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The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis

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ABSTRACT

INTRODUCTION: Patellofemoral (PF) osteoarthritis (OA) is a common and burdensome subgroup of knee OA, with very little evidence for effective treatments. Prefabricated foot orthoses are an affordable and accessible intervention that have been shown to reduce PF pain in younger adults. Similarities between PF pain and PFOA, as well as our pilot work, suggest that foot orthoses may also be an effective intervention for PFOA. The primary objective of this study is to compare the 3-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on knee pain severity.

METHODS AND ANALYSIS: The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a 3-month observation period (pre-randomisation) and 12-month follow-up. 160 participants with a clinical diagnosis of PFOA will be recruited from three sites in Australia, and randomised to one of two groups (prefabricated foot orthoses or flat shoe inserts). The primary outcome is worst knee pain severity during a self-nominated aggravating activity in the previous week (100mm visual analogue scale) at three months, with a secondary endpoint at 12 months. Secondary outcomes include global rating of change, symptoms, function, health-related quality of life, kinesiophobia, self-efficacy and use of co-interventions for knee pain. Blinded, intention-to-treat analyses of primary and secondary patient-reported outcomes will be performed, as well as economic analyses.

ETHICS AND DISSEMINATION: Ethical approval has been granted by La Trobe University's Human Ethics Committee and The University of Queensland's Medical Research Ethics Committee. Study outcomes will be disseminated via peer-reviewed journals, conference presentations targeting a range of healthcare disciplines, and an open access website with clinician resources.

TRIAL REGISTRATION NUMBER: Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study is the first full-scale RCT to evaluate simple, prefabricated foot orthoses as a treatment for patellofemoral osteoarthritis.
- The proposed project will recruit a large sample of people with patellofemoral osteoarthritis, with sample size estimates based on our pilot work.
- Outcomes will be measured at three months (primary endpoint), as well as 12 months to evaluate the longer-term efficacy of foot orthoses for this chronic condition.
- Economic analyses will provide cost-effectiveness ratios and costs per additional quality-adjusted life year, to inform clinical decision-making.
- While participants and outcome assessors are blinded, it is not possible to blind the therapists issuing the interventions, due to visual differences between the prefabricated foot orthoses and flat shoe inserts.

INTRODUCTION

Patellofemoral (PF) osteoarthritis (OA) is an important subgroup of knee OA, whose burden is becoming increasingly evident. Radiographic PFOA is more common than tibiofemoral (TF) OA in people with chronic knee pain (64 to 69% compared to 44 to 45%).[1 2] The PF joint is often the first knee joint compartment affected by OA, and increases the risk of TFOA development and progression.[3] Structural features of PFOA show greater association with knee symptoms than TFOA features. Patellofemoral osteophytes (but not TF osteophytes) are associated with knee pain (odds ratio 2.3, 95% CI 1.1 to 4.8),[4] and reduced patellar cartilage volume (but not femoral or tibial) is related to greater pain and functional impairment.[5] Importantly, compared to TFOA, PFOA tends to occur in younger people,[1] who often have greater daily physical demands due to occupational and/or childcare responsibilities. Considering the progressive nature of PFOA, the side effects of long-term medication use, and that pain and functional limitations are primary barriers to physical activity[6] and indications for total knee replacement,[7] interventions that can effectively reduce PFOA pain are urgently required.

Despite the burden of PFOA, and best-practice guidelines recommending non-surgical, non-drug interventions as the first line strategy for knee OA management,[7] there is very little evidence for effective treatments for PFOA. Although combined interventions (e.g. PF taping, knee/hip exercises, manual therapy, education)[8 9] and knee braces[10] have some evidence of efficacy, their longer-term effects appear to be limited by poor treatment adherence.[11 12] This is particularly relevant for middle-aged adults with PFOA, whose busy lifestyles and family and work commitments are likely to influence adherence to exercise programs.[11] Issues with knee brace bulkiness and interference with clothing[12] are likely to be barriers to brace wear. For braces and orthoses to be effective, they must be comfortable and unobtrusive to daily living to ensure maximal adherence and patient outcomes.

Foot orthoses are inserts worn in everyday footwear that are contoured to match the shape of the foot. Prefabricated foot orthoses are affordable and accessible, and are an effective treatment for PF pain in young adults (aged 18 to 40 years).[13 14] Based on similarities in symptoms, biomechanics and muscle function between PF pain and

PFOA,[15-17] it is plausible that foot orthoses could also have positive effects in people with PFOA. Pilot data show that people with PFOA (n=23, mean age 59±10) report immediate improvements in pain when performing a step-down task with foot orthoses, compared to shoes alone.[18] We observed high adherence and only transient, minor adverse events in our previous trial of foot orthoses in PF pain,[19] suggesting the feasibility of long-term wear. It is therefore timely to conduct a randomised clinical trial (RCT) to evaluate foot orthoses efficacy in this population. The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) will investigate the efficacy of prefabricated foot orthoses for people with PFOA.

OBJECTIVES

Primary objective

The primary objective is to compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts on knee pain severity in people with PFOA. *We hypothesise that, compared to flat inserts, foot orthoses will result in greater improvements in knee pain during a nominated aggravating activity at three months (H1).*

Key secondary objectives

1. Compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on patient-reported global rating of change (GROC). *We hypothesise that, compared to flat inserts, foot orthoses will result in more participants reporting marked improvement at three months (H2).*
2. Compare the 12-month efficacy of prefabricated foot orthoses and flat shoe inserts on GROC, knee pain severity, function, quality of life, kinesiophobia, self-efficacy and use of co-interventions, in people with PFOA.
   We hypothesise that foot orthoses will yield: (i) more participants reporting marked improvement, and greater improvements in knee pain during a nominated aggravating activity, at 12 months (H3); and (ii) greater improvements in knee pain severity, the Knee injury and Osteoarthritis Outcome Score (KOOS),

Anterior Knee Pain Scale, Short-Form 12, EuroQol-5D, Tampa Scale for Kinesiophobia and Arthritis Self Efficacy Scale, and less co-intervention use at three and 12 months (H4).

3. Evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts in people with PFOA.
   We hypothesise that foot orthoses will yield better cost-effectiveness ratios and lower costs per additional quality-adjusted life year after 12 months (H5).

Other secondary objectives

Alongside primary and secondary RCT outcomes, we will investigate the following additional secondary objectives, in people with PFOA.

1. Identify factors that predict change in patient-reported symptoms over a three-month wait-and-see period.
2. Describe characteristics of people with PFOA, including patterns of pain location.
3. Investigate whether foot mobility is related to radiographic features of PF and TF joint alignment and radiographic features of OA.
4. Identify clinically applicable factors that predict poor prognosis at three and 12 months, and determine baseline values of predictor variables to facilitate clinical identification of people with a poor prognosis.
5. Determine the three-month effect of prefabricated foot orthoses on physical activity level compared to flat shoe inserts.
6. Explore factors that are associated with clinical outcomes with prefabricated foot orthoses at three and 12 months.

METHODS AND ANALYSIS

Trial design

The FOOTPATH Study is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a three-month observation period (pre-randomisation) and 12-month follow-up. Equal numbers of participants will be randomised to each group, with the primary endpoint of GROC and pain after three

months. The trial will be conducted across two university sites in Melbourne and Brisbane, Australia, with a satellite site in Hobart, Tasmania. The trial protocol was developed in consultation with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement[20 21] and the Osteoarthritis Research Society (OARSI) recommendations.[22] The trial was prospectively registered (Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347).

Ethics approval

Ethical approval has been granted by La Trobe University's Human Ethics Committee (HEC16-113) and The University of Queensland's Medical Research Ethics Committee (2017000284). In the event that a substantive modification to the study protocol is required (i.e. modifications that affect the conduct of the study), a formal protocol amendment will be prepared, and all proposed amendments reviewed by the two ethics committees. These will be reported in the ANZCTR and study publications.

Participant recruitment and eligibility criteria

Figure 1 summarises the flow of participants through the study. Participants will be recruited from the community in Melbourne, Brisbane, Hobart and regional Victoria. We will utilise a multifaceted recruitment strategy that has successfully recruited people of all ages with knee pain in our previous studies. This will include strategies such as paid and free advertisements in local newspapers, community magazines and newsletters (e.g. University staff bulletins, seniors newsletters); posters in senior citizen's centres, golf and bowling clubs, and retirement villages; sandwich boards and handouts at community events (e.g. fun runs, farmer's markets); radio and television media releases; mail-outs to health practitioners in recruitment areas (e.g. general practitioners, orthopaedic surgeons, physiotherapists); posts on university and research centre websites (La Trobe University, The University of Queensland); social media (e.g. Facebook, Twitter); and patients from the La Trobe University Health Sciences (Podiatry) Clinic, community health care centres, and hospital waiting lists. Based on recruitment rates of 6 participants per month during our feasibility trial (single site), as well as known periods of slow recruitment (e.g.

December/January), conservative estimates indicate that the duration of recruitment will be approximately 20 months. Recruitment rates across all sites will be monitored during the trial, and recruitment strategies adjusted accordingly to meet recruitment targets. There will be no incentives provided to trial investigators or participants for enrolment.

Volunteers who respond to advertisements will be screened for eligibility using a two-stage screening process. This will be conducted by an experienced musculoskeletal health professional (physiotherapist or podiatrist with a minimum of five years of musculoskeletal clinical experience). Preliminary screening questions will be asked via telephone or email. Potentially suitable volunteers will then be invited to attend a physical screening appointment at La Trobe University, The University of Queensland or a private practice (if in regional Victoria or Hobart), where a comprehensive musculoskeletal examination will be completed.

We will use a clinical diagnosis of PFOA, adapted from the NICE guidelines.[23] This is to facilitate generalisation of findings to clinical practice, without the need for imaging. Inclusion criteria will be: (i) age 50 years and over; (ii) predominant symptom of anterior or retropatellar knee pain aggravated by at least two PF joint loading activities (e.g. stairs, squatting, rising from sitting); (iii) pain present during these activities on most days of the previous month; (iv) pain severity of at least three on an 11-point numerical rating scale (NRS, 0-10) during aggravating activities; (v) duration of symptoms of at least three months; and (vi) either no morning joint-related stiffness, or morning stiffness that lasts no longer than 30 minutes.

Volunteers will be excluded if they have: (i) knee pain symptoms predominantly from other knee (TF joint) structures, hip or lumbar spine; (ii) knee injections or use of any shoe inserts within the previous three months; (iii) recent commencement of new physiotherapy treatment for PF pain (i.e. new intervention, or modifications to existing intervention such as therapeutic exercise); (iv) any foot condition precluding the use of foot orthoses or flat shoe inserts; (v) history of lower limb surgery involving major reconstructive procedure (e.g. anterior cruciate ligament reconstruction, osteotomy, arthroplasty); (vi) planned lower limb surgery in the following 12 months; (vii) neurological or systemic arthritis conditions; (viii) major medical conditions (e.g.

cancer); (ix) contraindications to x-ray (pregnancy, breastfeeding); or (x) an inability to understand written and spoken English.

Informed consent

All volunteers who meet the study eligibility criteria will be provided with a participant information sheet. This will provide details of the first phase of the study (observation period), and outline procedures for the second phase of the study (intervention). A trained investigator will discuss the study with volunteers, and provide opportunities for volunteers to ask any questions. The lead investigator at each university site (Melbourne: KMC; Brisbane: NJC) will be available for consultation as required. All participants will provide written informed consent prior to participation. At the conclusion of the observation period, participants will provide additional consent for the intervention phase of the study (detailed below). Participant information and consent forms for all components of the study are included in Supplementary file 1.

Baseline assessment

Participants will attend a single session at La Trobe University, The University of Queensland, or a private physiotherapy/podiatry clinic (if in regional Victoria or Hobart) for baseline assessment. Structured questionnaires and established patient-reported outcome measures will be used. These will be administered in an electronic format (via computer or tablet) to familiarise participants with the electronic platform. Participants will then nominate their preferred methods of communication (e.g. phone, email) and questionnaire completion (paper or electronic format [24]) for the duration of the study.

Participant characteristics will include age, sex, occupation, duration of knee pain symptoms, major medical conditions, other joint complaints in the past month,[25] and medication use.

Patient-reported outcome measures are outlined in Figure 2 and detailed in Supplementary file 2. Pain will be evaluated as knee pain severity over the past week (100mm visual analogue scales [VAS]),[26] PainDetect[27] and Navigate Pain.[28]

The KOOS[29] and patellofemoral subscale[30] will evaluate pain severity, other symptoms, function, knee-related quality of life and patellofemoral symptoms. Other measures include the Anterior Knee Pain Scale (AKPS),[31] Short-Form-12 (SF-12) questionnaire,[32] EuroQol (EQ) 5D-5L questionnaire,[33] Tampa Scale for Kinesiophobia,[34] Pain Catastrophising Scale,[35] Arthritis Self Efficacy Scale[36], and sport and physical activity participation.

Participants will also complete a battery of clinical measures and tests (detailed in Supplementary file 3), which were selected based on their potential to predict PFOA prognosis and/or response to foot orthoses. These include height, mass, body mass index (BMI), waist circumference, presence of knee clicking and crepitus,[37] Foot Posture Index (FPI),[38] foot mobility (Foot Assessment Platform),[39] weight-bearing ankle dorsiflexion (knee to wall test),[40] Footwear Assessment Tool,[41] knee extension torque,[42] and the timed 10-metre walk test.[43]

Radiographic assessment

All participants will attend a private radiology clinic to have radiographs taken of their nominated study knee (most symptomatic eligible knee if pain is bilateral). These will be used to characterise the cohort, and used as predictor variables in other secondary analyses. Several radiology clinics in Melbourne, regional Victoria, Hobart and Brisbane will be used to minimise participant travel time. Weight-bearing anteroposterior, lateral and skyline views will be obtained using standard clinical protocols. Radiographs will be used to grade the presence and severity of OA features in the PF and TF joint compartments. Radiographic features of joint space narrowing and osteophytes will be graded, and the presence of PF and TF OA determined using the Kellgren-Lawrence grading system[44] and a radiographic atlas.[45] Each radiograph will be graded by two experienced investigators (NJC, KMC). Anteroposterior radiographs will also be used to measure frontal plane TF alignment,[46] while lateral and skyline views will be used to measure PF alignment using established protocols.[47]

Observation period

Participants will undergo a three-month observation period, where they will not receive any treatment for their knee pain as part of the study. This is to ensure that only participants with ongoing chronic symptoms that do not improve with time are enrolled in the RCT. Participants will be informed that they will be observed for a three-month period before receiving their intervention.

During the observation period, a subgroup of participants will undergo physical activity monitoring. This subgroup will consist of the first 60 participants who have access to the internet and a smartphone or laptop, and who agree to participate. They will be asked to wear a Fitbit® device (Flex™ / Flex 2™, Fitbit Inc., San Francisco, USA) for the duration of the three-month observation period. This is to familiarise participants with the device and to facilitate adherence with wear during the next phase of the study. Data for physical activity will be remotely extracted from the Fitbit® website.

To maintain contact during the observation period, participants will be contacted via phone or email six weeks after their baseline measures, and will be asked to rate their average and worst knee pain severity over the past week during their nominated aggravating activity (11-point numerical rating scale). Patient-reported outcome measures taken at baseline will be repeated three months after initial assessment. Participants who rate their pain during aggravating activities as less than 30mm on a 100mm visual analogue scale will not be invited to participate in the RCT. They will be offered a pair of contoured sandals (Vionic®, Arundel, Queensland, Australia), and be invited to participate in a prospective longitudinal cohort study (a separate consent process). This will require participants to complete the same battery of questionnaires that they completed at baseline and three months, at yearly intervals from the date of their baseline assessment (up to five years). This study will occur alongside, but separate to, the RCT.

Participants who rate their worst knee pain at least 30mm on the 100mm VAS during their nominated aggravating activity will be invited to participate in the RCT evaluating the efficacy of prefabricated foot orthoses, compared to flat shoe inserts.

Randomised clinical trial

Informed consent

Participants who are eligible to participate in the RCT will provide separate informed consent for the RCT, and for the release of their Medicare and Pharmaceutical Benefits Scheme data for economic analyses.

RCT baseline measures

Three-month follow-up outcomes from the observation period will serve as baseline data for the RCT. Participants will also complete the Credibility and Expectancy Questionnaire (CEQ) to evaluate treatment expectations.[48]

Allocation, concealment and blinding

Once baseline outcome measures are completed, participants will be randomised to receive prefabricated foot orthoses or flat shoe inserts. To ensure concealed allocation, we will use an offsite, telephone-based interactive voice response randomisation service (NHMRC Clinical Trials Centre; randomisation will be performed using a computer-generated minimisation programme with study site as a minimisation factor). Each participant's allocated intervention will be revealed to a single investigator (JMT), who will communicate this to the participant's nominated study practitioner, or to the Brisbane site research assistant (GC) who will liaise with local study practitioners. Because we are comparing two shoe inserts with different shapes, it is not possible to blind study practitioners to group allocation. As the primary outcomes are self-reported, participants are considered assessors. To ensure participant (and thus assessor) blinding, consent will involve limited disclosure. As in our recent RCT,[8] participants will be informed that they will be randomised to one of two shoe insert interventions, but will not be informed of the treatment elements or our hypotheses. Trial participants will be unblinded once data analyses have been finalised. Because we are evaluating two different shoe inserts known to have minimal associated adverse events,[19] it is anticipated that emergency unblinding will not be required.

Interventions

Forty registered podiatrists and physiotherapists with at least five years musculoskeletal experience will fit participants with their allocated intervention. All study practitioners will fit interventions for participants allocated to both groups. To minimise participant burden, study practitioners will be located at multiple private practice clinics across greater Melbourne, Brisbane, Hobart and regional Victoria. To ensure consistency in prescription of foot orthoses and flat shoe inserts, study practitioners will undergo formal training in standardised fitting procedures for both interventions, as used in our previous RCT of prefabricated foot orthoses and flat shoe inserts for young adults with PF pain.[19 49] Study practitioners will also be provided with a comprehensive manual and video outlining study procedures, and will have email and phone access to an unblinded investigator to discuss interventions as required (Melbourne, SEM; Brisbane, BV). Participants will attend an appointment with their study practitioner within one week of baseline assessment to undergo fitting of their allocated intervention.

Participants will be asked to wear their allocated inserts as much as possible, and will be able to transfer them between footwear. This reflects current clinical practice, and will ensure maximal wear time and potential effects.

Prefabricated foot orthoses

The prefabricated foot orthoses will replicate the intervention used in our previous RCT in young adults with PF pain.[19 49] Participants will receive prefabricated foot orthoses from a commercially available range (Vasyli Medical®, Labrador, Australia) (Figure 3A, 3B). The foot orthoses are manufactured from ethylene-vinyl acetate (EVA) of high density (hard, Shore A 70°), medium density (Shore A 55°) and low density (soft, Shore A 45°), and have an inbuilt arch support and 6° varus wedging. A variety of lengths and shapes are available to fit the shape of different footwear. At their first appointment with their chosen study practitioner, participants will bring up to three pairs of shoes that they most commonly wear (e.g. work shoes, casual shoes and sports shoes). Study practitioners will fit one pair of foot orthoses to one

pair of the participant's shoes. This will be based on which of the participant's shoes are able to accommodate the foot orthoses and provide the most support, as prefabricated foot orthoses have superior effects when used with supportive footwear.[50] Where possible, the orthoses will be able to be transferred across their usual footwear. Study practitioners will ensure that the foot orthoses are comfortable, using procedures used in our previous RCT[19 49] (Figure 4). Comfort will be enhanced by adding wedges to the forefoot, rearfoot or heel, or by gently heat moulding the orthoses. Comfortable foot orthoses can effectively reduce PF pain in younger adults,[51] and are proposed to optimise adherence and potential therapeutic effects. Participants will be given written instructions for using and adapting to the foot orthoses.

To reflect current clinical practice, and to provide sufficient opportunity to ensure adequate comfort and prescribe additional foot orthoses, participants will attend up to six appointments with the study practitioner in the first six weeks of the study. Appointments will be scheduled as follows, where appropriate for individual participants: two appointments in week one; one appointment in week two (with an additional appointment in the same week as needed); one appointment in week three or four; one appointment in week six. Participants will be provided with up to four pairs of foot orthoses, fitted to multiple pairs of commonly worn shoes, in order to maximise wear time.

To maximise outcomes of wearing a comfortable, contoured device, participants will receive one pair of sandals from the Vionic range (Vionic®, Arundel, Queensland, Australia). Participants will be encouraged to wear these during times that they do not normally wear enclosed footwear that accommodates foot orthoses (e.g. at home or during warmer weather). Feedback from our previous RCT in young adults with PF pain[19] indicated that participants often chose to wear sandal-type footwear in warm weather, for a large proportion of the year. The Vasyli® sandals offered as an adjunct to foot orthoses were well received by participants in our previous RCT, and increased the time that participants wore a contoured device.

Participants with a high BMI (≥30 kg/m^2) will be invited to attend a follow-up appointment at six months post-randomisation, to receive new foot orthoses. This will not be necessary for those with a BMI <30 kg/m^2, as the pressure-redistributing properties of prefabricated foot orthoses are maintained after 12 months.[52] However, participants will be offered an additional appointment at six months and/or nine months if they are having any issues with the foot orthoses (e.g. increase in pain, excessive wear of orthoses).

