will be calculated.

As is usual with an embedded trial within a trial, no formal power calculation will be undertaken for the study, as the sample size will be constrained by the number of recruiting sites and the number of potential participants approached to take part in the trial per site.

8. Statistical considerations

8.1 Sample size

The developers of the OxAFQ-C have suggested that changes in scores of, or exceeding, six to eight points might be important but further work is required to refine the estimates of the minimal clinically important difference (MCID) (15). We shall assume a standard

deviation of 24 points, (15, 20) and aim to have 90% power (2p = 0.05) to detect a difference of 8 points between the orthoses and exercise and advice groups. Allowing for 20% attrition at 12 months, we require 478 participants to be recruited and randomised in a 1:1 allocation ratio.

8.2 Internal pilot - monitoring trial recruitment and retention

We aim to recruit the 478 participants over 12 months from 18 sites, and to open the sites at a rate of 2 or 3 a month in the first seven months to allow each site to recruit for at least five months. We therefore require sites to recruit participants at an average rate of 3 a month to achieve the target sample size. After six months of recruitment we will review trial progress in terms of site and participant recruitment and follow-up rates at the three month time point. This will complement the mixed methods process evaluation (section 7.2), which will consider barriers and facilitators to trial recruitment.

We will consult with the joint independent Trial Steering Committee and Data Monitoring and Ethics Committee (TSC/DMEC) before we start recruitment into the trial to ask for their view on the following proposed progression criteria:

(1) Number of sites open to recruitment: red = <8; amber = 8-11; green = ≥12
(2) Number of participants randomised: red = <75; amber = 75-119; green = ≥120
(3) Child questionnaire return rates at three months: red = <50%; amber = 50-79%; green = ≥80%

After six months of recruitment, data on site and participant recruitment and questionnaire return rates will be presented descriptively to the TSC/DMEC who will review progress against the agreed criteria. They will recommendations as to whether the trial should continue in its current form, continue with minor amendments to improve site/participant recruitment or follow-up, or continue with major amendments/close.

8.3 Statistical analysis for the main OSTRICH trial

Analyses will be described in detail in a Statistical Analysis Plan drafted by the study statisticians and reviewed by the Trial Management Group and the Trial Steering/Data Monitoring and Ethics Committee prior to the completion of follow-up. The main planned analyses are summarised below.

There will be one single analysis at the end of the trial. All analyses will be conducted in Stata v15 or later (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA) using two-sided statistical tests at the 5% significance level. This trial will be reported according to the CONSORT guidelines for clinical trials (Consolidated Standards Of Reporting Trials statement (http://www.consort-statement.org/). Baseline data (sex, age) will be summarised descriptively and presented in tabular form for participants as randomised, and as included in the primary analysis model. No formal statistical comparisons will be undertaken on baseline data. Continuous measures will be reported as means and standard deviations whilst the categorical data will be reported as counts and percentages. Analyses will be conducted following the principles of intention-to-treat with participant's outcomes analysed according to their original, randomised group, where data are available, irrespective of deviations based on non-compliance.

8.4 Primary outcome for the main OSTRICH trial

The score on the physical subscale of the child-reported OxAFQ will be compared between the groups using a linear covariance pattern mixed model incorporating the three post-randomisation time points (three, six and 12 months). The model will control for child-reported OxAFQ-C physical subscale score at baseline, time point, allocation, and a time-by-allocation interaction. Participant (to account for the repeated measures) and site will be included as random effects. The correlation of observations within participants over time will be modelled by a covariance structure. The Akaike information criterion will be used to compare models specifying different covariance structures (smaller values preferred) [7]. The pairwise mean differences with their associated 95% confidence interval (CI) and p-value for the treatment effect overall (primary endpoint), and at three, six and 12 months (secondary endpoints) will be extracted from the model.

8.5 Secondary outcomes for the main OSTRICH trial

The secondary outcomes of proxy-completed OxAFQ-C physical domain score, child- and proxy-reported OxAFQ-C 'School and Play' and 'Emotional' subscales and the 'Footwear' item, and pain scores will be analysed similarly to the primary outcome.

8.6 Subgroup analyses

Subgroup analyses for the primary outcome will be considered to investigate the presence of differential treatment effects according to the Foot Posture Index score at baseline.