Flat shoe inserts

Flat shoe inserts will be used as the comparator intervention (Figure 3C). This is because the contour and wedging of the foot orthoses are proposed to exert mechanical effects on the foot and lower limb, which is thought to be the basis for symptom improvement. Participants will be informed that the study aims to compare two different types of shoe inserts. The flat inserts will be described as an intervention designed to enhance sensory feedback, supported by findings from our previous RCT in PF pain, where those who received flat inserts also experienced improvements in pain over 12 months.[19] The flat inserts will be the same as those used in our previous RCT, with identical covering fabric to the foot orthoses. To control for gradual contouring that occurs with repeated wear of low-density inserts (a limitation of previous studies), the flat inserts will be made of high-density EVA (Shore A 70°). Standardised guidelines for fitting and follow-up of the flat inserts will aim to ensure these are perceived as a credible intervention (Figure 5). As with the foot orthoses, participants will be provided with up to four pairs of flat inserts fit to multiple pairs of commonly worn shoes. To address the potential influence of therapist contact, those randomised to this group will also attend an initial appointment with a study practitioner for fitting of flat inserts, and up to two follow-up appointments to ensure adequate comfort and fit. At six months post-randomisation, a follow-up appointment will be made with the study practitioner to issue new flat inserts, to minimise the effects of cumulative contouring with repeated wear.

At the conclusion of the study, if prefabricated foot orthoses are found to be more efficacious than flat inserts, those randomised to the flat insert group will be offered

one pair of foot orthoses and one additional appointment with one of the study practitioners at no cost to them.

Criteria for discontinuing or modifying allocated intervention

The occurrence of adverse events will be monitored throughout the duration of the RCT by study practitioners, participant logbooks, and three-monthly telephone calls to participants. In the event of minor adverse events (e.g. rubbing, blisters) associated with either intervention, study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms described above. This may include replacement of foot orthoses with a softer device. If participants still report discomfort, they will be encouraged to halve their foot orthoses or flat insert wear time for a period of two weeks, and then gradually increase wear time as tolerated. If comfort is unable to be achieved, the intervention will be ceased, as this reflects current clinical practice.

In the event of a sustained increase in knee pain, or aggravation of another area of pain (e.g. low back pain), study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms. If this does not relieve the participant's symptoms immediately, then intervention will be ceased. Participants who cease their allocated intervention will be encouraged to remain in the trial to enable follow-up data collection at all nominated time points.

Strategies for improving and monitoring adherence to interventions

Study personnel will maintain regular communication with participants over the study period (e.g. email, phone), and will encourage adherence to the interventions at each time of contact. Adherence to foot orthoses or flat insert wear will be monitored using a variety of strategies. Study practitioners will record attendance at each appointment. To reduce participant burden associated with daily diary entries, participants will report their adherence at three-monthly intervals during the RCT. This will be recorded as the average days per week and hours per day that they wore the foot orthoses or flat inserts over the preceding four weeks.[53]

Concomitant care and interventions

During the observation and intervention periods, participants will be able to continue with stable medication doses and exercise programs, and use some concomitant interventions (e.g. analgesics, heat/cold, general exercise).[54] New physical therapies (e.g. exercise, manual therapy, taping, bracing), intra-articular injections and surgery will be discouraged. If participants have problems with their allocated intervention or wish to seek additional treatment outside the trial, they will be asked to contact the unblinded investigator at their trial site to discuss this (Melbourne, Hobart, JMT/SEM; Brisbane, BV). Use of concomitant interventions will be recorded during the intervention period using monthly logbooks (issued at RCT baseline) and structured questionnaires at three-monthly intervals.

Participant retention

Study personnel will utilise established methods to maximise participant retention. Following enrolment in the study at the commencement of the observation period, participants will be contacted at regular intervals throughout the study period to collect outcome data, ascertain any issues with the intervention, and maintain communication. We have endeavoured to minimise participant burden by utilising an online data collection platform, and limiting the number of appointments that participants are required to attend in-person (one screening/baseline appointment; one x-ray appointment; maximum of seven practitioner appointments over 12 months). Although financial incentives will not be provided, financial reimbursement for travel costs will be available for participants if required. Participants who discontinue use of the intervention will be encouraged to complete outcome measures for the duration of the study to minimise missing data.

Outcomes

Outcome assessment will occur at three, six, nine and 12 months. Three months is the *a priori* primary end-point of interest, as early improvement in symptoms is likely to influence ongoing adherence with foot orthoses or flat inserts. Twelve-month

follow-up will evaluate longer-term effects and economic efficiency of foot orthoses, which is important given the chronic nature of PFOA, and reflects clinical practice.

At entry into the study, participants will be asked their preferred method of receiving and completing outcome measures. Where possible, outcome data will be collected using an internet-based platform, which has equivalent measurement properties to paper-based completion.[24] This strategy was used in our pilot studies on people with PFOA,[55] ensuring feasibility of online data collection in this population. However, for participants who do not have internet access or would prefer to complete outcome measures in paper format, paper versions and reply-paid envelopes will be mailed.

Outcome measures of GROC, pain and function have been selected based on international recommendations for knee OA.[56] These are listed below and detailed in Supplementary file 2.

We have selected patient-reported outcomes over imaging and surgical endpoints, aligning with international recommendations highlighting the importance of patient-centred outcomes.[22 56] Considering the financial cost and participant burden of repeated magnetic resonance imaging (MRI), and the lack of correlation between symptoms and imaging,[57] it is important to first determine whether prefabricated foot orthoses improve pain and function. This will ensure continued adherence and greater potential for longer-term effects on joint structure. Whilst total knee replacement is usually recommended for end-stage joint disease, severe pain and functional limitations,[7 54] other factors such as race, ethnicity, socioeconomic status and patient preferences can also influence decisions for surgery.[58] Thus, patient-reported outcomes are, at present, the ideal method to evaluate foot orthoses outcomes for PFOA. Indeed, regulatory agencies such as the United States Food and Drug Administration require the use of patient-reported outcomes in the development of medical products to support labelling claims.[59]

Primary outcome (three months)

Knee pain is the predominant symptom of PFOA and the primary indication for undergoing total knee replacement.[7 54] Pain will be evaluated as *worst knee pain*

severity during a self-nominated aggravating activity in the previous week.[8 10] Participants will nominate one of three everyday activities that they experience the greatest pain severity (rising from sitting, squatting or stair ambulation). Pain severity will be measured on a 100mm VAS (terminal descriptors 0=no pain, 100=worst pain possible). VAS measures of pain severity have well-established reliability and validity, including in PF pain.[26] This will be measured at baseline, six weeks, three months (time of primary interest), and six, nine and 12 months.

Secondary outcomes

Secondary outcomes will be administered at baseline, six weeks (knee pain severity and GROC), three months, six and nine months (knee pain severity and EQ-5D-5L), and 12 months (Figure 2).

- Knee pain severity over the past week (100mm visual analogue scales).[26]
- GROC (7-point Likert Scale: 'much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'; dichotomised to 'improved' ('much better, 'better') *vs.* 'not improved' ('a little better' to 'much worse').
- KOOS subscales: symptoms, pain, function in daily activities, function in sport/recreation, knee-related quality of life, patellofemoral symptoms.[29 30]
- AKPS.[31]
- SF-12.[32]
- EQ-5D-5L.[33]
- Tampa Scale for Kinesiophobia.[34]
- Arthritis Self Efficacy Scale.[36]
- Use of co-interventions for knee pain.[60]

Physical activity will be monitored in the subgroup of participants who received a Fitbit® physical activity monitor during the observation period. Data relating to physical activity levels (e.g. steps, distance) will be extracted weekly for each participant, for the first three months after randomisation. Data will be analysed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) for total step count and time spent in low, moderate and high-intensity activity bands (defined as step count per 15-minute epoch). All physical activity data will be remotely downloaded

from the Fitbit® data server using a freely available R package (Fitbit Scraper), and imported into Microsoft Excel for analysis.

Other outcomes

Treatment adherence and adverse events: Every three months, participants will complete a short questionnaire for physical activity, footwear worn and foot orthoses or flat insert wear time, and adverse events.[53] Evaluation of 12-month adherence is vital to determine whether frequency of wear is maintained long-term. This will assist with translating outcomes into clinical practice guidelines. Study practitioners will record attendance, prescription notes and adverse effects during fitting and follow-up.

Treatment credibility and expectations: The CEQ will be completed again at three and 12 months.[48]

Economic outcomes

Data on direct health costs will be sourced from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. Direct and indirect health costs (e.g. medication use, hospital admissions, other co-interventions such as physiotherapy, time off work due to PFOA or treatment) will be captured from the following sources: (i) monthly participant logbooks; (ii) 3-monthly telephone interviews; and (iii) the Institute for Medical Technology Assessment (iMTA) Productivity Costs Questionnaire (iPCQ).[61] The EQ-5D is a reliable and valid measure of health-related quality of life, and considers mobility, self-care, usual activity, pain/distress and depression/anxiety.[33 62] EQ-5D will be measured at baseline, and at three, six, nine and 12 months, and used to calculate quality-adjusted life years.

Long-term follow-up

After completion of the RCT 12-month follow-up, participants will be asked to complete the same battery of patient-reported outcome measures at yearly intervals, up to four years after completion of the RCT (five years from baseline). This will

allow us to conduct prognostic analyses to identify pain trajectories and predictors of long-term outcome, as in our previous RCTs.[63]

Sample size

Treatment efficacy will be evaluated by between-group comparisons on the primary outcome measure, which is worst knee pain severity during a self-nominated aggravating activity in the previous week, measured on a 100mm VAS). The minimal clinically important difference for pain on a VAS is 15mm.[64] Sample size calculations are based on an analysis of covariance (ANCOVA) adjusting for baseline of the outcome variable, and assume a between-person standard deviation of 30mm (based on pilot data in people with PFOA) and baseline to three-month correlation of 0.5. A sample of 160 (80 per group) provides a minimum 90% power (α=0.05) to detect significant between-group differences, and allows for ~20% dropouts.

Observation period: In people with chronic knee pain, pain severity has been shown to improve naturally over three months when people are being monitored by a general practitioner.[65] Thus, to ensure that participants in the RCT have sufficient levels of pain at baseline, and that any observed improvements in pain during the three-month time of primary interest are attributable to the intervention, we will include a three- month observation period prior to randomisation. Based on previous findings, it is anticipated that some participants will experience natural improvement in their pain severity during this time.[65] Thus, we will continue to recruit participants into the observation period until we have recruited the required sample size into the RCT (n=160). Based on conservative estimates that approximately two thirds of participants will qualify for the RCT at three months, it is anticipated that a total of ~230 participants will be recruited. This will be revised throughout the study period.

Data management and storage

The majority of outcome data will be collected electronically, facilitating simultaneous data entry. For paper-based data collection, data will be entered by a single trained investigator (JWD). A second investigator will check a random subset of manually

entered documents to ensure accuracy. Once data entry is finalised, quality checks will ensure that all data points are within expected values. Only named investigators will have access to the full dataset.

Personal data, including informed consent forms, participant names, contact details and date of birth will be stored on a password-locked computer hard drive, separately from patient-reported or other study data, in order to ensure data de-identification. All subsequent study data will be identified by participant number only, and will be stored on the La Trobe University server Research Data Storage, which is only accessible only by the research team through secure means. All project documentation will be stored on a secure, password locked external hard drive, overseen by an external company (DS PRIMA, Port Melbourne, Victoria, Australia). No persons external to the research team will have access to information stored on this server. Appropriate ethical procedures will be followed for all data (e.g. participant coding, data file encryption, storage in locked filing cabinets). Any paper containing participant details, such as baseline questionnaires, will remain in the locked filing cabinet and will not be accessible outside the premises. Data pertaining to participant characteristics, questionnaires and clinical tests will be preserved for possible future use by the investigators. De-identified data will be stored in an Excel spreadsheet. If researchers other than those listed as investigators wish to use the data, prior approval will be sought from the La Trobe University human ethics committee. Participants will be made aware of this in the Participant Information Statement, ensuring that they are aware of the possibility that their data will be used for future studies, and are able to provide written informed consent.

Due to the minimal known risks associated with the interventions being evaluated, this study will not require a formal data monitoring committee or planned interim analysis.

Statistical methods

Primary and key secondary objectives

Intention to treat analyses will be performed, with all randomised participants included regardless of protocol adherence. Blinded analyses of primary and secondary patient-reported outcomes will be performed. The dichotomised measure of GROC will be expressed from blinded analyses as relative risk (RR) and number needed to treat (NNT), with 95% confidence intervals, to facilitate clinical guidelines.[19 66] For the primary outcome and continuous secondary outcome measures, linear mixed models (with baseline value as a covariate and treatment condition as a fixed factor) will be used to evaluate the treatment effect and 95% confidence interval at three months and 12 months ($p<0.05$). Linear mixed models utilising repeated measures at all time-points will allow non-biased estimates of treatment effect in the presence of any potential missing cases. This likelihood-based estimation procedure results in non-biased estimates, providing data are missing at random and models are adjusted for any imbalance between groups in potential confounders at baseline (age, sex, weight, symptom duration, PF/TF OA radiographic severity). Relative risk (95% confidence intervals) will be calculated for use of co-interventions and adverse events.

Economic evaluation

Blinded economic analyses will be conducted to evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts, from the societal perspective. Hospitalisations will be converted to costs using the National Weighted Activity Unit costing model. Incremental cost-effectiveness analyses will use the formula $[(DC_{foot\ orthoses} + IC_{foot\ orthoses}) - (DC_{flat\ inserts} + IC_{flat\ inserts}) / (E_{foot\ orthoses} - E_{flat\ inserts})]$, where DC=mean direct health costs, IC=mean indirect costs, E=effect, $_{foot\ orthoses}$= foot orthoses group, and $_{flat\ inserts}$=flat insert group. Effect for the primary economic evaluation will be the proportion of participants who 'improve' (measured on the GROC) within each group at 12 months. Thus, the cost-effectiveness ratio will reflect the marginal cost per additional 'improved' participant from the societal perspective over a 12-month time horizon. Uncertainty in this ratio will be examined by constructing a 95% confidence ellipse on a cost-effectiveness plane, and transforming these to cost-effectiveness acceptability curves using non-parametric bootstrap resampling of primary data. Sensitivity analyses will be conducted, varying the threshold of 'improvement' on the GROC to reflect increasingly higher

thresholds. Quality-adjusted life year scores for each participant (calculated as area under the curve applied to utility measures calculated from EQ-5D) will be substituted for GROC scores as the effect measure, creating an incremental cost-utility ratio to determine the marginal cost per additional quality-adjusted life year for the more effective intervention.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not directly involved in the development of the research question, study design or selection of outcome measures. Patients will not be directly involved in the recruitment to or conduct of the study, except as participants if they meet the eligibility criteria and provide informed consent. At the conclusion of the study, overall study findings and individual participant data will be provided to study participants on request.

ETHICS AND DISSEMINATION

This study complies with the Declaration of Helsinki, and has been approved by ethics committees at La Trobe University and The University of Queensland. All participants will provide written informed consent prior to baseline data collection and enrolment in the three-month observation period. Participant information and consent forms for each phase of the study are included in Supplementary file 1. Participants will undergo knee radiographs at a single time point as part of this trial, ensuring that the amount of ionising radiation is consistent with standard clinical exposure. When prescribed by trained health practitioners, prefabricated foot orthoses and flat shoe inserts are associated with minimal and transient adverse events.[19] Thus, there are minimal ethical and safety considerations associated with this trial.

Study outcomes will be widely disseminated through a variety of sources. Primary and key secondary objectives will be submitted to a high-impact peer-reviewed journal in the field. Because study outcomes are applicable to a broad range of health professionals, we will target a general medical journal to facilitate wider dissemination of findings to key stakeholders (e.g. general practitioners). Each of the other secondary objectives will be addressed in separate publications, and submitted

to appropriate journals in the field. Authorship will be in accordance with guidelines provided by the International Committee of Medical Journal Editors [67]. We will also submit articles to key professional magazines to enhance dissemination to clinicians. Our publication strategy will be complemented by submission of abstracts to key national and international conferences, covering multiple discipline groups (e.g. physiotherapy, podiatry, general practice), as well as OA conferences. We will also develop an open access website and resources for clinicians, including videos detailing how to prescribe foot orthoses, and run workshops on PFOA and foot orthoses for registered health professionals. This will facilitate translation of findings to clinical practice, especially practitioners located in rural or remote areas.

The trial protocol, anonymised participant level dataset, and statistical code used in primary and secondary analyses, will be made publicly available through institutional data repositories (La Trobe University: http://arrow.latrobe.edu.au:8080/vital/access/manager/Index).

DISCUSSION

PFOA is a major public health problem, and has no cure. Pain and stiffness experienced during daily activities, occupational tasks and exercise can reduce active participation. Importantly, PFOA in middle-aged adults can affect productivity and contribution to society, and result in more years of knee pain and disability across the lifespan. Along with direct personal and economic costs of PFOA, indirect costs associated with consequences of physical inactivity are a major burden on health expenditure.

This RCT will be the first to evaluate patient-reported benefits of foot orthoses – a simple, low-cost, low-risk intervention that is widely accessible to people with PFOA. Findings of efficacy and cost-effectiveness of prefabricated foot orthoses could represent a turning point in the effective long-term management of PFOA. When worn in everyday and exercise footwear, foot orthoses have the potential to reduce pain every time the foot hits the ground, substantially increasing an individual's capacity and motivation to be physically active. This has important implications for maintenance of general and mental health with increasing age. Importantly, the ease

of daily use of foot orthoses, with minimal patient burden, is likely to maximise adherence, enhance outcomes, and reduce reliance on health practitioner resources.

AUTHORS' CONTRIBUTIONS

NJC, KMC, HBM, TGR, AJS, RSH, BV and TPH conceived the study and obtained funding. NJC, KMC and HBM designed the trial protocol with input from TGR, AJS, RSH, BV, TPH, SEM and JMT. AJS and TPH provided statistical expertise. AJS will conduct primary statistical analysis. NJC drafted the manuscript with input from KMC, HBM, TGR, AJS, RSH, BV, TPH, SEM, JMT, HFH, BEP, GC, JWD and LRM. All authors have read and approved the final manuscript.

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COMPETING INTERESTS STATEMENT

Professor Vicenzino reports non-financial support from Vionic®, outside the submitted work. He is a member (non-paid affiliation) of the Vasyli Think Tank™, which was founded in 2011 to foster collaboration and cooperative thought among a leading group of health professionals specialising in the field of lower limb biomechanics. All other authors have no conflicts of interest to declare.

REFERENCES

1. Hinman RS, Lentzos J, Vicenzino B, et al. Is patellofemoral osteoarthritis common in middle-aged people with chronic patellofemoral pain? *Arthritis Care Res (Hoboken)* 2014;66(8):1252-7. doi: 10.1002/acr.22274
2. Duncan RC, Hay EM, Saklatvala J, et al. Prevalence of radiographic osteoarthritis--it all depends on your point of view. *Rheumatology (Oxford)* 2006;45(6):757-60. doi: 10.1093/rheumatology/kei270
3. Duncan R, Peat G, Thomas E, et al. Incidence, progression and sequence of development of radiographic knee osteoarthritis in a symptomatic population. *Ann Rheum Dis* 2011;70(11):1944-8. doi: 10.1136/ard.2011.151050
4. Kornaat PR, Bloem JL, Ceulemans RY, et al. Osteoarthritis of the knee: association between clinical features and MR imaging findings. *Radiology* 2006;239(3):811-7. doi: 10.1148/radiol.2393050253
5. Hunter DJ, March L, Sambrook PN. The association of cartilage volume with knee pain. *Osteoarthritis Cartilage* 2003;11(10):725-9. doi: S1063458403001602 [pii]
6. Hendry M, Williams NH, Markland D, et al. Why should we exercise when our knees hurt? A qualitative study of primary care patients with osteoarthritis of the knee. *Fam Pract* 2006;23(5):558-67. doi: 10.1093/fampra/cml022
7. Carr AJ, Robertsson O, Graves S, et al. Knee replacement. *Lancet* 2012;379(9823):1331-40. doi: 10.1016/S0140-6736(11)60752-6
8. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64. doi: 10.1016/j.joca.2015.04.024
9. Quilty B, Tucker M, Campbell R, et al. Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol* 2003;30(6):1311-7. doi: 0315162X-30-1311 [pii]
10. Callaghan MJ, Parkes MJ, Hutchinson CE, et al. A randomised trial of a brace for patellofemoral osteoarthritis targeting knee pain and bone marrow lesions. *Ann Rheum Dis* 2015;74(6):1164-70. doi: 10.1136/annrheumdis-2014-206376
11. Campbell R, Evans M, Tucker M, et al. Why don't patients do their exercises? Understanding non-compliance with physiotherapy in patients with osteoarthritis of the knee. *J Epidemiol Community Health* 2001;55(2):132-8.
12. Squyer E, Stamper DL, Hamilton DT, et al. Unloader knee braces for osteoarthritis: do patients actually wear them? *Clin Orthop Relat Res* 2013;471(6):1982-91. doi: 10.1007/s11999-013-2814-0
13. Crossley KM, van Middelkoop M, Callaghan MJ, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br J Sports Med* 2016;50(14):844-52. doi: 10.1136/bjsports-2016-096268
14. Barton CJ, Lack S, Hemmings S, et al. The 'Best Practice Guide to Conservative Management of Patellofemoral Pain': incorporating level 1 evidence with expert clinical reasoning. *Br J Sports Med* 2015;49(14):923-34. doi: 10.1136/bjsports-2014-093637
15. Crossley KM, Hinman RS. The patellofemoral joint: the forgotten joint in knee osteoarthritis. *Osteoarthritis Cartilage* 2011;19(7):765-7. doi: 10.1016/j.joca.2011.05.005

16. Wyndow N, Collins N, Vicenzino B, et al. Is There a Biomechanical Link Between Patellofemoral Pain and Osteoarthritis? A Narrative Review. *Sports Med* 2016;46(12):1797-808. doi: 10.1007/s40279-016-0545-6
17. Crossley KM, Schache AG, Ozturk H, et al. Pelvic and Hip Kinematics During Walking in People With Patellofemoral Joint Osteoarthritis Compared to Healthy Age-Matched Controls. *Arthritis Care Res (Hoboken)* 2018;70(2):309-14. doi: 10.1002/acr.23261
18. Collins NJ, Hinman RS, Menz HB, et al. Immediate effects of foot orthoses on pain during functional tasks in people with patellofemoral osteoarthritis: A cross-over, proof-of-concept study. *Knee* 2017;24(1):76-81. doi: 10.1016/j.knee.2016.09.016
19. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735. doi: 10.1136/bmj.a1735
20. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583
21. Chan AW, Tetzlaff JM, Gotzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586. doi: 10.1136/bmj.e7586
22. McAlindon TE, Driban JB, Henrotin Y, et al. OARSI Clinical Trials Recommendations: Design, conduct, and reporting of clinical trials for knee osteoarthritis. *Osteoarthritis Cartilage* 2015;23(5):747-60. doi: 10.1016/j.joca.2015.03.005
23. National Institute for Health and Care Excellence. Osteoarthritis: care and management 2014 [Available from: https://www.nice.org.uk/guidance/cg177 accessed 8 July 2018.
24. Gudbergsen H, Bartels EM, Krusager P, et al. Test-retest of computerized health status questionnaires frequently used in the monitoring of knee osteoarthritis: a randomized crossover trial. *BMC Musculoskelet Disord* 2011;12:190. doi: 10.1186/1471-2474-12-190
25. de Klerk BM, Willemsen S, Schiphof D, et al. Development of radiological knee osteoarthritis in patients with knee complaints. *Ann Rheum Dis* 2012;71(6):905-10. doi: 10.1136/annrheumdis-2011-200172
26. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
27. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20. doi: 10.1185/030079906X132488
28. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160. doi: 10.1186/s12891-017-1521-5
29. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.
30. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation

using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776
31. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
32. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.
33. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33(5):337-43.
34. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.
35. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.
36. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44.
37. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8. doi: 10.1016/j.joca.2014.02.008
38. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98. doi: 10.1016/j.clinbiomech.2005.08.002
39. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.
40. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80.
41. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.
42. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.
43. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30. doi: 10.1519/JPT.0b013e318248e20d
44. Kellgren JH, Jeffrey MR, Ball J. The Epidemiology of Chronic Rheumatism: Atlas of Standard Radiographs. Oxford: Blackwell Scientific 1963.
45. Altman RD, Hochberg M, Murphy WA, Jr., et al. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995;3 Suppl A:3-70.
46. Moyer R, Wirth W, Duryea J, et al. Anatomical alignment, but not goniometry, predicts femorotibial cartilage loss as well as mechanical alignment: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2016;24(2):254-61. doi: 10.1016/j.joca.2015.08.016
47. Macri EM, Stefanik JJ, Khan KK, et al. Is tibiofemoral or patellofemoral alignment or trochlear morphology associated with patellofemoral osteoarthritis? A systematic review. *Arthritis Care Res (Hoboken)* 2016;68(10):1453-70. doi: 10.1002/acr.22842

48. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.
49. Vicenzino B, Collins N, Crossley K, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: a randomised clinical trial. *BMC Musculoskelet Disord* 2008;9:27. doi: 10.1186/1471-2474-9-27
50. Barton CJ, Menz HB, Crossley KM. Clinical predictors of foot orthoses efficacy in individuals with patellofemoral pain. *Med Sci Sports Exerc* 2011;43(9):1603-10. doi: 10.1249/MSS.0b013e318211c45d
51. Mills K, Blanch P, Dev P, et al. A randomised control trial of short term efficacy of in-shoe foot orthoses compared with a wait and see policy for anterior knee pain and the role of foot mobility. *Br J Sports Med* 2012;46(4):247-52. doi: 10.1136/bjsports-2011-090204
52. Cronkwright DG, Spink MJ, Landorf KB, et al. Evaluation of the pressure-redistributing properties of prefabricated foot orthoses in older people after at least 12 months of wear. *Gait Posture* 2011;34(4):553-7. doi: 10.1016/j.gaitpost.2011.07.016
53. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198. doi: 10.1186/s13063-017-1936-1
54. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008;16(2):137-62. doi: 10.1016/j.joca.2007.12.013
55. Wyndow N, Crossley KM, Vicenzino B, et al. A single-blinded, randomized, parallel group superiority trial investigating the effects of footwear and custom foot orthoses versus footwear alone in individuals with patellofemoral joint osteoarthritis: a phase II pilot trial protocol. *J Foot Ankle Res* 2017;10:19. doi: 10.1186/s13047-017-0200-y
56. Bellamy N, Kirwan J, Boers M, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. *J Rheumatol* 1997;24(4):799-802.
57. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord* 2008;9:116. doi: 10.1186/1471-2474-9-116
58. Gossec L, Paternotte S, Maillefert JF, et al. The role of pain and functional impairment in the decision to recommend total joint replacement in hip and knee osteoarthritis: an international cross-sectional study of 1909 patients. Report of the OARSI-OMERACT Task Force on total joint replacement. *Osteoarthritis Cartilage* 2011;19(2):147-54. doi: 10.1016/j.joca.2010.10.025
59. Health USDo, Human Services FDACfDE, Research, et al. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* 2006;4:79. doi: 10.1186/1477-7525-4-79
60. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94. doi: 10.1136/bjsports-2014-093845
61. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-

Related Productivity Losses. *Value Health* 2015;18(6):753-8. doi: 10.1016/j.jval.2015.05.009
62. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24. doi: 10.1002/acr.20640
63. Collins NJ, Bierma-Zeinstra SM, Crossley KM, et al. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med* 2013;47(4):227-33. doi: 10.1136/bjsports-2012-091696
64. Salaffi F, Stancati A, Silvestri CA, et al. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004;8(4):283-91.
65. Kastelein M, Luijsterburg PA, Belo JN, et al. Six-year course and prognosis of nontraumatic knee symptoms in adults in general practice: a prospective cohort study. *Arthritis Care Res (Hoboken)* 2011;63(9):1287-94. doi: 10.1002/acr.20522
66. Crossley K, Bennell K, Green S, et al. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.
67. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication. 2010 [Available from: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html accessed 23 November 2017.

FIGURE CAPTIONS

Figure 1. Flow of participants through the study.

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

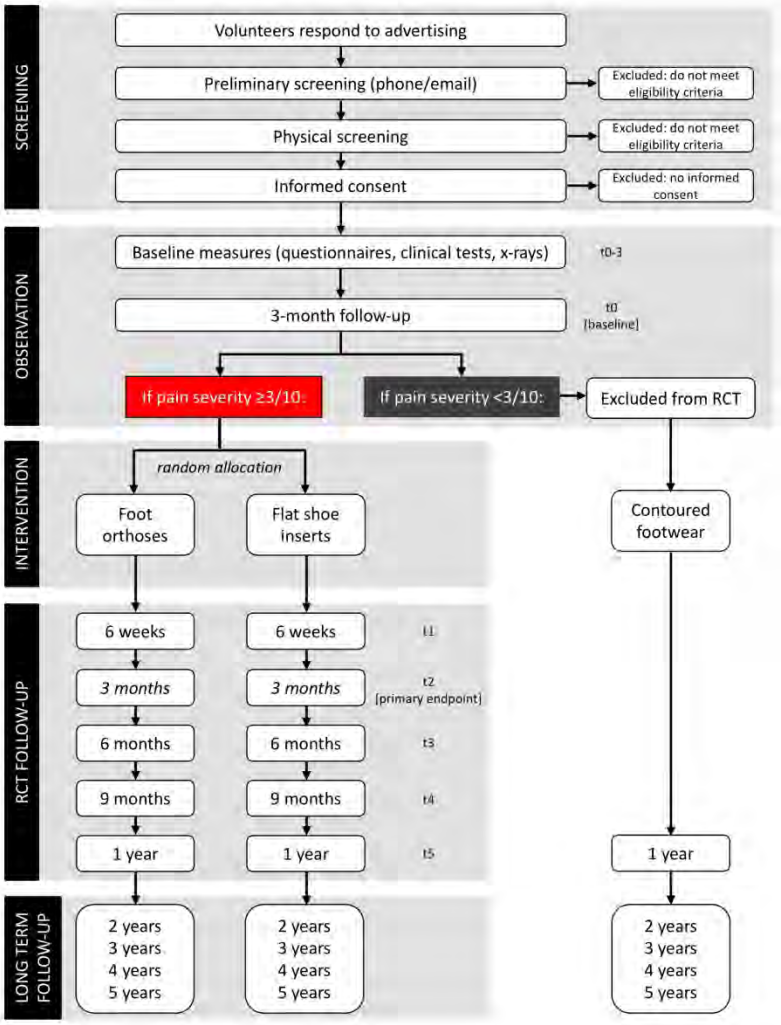

Figure 1. Flow of participants through the study.

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	STUDY PERIOD						
	Enrolment / Baseline		Post-allocation				Close-out
TIMEPOINT*	t0-3	t0	t1	t2	t3	t4	t5
ENROLMENT:							
Eligibility screen	X						
Informed consent	X	X					
Allocation		X					
INTERVENTIONS:							
Contoured shoe inserts		◆	—	—	—	—	◆
Flat shoe inserts		◆	—	—	—	—	◆
ASSESSMENTS:							
Participant characteristics	X						
Knee pain severity	X						
Navigate Pain	X						
PainDetect	X						
Pain Catastrophising Scale (PCS)	X						
Sport and physical activity participation	X						
Anthropometric measures	X						
Knee clicking and crepitus	X						
Knee extension torque	X						
Foot Posture Index (FPI)	X						
Foot mobility	X						
Weight bearing ankle dorsiflexion range of motion	X						
Footwear Assessment Tool	X						
10-metre Walk Test	X						
Primary outcome measure:							
Worst knee pain severity during self-nominated aggravating activity in the previous week	X	X	X	X	X	X	X
Secondary outcome measures:							
Patient-reported global rating of change (GROC)			X	X			X
Pain visual analogue scales	X	X	X	X	X	X	X
Knee injury and Osteoarthritis Outcome Score (KOOS)	X	X		X			X
Anterior Knee Pain Scale (AKPS)	X	X		X			X
Arthritis Self-Efficacy Scale (ASES)	X	X		X			X
Tampa Scale for Kinesiophobia (TSK)	X	X		X			X
Short-form 12 (SF-12)	X	X		X			X
Euroqol-5D-5L (EQ-5D)	X	X		X	X	X	X
Other outcomes:							
Use of co-interventions for knee pain				X	X	X	X
Adverse events				X	X	X	X
Direct health care costs				X	X	X	X
iMTA Productivity Cost Questionnaire (iPCQ)				X	X	X	X
Credibility and Expectancy Questionnaire (CEQ)		X		X			X

* t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months; t3 = 6 months; t4 = 9 months; t5 = 12 months

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

275x397mm (300 x 300 DPI)

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

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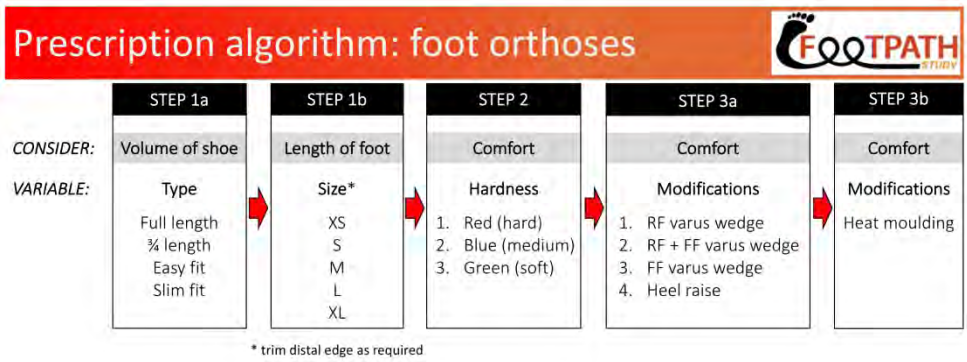

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

338x190mm (300 x 300 DPI)

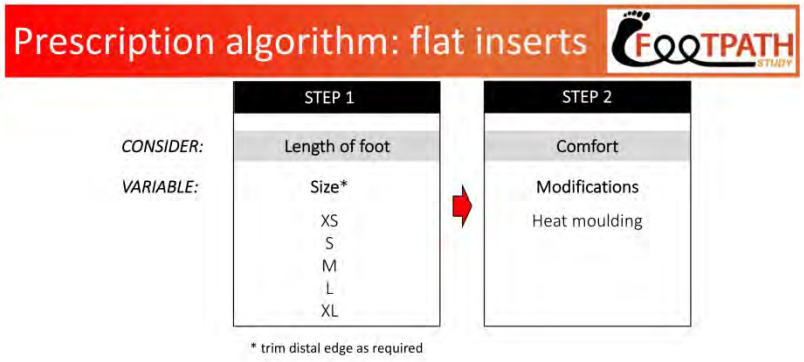

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

338x190mm (300 x 300 DPI)

Supplementary file 1. Participant information and consent forms.

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PARTICIPANT INFORMATION STATEMENT: PART A

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
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Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
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Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au
Dr Harvi Hart	School of Allied Health, La Trobe University	h.hart@latrobe.edu.au
Ms Brooke Patterson	School of Allied Health, La Trobe University	b.patterson@latrobe.edu.au

We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether footwear interventions can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether specific footwear interventions are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

If you are potentially eligible for the trial, you will be screened via telephone, and attend La Trobe University for a knee examination. If you are included in the trial, you will undergo baseline assessment at the same venue as your knee examination. For the first 3 months of the trial, we will monitor your knee condition using questionnaires. You will then be provided with a footwear intervention to take home and wear for 1 year, and be asked to complete a series of questionnaires online or via mail.

All assessments and footwear interventions will be provided at no cost to you.

At baseline, you will be asked to complete:

- Questionnaires, including:
  - Age, gender, occupational and sporting history, mechanism of injury, symptom duration, rehabilitation, medication use, and family history of arthritis
  - Your expectations and values regarding your condition and its management
  - Physical activity (type, frequency and dosage)
  - Knee-related pain, symptoms, function and quality of life
  - General health and self-efficacy
- Physical testing, including:
  - Height, weight and waist circumference
  - Movement and palpation of your knee
  - Foot and ankle mobility measures
  - Knee strength: The maximal strength of your leg muscles will be measured using a special device. The examiner will ask you to push against it, as hard as you can, in one direction.
  - Functional performance tests, including walking and hopping
  - Measures of pressure pain onset: The examiner will apply a pressure stimulus with a probe to 4 points around your knee, and one point at your elbow. As the pressure increases, you will be asked to press a button to indicate the precise moment that the pressure sensation changes to one of pressure and the first onset of pain. At this point the pressure will cease. Three measures will be taken at each site, and repeated on both knees and elbows.
- X-rays of your knee:
  - You will undergo the x-rays at a private radiology clinic that is convenient to your home or workplace. This will take approximately 30 minutes.

You will be invited to attend the La Trobe University Health Sciences Clinic, at the Bundoora Campus of La Trobe University, to undergo the baseline assessment. This will take approximately 2 hours of your time. You will first complete a series of questionnaires about your knee pain, as outlined above. You will then undergo the physical tests described above, including measures of foot and ankle motion, knee strength, and functional performance. For the physical tests, you will be asked to change into shorts. You may either bring your own shorts or we can provide some for you.

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During the telephone screening, you may be asked if you would like to participate in a sub-study that will monitor your physical activity with a Fitbit™ device for 3 months. If you choose to participate in the sub-study, you will be issued a Fitbit™ device to wear on daily basis for 3 months. Your decision to take part or not in the sub-study will not impact on your participation in the main study. For this sub-study, you will be required to have access to the internet (home, public library etc.) and a smartphone/laptop. During the baseline assessment, the Fitbit™ application will be installed on your device to ensure that the researchers at La Trobe University can remotely extract the data from your Fitbit™.

Your knee condition will then be monitored for 3 months, during which time you will receive no intervention. This is a novel and important part of this study, to learn more about the natural course of kneecap arthritis. At the conclusion of the 3-month observation period, you will be asked to repeat the same questionnaires that you completed at baseline.

You will then be contacted by a member of the study team, regarding your footwear intervention. At this time, they will explain in more detail what is involved, and will ask you to provide consent. You will then be given a footwear intervention to take home and wear for a period of 1 year. This may involve a sandal, or a special insole to wear in your own shoes. These be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the footwear intervention in safely. You will be encouraged to use the footwear intervention as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At the conclusion of the 3-month observation period, you may be invited to participate in the sub study which will require you to continue to wear your Fitbit™ device for the duration of the main study. Your decision to take part or not in the sub study will not impact on your participation in the main study.

During this time, you may be provided with a diary where you can record your physical activity, how often you wear the footwear intervention, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the footwear intervention, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the questionnaires outlined above (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. You may ask for a copy of your assessment results. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years.

We may also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period
During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?
You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy) or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research
Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

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X-ray: You will be asked to have an x-ray of your knee. This involves exposure to a very small amount of radiation from x-ray imaging. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from the x-rays of your knee is less than 0.015 mSv. At this dose level, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be very low.

It is important to be aware that with any imaging investigation, there is a small chance of a previously unknown medical condition being detected. In the unlikely event that this occurs, we will contact you directly and inform you of the findings. Should you require further medical review, we will also organise a referral to your chosen GP. It must be emphasized that the purpose of this study is to investigate your knee pain and not to identify other potential medical conditions. While we will ensure that you are made aware of any incidental findings reported on by the consulting radiologist, neither the investigators, the radiologist, nor the Universities involved, will be held accountable if a medical condition exists that is not detected during the process.

Physical testing: The physical tests are routinely performed by Physiotherapists and Podiatrists, and are not associated with any risks. You may experience a small amount of discomfort in your joints or muscles during the physical examination or testing procedures. Please report to the researcher any undue discomfort or pain experienced during the testing. If the pain or discomfort is deemed to be excessive by yourself or the investigators, testing will cease.

If required, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

Footwear intervention: You may feel some discomfort in your feet or knees when starting to use the footwear intervention. Occasionally, footwear interventions can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the footwear intervention and/or wearing time.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

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What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part A

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator: Date:

Name and phone number of contact person in case of an emergency:

Name: Phone:

Family Doctor: Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature: Date:

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La Trobe University

PARTICIPANT INFORMATION STATEMENT: PART B

Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
Prof Hylton Menz	School of Allied Health, La Trobe University	h.menz@latrobe.edu.au
Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
Prof Trevor Russell	School of Health and Rehabilitation Sciences, The University of Queensland	t.russell1@uq.edu.au
A/Prof Anne Smith	School of Physiotherapy and Exercise Science, Curtin University	anne.smith@curtin.edu.au
Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au
Dr Harvi Hart	School of Allied Health, La Trobe University	h.hart@latrobe.edu.au
Ms Brooke Patterson	School of Allied Health, La Trobe University	b.patterson@latrobe.edu.au

We invite you to participate in our research project "Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple shoe inserts are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether shoe inserts can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether shoe inserts are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a shoe insert intervention to take home and wear for 1 year, and ask you to complete a series of questionnaires online or via mail.

All assessments and shoe insert interventions will be provided at no cost to you.

You will be randomly allocated to receive one of two different shoe inserts, to wear in your own shoes. Although they are slightly different in design and possible mechanism of effect, both of these inserts have been shown to reduce kneecap pain in younger adults. These will be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the shoe inserts in safely. You will be encouraged to use the shoe inserts as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

During this time, you will be provided with a diary where you can record your daily physical activity, how often you wear the shoe inserts, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the shoe inserts, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years. You may ask for a copy of your assessment results.

You may also be provided with a FitBit to record your physical activity. This is a simple device worn on your wrist, which records your daily step count. If you do receive a FitBit, we will provide you with information and instructions on how to use the device.

We will also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. You will be asked to fill out a consent form authorising the study to access your complete Medicare and Pharmaceutical Benefits Scheme (PBS) data as outlined on the back of the consent form, and in Appendix A of this information statement. Medicare collects information on your medical visits and procedures, and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to the Department of Human Services who holds this information confidentially. You will also receive a phone call from one of the study personnel at 3-monthly intervals, who will ask you questions about how your knee is going (e.g. time off work, impact on daily activities, use of other interventions, hospital admissions). This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period

During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies (with the exception of Medicare and PBS data). Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

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What are the possible risks of participating in this project?
You may feel some discomfort in your feet or knees when starting to wear the shoe inserts. Occasionally, shoe inserts can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the shoe inserts and/or wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?
Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?
The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Electronic data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of consent forms and questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for 15 years after completion of the project in the Health Sciences storage vault, Building 3, level 1. After 15 years, hard copies will be shredded and placed in a secure document disposal bin, and computer files will be permanently deleted.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

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Funding
Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?
Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints
If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,
Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

Appendix A. Medicare and Pharmaceutical Benefits Scheme data fields

Medicare Benefits Schedule (MBS)	
Date of service	Date that the service was rendered by the provider, to the patient
MBS Item number	Items Numbers as per the Medicare Benefits Schedule
MBS Item description	Describes the service as per the Medicare Benefits Schedule
Provider charge	The dollar amount the provider charged for the service
Benefit paid	The benefit paid to the patient
Patient Out of Pocket	The dollar amount the patient is out of pocket
Hospital Indicator	Indication of whether or not the service was provided in hospital
Pharmaceutical Benefits Scheme (PBS)	
Date of supply	Date the prescription was supplied by the pharmacy
PBS Item Number	Items Numbers reflected in the PBS
PBS Item Description	The item description as noted in the PBS
Patient contribution	The contribution paid by the patient
PBS Net Benefit	Amount paid by the Government
Form category	Original or repeat prescription
ATC Code	The ATC Code is defined by the Commonwealth Department of Health which may be different to the code allocated by the WHO Collaborating Centre for Drug Statistics Methodology
ATC Name	The group the drug falls under in the Anatomical Therapeutic Chemical (ATC) classification system

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): PART B

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator:	Date:

Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature:	Date:

Participant ID:

PARTICIPANT CONSENT FORM

Consent to release of Medicare and/or Pharmaceutical Benefits Scheme (PBS) claims information for the purposes of the FOOTPATH Study

Important Information

Complete this form to request the release of personal Medicare claims information and/or PBS claims information to the FOOTPATH Study.