8.7 Missing data

Any response bias will be partially minimised by using a mixed-effect, repeated measures model in the primary analysis, which allows the inclusion of intermittent responders across the follow-up timepoints. Multiple imputation by chained equations will also be conducted to handle missing OxAFQ-C physical subscale scores.

8.8 Intervention adherence

A complier average causal effect analysis for the primary outcome will be considered to account for non-compliance with the intervention.

8.9 Economic analysis

A detailed health economics analysis plan will be written by the trial Health Economist prior to completion of follow-up, which will be reviewed by the Trial Management Group and the Trial Steering/Data Monitoring and Ethics Committee. The main planned analyses are summarised below.

The objective of the economic analysis is to establish whether the use of prefabricated orthoses as well as exercise and advice is cost-effective compared with exercise and advise alone.

The primary economic analysis will use patient-level trial data and be carried out on an intention to treat basis. It will take the form of a cost-utility analysis, in terms of the cost per quality-adjusted life year (QALY) gained, oer a 12-month time horizon. The perspective of the primary analysis will be the NHS and personal social services, in line with NICE

recommendations (21). However, we will undertake a secondary analysis, which will consider a societal perspective. Due to the 12-month follow-up period for the trial, discounting of future costs and health outcomes will not be required, hence will not be undertaken. All costs will be evaluated in pound sterling (£) for the appropriate year (e.g. 2021), with any costs that are sourced from previously published data inflated to the appropriate year figures.

Outcome data

The health outcomes feeding into the cost-utility analysis will be elicited via the EQ-5D-Y (22), which is the youth version of the EQ-5D, and the Child Health Utility 9D (CHU9D) (23) . The EQ-5D-Y is designed to be child-friendly and is for use in both children and adolescents. There are two pages of the questionnaire, comprising the EQ-5D-Y descriptive system and the EQ visual analogue scale (VAS), whereby the descriptive system consists of the same five dimensions as the EQ-5D-3L and 5L, using wording that is child-friendly. The five dimensions are: mobility; looking after myself; doing usual activities; having pain or discomfort; and feeling worried, sad or unhappy. Currently, there is no value set available for the EQ-5D-Y, although work is ongoing regarding the development of a protocol for the valuation of the EQ-5D-Y (24). Therefore, the current EuroQol/NICE guidance will be followed at the time of analysis. EQ-5D-Y data will be collected at baseline, and at three, six and 12 months follow-up.

In addition to the EQ-5D-Y, the CHU9D will be administered for the purpose of eliciting utilities for the cost-utility analysis. The CHU9D is a paediatric generic preference-based measure of health-related quality of life which can be used for children and adolescents aged seven-17 years (25). For children who are aged 6 years at the time of completing the CHU9D, a proxy version, which is currently being trialled for children aged 5-7 years, will be used. The CHU9D comprises a descriptive system and a set of preference weights, which enable QALYs to be calculated through utility values being given for each health state described by the descriptive system. The questionnaire consists of nine dimensions, and each dimension contains five response options.

The inclusion of the CHU9D will ensure that we can generate QALYs for the economic evaluation, in the situation where the EQ-5D-Y value set is still unavailable at the time of analysis. If the EQ-5D-Y value set does become available however, we will be able to undertake a useful comparison of EQ-5D-Y and CHU9D data.

Cost data

Costs will be collected through a combination of parent/legal guardian questionnaires (at baseline, three, six and 12 months) and medical records. For each participant, health care resource use will be obtained, within both primary care and the community (e.g. visits to the GP, nurse, podiatrist, physiotherapist, occupational therapist, etc.) and within secondary care (i.e. outpatient attendances, day cases, inpatient stays and accident and emergency attendances). Unit costs will be applied to the items of resource use in order to estimate a total cost per participant, with the unit costs estimated using established costing sources such as NHS Reference Costs (26) and PSSRU Unit Costs of Health and Social Care (27). Costs will be attached to the orthoses, based on costs of the actual devices used, which will be provided either by the manufacturer or the finance office of the purchasing Trusts. A

sensitivity analysis will vary the costs of the orthoses from the cheapest to the most expensive device used.

For the secondary analysis to be undertaken from the societal perspective, further costs will be collected, such as parental/legal guardian time off work to attend appointments. Time taken out of school due to symptoms or attendance of health care appointments will be listed as a 'consequence' of the condition and compared between groups but will not be formally valued in monetary terms.

Analysis methods

Mean within-trial cost and health benefits will be estimated using regression methods, adjusting for baseline covariates as well as any correlation between costs and utility. The results will be presented as mean costs and effects and the marginal cost-utility ratios between the groups, i.e. in terms of incremental cost-effectiveness ratios (ICERs). The ICER is calculated by dividing the difference in mean cost estimates between the two groups under consideration by the difference in mean health benefit estimates between the two groups. Net health benefit (28) will also be used to present the findings. Multiple imputation methods will be used to deal with missing data where needed (29).

The cost-effectiveness analysis methods outlined above will be applied to the comparison of the prefabricated orthoses group versus exercise and advice, by comparing the costs and QALYs for the two groups. The incremental cost-effectiveness will be evaluated following standard decision rules (30) regarding dominance and extended dominance, with further detail provided in the health economics analysis plan.

Uncertainty

Uncertainty will be described using confidence intervals and cost-effectiveness acceptability curves (CEACs), which are used to graphically represent and quantify uncertainty in the economic evaluation of health care technologies (31). The CEAC depicts the probability that an intervention is cost-effective when compared with an alternative, for a range of willingness-to-pay threshold values, based on the observed data (32). Hence, such curves can be used to understand the uncertainty surrounding a decision regarding whether a new intervention should be approved or rejected. Sensitivity analysis will be undertaken in order to investigate the impact of underlying assumptions of the analysis and varying key cost parameters in terms of the cost-effectiveness findings.

8.10 Definition of the end of the trial

The end of the study is defined as either the date when the last randomised participant is due to respond to their 12-month postal questionnaire or when the last qualitative interview/focus group has been conducted (whichever is the latter date). The trial will be stopped prematurely if:

- Funding for the trial ceases
- The Trial Steering Committee recommends it
- It is mandated by the Research Ethics Committee or the University of York's Research Governance Committee

- It is mandated by the University of York's, Department of Health Sciences Research Governance Committee

9. Adverse Event Reporting

9.1 Adverse Events and side effects of treatment

Details of any adverse events or side effects of treatment will be reported to the YTU either directly by the participant or by a member of the research team at the recruiting site. Adverse events will be recorded using the appropriate OSTRICH adverse event forms although expected side effects of treatment such as pain, discomfort, blisters, calluses, skin irritation or other foot problems will be collected on routine follow up questionnaires and not reported as adverse events.

9.2 Definition of Serious Adverse Events

A Serious Adverse Event (SAE) is defined as any untoward occurrence that:
(a) Results in death
(b) Is life threatening
(c) Requires hospitalisation or prolongation of existing hospitalisation
(d) Results in persistent or significant disability or incapacity
(e) Consists of a congenital anomaly or birth defect
(f) Is otherwise considered medically significant by the investigator.

9.3 Expected Adverse Events and expected side effects

Expected adverse events and side effects of treatment which are related to the intervention include: aches, pains, unusual feelings and discomfort in the lower limb or other parts of the body as a result of altered biomechanics, or as a result of undertaking a new exercise regimen, new callus/corn formation, blisters, ulcers, skin irritation/injury including pressure sores, soft tissue injury, heat foot, tight shoes, feeling unstable and falls. It is very unlikely (although not impossible) that death may occur, for example, following the result of an accident from wearing the orthoses. An 'unexpected event' is defined as: a type of event not listed in the protocol as an expected occurrence.

9.4 Definition of a related event

An event is defined as 'related' if the event was due to the administration of any research procedure.

9.5 Reporting adverse events

The adverse event reporting period for the trial begins once the participant is randomised and ends 12 months after they randomised i.e. after they are sent their final postal follow-up questionnaire.

This study will record details of any serious adverse events (SAEs) that are required to be reported to the Research Ethics Committee (REC) under the current terms of the Standard Operating Procedures for RECs. In the context of this study, SAEs will only be recorded and reported if the event is:

(i) suspected to be related to an aspect of the research procedures (e.g. wearing the orthotic, undertaking the exercise programme, completion of follow-up questionnaires, participation in the qualitative study)
AND
(ii) it is an unexpected occurrence

The following events will not be recorded or reported:

- Normal childhood illnesses are expected in the study population, they will therefore only be reported as SAEs if they appear to be related to an aspect of taking part in the study.
- Hospitalisation that was planned prior to entry into the study
- Pre-existing conditions
- In very rarely instances, death may occur in the population, e.g. due to an illness such as cancer, or an accident which are unrelated to taking part in the study.