Any changes to this form must be initialled by the signatory. Incomplete forms may result in the study not being provided with your information.

By signing this form, I acknowledge that I have been fully informed and have been provided with information about this study. I have been given an opportunity to ask questions and understand the possibilities of disclosures of my personal information.

PARTICIPANT DETAILS

1. Mr ☐ Mrs ☐ Miss ☐ Ms ☐ Other ☐

Family name: _____ First given name: _____

Other given name (s): _____

Date of birth: DD/MM/YYYY

2. Medicare card number: _____

3. Permanent address: _____

Postal address (if different to above): _____

AUTHORISATION

4. I authorise the Department of Human Services to provide my:

☐ Medicare claims history OR

☐ PBS claims history OR

☐ Medicare & PBS claims history

for the period* DD/MM/YYYY to: DD/MM/YYYY to the FOOTPATH Study.

*Note: The Department of Human Services can only extract 4.5 years of data (prior to the date of extraction), The consent period above may result in multiple extractions.

DECLARATION

I declare that the information on this form is true and correct.

5. Signed: _____ (participant's signature) Dated: DD/MM/YYYY **OR**

6. Signed by _____ (full name) _____ (signature) on behalf of participant

Dated: DD/MM/YYYY

☐ Power of attorney* ☐ Guardianship order*

* Please attach supporting evidence

APP 5 – PRIVACY NOTICE

Your personal information is protected by law, including the Privacy Act 1988, and is collected by the Australian Government Department of Human Services. The collection of your personal information by the department is necessary for administering requests for statistical and other data.

Your information may be used by the department or given to other parties for the purposes of research, investigation or where you have agreed or it is required or authorised by law.

You can get more information about the way in which the Department of Human Services will manage your personal information, including our privacy policy at humanservices.gov.au/privacy or by requesting a copy from the department.

Power of attorney – A power of attorney is a document that appoints a person to act on behalf of another person who grants that power. In particular, an enduring power of attorney allows the appointed person to act on behalf of another person even when that person has become mentally incapacitated. The powers under a power of attorney may be unlimited or limited to specific acts.

Guardianship order – A Guardianship order is an order made by a Guardianship Board/Tribunal that appoints a guardian to make decisions for another person. A Guardianship order may be expressed broadly or limited to particular aspects of the care of another person.

A sample of the information that may be included in your Medicare claims history:

Date of service	Item number	Item description	Provider charge	Benefit paid	Patient out of pocket	Hospital indicator
20/04/09	00023	Level B consultation	$38.30	$34.30	$4.00	N
22/06/09	11700	ECG	$29.50	$29.50		N

A sample of the information that may be included in your PBS claims history:

Date of supply	PBS item code	Item description	Patient contribution (this includes under copayment amounts**)	Net Benefit (this includes under copayment amounts**)	Form Category	ATC Code	ATC Name
06/03/09	03133X	Oxazepham Tablet 30 mg	$5.30	$25.55	Original	N05 B A 04	Oxazepam
04/07/09	03161J	Diazepam Tablet 2 mg	$30.85		Repeat	N05 B A 01	Diazepam

** Under co-payments can now be provided for data after 1 June 2012

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PARTICIPANT INFORMATION STATEMENT: PART C

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
Prof Hylton Menz	School of Allied Health, La Trobe University	h.menz@latrobe.edu.au
Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
Prof Trevor Russell	School of Health and Rehabilitation Sciences, The University of Queensland	t.russell1@uq.edu.au
A/Prof Anne Smith	School of Physiotherapy and Exercise Science, Curtin University	anne.smith@curtin.edu.au
Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au

We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The primary aim of this project is to determine whether footwear can reduce pain and improve outcome in people with kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a footwear intervention to take home and wear, and ask you to complete a series of questionnaires online or via mail at yearly intervals for the next 5 years.

All assessments and footwear interventions will be provided at no cost to you.

You will be contacted by one of the study personnel (who is an experienced Podiatrist or Physiotherapist) to confirm your shoe size. They will determine the best method of prescribing the footwear intervention to you. This may require you to attend an appointment at La Trobe University. We will give you instructions on how to break the footwear in safely. You will be encouraged to wear the footwear as much as is comfortable for you, when you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At yearly intervals, for a period of 5 years, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. You may ask for a copy of your assessment results.

Use of pain-relieving medications and other forms of treatment during the trial period

You are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

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Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

You may feel some discomfort in your feet or knees when starting to wear the footwear. Occasionally, footwear can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under

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guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu,

Ms Jade Tan

(on behalf of the research team)

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part C

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:
Investigator:		Date:

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Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

Participant's signature:	Date:

Supplementary file 2. Outcome measures used in the FOOTPATH Study.

	Description	t0-3	t0	t1	t2	t3	t4	t5
Primary outcomes								
Worst knee pain severity during self-nominated aggravating activity in the previous week	Participants nominate one of three everyday activities that they experience the greatest knee pain severity with (rising from sitting, stair ambulation, squatting). Pain severity during this activity is measured on a 100mm visual analogue scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). Pain visual analogue scales are reliable, valid and responsive in people with patellofemoral pain.[1] Pain severity associated with a self-nominated aggravating activity is sensitive to change in people with PFOA and knee OA.[2]	•	•	•	•	•	•	•
Secondary outcomes								
Self-reported global rating of change (GROC)	Participants will respond to the question 'overall, how has your knee pain changed since the start of the study?' on a 7-point Likert scale ('much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'). This will be dichotomised to 'improved' ('much better, 'better') and 'not improved' ('a little better' to 'much worse'). GROC has been used in previous PF pain RCTs to calculate relative risks and number needed to treat for clinical guidelines.[3 4] This is a clinically relevant and stable concept for evaluating an individual patient's perspective on meaningful improvement.[5]			•	•			•
Pain visual analogue scales	Participants will complete a series of pain visual analogue scales, rating the severity of their knee pain on a 100mm scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). This will include: (i) usual pain over the past week; (ii) worst pain over the past week); (iii) maximum pain when walking; (iv) maximum pain when sitting for one hour; (v) maximum pain when rising from sitting; (vi) maximum pain when going up and down stairs; (vii) maximum pain when squatting; and (viii) maximum pain when running. Reliability, validity and responsiveness of pain visual analogue scales have been established in patellofemoral pain.[1]	•	•	•	•	•	•	•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Knee injury and Osteoarthritis Outcome Score (KOOS)	The KOOS consists of 42 items across five subscales: (i) symptoms; (ii) pain; (iii) function in daily activities; (iv) function in sport/recreation; and (v) knee-related quality of life.[6] Participants will also complete the 11-item KOOS-PF, a subscale developed to be used in people with patellofemoral pain conditions in conjunction with the original KOOS.[7] Participants respond to each item using a 4-point Likert scale, and a normalised score from 0-100 is calculated for each subscale (100 = no knee problems, 0 = extreme knee problems. The KOOS and KOOS-PF are reliable and valid in people with patellofemoral pain and osteoarthritis.[7]	•	•		•			•
Anterior Knee Pain Scale (AKPS)	The AKPS, or Kujala Patellofemoral Score, consists of 13 items describing common symptoms and functional impairments associated with patellofemoral pain conditions.[8] Weighted scores from each item are summed to give an overall score (100 = no disability, 0 = maximal disability). The AKPS is reliable, valid and responsive to change in people with patellofemoral pain.[1 8 9]	•	•		•			•
Arthritis Self-Efficacy Scale (ASES)	The ASES consists of 20 items across three subscales: (i) self-efficacy for managing pain; (ii) self-efficacy for physical function; and (iii) self-efficacy for controlling other symptoms.[10] For each item, participants rate on a 10-point scale how certain they are that they can perform specific tasks or manage their knee pain symptoms. Item scores are summed to provide an overall score from 10-100, where higher scores represent greater self-efficacy.[11] The ASES has adequate reliability, validity and responsiveness for research use.[11]	•	•		•			•
Tampa Scale for Kinesiophobia (TSK)	The TSK evaluates fear of movement and re-injury.[12] Participants use a 4-point Likert scale to rate their agreement with 17 items (1=strongly disagree, 4=strongly agree). Items 4, 8, 12 and 16 are reverse scored, and a total score calculated ranging from 17 to 68, where higher scores indicate greater fear of movement and re-injury. While evaluation of psychometric properties has not been performed in people with patellofemoral pain, the Thai language version of the TSK demonstrated adequate measurement properties in people with knee osteoarthritis .[13]	•	•		•			•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Short-form 12 (SF-12)	The SF-12 (version 2) comprises 12 items across eight domains: bodily pain (BP), physical functioning (PF), role limitations due to physical health problems (RP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH).[14] A physical component score (PCS) is calculated from the BP, PF, RP and GH subscales, and a mental component score (MCS) calculated from the VT, SF, RE and MH subscale. Transformed scores for each subscale range from 0 (worst health state) to 100 (best health state). The SF-12 is valid for reproducing the PCS and MCS of the Short-form 36 (SF-36).[15]	•	•		•			•
Euroqol-5D-5L (EQ-5D)	The EQ-5D consists of five items encompassing five dimensions: mobility, self-care, usual activity, pain and discomfort, and anxiety and depression. Participants select the best of five possible responses. The EQ-5D Index is calculated from a predefined algorithm, with a score of 1 representing the best imaginable health state, 0 representing death, and negative scores indicating a state worse than death.[16] Participants will also complete the EQ-5D visual analogue scale evaluating self-reported health state (0=worst imaginable health state, 100=best imaginable health state). EQ-5D has been validated in knee pain cohorts.[17]	•	•		•	•	•	•
Use of co-interventions for knee pain	The number of participants who report using co-interventions specifically for their knee pain (e.g. medication, allied health services such as physiotherapy, complementary medicines such as osteopathy, topical medicines, or taping/bracing) will be recorded from a number of sources (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[18]				•	•	•	•
Adverse events	Adverse events (e.g. new pains in the body, rolled ankles, blisters, swelling) will be recorded from a number of sources specifically designed for this study (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[19]				•	•	•	•

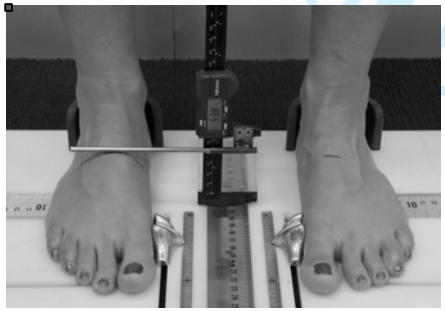
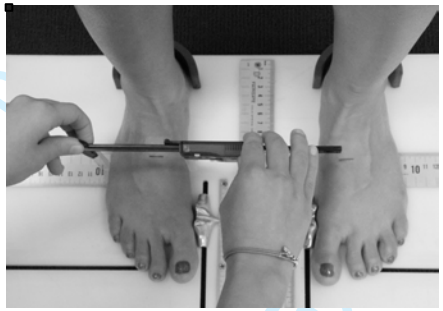
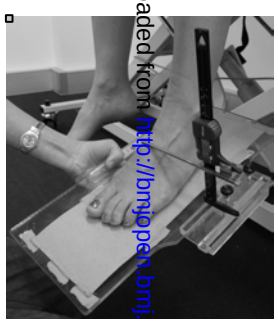
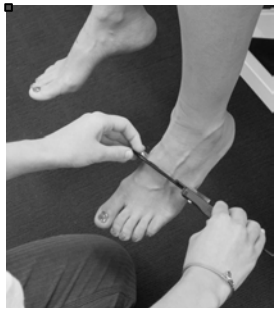
	Description	t0-3	t0	t1	t2	t3	t4	t5
Direct health care costs	Direct health costs will be captured from multiple sources, for use in economic analyses: (i) Medicare Australia and Pharmaceutical Benefits Scheme (PBS) databases; (ii) participant self-report (monthly log-books; 3-monthly telephone interviews); and (iii) costs associated with delivering the study intervention.				•	•	•	•
Institute for Medical Technology Assessment (iMTA) Productivity Cost Questionnaire (iPCQ)	The iPCQ will be used to capture indirect / productivity costs, for use in economic analyses. It consists of 18 questions and three modules: (i) productivity loss due to absence from paid work; (ii) productivity loss during paid work due to health reasons; and (iii) productivity loss of unpaid work.[20] The iPCQ will be administered via telephone interview.				•	•	•	•
Credibility and Expectancy Questionnaire (CEQ)	The six-item CEQ was used to evaluate the credibility and expectancy of treatment received.[21 22] Items 1, 2, 3 and 5 are scored on a nine-point Likert scale, while items 4 and 6 are scored from 0-100%. Higher scores indicate greater perceived credibility and benefit. The CEQ has demonstrated adequate internal consistency and test-retest reliability.[22]		•		•			•
Other measures								
Knee pain severity	Participants will respond to the question "how bad would you say your knee pain is now?" by selecting one of four responses: 'no pain', 'mild', 'moderate', 'severe'.	•	•	•	•	•	•	•
Navigate Pain	Participants will record the location of their knee pain on a high-resolution 3D schema of the lower limb, using a custom application (Navigate Pain, Aalborg University, Denmark)[23 24] on a personal computer tablet (Samsung Galaxy, Samsung, Seoul, South Korea). Pain areas will be individually extracted and expressed as total pixels by the software, and visually classified for location.[25] The touch screen interface has high agreement with paper-based pain maps.[24]	•						

	Description	t0-3	t0	t1	t2	t3	t4	t5
PainDetect	PainDetect will be administered to identify neuropathic pain components.[26] Nine items evaluating gradation of pain, pain course pattern and pain radiation are summed to give an overall score from -1 to 38. The presence of neuropathic pain is likely if the total score is ≥19, while a score ≤12 suggests that pain is unlikely to have a neuropathic component.[26] PainDetect is reliable[27] and recommended as a screening measure for neuropathic pain.[28]	•						
Pain Catastrophising Scale (PCS)	The PCS is a 13-item questionnaire used to evaluate pain-related catastrophising.[29] Participants use a 5-point Likert scale to indicate the degree to which they experienced each thought/feeling when they have pain. An overall score is calculated by summing all 13 items (range 0-52), as well as three subscale scores for rumination, magnification and helplessness. Higher scores indicate higher degrees of pain catastrophizing. The PCS has sufficient reliability and validity for use in adults.[29]	•						
Sport and physical activity participation	Participants will complete a standardised questionnaire about their current and previous physical activity. Items include: (i) current regular physical activity (>30mins duration); (ii) other physical activity or competitive sport prior to knee pain onset; (iii) whether they have changes their physical activity because of their knee pain, and why; and (iv) whether they plan to return to sport if they have modified their physical activity.	•						

t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months (time of primary interest); t3 = 6 months; t4 = 9 months; t5 = 12 months (close out)

Supplementary file 3. Clinical tests performed prior to commencing the observation period (t0-3).

Test	Description
Anthropometric measures	Height will be measured using a stadiometer. Body mass will be measured using digital scales. Body mass index (BMI) will be calculated as mass (kg) / height (m)^2. Waist circumference will be measured with a tape measure, at the narrowest point or midpoint of the lower costal border (10th rib) and iliac crest.
Knee clicking and crepitus	The presence of knee clicking and crepitus will be evaluated bilaterally using methods described by Schiphof et al.[30] Participants will be seated comfortably on a standard chair. The tester will rest their hand over the participants' patella of the test limb, and ask the participant to actively extend their knee from 90° of knee flexion to 0° of knee extension (if possible) 3 times. Crepitus will be defined as an audible grinding noise and/or palpable vibrations in the knee during active movement.
Knee extension torque	Knee extension force will be measured bilaterally using previously described methods .[31] Participants will sit comfortably on a high stool, with their knees in 90° flexion, and their thighs secured to the chair with a seatbelt (Figure 1). Participants may hold the seat of the chair with their arms in full extension. A strain gauge will be secured to the posterior aspect of the chair and strapped around the test ankle, at a point 10cm above the lateral malleolus. Participants will be instructed to extend their knee to end of range and push maximally for three seconds. Three trials will be performed on each side. To calculate knee extension torque, force will be multiplied by leg length (distance between the lateral femoral epicondyle and lateral malleolus).  Figure 1. Test position.
Foot Posture Index (FPI)	The FPI is a valid and reliable method of quantifying weight bearing static foot posture.[32] Methods are detailed in the user guide and manual (available online).[33] Participants will stand in relaxed bilateral stance, with their arms by their side and looking straight ahead. Six aspects of static foot posture are evaluated on each foot: (i) talar head palpation; (ii) supra and infra malleolar curvature; (iii) calcaneal frontal plane position; (iv) bulging in the region of the talonavicular joint; (v) height and congruence of the medial longitudinal arch; and (vi) abduction/adduction of the forefoot on the rearfoot. Each feature is scored on a five-point scale (-2 = supinated; 0 = neutral; +2 = pronated). A total score for each foot is calculated by summing each of the six items. Total scores range from -12 (supinated) to +12 (pronated).

Foot mobility	Foot mobility will be evaluated bilaterally using the Foot Assessment Platform.[34] For weight bearing (WB) measures, participants will be positioned in bilateral stance on a custom-designed platform. Total foot length will be measured, and the dorsum of the foot marked at 50% of total foot length. Midfoot height and midfoot width will be measured (in millimetres) at 50% foot length using digital calipers (Figure 2A and 2B). Participants will then be seated on the edge of a plinth to capture non-weight bearing (NWB) foot measures. With the femur horizontal, tibia vertical, and foot and ankle hanging relaxed in space, a custom-made platform will be used to measure midfoot height at 50% foot length (Figure 2C). Midfoot width at 50% foot length will be measured in the same position, using digital calipers (Figure 2D). Foot mobility will be defined in three ways: (i) midfoot height mobility, calculated as the difference between NWB and WB midfoot height; (ii) midfoot width mobility, calculated as the difference between WB and NWB midfoot width; and (iii) foot mobility magnitude (calculated as: $\sqrt{(\text{midfoot height mobility})^2 + (\text{midfoot width mobility})^2}$).  Fig 2A. WB midfoot height.  Fig 2B. WB midfoot width.  Fig 2C. NWB midfoot height.  Fig 2D. NWB midfoot width.
Weight bearing ankle dorsiflexion range of motion	Ankle dorsiflexion range of motion will be measured in weight bearing using established methods.[35] The plane of movement will be marked using a line of tape on the floor perpendicular to the wall (horizontal line), with the tape continuing vertically up the wall to approximately knee height. Participants will stand in front of the wall with the midpoint of the calcaneus and second toe of the test limb aligned on the horizontal line. Participants will be instructed to lunge forward to touch their kneecap to the vertical line on the wall, while maintaining their heel on the floor. The assessor will ensure that the heel stays in contact with the floor. The foot will be moved back gradually along the horizontal line until the point where the kneecap just touches the wall, and the heel is almost lifting off the floor (Figure 3). The distance between the wall and the longest toe will be measured (centimetres). The test will be performed three times on each limb.  Fig 3. Test position

Footwear Assessment Tool	The participant's footwear will be assessed using selected items from the Footwear Assessment Tool, which has established reliability.[36] We will evaluate one pair of shoes that they wear most frequently. Shoe fit (Item 1) will be evaluated in terms of the length between the longest toe and end of shoe (too short: < ½ thumb's width; good: 1 to 1 ½ thumb widths; too long: > 1 ½ thumb widths); width of the shoe when the upper is grasped across the metatarsal heads (too wide: excessive bunching; good: slight bunching; too narrow: taught upper unable to be grasped); and depth (adequate; too shallow). General features will also be recorded (Item 2), including age of the shoe (months); footwear type (selected from existing template [36]); and shoe weight (grams) and length (millimetres). Structural features (Item 3) will include heel and forefoot height (millimetres); and forefoot sole flexion point (at 1st metatarsophalangeal (MTP) joint; proximal to 1st MTP joint; distal to 1st MTP joint). Motion control properties (Item 4) will consist of sagittal stability of the midfoot sole (minimal >45°; moderate <45°; rigid <10°). Cushioning (Item 5) will be evaluated be measuring lateral midsole hardness (penetrometer reading). Participants will also be asked to rate how comfortable they think their shoes are on a 100mm visual analogue scale (0=extremely uncomfortable; 100=extremely comfortable).
10-metre Walk Test	Temporospatial gait parameters (e.g. walking speed, step length) will be measured using the 10-Metre Walk Test.[37] A 10-metre walkway will be measured along a level corridor. Participants will be instructed to walk at their usual comfortable walking pace from the point when they cross the starting line (0 metres) until they cross the finish line (10 metres). The investigator will start timing the trial from the moment their first foot crosses the starting line, and stop when their first foot crosses the finish line. Participants will perform three warm-up repetitions, followed by three recorded trials, ensuring that the second and third recorded trials are within 5% of the first recorded time.

REFERENCES

1. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
2. Parkes MJ, Callaghan MJ, O'Neill TW, et al. Sensitivity to Change of Patient-Preference Measures for Pain in Patients With Knee Osteoarthritis: Data From Two Trials. *Arthritis Care Res (Hoboken)* 2016;68(9):1224-31.
3. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64.
4. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735.
5. ten Klooster PM, Drossaers-Bakker KW, Taal E, et al. Patient-perceived satisfactory improvement (PPSI): interpreting meaningful change in pain from the patient's perspective. *Pain* 2006;121(1-2):151-7.
6. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.
7. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776.
8. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
9. Watson CJ, Propps M, Ratner J, et al. Reliability and responsiveness of the lower extremity functional scale and the anterior knee pain scale in patients with anterior knee pain. *J Orthop Sports Phys Ther* 2005;35(3):136-46.
10. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44.
11. Brady TJ. Measures of self-efficacy: Arthritis Self-Efficacy Scale (ASES), Arthritis Self-Efficacy Scale-8 Item (ASES-8), Children's Arthritis Self-Efficacy Scale (CASE), Chronic Disease Self-Efficacy Scale (CDSES), Parent's Arthritis Self-Efficacy Scale (PASE), and Rheumatoid Arthritis Self-Efficacy Scale (RASE). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S473-85.
12. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.
13. Areeudomwong P, Buttagat V. Reliability and Validity of the Cross-Culturally Adapted Thai Version of the Tampa Scale for Kinesiophobia in Knee Osteoarthritis Patients. *Malays J Med Sci* 2017;24(2):61-67.
14. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.
15. Busija L, Pausenberger E, Haines TP, et al. Adult measures of general health and health-related quality of life: Medical Outcomes Study Short Form 36-Item (SF-36) and Short Form 12-Item (SF-12) Health Surveys, Nottingham Health Profile (NHP), Sickness Impact Profile (SIP), Medical Outcomes Study Short Form 6D (SF-6D), Health Utilities Index Mark 3 (HUI3), Quality of Well-Being Scale (QWB), and Assessment of Quality of Life (AQoL). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S383-412.

16. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24.
17. Barton GR, Sach TH, Avery AJ, et al. Comparing the performance of the EQ-5D and SF-6D when measuring the benefits of alleviating knee pain. *Cost Eff Resour Alloc* 2009;7:12.
18. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94.
19. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198.
20. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18(6):753-8.
21. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. *J Behav Therapy Exp Psychiatry* 1972;34:257-60.
22. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.
23. Boudreau SA, Spence R, Vasov G, et al. Feature Extraction APP for Pain Profiles. *Biosyst Biorobot* 2014;7:853-54.
24. Boudreau SA, Badsberg S, Christensen SW, et al. Digital Pain Drawings: Assessing Touch-Screen Technology and 3D Body Schemas. *Clin J Pain* 2016;32(2):139-45.
25. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160.
26. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20.
27. Tampin B, Bohne T, Callan M, et al. Reliability of the English version of the painDETECT questionnaire. *Curr Med Res Opin* 2017;33(4):741-48.
28. Turner KV, Moreton BM, Walsh DA, et al. Reliability and responsiveness of measures of pain in people with osteoarthritis of the knee: a psychometric evaluation. *Disabil Rehabil* 2017;39(8):822-29.
29. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.
30. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8.
31. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.
32. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98.

33. Redmond AC. The foot posture index: easy quantification of standing foot posture. Available at https://www.leeds.ac.uk/medicine/FASTER/z/pdf/FPI-manual-formatted-August-2005v2.pdf 2005 [Available from: http://courses.ki.se/fpi_manual-formatted_august_2005v2_1_.pdf?node=202687 accessed November 8, 2017.
34. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.
35. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80.
36. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.
37. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	***1***
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	***2***
	2b	All items from the World Health Organization Trial Registration Data Set	**-**
Protocol version	3	Date and version identifier	**-**
Funding	4	Sources and types of financial, material, and other support	***25***
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	***25***
	5b	Name and contact information for the trial sponsor	***25***
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	***25***
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	***25***

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	***4-5***
	6b	Explanation for choice of comparators	***14-15***
Objectives	7	Specific objectives or hypotheses	***5-6***
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	***6-7***
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	***6-7***
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	***8***
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	***12-16***
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	***16***
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	***16-17***
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	***16***
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	***17-20***
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	***Figure 2***

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	***20-21***
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	***7-8***
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	***12***
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	***12***
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	***12***
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	***12***
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	***12***
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	***9-11, 17-20***
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	***17***

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	***21-22***
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	***22-23***
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	***22-23***
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	***22***
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	***22***
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	***22***
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	***19-20***
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	**-**
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	***7***
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	***7***

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	***8-9, 11***
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	***8-9, 11***
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	***21-22***
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	***25-26***
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	***21-22, 24***
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	***15-16***
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	***23-24***
	31b	Authorship eligibility guidelines and any intended use of professional writers	**-**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	***24***
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	***Supplementary file 1***
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	***n/a***

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis

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The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis

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ABSTRACT

INTRODUCTION: Patellofemoral (PF) osteoarthritis (OA) is a common and burdensome subgroup of knee OA, with very little evidence for effective treatments. Prefabricated foot orthoses are an affordable and accessible intervention that have been shown to reduce PF pain in younger adults. Similarities between PF pain and PFOA, as well as our pilot work, suggest that foot orthoses may also be an effective intervention for PFOA. The primary objective of this study is to compare the 3-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on knee pain severity.

METHODS AND ANALYSIS: The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a 3-month observation period (pre-randomisation) and 12-month follow-up. 160 participants with a clinical diagnosis of PFOA will be recruited from three sites in Australia, and randomised to one of two groups (prefabricated foot orthoses or flat shoe inserts). The primary outcome is worst knee pain severity during a self-nominated aggravating activity in the previous week (100mm visual analogue scale) at three months, with a secondary endpoint at 12 months. Secondary outcomes include global rating of change, symptoms, function, health-related quality of life, kinesiophobia, self-efficacy and use of co-interventions for knee pain. Blinded, intention-to-treat analyses of primary and

secondary patient-reported outcomes will be performed, as well as economic analyses.

ETHICS AND DISSEMINATION: Ethical approval has been granted by La Trobe University's Human Ethics Committee and The University of Queensland's Medical Research Ethics Committee. Study outcomes will be disseminated via peer-reviewed journals, conference presentations targeting a range of healthcare disciplines, and an open access website with clinician resources.

TRIAL REGISTRATION NUMBER: Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study is the first full-scale RCT to evaluate simple, prefabricated foot orthoses as a treatment for patellofemoral osteoarthritis.
- The proposed project will recruit a large sample of people with patellofemoral osteoarthritis, with sample size estimates based on our pilot work.
- Outcomes will be measured at three months (primary endpoint), as well as 12 months to evaluate the longer-term efficacy of foot orthoses for this chronic condition.

- Economic analyses will provide cost-effectiveness ratios and costs per additional quality-adjusted life year, to inform clinical decision-making.
- While participants and outcome assessors are blinded, it is not possible to blind the therapists issuing the interventions, due to visual differences between the prefabricated foot orthoses and flat shoe inserts.

INTRODUCTION

Patellofemoral (PF) osteoarthritis (OA) is an important subgroup of knee OA, whose burden is becoming increasingly evident. Radiographic PFOA is more common than tibiofemoral (TF) OA in people with chronic knee pain (64 to 69% compared to 44 to 45%).[1 2] The PF joint is often the first knee joint compartment affected by OA, and increases the risk of TFOA development and progression.[3] Structural features of PFOA show greater association with knee symptoms than TFOA features. Patellofemoral osteophytes (but not TF osteophytes) are associated with knee pain (odds ratio 2.3, 95% CI 1.1 to 4.8),[4] and reduced patellar cartilage volume (but not femoral or tibial) is related to greater pain and functional impairment.[5] Importantly, compared to TFOA, PFOA tends to occur in younger people,[1] who often have greater daily physical demands due to occupational and/or childcare responsibilities. Considering the progressive nature of PFOA, the side effects of long-term medication use, and that pain and functional limitations are primary barriers to physical activity[6] and indications for total knee replacement,[7] interventions that can effectively reduce PFOA pain are urgently required.

Despite the burden of PFOA, and best-practice guidelines recommending non-surgical, non-drug interventions as the first line strategy for knee OA management,[7] there is very little evidence for effective treatments for PFOA. Although combined interventions (e.g. PF taping, knee/hip exercises, manual therapy, education)[8 9] and

knee braces[10] have some evidence of efficacy, their longer-term effects appear to be limited by poor treatment adherence.[11 12] This is particularly relevant for middle-aged adults with PFOA, whose busy lifestyles and family and work commitments are likely to influence adherence to exercise programs.[11] Issues with knee brace bulkiness and interference with clothing[12] are likely to be barriers to brace wear. For braces and orthoses to be effective, they must be comfortable and unobtrusive to daily living to ensure maximal adherence and patient outcomes.

Foot orthoses are inserts worn in everyday footwear that are contoured to match the shape of the foot. Prefabricated foot orthoses are affordable and accessible, and are an effective treatment for PF pain in young adults (aged 18 to 40 years).[13 14] Based on similarities in symptoms, biomechanics and muscle function between PF pain and PFOA,[15-17] it is plausible that foot orthoses could also have positive effects in people with PFOA. Pilot data show that people with PFOA (n=23, mean age 59±10) report immediate improvements in pain when performing a step-down task with foot orthoses, compared to shoes alone.[18] We observed high adherence and only transient, minor adverse events in our previous trial of foot orthoses in PF pain,[19] suggesting the feasibility of long-term wear. It is therefore timely to conduct a randomised clinical trial (RCT) to evaluate foot orthoses efficacy in this population. The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) will investigate the efficacy of prefabricated foot orthoses for people with PFOA.

OBJECTIVES

Primary objective

The primary objective is to compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts on knee pain severity in people with PFOA. *We hypothesise that, compared to flat inserts, foot orthoses will result in greater improvements in knee pain during a nominated aggravating activity at three months (H1).*

Key secondary objectives

1. Compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on patient-reported global rating of change (GROC). *We hypothesise that, compared to flat inserts, foot orthoses will result in more participants reporting marked improvement at three months (H2).*
2. Compare the 12-month efficacy of prefabricated foot orthoses and flat shoe inserts on GROC, knee pain severity, function, quality of life, kinesiophobia, self-efficacy and use of co-interventions, in people with PFOA.

   We hypothesise that foot orthoses will yield: (i) more participants reporting marked improvement, and greater improvements in knee pain during a nominated aggravating activity, at 12 months (H3); and (ii) greater improvements in knee pain

severity, the Knee injury and Osteoarthritis Outcome Score (KOOS), Anterior Knee Pain Scale, Short-Form 12, EuroQol-5D, Tampa Scale for Kinesiophobia and Arthritis Self Efficacy Scale, and less co-intervention use at three and 12 months (H4).

3. Evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts in people with PFOA.

   We hypothesise that foot orthoses will yield better cost-effectiveness ratios and lower costs per additional quality-adjusted life year after 12 months (H5).

Other secondary objectives

Alongside primary and secondary RCT outcomes, we will investigate the following additional secondary objectives, in people with PFOA.

1. Identify factors that predict change in patient-reported symptoms over a three-month wait-and-see period.
2. Describe characteristics of people with PFOA, including patterns of pain location.
3. Investigate whether foot mobility is related to radiographic features of PF and TF joint alignment and radiographic features of OA.
4. Identify clinically applicable factors that predict poor prognosis at three and 12 months, and determine baseline values of predictor variables to facilitate clinical identification of people with a poor prognosis.

5. Determine the three-month effect of prefabricated foot orthoses on physical activity level compared to flat shoe inserts.
6. Explore factors that are associated with clinical outcomes with prefabricated foot orthoses at three and 12 months.

METHODS AND ANALYSIS

Trial design

The FOOTPATH Study is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a three-month observation period (pre-randomisation) and 12-month follow-up. Equal numbers of participants will be randomised to each group, with the primary endpoint of GROC and pain after three months. The trial will be conducted across two university sites in Melbourne and Brisbane, Australia, with a satellite site in Hobart, Tasmania. The trial protocol was developed in consultation with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement[20 21] and the Osteoarthritis Research Society (OARSI) recommendations.[22] The trial was prospectively registered (Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347).

Ethics approval

Ethical approval has been granted by La Trobe University's Human Ethics Committee (HEC16-113) and The University of Queensland's Medical Research Ethics Committee (2017000284). In the event that a substantive modification to the study protocol is required (i.e. modifications that affect the conduct of the study), a formal protocol amendment will be prepared, and all proposed amendments reviewed by the two ethics committees. These will be reported in the ANZCTR and study publications.

Participant recruitment and eligibility criteria

Figure 1 summarises the flow of participants through the study. Participants will be recruited from the community in Melbourne, Brisbane, Hobart and regional Victoria. We will utilise a multifaceted recruitment strategy that has successfully recruited people of all ages with knee pain in our previous studies. This will include strategies such as paid and free advertisements in local newspapers, community magazines and newsletters (e.g. University staff bulletins, seniors newsletters); posters in senior citizen's centres, golf and bowling clubs, and retirement villages; sandwich boards and handouts at community events (e.g. fun runs, farmer's markets); radio and television media releases; mail-outs to health practitioners in recruitment areas (e.g. general practitioners, orthopaedic surgeons, physiotherapists); posts on university and research centre websites (La Trobe University, The University of Queensland); social media (e.g. Facebook, Twitter); and patients from the La Trobe University Health Sciences (Podiatry) Clinic, community health care centres, and hospital waiting lists.

Based on recruitment rates of 6 participants per month during our feasibility trial (single site), as well as known periods of slow recruitment (e.g. December/January), conservative estimates indicate that the duration of recruitment will be approximately 20 months. Recruitment rates across all sites will be monitored during the trial, and recruitment strategies adjusted accordingly to meet recruitment targets. There will be no incentives provided to trial investigators or participants for enrolment.

Volunteers who respond to advertisements will be screened for eligibility using a two-stage screening process. This will be conducted by an experienced musculoskeletal health professional (physiotherapist or podiatrist with a minimum of five years of musculoskeletal clinical experience). Preliminary screening questions will be asked via telephone or email. Potentially suitable volunteers will then be invited to attend a physical screening appointment at La Trobe University, The University of Queensland or a private practice (if in regional Victoria or Hobart), where a comprehensive musculoskeletal examination will be completed.

We will use a clinical diagnosis of PFOA[23], adapted from the NICE guidelines.[24] This is to facilitate generalisation of findings to clinical practice, without the need for imaging. Inclusion criteria will be: (i) age 50 years and over; (ii) predominant symptom of anterior or retropatellar knee pain aggravated by at least two PF joint loading activities (e.g. stairs, squatting, rising from sitting); (iii) pain present during these activities on most days of the previous month; (iv) pain severity of at least three on an

11-point numerical rating scale (NRS, 0-10) during aggravating activities; (v) duration of symptoms of at least three months; and (vi) either no morning joint-related stiffness, or morning stiffness that lasts no longer than 30 minutes.

Volunteers will be excluded if they have: (i) knee pain symptoms predominantly from other knee (TF joint) structures, hip or lumbar spine; (ii) knee injections or use of any shoe inserts within the previous three months; (iii) recent commencement of new physiotherapy treatment for PF pain (i.e. new intervention, or modifications to existing intervention such as therapeutic exercise); (iv) any foot condition precluding the use of foot orthoses or flat shoe inserts; (v) history of lower limb surgery involving major reconstructive procedure (e.g. anterior cruciate ligament reconstruction, osteotomy, arthroplasty); (vi) planned lower limb surgery in the following 12 months; (vii) neurological or systemic arthritis conditions; (viii) major medical conditions (e.g. cancer); (ix) contraindications to x-ray (pregnancy, breastfeeding); or (x) an inability to understand written and spoken English.

Informed consent

All volunteers who meet the study eligibility criteria will be provided with a participant information sheet. This will provide details of the first phase of the study (observation period), and outline procedures for the second phase of the study (intervention). A trained investigator will discuss the study with volunteers, and provide opportunities

for volunteers to ask any questions. The lead investigator at each university site (Melbourne: KMC; Brisbane: NJC) will be available for consultation as required. All participants will provide written informed consent prior to participation. At the conclusion of the observation period, participants will provide additional consent for the intervention phase of the study (detailed below). Participant information and consent forms for all components of the study are included in Supplementary file 1.

Baseline assessment

Participants will attend a single session at La Trobe University, The University of Queensland, or a private physiotherapy/podiatry clinic (if in regional Victoria or Hobart) for baseline assessment. Structured questionnaires and established patient-reported outcome measures will be used. These will be administered in an electronic format (via computer or tablet) to familiarise participants with the electronic platform. Participants will then nominate their preferred methods of communication (e.g. phone, email) and questionnaire completion (paper or electronic format [25]) for the duration of the study.

Participant characteristics will include age, sex, occupation, duration of knee pain symptoms, major medical conditions, other joint complaints in the past month,[26] and medication use.

Patient-reported outcome measures are outlined in Figure 2 and detailed in Supplementary file 2. Pain will be evaluated as knee pain severity over the past week (100mm visual analogue scales [VAS]),[27] PainDetect[28] and Navigate Pain.[29] The KOOS[30] and patellofemoral subscale[31] will evaluate pain severity, other symptoms, function, knee-related quality of life and patellofemoral symptoms. Other measures include the Anterior Knee Pain Scale (AKPS),[32] Short-Form-12 (SF-12) questionnaire,[33] EuroQol (EQ) 5D-5L questionnaire,[34] Tampa Scale for Kinesiophobia,[35] Pain Catastrophising Scale,[36] Arthritis Self Efficacy Scale[37], and sport and physical activity participation.

Participants will also complete a battery of clinical measures and tests (detailed in Supplementary file 3), which were selected based on their potential to predict PFOA prognosis and/or response to foot orthoses. These include height, mass, body mass index (BMI), waist circumference, presence of knee clicking and crepitus,[38] Foot Posture Index (FPI),[39] foot mobility (Foot Assessment Platform),[40] weight-bearing ankle dorsiflexion (knee to wall test),[41] Footwear Assessment Tool,[42] knee extension torque,[43] and the timed 10-metre walk test.[44]

Radiographic assessment

All participants will attend a private radiology clinic to have radiographs taken of their nominated study knee (most symptomatic eligible knee if pain is bilateral). These will

be used to characterise the cohort, and used as predictor variables in other secondary analyses. Several radiology clinics in Melbourne, regional Victoria, Hobart and Brisbane will be used to minimise participant travel time. Weight-bearing anteroposterior, lateral and skyline views will be obtained using standard clinical protocols. Radiographs will be used to grade the presence and severity of OA features in the PF and TF joint compartments. Radiographic features of joint space narrowing and osteophytes will be graded, and the presence of PF and TF OA determined using the Kellgren-Lawrence grading system[45] and a radiographic atlas.[46] Each radiograph will be graded by two experienced investigators (NJC, KMC). Anteroposterior radiographs will also be used to measure frontal plane TF alignment,[47] while lateral and skyline views will be used to measure PF alignment using established protocols.[48]

Observation period

Participants will undergo a three-month observation period, where they will not receive any treatment for their knee pain as part of the study. This is to ensure that only participants with ongoing chronic symptoms that do not improve with time are enrolled in the RCT. Participants will be informed that they will be observed for a three-month period before receiving their intervention.

During the observation period, a subgroup of participants will undergo physical activity monitoring. This subgroup will consist of the first 60 participants who have access to

the internet and a smartphone or laptop, and who agree to participate. They will be asked to wear a Fitbit® device (Flex™ / Flex 2™, Fitbit Inc., San Francisco, USA) for the duration of the three-month observation period. This is to familiarise participants with the device and to facilitate adherence with wear during the next phase of the study. Data for physical activity will be remotely extracted from the Fitbit® website.

To maintain contact during the observation period, participants will be contacted via phone or email six weeks after their baseline measures, and will be asked to rate their average and worst knee pain severity over the past week during their nominated aggravating activity (11-point numerical rating scale). Patient-reported outcome measures taken at baseline will be repeated three months after initial assessment. Participants who rate their pain during aggravating activities as less than 30mm on a 100mm visual analogue scale will not be invited to participate in the RCT. They will be offered a pair of contoured sandals (Vionic®, Arundel, Queensland, Australia), and be invited to participate in a prospective longitudinal cohort study (a separate consent process). The same battery of questionnaires administered at baseline will be completed at yearly intervals from the date of baseline assessment (up to five years), with the addition of questionnaires regarding GROC, use of co-interventions for knee pain, and adverse events). This study will occur alongside, but separate to, the RCT.

Participants who rate their worst knee pain at least 30mm on the 100mm VAS during their nominated aggravating activity will be invited to participate in the RCT evaluating the efficacy of prefabricated foot orthoses, compared to flat shoe inserts.

Randomised clinical trial

Informed consent

Participants who are eligible to participate in the RCT will provide separate informed consent for the RCT, and for the release of their Medicare and Pharmaceutical Benefits Scheme data for economic analyses.

RCT baseline measures

Three-month follow-up outcomes from the observation period will serve as baseline data for the RCT. Participants will also complete the Credibility and Expectancy Questionnaire (CEQ) to evaluate treatment expectations.[49]

Allocation, concealment and blinding

Once baseline outcome measures are completed, participants will be randomised to receive prefabricated foot orthoses or flat shoe inserts. To ensure concealed

allocation, we will use an offsite, telephone-based interactive voice response randomisation service (NHMRC Clinical Trials Centre; randomisation will be performed using a computer-generated minimisation programme with study site as a minimisation factor). Each participant's allocated intervention will be revealed to a single investigator (JMT), who will communicate this to the participant's nominated study practitioner, or to the Brisbane site research assistant (GC) who will liaise with local study practitioners. Because we are comparing two shoe inserts with different shapes, it is not possible to blind study practitioners to group allocation. As the primary outcomes are self-reported, participants are considered assessors. To ensure participant (and thus assessor) blinding, consent will involve limited disclosure. As in our recent RCT,[8] participants will be informed that they will be randomised to one of two shoe insert interventions, but will not be informed of the treatment elements or our hypotheses. Trial participants will be unblinded once data analyses have been finalised. Because we are evaluating two different shoe inserts known to have minimal associated adverse events,[19] it is anticipated that emergency unblinding will not be required.

Interventions

Forty registered podiatrists and physiotherapists with at least five years musculoskeletal experience will fit participants with their allocated intervention. All study practitioners will fit interventions for participants allocated to both groups. To

minimise participant burden, study practitioners will be located at multiple private practice clinics across greater Melbourne, Brisbane, Hobart and regional Victoria. To ensure consistency in prescription of foot orthoses and flat shoe inserts, study practitioners will undergo formal training in standardised fitting procedures for both interventions, as used in our previous RCT of prefabricated foot orthoses and flat shoe inserts for young adults with PF pain.[19 50] Study practitioners will also be provided with a comprehensive manual and video outlining study procedures, and will have email and phone access to an unblinded investigator to discuss interventions as required (Melbourne, SEM; Brisbane, BV). Participants will attend an appointment with their study practitioner within one week of baseline assessment to undergo fitting of their allocated intervention.