Non-serious adverse events will only be recorded and reported for the study if they are related to taking part in the trial or related to the trial treatments. Expected side effects of treatment such as discomfort, blisters, calluses, skin irritation or other foot problems will be recorded on the participant follow up questionnaires. Participants will be asked if they sought treatment for any problems caused by wearing the insoles or undertaking the exercises and if treatment has been sought whether the problems have fully resolved. If a participant or a member of the research team rings the York Trials Unit to notify the occurrence of an adverse event, or an adverse event is reported in information provided in the follow-up questionnaires, then the trial coordinator (or designated person) will complete the appropriate adverse event form if the event is considered to be related to the trial.

The trial coordinator (or designated person) will inform the Chief Investigator (CI) or designated person, and one other member of the Trial Management Group (TMG) about any potential SAEs, that require reporting to ethics. They will jointly decide if the event should be reported to the main REC as an SAE. Related and unexpected SAEs will be reported to the main REC within 15 days of the CI becoming aware of the event. Details of the assessment will be recorded on an 'adverse event review form'.

The occurrence of adverse events during the trial will be monitored by an independent Data Monitoring Ethics Committee (DMEC)/ Trial Steering Committee (TSC). The DMEC/TSC will immediately see all SAEs thought to be treatment related and they will see SAEs not thought to be treatment related by the Trial Management Group at the next scheduled meeting.

10. Trial monitoring

10.1 Site monitoring

Participating sites may be asked to assist in trial related monitoring when required for example audits, ethics committee review and regulatory inspections.

The YTU will undertake central monitoring of sites. This may include: review of consent forms; review of screening forms to confirm eligibility; cross checking delegation logs; and annual audits completed by sites and returned to the YTU.

See sections 13.4 and 13.5 for study oversight.

10.2 Standard Operating Procedures

The study will be run in accordance with the University of York, Department of Health Sciences, York Trials Unit's Standard Operating Procedures.

11. Service User Involvement

Patient and Public Involvement (PPI) has been central to the development of the research question and the design of the OSTRICH study. We will bring together the University of Brighton Paediatric Users Group and the NIHR@Leeds PPI Group, an NIHR Infrastructure PPI group. These groups will work together to create the Great Foundations Patient and Public Involvement Forum (GFPPIF), which will support the Trial. The group will meet approximately four times over the course of the trial and will give input in matters regarding the day-to-day running of the study such as:

- *Feedback and acceptability of treatment arms*
  A focus group will be undertaken with at least three GFPPIF parents/legal guardians and children on the acceptability of the trial interventions.
- *Review of participant facing literature*
  The PPI group have been consulted and asked for assistance with the design of all parent/legal guardian/child/public facing literature, including information sheets, consent forms, recruitment publicity and the standard advice provided in all treatment arms.
- *Membership of the Trial Steering Committee/Data Monitoring Ethics committee*
  The PPI group will provide two members (parents/legal guardians) on the OSTRICH Trial Steering Committee/Data Monitoring Ethics committee.
- *Public facing dissemination strategy plan*
  The PPI group will help develop a dissemination strategy which will target trial participants including an annual newsletter and website, presentations on trial progression to patient groups and relevant children and parent organisations. Dissemination will be developed specifically with the target audience in mind (age relevant material for children and younger people). Feedback from our Users' group also suggested that communication to schools should be explored.

12. Ethical issues

Participation in the study will be entirely voluntary. Participants will be able to withdraw from the study at any point without prejudice by contacting the trial coordinator or the treating clinician. Participants will be informed that they do not have to give a reason for their decision to withdraw, but if a reason is provided, then this will be recorded. Whilst we do not anticipate any major ethical problems with the study, the major issue in this study is

consenting participants under the age of 16 into the trial. The recruiting clinicians will obtain consent from the parent/legal guardian of participating children.

12.1 Obtaining consent

The process of obtaining informed consent from trial participants is described in section 5.6.1. The qualitative researcher will obtain informed consent from the participant for the qualitative part of the study.

Due to the aim of the SWATs it will not be possible to ask participants to give specific informed consent to enter these studies. However, we do not consider this to be a major ethical issue.

For the birthday card SWAT, we sought advice from our PPI group about the suitability of running this trial. They were supportive of the aim of this study and suggested that the cards should be as personal as possible but should not include anything that could cause offense and that they should be sent from the treating clinician. We will therefore minimise the risk of offending or upsetting recipients by ensuring that, for example, there are no religious elements to the card. Before conducting the study, we will ask the PPI's feedback on draft versions of the birthday card before deciding on the version to be sent out to participants. We are aware that Jehovah's Witnesses do not celebrate birthdays. Approximately 1 in 460 of the population follow this faith (33), so it is possible that one or two people following this faith will be entered into this study, each with only a two in three chance of being allocated to receive a birthday card; therefore, this risk is negligible. In addition to this we are not asking participants to undertake any additional tasks, so we are not increasing their burden.

For the MMI SWAT, participants will not be asked to consent to be in this part of the study, however, we do not consider this an ethical issue as the information given to all participants is the same, it is just presented in a different format. The design of the MMI SWAT is the same as the "Developing and evaluating multimedia information resources to improve engagement of children, adolescents and their parents with trials" (TRECA study). ISRCTN73136092 https://doi.org/10.1186/ISRCTN73136092. This study was approved by HRA Yorkshire & The Humber – Bradford Leeds Research Ehtics Committee reference number is 17/YH/0082. This ethics committee did not raise any objections to the design of this study.

12.2 Anticipated risks and benefits

We do not anticipate the risks of this study will be above those experienced in routine care as the treatments being used in the study are already used in routine clinical practice. Adverse events are uncommon and generally minor. The orthotic component does not involve a new medical device. The prefabricated foot orthotics will be CE marked and the clinician will be able to select from a list of orthotics, which has been compiled based on

those currently used within NHS sites. The exercise and footwear advice component of the intervention will be based on routine practice at recruiting sites.

We cannot guarantee that participants will benefit from taking part in the study, but the results of the study will help inform clinical practice on the treatment of pes planus.

12.3 Informing participants of anticipated risks and benefits

The participant information sheet (PIS) will provide information about the possible benefits and anticipated risks of taking part in the study. The PIS will be developed with the help of our PPI group. Participants will be given the opportunity to discuss trial participation with the treating clinician prior to consenting to participate. They will also be able to contact the trial coordinator if they have any day-to-day trial management related questions. Participants will be informed of any new information which comes to light that may affect their willingness to participate in the study.

12.4 Retention of study documentation

All data will be stored for a minimum of 20 years, or until the youngest participant turns 25 years old. Data will be archived in accordance with the current York Trials Unit's Standard Operating Procedures. All paper records will be stored in secure storage facilities. Personal identifiable paper records will be stored separately from anonymised paper records. All electronic records will be stored on a password protected server within the York Trials Unit.

13. Oversight

13.1 Sponsorship

The University of York will act as the sponsor for the study.

13.2 Indemnity

NHS indemnity covers NHS staff delivering the intervention and will apply for patients treated within the NHS sites. The University of York, University of Brighton and University of Salford will provide legal liability cover for their employed staff. Non negligent harm will not be covered.

13.3 Funding

This study is funded by the National Institute of Health Research (NIHR) Health Technology Assessment (HTA) Programme (NIHR reference number 127510).

13.4 Independent Steering Committee

Due to the low risk nature of this study, approval has been sought from the funders to set up one Independent Trial Steering and Data Monitoring and Ethics Committee to undertake the roles traditionally undertaken by the Trial Steering Committee and the Data Monitoring and Ethics Committee. This committee will comprise of an Independent Chair, who will be a clinician with expertise in symptomatic pes planus, a statistician, a physiotherapist, two members of the Patient Public Involvement Group, the Chief Investigator, Trial Manager and Trial Statistician. Other study collaborators may also attend the meeting. The role of the committee will include the review of all serious adverse events which are thought to be

treatment related and unexpected. The committee will meet at least annually or more frequently if the committee requests.

13.5 Trial Management Group (TMG)

A TMG will be set up. It will consist of the Chief Investigator (who will be in overall charge of the study), the trial manager (who will be in charge of the day-to-day management of the study); the study's grant co-applicants and the Principal Investigators or delegated person at sites delivering the intervention. Regular meetings will be held according to the needs of the trial. Trial progress will also be reviewed at the YTU Trial coordinator meetings. These meetings are held by the Director of the YTU approximately every two months.

13.6 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.

14. Publication policy

It is intended that the results of the study will be reported and disseminated regardless of the magnitude or direction of effect to key stakeholders and participants in several ways.