Participants will be asked to wear their allocated inserts as much as possible, and will be able to transfer them between footwear. This reflects current clinical practice, and will ensure maximal wear time and potential effects.

Prefabricated foot orthoses

The prefabricated foot orthoses will replicate the intervention used in our previous RCT in young adults with PF pain.[19 50] Participants will receive prefabricated foot orthoses from a commercially available range (Vasyli Medical®, Labrador, Australia) (Figure 3A, 3B). The foot orthoses are manufactured from ethylene-vinyl acetate (EVA) of high

density (hard, Shore A 70°), medium density (Shore A 55°) and low density (soft, Shore A 45°), and have an inbuilt arch support and 6° varus wedging. A variety of lengths and shapes are available to fit the shape of different footwear. At their first appointment with their chosen study practitioner, participants will bring up to three pairs of shoes that they most commonly wear (e.g. work shoes, casual shoes and sports shoes). Study practitioners will fit one pair of foot orthoses to one pair of the participant's shoes. This will be based on which of the participant's shoes are able to accommodate the foot orthoses and provide the most support, as prefabricated foot orthoses have superior effects when used with supportive footwear.[51] Where possible, the orthoses will be able to be transferred across their usual footwear. Study practitioners will ensure that the foot orthoses are comfortable, using procedures used in our previous RCT.[19 50] Figure 4 outlines the steps involved in the prescription algorithm. The first step involves selection of the type and size of orthoses based on shoe volume and foot length, respectively. Step two involves selection of the hardness of the device, based on participant comfort. If needed, study practitioners will then follow a series of sequential modifications until comfort has been achieved: (i) adding rearfoot varus wedge; (ii) adding forefoot varus to the rearfoot varus wedge; (iii) removing the rearfoot varus wedge; (iv) adding a heel raise; and (v) gently heat moulding the orthoses. Comfortable foot orthoses can effectively reduce PF pain in younger adults,[52] and are proposed to optimise adherence and potential therapeutic effects. Participants will be given written instructions for using and adapting to the foot orthoses.

To reflect current clinical practice, and to provide sufficient opportunity to ensure adequate comfort and prescribe additional foot orthoses, participants will attend up to six appointments with the study practitioner in the first six weeks of the study. Appointments will be scheduled as follows, where appropriate for individual participants: two appointments in week one; one appointment in week two (with an additional appointment in the same week as needed); one appointment in week three or four; one appointment in week six. Participants will be provided with up to four pairs of foot orthoses, fitted to multiple pairs of commonly worn shoes, in order to maximise wear time.

To maximise outcomes of wearing a comfortable, contoured device, participants will receive one pair of sandals (Shore A 50°) from the Vionic range (Vionic®, Arundel, Queensland, Australia). Participants will be encouraged to wear these during times that they do not normally wear enclosed footwear that accommodates foot orthoses (e.g. at home or during warmer weather). Feedback from our previous RCT in young adults with PF pain[19] indicated that participants often chose to wear sandal-type footwear in warm weather, for a large proportion of the year. The Vasyli® sandals offered as an adjunct to foot orthoses were well received by participants in our previous RCT, and increased the time that participants wore a contoured device.

Participants with a high BMI (≥30 kg/m^2) will be invited to attend a follow-up appointment at six months post-randomisation, to receive new foot orthoses. This will not be necessary for those with a BMI <30 kg/m^2, as the pressure-redistributing properties of prefabricated foot orthoses are maintained after 12 months.[53] However, participants will be offered an additional appointment at six months and/or nine months if they are having any issues with the foot orthoses (e.g. increase in pain, excessive wear of orthoses).

Flat shoe inserts

Flat shoe inserts will be used as the comparator intervention (Figure 3C). This is because the contour and wedging of the foot orthoses are proposed to exert mechanical effects on the foot and lower limb, which is thought to be the basis for symptom improvement. Participants will be informed that the study aims to compare two different types of shoe inserts. The flat inserts will be described as an intervention designed to enhance sensory feedback, supported by findings from our previous RCT in PF pain, where those who received flat inserts also experienced improvements in pain over 12 months.[19] The flat inserts will be the same as those used in our previous RCT, with identical covering fabric to the foot orthoses. To control for gradual contouring that occurs with repeated wear of low-density inserts (a limitation of previous studies), the flat inserts will be made of high-density EVA (Shore A 70°). Standardised guidelines for fitting and follow-up of the flat inserts will aim to ensure

these are perceived as a credible intervention (Figure 5). As with the foot orthoses, participants will be provided with up to four pairs of flat inserts fit to multiple pairs of commonly worn shoes. To address the potential influence of therapist contact, those randomised to this group will also attend an initial appointment with a study practitioner for fitting of flat inserts, and up to two follow-up appointments to ensure adequate comfort and fit. At six months post-randomisation, a follow-up appointment will be made with the study practitioner to issue new flat inserts, to minimise the effects of cumulative contouring with repeated wear.

At the conclusion of the study, if prefabricated foot orthoses are found to be more efficacious than flat inserts, those randomised to the flat insert group will be offered one pair of foot orthoses and one additional appointment with one of the study practitioners at no cost to them.

Criteria for discontinuing or modifying allocated intervention

The occurrence of adverse events will be monitored throughout the duration of the RCT by study practitioners, participant logbooks, and three-monthly telephone calls to participants. In the event of minor adverse events (e.g. rubbing, blisters) associated with either intervention, study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms described above. This may include replacement of foot orthoses with a softer device. If participants still report

discomfort, they will be encouraged to halve their foot orthoses or flat insert wear time for a period of two weeks, and then gradually increase wear time as tolerated. If comfort is unable to be achieved, the intervention will be ceased, as this reflects current clinical practice.

In the event of a sustained increase in knee pain, or aggravation of another area of pain (e.g. low back pain), study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms. If this does not relieve the participant's symptoms immediately, then intervention will be ceased. Participants who cease their allocated intervention will be encouraged to remain in the trial to enable follow-up data collection at all nominated time points.

Strategies for improving and monitoring adherence to interventions

Study personnel will maintain regular communication with participants over the study period (e.g. email, phone), and will encourage adherence to the interventions at each time of contact. Adherence to foot orthoses or flat insert wear will be monitored using a variety of strategies. Study practitioners will record attendance at each appointment. To reduce participant burden associated with daily diary entries, participants will report their adherence at three-monthly intervals during the RCT. This will be recorded as the average days per week and hours per day that they wore the foot orthoses or flat inserts over the preceding four weeks.[54]

Concomitant care and interventions

During the observation and intervention periods, participants will be able to continue with stable medication doses and exercise programs, and use some concomitant interventions (e.g. analgesics, heat/cold, general exercise).[55] New physical therapies (e.g. exercise, manual therapy, taping, bracing), intra-articular injections and surgery will be discouraged. If participants have problems with their allocated intervention or wish to seek additional treatment outside the trial, they will be asked to contact the unblinded investigator at their trial site to discuss this (Melbourne, Hobart, JMT/SEM; Brisbane, BV). Use of concomitant interventions will be recorded during the intervention period using monthly logbooks (issued at RCT baseline) and structured questionnaires at three-monthly intervals.

Participant retention

Study personnel will utilise established methods to maximise participant retention. Following enrolment in the study at the commencement of the observation period, participants will be contacted at regular intervals throughout the study period to collect outcome data, ascertain any issues with the intervention, and maintain communication. We have endeavoured to minimise participant burden by utilising an online data collection platform, and limiting the number of appointments that

participants are required to attend in-person (one screening/baseline appointment; one x-ray appointment; maximum of seven practitioner appointments over 12 months). Although financial incentives will not be provided, financial reimbursement for travel costs will be available for participants if required. Participants who discontinue use of the intervention will be encouraged to complete outcome measures for the duration of the study to minimise missing data.

Outcomes

Outcome assessment will occur at three, six, nine and 12 months. Three months is the *a priori* primary end-point of interest, as early improvement in symptoms is likely to influence ongoing adherence with foot orthoses or flat inserts. Twelve-month follow-up will evaluate longer-term effects and economic efficiency of foot orthoses, which is important given the chronic nature of PFOA, and reflects clinical practice.

At entry into the study, participants will be asked their preferred method of receiving and completing outcome measures. Where possible, outcome data will be collected using an internet-based platform, which has equivalent measurement properties to paper-based completion.[25] This strategy was used in our pilot studies on people with PFOA,[56] ensuring feasibility of online data collection in this population. However, for participants who do not have internet access or would prefer to complete outcome measures in paper format, paper versions and reply-paid envelopes will be mailed.

Outcome measures of GROC, pain and function have been selected based on international recommendations for knee OA.[57] These are listed below and detailed in Supplementary file 2.

We have selected patient-reported outcomes over imaging and surgical endpoints, aligning with international recommendations highlighting the importance of patient-centred outcomes.[22 57] Considering the financial cost and participant burden of repeated magnetic resonance imaging (MRI), and the lack of correlation between symptoms and imaging,[58] it is important to first determine whether prefabricated foot orthoses improve pain and function. This will ensure continued adherence and greater potential for longer-term effects on joint structure. Whilst total knee replacement is usually recommended for end-stage joint disease, severe pain and functional limitations,[7 55] other factors such as race, ethnicity, socioeconomic status and patient preferences can also influence decisions for surgery.[59] Thus, patient-reported outcomes are, at present, the ideal method to evaluate foot orthoses outcomes for PFOA. Indeed, regulatory agencies such as the United States Food and Drug Administration require the use of patient-reported outcomes in the development of medical products to support labelling claims.[60]

Primary outcome (three months)

Knee pain is the predominant symptom of PFOA and the primary indication for undergoing total knee replacement.[7 55] Pain will be evaluated as *worst knee pain severity during a self-nominated aggravating activity in the previous week.*[8 10] Participants will nominate one of three everyday activities that they experience the greatest pain severity (rising from sitting, squatting or stair ambulation). Pain severity will be measured on a 100mm VAS (terminal descriptors 0=no pain, 100=worst pain possible). VAS measures of pain severity have well-established reliability and validity, including in PF pain.[27] This will be measured at baseline, six weeks, three months (time of primary interest), and six, nine and 12 months.

Secondary outcomes

Secondary outcomes will be administered at baseline, six weeks (knee pain severity and GROC), three months, six and nine months (knee pain severity and EQ-5D-5L), and 12 months (Figure 2).

- Knee pain severity over the past week (100mm visual analogue scales).[27]
- GROC (7-point Likert Scale: 'much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'; dichotomised to 'improved' ('much better, 'better') *vs.* 'not improved' ('a little better' to 'much worse').
- KOOS subscales: symptoms, pain, function in daily activities, function in sport/recreation, knee-related quality of life, patellofemoral symptoms.[30 31]

- AKPS.[32]
- SF-12.[33]
- EQ-5D-5L.[34]
- Tampa Scale for Kinesiophobia.[35]
- Arthritis Self Efficacy Scale.[37]
- Use of co-interventions for knee pain.[61]

Physical activity will be monitored in the subgroup of participants who received a Fitbit® physical activity monitor during the observation period. Data relating to physical activity levels (e.g. steps, distance) will be extracted weekly for each participant, for the first three months after randomisation. Data will be analysed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) for total step count and time spent in low, moderate and high-intensity activity bands (defined as step count per 15-minute epoch). All physical activity data will be remotely downloaded from the Fitbit® data server using a freely available R package (Fitbit Scraper), and imported into Microsoft Excel for analysis.

Other outcomes

Treatment adherence and adverse events: Every three months, participants will complete a short questionnaire for physical activity, footwear worn and foot orthoses or flat insert wear time, and adverse events.[54] Evaluation of 12-month adherence is

vital to determine whether frequency of wear is maintained long-term. This will assist with translating outcomes into clinical practice guidelines. Study practitioners will record attendance, prescription notes and adverse effects during fitting and follow-up.

Treatment credibility and expectations: The CEQ will be completed again at three and 12 months.[49]

Economic outcomes

Data on direct health costs will be sourced from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. Direct and indirect health costs (e.g. medication use, hospital admissions, other co-interventions such as physiotherapy, time off work due to PFOA or treatment) will be captured from the following sources: (i) monthly participant logbooks; (ii) 3-monthly telephone interviews; and (iii) the Institute for Medical Technology Assessment (iMTA) Productivity Costs Questionnaire (iPCQ).[62] The EQ-5D is a reliable and valid measure of health-related quality of life, and considers mobility, self-care, usual activity, pain/distress and depression/anxiety.[34 63] EQ-5D will be measured at baseline, and at three, six, nine and 12 months, and used to calculate quality-adjusted life years.

Long-term follow-up

After completion of the RCT 12-month follow-up, participants will be asked to complete the same battery of patient-reported outcome measures at yearly intervals, up to four years after completion of the RCT (five years from baseline). This will allow us to conduct prognostic analyses to identify pain trajectories and predictors of long-term outcome, as in our previous RCTs.[64]

Sample size

Treatment efficacy will be evaluated by between-group comparisons on the primary outcome measure, which is worst knee pain severity during a self-nominated aggravating activity in the previous week, measured on a 100mm VAS). The minimal clinically important difference for pain on a VAS is 15mm.[65] Sample size calculations are based on an analysis of covariance (ANCOVA) adjusting for baseline of the outcome variable, and assume a between-person standard deviation of 30mm (based on pilot data in people with PFOA) and baseline to three-month correlation of 0.5. A sample of 160 (80 per group) provides a minimum 90% power (α=0.05) to detect significant between-group differences, and allows for ~20% dropouts.

Observation period: In people with chronic knee pain, pain severity has been shown to improve naturally over three months when people are being monitored by a general practitioner.[66] Thus, to ensure that participants in the RCT have sufficient levels of pain at baseline, and that any observed improvements in pain during the three-month

time of primary interest are attributable to the intervention, we will include a three-month observation period prior to randomisation. Based on previous findings, it is anticipated that some participants will experience natural improvement in their pain severity during this time.[66] Thus, we will continue to recruit participants into the observation period until we have recruited the required sample size into the RCT (n=160). Based on conservative estimates that approximately two thirds of participants will qualify for the RCT at three months, it is anticipated that a total of ~230 participants will be recruited. This will be revised throughout the study period.

Data management and storage

The majority of outcome data will be collected electronically, facilitating simultaneous data entry. For paper-based data collection, data will be entered by a single trained investigator (JWD). A second investigator will check a random subset of manually entered documents to ensure accuracy. Once data entry is finalised, quality checks will ensure that all data points are within expected values. Only named investigators will have access to the full dataset.

Personal data, including informed consent forms, participant names, contact details and date of birth will be stored on a password-locked computer hard drive, separately from patient-reported or other study data, in order to ensure data de-identification. All subsequent study data will be identified by participant number only, and will be stored

on the La Trobe University server Research Data Storage, which is only accessible only by the research team through secure means. All project documentation will be stored on a secure, password locked external hard drive, overseen by an external company (DS PRIMA, Port Melbourne, Victoria, Australia). No persons external to the research team will have access to information stored on this server. Appropriate ethical procedures will be followed for all data (e.g. participant coding, data file encryption, storage in locked filing cabinets). Any paper containing participant details, such as baseline questionnaires, will remain in the locked filing cabinet and will not be accessible outside the premises. Data pertaining to participant characteristics, questionnaires and clinical tests will be preserved for possible future use by the investigators. De-identified data will be stored in an Excel spreadsheet. If researchers other than those listed as investigators wish to use the data, prior approval will be sought from the La Trobe University human ethics committee. Participants will be made aware of this in the Participant Information Statement, ensuring that they are aware of the possibility that their data will be used for future studies, and are able to provide written informed consent.

Due to the minimal known risks associated with the interventions being evaluated, this study will not require a formal data monitoring committee or planned interim analysis.

Statistical methods

Primary and key secondary objectives

Intention to treat analyses will be performed, with all randomised participants included regardless of protocol adherence. Blinded analyses of primary and secondary patient-reported outcomes will be performed. The dichotomised measure of GROC will be expressed from blinded analyses as relative risk (RR) and number needed to treat (NNT), with 95% confidence intervals, to facilitate clinical guidelines.[19 67] For the primary outcome and continuous secondary outcome measures, linear mixed models (with baseline value as a covariate and treatment condition as a fixed factor) will be used to evaluate the treatment effect and 95% confidence interval at three months and 12 months ($p<0.05$). Linear mixed models utilising repeated measures at all time-points will allow non-biased estimates of treatment effect in the presence of any potential missing cases. This likelihood-based estimation procedure results in non-biased estimates, providing data are missing at random and models are adjusted for any imbalance between groups in potential confounders at baseline (age, sex, weight, symptom duration, PF/TF OA radiographic severity). Relative risk (95% confidence intervals) will be calculated for use of co-interventions and adverse events.

Economic evaluation

Blinded economic analyses will be conducted to evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts, from the

societal perspective. Hospitalisations will be converted to costs using the National Weighted Activity Unit costing model. Incremental cost-effectiveness analyses will use the formula $[(DC_{foot\ orthoses} + IC_{foot\ orthoses}) - (DC_{flat\ inserts} + IC_{flat\ inserts}) / (E_{foot\ orthoses} - E_{flat\ inserts})]$, where DC=mean direct health costs, IC=mean indirect costs, E=effect, $_{foot\ orthoses}$= foot orthoses group, and $_{flat\ inserts}$=flat insert group. Effect for the primary economic evaluation will be the proportion of participants who 'improve' (measured on the GROC) within each group at 12 months. Thus, the cost-effectiveness ratio will reflect the marginal cost per additional 'improved' participant from the societal perspective over a 12-month time horizon. Uncertainty in this ratio will be examined by constructing a 95% confidence ellipse on a cost-effectiveness plane, and transforming these to cost-effectiveness acceptability curves using non-parametric bootstrap resampling of primary data. Sensitivity analyses will be conducted, varying the threshold of 'improvement' on the GROC to reflect increasingly higher thresholds. Quality-adjusted life year scores for each participant (calculated as area under the curve applied to utility measures calculated from EQ-5D) will be substituted for GROC scores as the effect measure, creating an incremental cost-utility ratio to determine the marginal cost per additional quality-adjusted life year for the more effective intervention.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not directly involved in the development of the research question, study design or selection of outcome measures. Patients will not be directly involved in the recruitment to or conduct of the study, except as participants if they meet the eligibility criteria and provide informed consent. At the conclusion of the study, overall study findings and individual participant data will be provided to study participants on request.

ETHICS AND DISSEMINATION

This study complies with the Declaration of Helsinki, and has been approved by ethics committees at La Trobe University and The University of Queensland. All participants will provide written informed consent prior to baseline data collection and enrolment in the three-month observation period. Participant information and consent forms for each phase of the study are included in Supplementary file 1. Participants will undergo knee radiographs at a single time point as part of this trial, ensuring that the amount of ionising radiation is consistent with standard clinical exposure. When prescribed by trained health practitioners, prefabricated foot orthoses and flat shoe inserts are associated with minimal and transient adverse events.[19] Thus, there are minimal ethical and safety considerations associated with this trial.

Study outcomes will be widely disseminated through a variety of sources. Primary and key secondary objectives will be submitted to a high-impact peer-reviewed journal in

the field. Because study outcomes are applicable to a broad range of health professionals, we will target a general medical journal to facilitate wider dissemination of findings to key stakeholders (e.g. general practitioners). Each of the other secondary objectives will be addressed in separate publications, and submitted to appropriate journals in the field. Authorship will be in accordance with guidelines provided by the International Committee of Medical Journal Editors [68]. We will also submit articles to key professional magazines to enhance dissemination to clinicians. Our publication strategy will be complemented by submission of abstracts to key national and international conferences, covering multiple discipline groups (e.g. physiotherapy, podiatry, general practice), as well as OA conferences. We will also develop an open access website and resources for clinicians, including videos detailing how to prescribe foot orthoses, and run workshops on PFOA and foot orthoses for registered health professionals. This will facilitate translation of findings to clinical practice, especially practitioners located in rural or remote areas.

The trial protocol, anonymised participant level dataset, and statistical code used in primary and secondary analyses, will be made publicly available through institutional data repositories (La Trobe University: http://arrow.latrobe.edu.au:8080/vital/access/manager/Index).

DISCUSSION

PFOA is a major public health problem, and has no cure. Pain and stiffness experienced during daily activities, occupational tasks and exercise can reduce active participation. Importantly, PFOA in middle-aged adults can affect productivity and contribution to society, and result in more years of knee pain and disability across the lifespan. Along with direct personal and economic costs of PFOA, indirect costs associated with consequences of physical inactivity are a major burden on health expenditure.

This RCT will be the first to evaluate patient-reported benefits of foot orthoses – a simple, low-cost, low-risk intervention that is widely accessible to people with PFOA. Findings of efficacy and cost-effectiveness of prefabricated foot orthoses could represent a turning point in the effective long-term management of PFOA. When worn in everyday and exercise footwear, foot orthoses have the potential to reduce pain every time the foot hits the ground, substantially increasing an individual's capacity and motivation to be physically active. This has important implications for maintenance of general and mental health with increasing age. Importantly, the ease of daily use of foot orthoses, with minimal patient burden, is likely to maximise adherence, enhance outcomes, and reduce reliance on health practitioner resources.

AUTHORS' CONTRIBUTIONS

NJC, KMC, HBM, TGR, AJS, RSH, BV and TPH conceived the study and obtained funding. NJC, KMC and HBM designed the trial protocol with input from TGR, AJS, RSH, BV, TPH, SEM and JMT. AJS and TPH provided statistical expertise. AJS will conduct primary statistical analysis. NJC drafted the manuscript with input from KMC, HBM, TGR, AJS, RSH, BV, TPH, SEM, JMT, HFH, BEP, GC, JWD and LRM. All authors have read and approved the final manuscript.