- We will publicise major milestones in professional publications (e.g. Podiatry Now, Frontline, etc)
- We will publish the findings of the study in peer-reviewed scientific journals such as the BMJ or similar. In addition to the main trial paper, we will submit papers reporting the health economics and qualitative findings, as well as the trial protocol. The full trial report will be open access and made available as a permanent archive in the NIHR Journals Library. Publications for the study team will be listed in their Institution's website.
- Conference presentations and stands within the UK, such as the College of Podiatry, British Orthopaedic Foot and Ankle Society Annual Conference, the Great Foundations "children's foot health symposia" and overseas (e.g. Australasian Podiatry Conference).
- Resources to assist in the general clinical and research activities with this population such as an exercise and information booklet for children and parents/legal guardian, will be produced.
- In addition to annual newsletters, a short summary of the results of the study will be distributed to all trial participants.
- Results will be posted on websites, forums and blogs, such as the Great Foundations website https://greatfoundations.org.uk/, Talking Feet https://talkingfeet.online/, Honest Dad https://honestdadofficial.com/ and Mum's net https://www.mumsnet.com/Talk
- Presentations to patient groups, school teachers, etc.
- Social media e.g. Twitter, Facebook, Science Fairs e.g. Brains at the Bevy, and national festivals e.g. British Science Festival
- We will publish our findings on the nested SWATs we have run, regarding recruitment and retention in paediatric trials. The findings of the SWATs may be presented at the

Trials Methodology Conferences such as the International Clinical Trials Methodology Conference/Society for Clinical Trials.

15. List of abbreviations

Abbreviation	Explanation
AE	Adverse event
CHU9D	Child Health Utility 9D
CONSORT	Consolidated Standards of Reporting Trials
GP	General Practitioner
NIHR	National Institute of Health Research
OSTRICH	Orthotics for Treatment of Symptomatic Flat Feet in Children
SAE	Serious Adverse Event
SWAT	Study within a Trial
TMG	Trial Management Group
TSC/DMEC	Trial Steering Committee/Data Monitoring and Ethics Committee
YTU	York Trials Unit

16. Table of protocol changes

Version number	Date of protocol	Summary of changes
2.0		Adaptations to enable delivery during COVID-19 pandemic. Removed custom-made orthoses group, and changed to equal randomisation ratio. This, in turn, reduces the sample size and simplifies the analysis.

3.0		Change in design from a 3 to a 2 arm trial (custom insoles arm removed) and changes to sample size an statistical analysis as a result of this change.
4.0	07.01.2022	Clarification to how the Birthday card SWAT will be run and inclusion of a new MMI SWAT. Inclusion of social enterprises or community interest companies to recruit patients who provide services for the NHS. Participatant may be given the invitation pack in clinic and if eligible and they consent may be recruited to study on the same day.
5.0	25.03.2022	Addition of a new sub study to 3D map children's foot shape. Recruitment: participants may take study documentation home with them and come back into clinic on another day to be enrolled into the study.

REFERENCES

1. Martinez-Nova A, Gijon-Nogueron G, Alfageme-Garcia P, Montes-Alguacil J, Evans AM. Foot posture development in children aged 5 to11 years: A three-year prospective study. Gait & posture. 2018;62:280-4.
2. Morrison SC, McClymont J, Price C, Nester C. Time to revise our dialogue: how flat is the paediatric flatfoot? Journal of foot and ankle research. 2017;10:50.
3. Pfeiffer M, Kotz R, Ledl T, Hauser G, Sluga M. Prevalence of flat foot in preschool-aged children. Pediatrics. 2006;118(2):634-9.
4. Roth-Isigkeit A, Thyen U, Stoven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: restrictions in daily living and triggering factors. Pediatrics. 2005;115(2):e152-62.
5. Wrotniak BH, Epstein LH, Dorn JM, Jones KE, Kondilis VA. The relationship between motor proficiency and physical activity in children. Pediatrics. 2006;118(6):e1758-65.
6. Luhmann SJ, Rich MM, Schoenecker PL. Painful idiopathic rigid flatfoot in children and adolescents. Foot & ankle international. 2000;21(1):59-66.
7. Rome K, Ashford RL, Evans A. Non-surgical interventions for paediatric pes planus. The Cochrane database of systematic reviews. 2010(7):CD006311.
8. Kothari A, Stebbins J, Zavatsky AB, Theologis T. Health-related quality of life in children with flexible flatfeet: a cross-sectional study. Journal of children's orthopaedics. 2014;8(6):489-96.
9. Nester CJ, Graham A, Martinez-Santos A, Williams AE, McAdam J, Newton V. National profile of foot orthotic provision in the United Kingdom, part 1: practitioners and scope of practice. Journal of foot and ankle research. 2017;10:35.
10. Harris EJ, Vanore JV, Thomas JL, Kravitz SR, Mendelson SA, Mendicino RW, et al. Diagnosis and treatment of pediatric flatfoot. The Journal of Foot and Ankle Surgery. 2004;43(6):341-73.
11. Jane MacKenzie A, Rome K, Evans AM. The efficacy of nonsurgical interventions for pediatric flexible flat foot: a critical review. Journal of pediatric orthopedics. 2012;32(8):830-4.
12. Dars S, Uden H, Banwell HA, Kumar S. The effectiveness of non-surgical intervention (Foot Orthoses) for paediatric flexible pes planus: A systematic review: Update. PloS one. 2018;13(2):e0193060.
13. Dars S, Uden H, Kumar S, Banwell HA. When, why and how foot orthoses (FOs) should be prescribed for children with flexible pes planus: a Delphi survey of podiatrists. PeerJ. 2018;6:e4667.

14. Castori M, Tinkle B, Levy H, Grahame R, Malfait F, Hakim A. A framework for the classification of joint hypermobility and related conditions. Am J Med Genet C Semin Med Genet. 2017;175(1):148-57.
15. Morris C, Doll H, Davies N, Wainwright A, Theologis T, Willett K, et al. The Oxford Ankle Foot Questionnaire for children: responsiveness and longitudinal validity. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2009;18(10):1367-76.
16. Morris C, Doll HA, Wainwright A, Theologis T, Fitzpatrick R. The Oxford ankle foot questionnaire for children: scaling, reliability and validity. The Journal of bone and joint surgery British volume. 2008;90(11):1451-6.
17. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Med. 2010;8:63.
18. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol. 2013;13:117.
19. York, Trials, Unit. Trial Forge Studies Within A Trial (SWAT) Centre 2019 [Available from: https://www.york.ac.uk/healthsciences/research/trials/research/swats/.
20. Kothari A, Dixon PC, Stebbins J, Zavatsky AB, Theologis T. The relationship between quality of life and foot function in children with flexible flatfeet. Gait & posture. 2015;41(3):786-90.
21. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal. London: NICE; 2013.
22. Wille N, Badia X, Bonsel G, Burstrom K, Cavrini G, Devlin N, et al. Development of the EQ-5D-Y: a child-friendly version of the EQ-5D. Qual Life Res. 2010;19(6):875-86.
23. Stevens K. Developing a descriptive system for a new preference-based measure of health-related quality of life for children. Quality of Life Research. 2009;18(8):1105-13.
24. EuroQol Group. EQ-5D-Y User Guide. Basic information on how to use the EQ-5D-Y instrument. Version 1.0. August 2014. https://euroqol.org/wp-content/uploads/2016/09/EQ-5D-Y_User_Guide_v1.0_2014.pdf; 2014.
25. Rose NE, Feiwell LA, Cracchiolo A, 3rd. A method for measuring foot pressures using a high resolution, computerized insole sensor: the effect of heel wedges on plantar pressure distribution and center of force. Foot & ankle. 1992;13(5):263-70.
26. Department of Health. NHS Reference Costs 2017/18 https://improvement.nhs.uk/resources/reference-costs/: Department of Health; 2018 [
27. Curtis L, Burns A. Unit Costs of Health and Social Care 2018. University of Kent: Personal Social Services Research Unit; 2018. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/.
28. Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. Med Decis Making. 1998;18(2 Suppl):S68-80.
29. Manca A, Palmer S. Handling missing data in patient-level cost-effectiveness analysis alongside randomised clinical trials. Applied health economics and health policy. 2005;4(2):65-75.
30. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. Methods fo the Economic Evaluation of Health Care Programmes. 3rd ed. Oxford: Oxford University press; 2005.
31. Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves – facts, fallacies and frequently asked questions. Health Economics. 2004;13(5):405-15.
32. Fenwick E, Marshall DA, Levy AR, Nichol G. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. BMC health services research. 2006;6:52-.
33. JW.org. 2019 Grand Totals [Internet]; 2019 [cited 2022 April 8]. Available from https://www.jw.org/en/library/books/2019-service-year-report/2019-grand-totals/

Appendix 1: Foot Scan Sub study

Background

Feet are complex structures with a wide variation in their 3D shape. The importance of this variation in a clinical context is poorly understood, and it is not clear whether the shape of a person's feet influences their response to orthoses. Similarly, there is a lack of evidence as to how the 3D shape of a child's foot changes over time.