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COMPETING INTERESTS STATEMENT

Professor Vicenzino reports non-financial support from Vionic®, outside the submitted work. He is a member (non-paid affiliation) of the Vasyli Think Tank™, which was founded in 2011 to foster collaboration and cooperative thought among a leading group of health professionals specialising in the field of lower limb biomechanics. All other authors have no conflicts of interest to declare.

REFERENCES

1. Hinman RS, Lentzos J, Vicenzino B, et al. Is patellofemoral osteoarthritis common in middle-aged people with chronic patellofemoral pain? *Arthritis Care Res (Hoboken)* 2014;66(8):1252-7. doi: 10.1002/acr.22274

2. Duncan RC, Hay EM, Saklatvala J, et al. Prevalence of radiographic osteoarthritis--it all depends on your point of view. *Rheumatology (Oxford)* 2006;45(6):757-60. doi: 10.1093/rheumatology/kei270 [published Online First: 2006/01/19]

3. Duncan R, Peat G, Thomas E, et al. Incidence, progression and sequence of development of radiographic knee osteoarthritis in a symptomatic population. *Ann Rheum Dis* 2011;70(11):1944-8. doi: 10.1136/ard.2011.151050 [published Online First: 2011/08/04]

4. Kornaat PR, Bloem JL, Ceulemans RY, et al. Osteoarthritis of the knee: association between clinical features and MR imaging findings. *Radiology* 2006;239(3):811-7. doi: 10.1148/radiol.2393050253 [published Online First: 2006/05/23]

5. Hunter DJ, March L, Sambrook PN. The association of cartilage volume with knee pain. *Osteoarthritis Cartilage* 2003;11(10):725-9. doi: S1063458403001602 [pii] [published Online First: 2003/09/18]

6. Hendry M, Williams NH, Markland D, et al. Why should we exercise when our knees hurt? A qualitative study of primary care patients with osteoarthritis of the knee. *Fam Pract* 2006;23(5):558-67. doi: 10.1093/fampra/cml022 [published Online First: 2006/05/30]

7. Carr AJ, Robertsson O, Graves S, et al. Knee replacement. *Lancet* 2012;379(9823):1331-40. doi: 10.1016/S0140-6736(11)60752-6 [published Online First: 2012/03/09]

8. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64. doi: 10.1016/j.joca.2015.04.024

9. Quilty B, Tucker M, Campbell R, et al. Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol* 2003;30(6):1311-7. doi: 0315162X-30-1311 [pii] [published Online First: 2003/06/05]

10. Callaghan MJ, Parkes MJ, Hutchinson CE, et al. A randomised trial of a brace for patellofemoral osteoarthritis targeting knee pain and bone marrow lesions. *Ann Rheum Dis* 2015;74(6):1164-70. doi: 10.1136/annrheumdis-2014-206376

11. Campbell R, Evans M, Tucker M, et al. Why don't patients do their exercises? Understanding non-compliance with physiotherapy in patients with osteoarthritis of the knee. *J Epidemiol Community Health* 2001;55(2):132-8. [published Online First: 2001/01/12]

12. Squyer E, Stamper DL, Hamilton DT, et al. Unloader knee braces for osteoarthritis: do patients actually wear them? *Clin Orthop Relat Res* 2013;471(6):1982-91. doi: 10.1007/s11999-013-2814-0

13. Crossley KM, van Middelkoop M, Callaghan MJ, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br J Sports Med* 2016;50(14):844-52. doi: 10.1136/bjsports-2016-096268

14. Barton CJ, Lack S, Hemmings S, et al. The 'Best Practice Guide to Conservative Management of Patellofemoral Pain': incorporating level 1 evidence with expert clinical reasoning. *Br J Sports Med* 2015;49(14):923-34. doi: 10.1136/bjsports-2014-093637

15. Crossley KM, Hinman RS. The patellofemoral joint: the forgotten joint in knee osteoarthritis. *Osteoarthritis Cartilage* 2011;19(7):765-7. doi: 10.1016/j.joca.2011.05.005 [published Online First: 2011/06/21]

16. Wyndow N, Collins N, Vicenzino B, et al. Is There a Biomechanical Link Between Patellofemoral Pain and Osteoarthritis? A Narrative Review. *Sports Med* 2016;46(12):1797-808. doi: 10.1007/s40279-016-0545-6 [published Online First: 2016/05/05]

17. Crossley KM, Schache AG, Ozturk H, et al. Pelvic and Hip Kinematics During Walking in People With Patellofemoral Joint Osteoarthritis Compared to Healthy Age-Matched Controls. *Arthritis Care Res (Hoboken)* 2018;70(2):309-14. doi: 10.1002/acr.23261 [published Online First: 2017/04/25]

18. Collins NJ, Hinman RS, Menz HB, et al. Immediate effects of foot orthoses on pain during functional tasks in people with patellofemoral osteoarthritis: A

cross-over, proof-of-concept study. *Knee* 2017;24(1):76-81. doi: 10.1016/j.knee.2016.09.016 [published Online First: 2016/11/09]

19. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735. doi: 10.1136/bmj.a1735 [published Online First: 2008/10/28]

20. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583 [published Online First: 2013/01/09]

21. Chan AW, Tetzlaff JM, Gotzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586. doi: 10.1136/bmj.e7586 [published Online First: 2013/01/11]

22. McAlindon TE, Driban JB, Henrotin Y, et al. OARSI Clinical Trials Recommendations: Design, conduct, and reporting of clinical trials for knee osteoarthritis. *Osteoarthritis Cartilage* 2015;23(5):747-60. doi: 10.1016/j.joca.2015.03.005

23. van Middelkoop M, Bennell KL, Callaghan MJ, et al. International patellofemoral osteoarthritis consortium: Consensus statement on the diagnosis, burden, outcome measures, prognosis, risk factors and treatment. *Semin Arthritis Rheum* 2018;47(5):666-75. doi: 10.1016/j.semarthrit.2017.09.009 [published Online First: 2017/09/23]

24. National Institute for Health and Care Excellence. Osteoarthritis: care and management 2014 [Available from: https://www.nice.org.uk/guidance/cg177 accessed 8 July 2018.

25. Gudbergsen H, Bartels EM, Krusager P, et al. Test-retest of computerized health status questionnaires frequently used in the monitoring of knee osteoarthritis: a randomized crossover trial. *BMC Musculoskelet Disord* 2011;12:190. doi: 10.1186/1471-2474-12-190 [published Online First: 2011/08/20]

26. de Klerk BM, Willemsen S, Schiphof D, et al. Development of radiological knee osteoarthritis in patients with knee complaints. *Ann Rheum Dis* 2012;71(6):905-10. doi: 10.1136/annrheumdis-2011-200172

27. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.

28. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20. doi: 10.1185/030079906X132488

29. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160. doi: 10.1186/s12891-017-1521-5 [published Online First: 2017/04/20]

30. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.

31. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776 [published Online First: 2017/03/05]

32. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.

33. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.

34. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33(5):337-43. [published Online First: 2001/08/09]

35. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.

36. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.

37. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44. [published Online First: 1989/01/01]

38. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8. doi: 10.1016/j.joca.2014.02.008

39. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98. doi: 10.1016/j.clinbiomech.2005.08.002 [published Online First: 2005/09/27]

40. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.

41. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80. [published Online First: 2001/10/26]

42. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.

43. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.

44. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30. doi: 10.1519/JPT.0b013e318248e20d

45. Kellgren JH, Jeffrey MR, Ball J. The Epidemiology of Chronic Rheumatism: Atlas of Standard Radiographs. Oxford: Blackwell Scientific 1963.

46. Altman RD, Hochberg M, Murphy WA, Jr., et al. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995;3 Suppl A:3-70. [published Online First: 1995/09/01]

47. Moyer R, Wirth W, Duryea J, et al. Anatomical alignment, but not goniometry, predicts femorotibial cartilage loss as well as mechanical alignment: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2016;24(2):254-61. doi: 10.1016/j.joca.2015.08.016

48. Macri EM, Stefanik JJ, Khan KK, et al. Is tibiofemoral or patellofemoral alignment or trochlear morphology associated with patellofemoral osteoarthritis? A systematic review. *Arthritis Care Res (Hoboken)* 2016;68(10):1453-70. doi: 10.1002/acr.22842

49. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.

50. Vicenzino B, Collins N, Crossley K, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: a randomised clinical trial. *BMC Musculoskelet Disord* 2008;9:27. doi: 10.1186/1471-2474-9-27 [published Online First: 2008/02/29]

51. Barton CJ, Menz HB, Crossley KM. Clinical predictors of foot orthoses efficacy in individuals with patellofemoral pain. *Med Sci Sports Exerc* 2011;43(9):1603-10. doi: 10.1249/MSS.0b013e318211c45d

52. Mills K, Blanch P, Dev P, et al. A randomised control trial of short term efficacy of in-shoe foot orthoses compared with a wait and see policy for anterior knee pain and the role of foot mobility. *Br J Sports Med* 2012;46(4):247-52. doi: 10.1136/bjsports-2011-090204 [published Online First: 2011/09/21]

53. Cronkwright DG, Spink MJ, Landorf KB, et al. Evaluation of the pressure-redistributing properties of prefabricated foot orthoses in older people after at least 12 months of wear. *Gait Posture* 2011;34(4):553-7. doi: 10.1016/j.gaitpost.2011.07.016 [published Online First: 2011/08/23]

54. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198. doi: 10.1186/s13063-017-1936-1 [published Online First: 2017/04/30]

55. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008;16(2):137-62. doi: 10.1016/j.joca.2007.12.013 [published Online First: 2008/02/19]

56. Wyndow N, Crossley KM, Vicenzino B, et al. A single-blinded, randomized, parallel group superiority trial investigating the effects of footwear and custom foot orthoses versus footwear alone in individuals with patellofemoral joint osteoarthritis: a phase II pilot trial protocol. *J Foot Ankle Res* 2017;10:19. doi: 10.1186/s13047-017-0200-y [published Online First: 2017/04/30]

57. Bellamy N, Kirwan J, Boers M, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. *J Rheumatol* 1997;24(4):799-802.

58. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord* 2008;9:116. doi: 10.1186/1471-2474-9-116

59. Gossec L, Paternotte S, Maillefert JF, et al. The role of pain and functional impairment in the decision to recommend total joint replacement in hip and knee osteoarthritis: an international cross-sectional study of 1909 patients. Report of the OARSI-OMERACT Task Force on total joint replacement. *Osteoarthritis Cartilage* 2011;19(2):147-54. doi: 10.1016/j.joca.2010.10.025 [published Online First: 2010/11/04]

60. Health USDo, Human Services FDACfDE, Research, et al. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* 2006;4:79. doi: 10.1186/1477-7525-4-79 [published Online First: 2006/10/13]

61. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94. doi: 10.1136/bjsports-2014-093845 [published Online First: 2014/09/24]

62. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18(6):753-8. doi: 10.1016/j.jval.2015.05.009

63. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24. doi: 10.1002/acr.20640

64. Collins NJ, Bierma-Zeinstra SM, Crossley KM, et al. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med* 2013;47(4):227-33. doi: 10.1136/bjsports-2012-091696 [published Online First: 2012/12/18]

65. Salaffi F, Stancati A, Silvestri CA, et al. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004;8(4):283-91.

66. Kastelein M, Luijsterburg PA, Belo JN, et al. Six-year course and prognosis of nontraumatic knee symptoms in adults in general practice: a prospective

cohort study. *Arthritis Care Res (Hoboken)* 2011;63(9):1287-94. doi: 10.1002/acr.20522

67. Crossley K, Bennell K, Green S, et al. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.

68. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication. 2010 [Available from: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html accessed 23 November 2017.

FIGURE CAPTIONS

Figure 1. Flow of participants through the study.

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

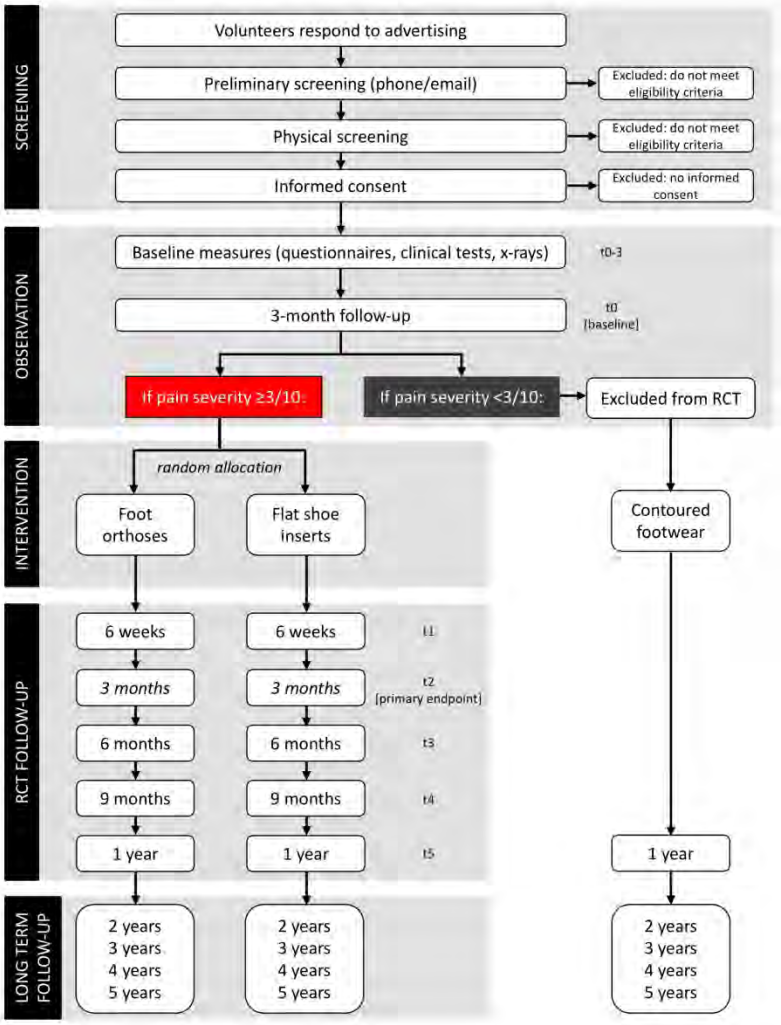

Figure 1. Flow of participants through the study.

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	STUDY PERIOD						
	Enrolment / Baseline		Post-allocation				Close-out
TIMEPOINT*	t0-3	t0	t1	t2	t3	t4	t5
ENROLMENT:							
Eligibility screen	X						
Informed consent	X	X					
Allocation		X					
INTERVENTIONS:							
Contoured shoe inserts		◆	—	—	—	—	◆
Flat shoe inserts		◆	—	—	—	—	◆
ASSESSMENTS:							
Participant characteristics	X						
Knee pain severity	X						
Navigate Pain	X						
PainDetect	X						
Pain Catastrophising Scale (PCS)	X						
Sport and physical activity participation	X						
Anthropometric measures	X						
Knee clicking and crepitus	X						
Knee extension torque	X						
Foot Posture Index (FPI)	X						
Foot mobility	X						
Weight bearing ankle dorsiflexion range of motion	X						
Footwear Assessment Tool	X						
10-metre Walk Test	X						
Primary outcome measure:							
Worst knee pain severity during self-nominated aggravating activity in the previous week	X	X	X	X	X	X	X
Secondary outcome measures:							
Patient-reported global rating of change (GROC)			X	X			X
Pain visual analogue scales	X	X	X	X	X	X	X
Knee injury and Osteoarthritis Outcome Score (KOOS)	X	X		X			X
Anterior Knee Pain Scale (AKPS)	X	X		X			X
Arthritis Self-Efficacy Scale (ASES)	X	X		X			X
Tampa Scale for Kinesiophobia (TSK)	X	X		X			X
Short-form 12 (SF-12)	X	X		X			X
Euroqol-5D-5L (EQ-5D)	X	X		X	X	X	X
Other outcomes:							
Use of co-interventions for knee pain				X	X	X	X
Adverse events				X	X	X	X
Direct health care costs				X	X	X	X
iMTA Productivity Cost Questionnaire (iPCQ)				X	X	X	X
Credibility and Expectancy Questionnaire (CEQ)		X		X			X

* t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months; t3 = 6 months; t4 = 9 months; t5 = 12 months

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

275x397mm (300 x 300 DPI)

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

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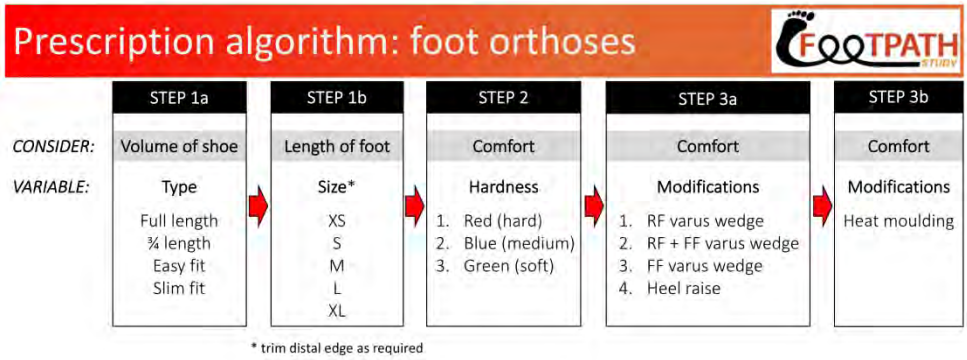

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

338x190mm (300 x 300 DPI)

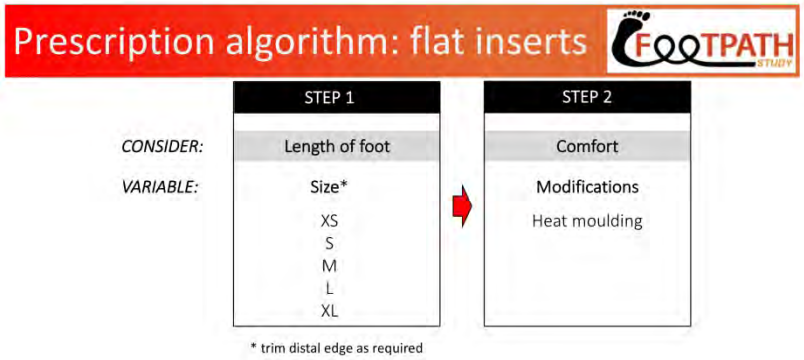

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

338x190mm (300 x 300 DPI)

Supplementary file 1. Participant information and consent forms.

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PARTICIPANT INFORMATION STATEMENT: PART A

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

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Dr Harvi Hart	School of Allied Health, La Trobe University	h.hart@latrobe.edu.au
Ms Brooke Patterson	School of Allied Health, La Trobe University	b.patterson@latrobe.edu.au

We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether footwear interventions can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether specific footwear interventions are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

If you are potentially eligible for the trial, you will be screened via telephone, and attend La Trobe University for a knee examination. If you are included in the trial, you will undergo baseline assessment at the same venue as your knee examination. For the first 3 months of the trial, we will monitor your knee condition using questionnaires. You will then be provided with a footwear intervention to take home and wear for 1 year, and be asked to complete a series of questionnaires online or via mail.

All assessments and footwear interventions will be provided at no cost to you.

At baseline, you will be asked to complete:

- Questionnaires, including:
  - Age, gender, occupational and sporting history, mechanism of injury, symptom duration, rehabilitation, medication use, and family history of arthritis
  - Your expectations and values regarding your condition and its management
  - Physical activity (type, frequency and dosage)
  - Knee-related pain, symptoms, function and quality of life
  - General health and self-efficacy
- Physical testing, including:
  - Height, weight and waist circumference
  - Movement and palpation of your knee
  - Foot and ankle mobility measures
  - Knee strength: The maximal strength of your leg muscles will be measured using a special device. The examiner will ask you to push against it, as hard as you can, in one direction.
  - Functional performance tests, including walking and hopping
  - Measures of pressure pain onset: The examiner will apply a pressure stimulus with a probe to 4 points around your knee, and one point at your elbow. As the pressure increases, you will be asked to press a button to indicate the precise moment that the pressure sensation changes to one of pressure and the first onset of pain. At this point the pressure will cease. Three measures will be taken at each site, and repeated on both knees and elbows.
- X-rays of your knee:
  - You will undergo the x-rays at a private radiology clinic that is convenient to your home or workplace. This will take approximately 30 minutes.

You will be invited to attend the La Trobe University Health Sciences Clinic, at the Bundoora Campus of La Trobe University, to undergo the baseline assessment. This will take approximately 2 hours of your time. You will first complete a series of questionnaires about your knee pain, as outlined above. You will then undergo the physical tests described above, including measures of foot and ankle motion, knee strength, and functional performance. For the physical tests, you will be asked to change into shorts. You may either bring your own shorts or we can provide some for you.

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During the telephone screening, you may be asked if you would like to participate in a sub-study that will monitor your physical activity with a Fitbit™ device for 3 months. If you choose to participate in the sub-study, you will be issued a Fitbit™ device to wear on daily basis for 3 months. Your decision to take part or not in the sub-study will not impact on your participation in the main study. For this sub-study, you will be required to have access to the internet (home, public library etc.) and a smartphone/laptop. During the baseline assessment, the Fitbit™ application will be installed on your device to ensure that the researchers at La Trobe University can remotely extract the data from your Fitbit™.

Your knee condition will then be monitored for 3 months, during which time you will receive no intervention. This is a novel and important part of this study, to learn more about the natural course of kneecap arthritis. At the conclusion of the 3-month observation period, you will be asked to repeat the same questionnaires that you completed at baseline.

You will then be contacted by a member of the study team, regarding your footwear intervention. At this time, they will explain in more detail what is involved, and will ask you to provide consent. You will then be given a footwear intervention to take home and wear for a period of 1 year. This may involve a sandal, or a special insole to wear in your own shoes. These be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the footwear intervention in safely. You will be encouraged to use the footwear intervention as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At the conclusion of the 3-month observation period, you may be invited to participate in the sub study which will require you to continue to wear your Fitbit™ device for the duration of the main study. Your decision to take part or not in the sub study will not impact on your participation in the main study.