Currently, foam impression boxes are the most popular method clinicians use to capture foot shape as part of the manufacturing process of custom-made orthoses [1, 2]. The patient's foot is pressed into a foam box, which compresses and leaves the imprint of their foot in the foam. This imprint can then be scanned with a 3D scanner to accurately extract the shape through precise measurements from the impression. As such, 3D scanning is now increasingly used for the development of individually customised devices [3].

This sub study aims to answer three research questions:

i) Does the 3D shape of a child/young person's feet influence their response to the prefabricated orthoses used in the main trial?

ii) What changes in children/young people's foot posture occur over a 12-month period and do orthoses influence change in foot posture?

Methods

Collecting the impressions

Recruitment will take place within a subset of research sites from the main trial that opt into this sub study. There are no additional eligibility criteria beyond those of the main trial. Participation in this sub study will not be restricted to participants allocated to any particular group in the main trial.

Additional consent will be required to participate in this sub study, so potential participants will be provided with an age appropriate information sheet and assent/consent form. If either the parent or child does not want to participate in the sub study this will not prejudice their involvement in the main trial. If the child/young person and their parent/guardian are willing to take part in the sub study, they will complete the assent and consent forms with the clinician. Participants will have the right to withdraw from this sub study at any point without it affecting their participation in the main trial.

Those participating in this sub study, will receive an impression box in the post within 1 month of their baseline appointment within the main trial. They will be provided with brief simple instructions, and the child will then take an impression of each foot, with assistance from their parent as required. The impression box will be returned to the University of Salford using pre-paid postage. Then at the time of the 12 month questionnaire, participants in this sub study will be posted a second impression box along with the instructions to capture a final impression of both feet, this will then be returned by pre-paid postage to the University of Salford for analysis.

Creating the model

The returned impression boxes will be scanned using a handheld impression box scanner at the University of Salford. Both left and right feet impressions will be scanned and exported in STL file format (used for 3D systems). The STL data will be imported into MATLAB software for visual inspection, alignment and analysis. A quality assessment will be conducted to ensure foot shape has been adequately captured and then the most symptomatic foot (as determined from the self-reported pain scales on the baseline CRF) will be used for subsequent analysis. When both feet are equally symptomatic, or the child is unable to determine the most symptomatic, the right foot will be used for subsequent analysis.

Data for each study arm will be used to generate a mean foot shape and map of variation across foot surface to generate a 3D statistical model. Foot shape characteristics describing the arch will be determined for the mean foot shape including a 3D shape index to characterise arch curvature, arch height, and arch surface area along with other measures of foot posture.

Statistical analysis

i) The primary outcome will be the relationship between foot shape characteristics describing the arch and score on the physical domain scale of the OxAFQ-C. This will be assessed via prediction analysis; an analysis of covariance will also be conducted.

ii) To assess the change in foot shape over time, baseline and 12-month scans will be directly compared to detect regions of greatest variation and significant difference. An analysis of variance will be conducted to identify the effect of intervention type on change in foot shape over time.

No formal power analysis has been conducted due to the embedded nature of this study and lack of relevant data published in the literature. An indicative sample size of 100 participants per study arm (total 200 participants) is considered feasible. To meet this target, we will aim for 50% of sites to participate in this sub study.

References:

1. Chapman, L.S., et al., A survey of foot orthoses prescription habits amongst podiatrists in the UK, Australia and New Zealand. J Foot Ankle Res, 2018. **11**: p. 64.
2. Nester, C.J., et al., National profile of foot orthotic provision in the United Kingdom, part 1: practitioners and scope of practice. J Foot Ankle Res, 2017. **10**: p. 35.
3. Telfer, S. and J. Woodburn, The use of 3D surface scanning for the measurement and assessment of the human foot. Journal of Foot and Ankle Research, 2010. **3**(1): p. 1-9.