During this time, you may be provided with a diary where you can record your physical activity, how often you wear the footwear intervention, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the footwear intervention, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the questionnaires outlined above (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. You may ask for a copy of your assessment results. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years.

We may also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period
During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?
You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy) or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research
Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

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X-ray: You will be asked to have an x-ray of your knee. This involves exposure to a very small amount of radiation from x-ray imaging. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from the x-rays of your knee is less than 0.015 mSv. At this dose level, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be very low.

It is important to be aware that with any imaging investigation, there is a small chance of a previously unknown medical condition being detected. In the unlikely event that this occurs, we will contact you directly and inform you of the findings. Should you require further medical review, we will also organise a referral to your chosen GP. It must be emphasized that the purpose of this study is to investigate your knee pain and not to identify other potential medical conditions. While we will ensure that you are made aware of any incidental findings reported on by the consulting radiologist, neither the investigators, the radiologist, nor the Universities involved, will be held accountable if a medical condition exists that is not detected during the process.

Physical testing: The physical tests are routinely performed by Physiotherapists and Podiatrists, and are not associated with any risks. You may experience a small amount of discomfort in your joints or muscles during the physical examination or testing procedures. Please report to the researcher any undue discomfort or pain experienced during the testing. If the pain or discomfort is deemed to be excessive by yourself or the investigators, testing will cease.

If required, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

Footwear intervention: You may feel some discomfort in your feet or knees when starting to use the footwear intervention. Occasionally, footwear interventions can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the footwear intervention and/or wearing time.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

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What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part A

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator: Date:

Name and phone number of contact person in case of an emergency:

Name: Phone:

Family Doctor: Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature: Date:

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PARTICIPANT INFORMATION STATEMENT: PART B

Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

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Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
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Dr Harvi Hart	School of Allied Health, La Trobe University	h.hart@latrobe.edu.au
Ms Brooke Patterson	School of Allied Health, La Trobe University	b.patterson@latrobe.edu.au

We invite you to participate in our research project "Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple shoe inserts are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether shoe inserts can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether shoe inserts are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a shoe insert intervention to take home and wear for 1 year, and ask you to complete a series of questionnaires online or via mail.

All assessments and shoe insert interventions will be provided at no cost to you.

You will be randomly allocated to receive one of two different shoe inserts, to wear in your own shoes. Although they are slightly different in design and possible mechanism of effect, both of these inserts have been shown to reduce kneecap pain in younger adults. These will be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the shoe inserts in safely. You will be encouraged to use the shoe inserts as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

During this time, you will be provided with a diary where you can record your daily physical activity, how often you wear the shoe inserts, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the shoe inserts, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years. You may ask for a copy of your assessment results.

You may also be provided with a FitBit to record your physical activity. This is a simple device worn on your wrist, which records your daily step count. If you do receive a FitBit, we will provide you with information and instructions on how to use the device.

We will also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. You will be asked to fill out a consent form authorising the study to access your complete Medicare and Pharmaceutical Benefits Scheme (PBS) data as outlined on the back of the consent form, and in Appendix A of this information statement. Medicare collects information on your medical visits and procedures, and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to the Department of Human Services who holds this information confidentially. You will also receive a phone call from one of the study personnel at 3-monthly intervals, who will ask you questions about how your knee is going (e.g. time off work, impact on daily activities, use of other interventions, hospital admissions). This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period

During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies (with the exception of Medicare and PBS data). Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

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What are the possible risks of participating in this project?
You may feel some discomfort in your feet or knees when starting to wear the shoe inserts. Occasionally, shoe inserts can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the shoe inserts and/or wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?
Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?
The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Electronic data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of consent forms and questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for 15 years after completion of the project in the Health Sciences storage vault, Building 3, level 1. After 15 years, hard copies will be shredded and placed in a secure document disposal bin, and computer files will be permanently deleted.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

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Funding
Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?
Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints
If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,
Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

Appendix A. Medicare and Pharmaceutical Benefits Scheme data fields

Medicare Benefits Schedule (MBS)	
Date of service	Date that the service was rendered by the provider, to the patient
MBS Item number	Items Numbers as per the Medicare Benefits Schedule
MBS Item description	Describes the service as per the Medicare Benefits Schedule
Provider charge	The dollar amount the provider charged for the service
Benefit paid	The benefit paid to the patient
Patient Out of Pocket	The dollar amount the patient is out of pocket
Hospital Indicator	Indication of whether or not the service was provided in hospital
Pharmaceutical Benefits Scheme (PBS)	
Date of supply	Date the prescription was supplied by the pharmacy
PBS Item Number	Items Numbers reflected in the PBS
PBS Item Description	The item description as noted in the PBS
Patient contribution	The contribution paid by the patient
PBS Net Benefit	Amount paid by the Government
Form category	Original or repeat prescription
ATC Code	The ATC Code is defined by the Commonwealth Department of Health which may be different to the code allocated by the WHO Collaborating Centre for Drug Statistics Methodology
ATC Name	The group the drug falls under in the Anatomical Therapeutic Chemical (ATC) classification system

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): PART B

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator:	Date:

Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature:	Date:

Participant ID:

PARTICIPANT CONSENT FORM

Consent to release of Medicare and/or Pharmaceutical Benefits Scheme (PBS) claims information for the purposes of the FOOTPATH Study

Important Information

Complete this form to request the release of personal Medicare claims information and/or PBS claims information to the FOOTPATH Study.

Any changes to this form must be initialled by the signatory. Incomplete forms may result in the study not being provided with your information.

By signing this form, I acknowledge that I have been fully informed and have been provided with information about this study. I have been given an opportunity to ask questions and understand the possibilities of disclosures of my personal information.

PARTICIPANT DETAILS

1. Mr ☐ Mrs ☐ Miss ☐ Ms ☐ Other ☐

Family name: _____ First given name: _____

Other given name (s): _____

Date of birth: DD/MM/YYYY

2. Medicare card number: _____

3. Permanent address: _____

Postal address (if different to above): _____

AUTHORISATION

4. I authorise the Department of Human Services to provide my:

☐ Medicare claims history OR

☐ PBS claims history OR

☐ Medicare & PBS claims history

for the period* DD/MM/YYYY to: DD/MM/YYYY to the FOOTPATH Study.

*Note: The Department of Human Services can only extract 4.5 years of data (prior to the date of extraction), The consent period above may result in multiple extractions.

DECLARATION

I declare that the information on this form is true and correct.

5. Signed: _____ (participant's signature) Dated: DD/MM/YYYY **OR**

6. Signed by _____ (full name) _____ (signature) on behalf of participant

Dated: DD/MM/YYYY

☐ Power of attorney* ☐ Guardianship order*

* Please attach supporting evidence

APP 5 – PRIVACY NOTICE

Your personal information is protected by law, including the Privacy Act 1988, and is collected by the Australian Government Department of Human Services. The collection of your personal information by the department is necessary for administering requests for statistical and other data.

Your information may be used by the department or given to other parties for the purposes of research, investigation or where you have agreed or it is required or authorised by law.

You can get more information about the way in which the Department of Human Services will manage your personal information, including our privacy policy at humanservices.gov.au/privacy or by requesting a copy from the department.

Power of attorney – A power of attorney is a document that appoints a person to act on behalf of another person who grants that power. In particular, an enduring power of attorney allows the appointed person to act on behalf of another person even when that person has become mentally incapacitated. The powers under a power of attorney may be unlimited or limited to specific acts.

Guardianship order – A Guardianship order is an order made by a Guardianship Board/Tribunal that appoints a guardian to make decisions for another person. A Guardianship order may be expressed broadly or limited to particular aspects of the care of another person.

A sample of the information that may be included in your Medicare claims history:

Date of service	Item number	Item description	Provider charge	Benefit paid	Patient out of pocket	Hospital indicator
20/04/09	00023	Level B consultation	$38.30	$34.30	$4.00	N
22/06/09	11700	ECG	$29.50	$29.50		N

A sample of the information that may be included in your PBS claims history:

Date of supply	PBS item code	Item description	Patient contribution (this includes under copayment amounts**)	Net Benefit (this includes under copayment amounts**)	Form Category	ATC Code	ATC Name
06/03/09	03133X	Oxazepham Tablet 30 mg	$5.30	$25.55	Original	N05 B A 04	Oxazepam
04/07/09	03161J	Diazepam Tablet 2 mg	$30.85		Repeat	N05 B A 01	Diazepam

** Under co-payments can now be provided for data after 1 June 2012

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PARTICIPANT INFORMATION STATEMENT: PART C

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
Prof Hylton Menz	School of Allied Health, La Trobe University	h.menz@latrobe.edu.au
Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
Prof Trevor Russell	School of Health and Rehabilitation Sciences, The University of Queensland	t.russell1@uq.edu.au
A/Prof Anne Smith	School of Physiotherapy and Exercise Science, Curtin University	anne.smith@curtin.edu.au
Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au

We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The primary aim of this project is to determine whether footwear can reduce pain and improve outcome in people with kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a footwear intervention to take home and wear, and ask you to complete a series of questionnaires online or via mail at yearly intervals for the next 5 years.

All assessments and footwear interventions will be provided at no cost to you.

You will be contacted by one of the study personnel (who is an experienced Podiatrist or Physiotherapist) to confirm your shoe size. They will determine the best method of prescribing the footwear intervention to you. This may require you to attend an appointment at La Trobe University. We will give you instructions on how to break the footwear in safely. You will be encouraged to wear the footwear as much as is comfortable for you, when you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At yearly intervals, for a period of 5 years, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. You may ask for a copy of your assessment results.

Use of pain-relieving medications and other forms of treatment during the trial period

You are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

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Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

You may feel some discomfort in your feet or knees when starting to wear the footwear. Occasionally, footwear can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under

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guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu,

Ms Jade Tan

(on behalf of the research team)

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part C

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:
Investigator:		Date:

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La Trobe University

Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

Participant's signature:	Date:

Supplementary file 2. Outcome measures used in the FOOTPATH Study.

	Description	t0-3	t0	t1	t2	t3	t4	t5
Primary outcomes								
Worst knee pain severity during self-nominated aggravating activity in the previous week	Participants nominate one of three everyday activities that they experience the greatest knee pain severity with (rising from sitting, stair ambulation, squatting). Pain severity during this activity is measured on a 100mm visual analogue scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). Pain visual analogue scales are reliable, valid and responsive in people with patellofemoral pain.[1] Pain severity associated with a self-nominated aggravating activity is sensitive to change in people with PFOA and knee OA.[2]	•	•	•	•	•	•	•
Secondary outcomes								
Self-reported global rating of change (GROC)	Participants will respond to the question 'overall, how has your knee pain changed since the start of the study?' on a 7-point Likert scale ('much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'). This will be dichotomised to 'improved' ('much better, 'better') and 'not improved' ('a little better' to 'much worse'). GROC has been used in previous PF pain RCTs to calculate relative risks and number needed to treat for clinical guidelines.[3 4] This is a clinically relevant and stable concept for evaluating an individual patient's perspective on meaningful improvement.[5]			•	•			•
Pain visual analogue scales	Participants will complete a series of pain visual analogue scales, rating the severity of their knee pain on a 100mm scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). This will include: (i) usual pain over the past week; (ii) worst pain over the past week); (iii) maximum pain when walking; (iv) maximum pain when sitting for one hour; (v) maximum pain when rising from sitting; (vi) maximum pain when going up and down stairs; (vii) maximum pain when squatting; and (viii) maximum pain when running. Reliability, validity and responsiveness of pain visual analogue scales have been established in patellofemoral pain.[1]	•	•	•	•	•	•	•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Knee injury and Osteoarthritis Outcome Score (KOOS)	The KOOS consists of 42 items across five subscales: (i) symptoms; (ii) pain; (iii) function in daily activities; (iv) function in sport/recreation; and (v) knee-related quality of life.[6] Participants will also complete the 11-item KOOS-PF, a subscale developed to be used in people with patellofemoral pain conditions in conjunction with the original KOOS.[7] Participants respond to each item using a 4-point Likert scale, and a normalised score from 0-100 is calculated for each subscale (100 = no knee problems, 0 = extreme knee problems. The KOOS and KOOS-PF are reliable and valid in people with patellofemoral pain and osteoarthritis.[7]	•	•		•			•
Anterior Knee Pain Scale (AKPS)	The AKPS, or Kujala Patellofemoral Score, consists of 13 items describing common symptoms and functional impairments associated with patellofemoral pain conditions.[8] Weighted scores from each item are summed to give an overall score (100 = no disability, 0 = maximal disability). The AKPS is reliable, valid and responsive to change in people with patellofemoral pain.[1 8 9]	•	•		•			•
Arthritis Self-Efficacy Scale (ASES)	The ASES consists of 20 items across three subscales: (i) self-efficacy for managing pain; (ii) self-efficacy for physical function; and (iii) self-efficacy for controlling other symptoms.[10] For each item, participants rate on a 10-point scale how certain they are that they can perform specific tasks or manage their knee pain symptoms. Item scores are summed to provide an overall score from 10-100, where higher scores represent greater self-efficacy.[11] The ASES has adequate reliability, validity and responsiveness for research use.[11]	•	•		•			•
Tampa Scale for Kinesiophobia (TSK)	The TSK evaluates fear of movement and re-injury.[12] Participants use a 4-point Likert scale to rate their agreement with 17 items (1=strongly disagree, 4=strongly agree). Items 4, 8, 12 and 16 are reverse scored, and a total score calculated ranging from 17 to 68, where higher scores indicate greater fear of movement and re-injury. While evaluation of psychometric properties has not been performed in people with patellofemoral pain, the Thai language version of the TSK demonstrated adequate measurement properties in people with knee osteoarthritis .[13]	•	•		•			•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Short-form 12 (SF-12)	The SF-12 (version 2) comprises 12 items across eight domains: bodily pain (BP), physical functioning (PF), role limitations due to physical health problems (RP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH).[14] A physical component score (PCS) is calculated from the BP, PF, RP and GH subscales, and a mental component score (MCS) calculated from the VT, SF, RE and MH subscale. Transformed scores for each subscale range from 0 (worst health state) to 100 (best health state). The SF-12 is valid for reproducing the PCS and MCS of the Short-form 36 (SF-36).[15]	•	•		•			•
Euroqol-5D-5L (EQ-5D)	The EQ-5D consists of five items encompassing five dimensions: mobility, self-care, usual activity, pain and discomfort, and anxiety and depression. Participants select the best of five possible responses. The EQ-5D Index is calculated from a predefined algorithm, with a score of 1 representing the best imaginable health state, 0 representing death, and negative scores indicating a state worse than death.[16] Participants will also complete the EQ-5D visual analogue scale evaluating self-reported health state (0=worst imaginable health state, 100=best imaginable health state). EQ-5D has been validated in knee pain cohorts.[17]	•	•		•	•	•	•
Use of co-interventions for knee pain	The number of participants who report using co-interventions specifically for their knee pain (e.g. medication, allied health services such as physiotherapy, complementary medicines such as osteopathy, topical medicines, or taping/bracing) will be recorded from a number of sources (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[18]				•	•	•	•
Adverse events	Adverse events (e.g. new pains in the body, rolled ankles, blisters, swelling) will be recorded from a number of sources specifically designed for this study (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[19]				•	•	•	•

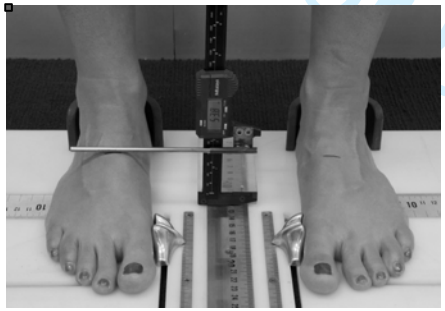
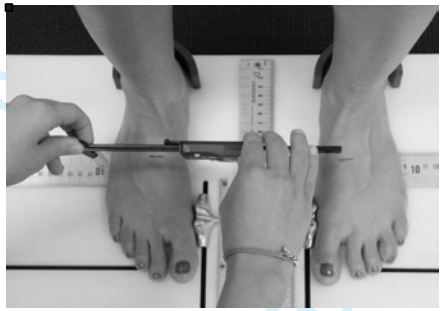
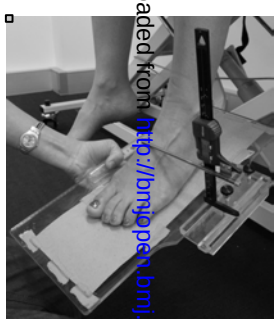
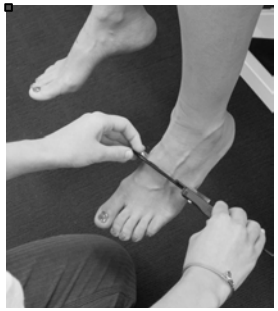
	Description	t0-3	t0	t1	t2	t3	t4	t5
Direct health care costs	Direct health costs will be captured from multiple sources, for use in economic analyses: (i) Medicare Australia and Pharmaceutical Benefits Scheme (PBS) databases; (ii) participant self-report (monthly log-books; 3-monthly telephone interviews); and (iii) costs associated with delivering the study intervention.				•	•	•	•
Institute for Medical Technology Assessment (iMTA) Productivity Cost Questionnaire (iPCQ)	The iPCQ will be used to capture indirect / productivity costs, for use in economic analyses. It consists of 18 questions and three modules: (i) productivity loss due to absence from paid work; (ii) productivity loss during paid work due to health reasons; and (iii) productivity loss of unpaid work.[20] The iPCQ will be administered via telephone interview.				•	•	•	•
Credibility and Expectancy Questionnaire (CEQ)	The six-item CEQ was used to evaluate the credibility and expectancy of treatment received.[21 22] Items 1, 2, 3 and 5 are scored on a nine-point Likert scale, while items 4 and 6 are scored from 0-100%. Higher scores indicate greater perceived credibility and benefit. The CEQ has demonstrated adequate internal consistency and test-retest reliability.[22]		•		•			•
Other measures								
Knee pain severity	Participants will respond to the question "how bad would you say your knee pain is now?" by selecting one of four responses: 'no pain', 'mild', 'moderate', 'severe'.	•	•	•	•	•	•	•
Navigate Pain	Participants will record the location of their knee pain on a high-resolution 3D schema of the lower limb, using a custom application (Navigate Pain, Aalborg University, Denmark)[23 24] on a personal computer tablet (Samsung Galaxy, Samsung, Seoul, South Korea). Pain areas will be individually extracted and expressed as total pixels by the software, and visually classified for location.[25] The touch screen interface has high agreement with paper-based pain maps.[24]	•						

	Description	t0-3	t0	t1	t2	t3	t4	t5
PainDetect	PainDetect will be administered to identify neuropathic pain components.[26] Nine items evaluating gradation of pain, pain course pattern and pain radiation are summed to give an overall score from -1 to 38. The presence of neuropathic pain is likely if the total score is ≥19, while a score ≤12 suggests that pain is unlikely to have a neuropathic component.[26] PainDetect is reliable[27] and recommended as a screening measure for neuropathic pain.[28]	•						
Pain Catastrophising Scale (PCS)	The PCS is a 13-item questionnaire used to evaluate pain-related catastrophising.[29] Participants use a 5-point Likert scale to indicate the degree to which they experienced each thought/feeling when they have pain. An overall score is calculated by summing all 13 items (range 0-52), as well as three subscale scores for rumination, magnification and helplessness. Higher scores indicate higher degrees of pain catastrophizing. The PCS has sufficient reliability and validity for use in adults.[29]	•						
Sport and physical activity participation	Participants will complete a standardised questionnaire about their current and previous physical activity. Items include: (i) current regular physical activity (>30mins duration); (ii) other physical activity or competitive sport prior to knee pain onset; (iii) whether they have changes their physical activity because of their knee pain, and why; and (iv) whether they plan to return to sport if they have modified their physical activity.	•						

t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months (time of primary interest); t3 = 6 months; t4 = 9 months; t5 = 12 months (close out)

Supplementary file 3. Clinical tests performed prior to commencing the observation period (t0-3).

Test	Description
Anthropometric measures	Height will be measured using a stadiometer. Body mass will be measured using digital scales. Body mass index (BMI) will be calculated as mass (kg) / height (m)^2. Waist circumference will be measured with a tape measure, at the narrowest point or midpoint of the lower costal border (10th rib) and iliac crest.
Knee clicking and crepitus	The presence of knee clicking and crepitus will be evaluated bilaterally using methods described by Schiphof et al.[30] Participants will be seated comfortably on a standard chair. The tester will rest their hand over the participants' patella of the test limb, and ask the participant to actively extend their knee from 90° of knee flexion to 0° of knee extension (if possible) 3 times. Crepitus will be defined as an audible grinding noise and/or palpable vibrations in the knee during active movement.
Knee extension torque	Knee extension force will be measured bilaterally using previously described methods .[31] Participants will sit comfortably on a high stool, with their knees in 90° flexion, and their thighs secured to the chair with a seatbelt (Figure 1). Participants may hold the seat of the chair with their arms in full extension. A strain gauge will be secured to the posterior aspect of the chair and strapped around the test ankle, at a point 10cm above the lateral malleolus. Participants will be instructed to extend their knee to end of range and push maximally for three seconds. Three trials will be performed on each side. To calculate knee extension torque, force will be multiplied by leg length (distance between the lateral femoral epicondyle and lateral malleolus).  Figure 1. Test position.
Foot Posture Index (FPI)	The FPI is a valid and reliable method of quantifying weight bearing static foot posture.[32] Methods are detailed in the user guide and manual (available online).[33] Participants will stand in relaxed bilateral stance, with their arms by their side and looking straight ahead. Six aspects of static foot posture are evaluated on each foot: (i) talar head palpation; (ii) supra and infra malleolar curvature; (iii) calcaneal frontal plane position; (iv) bulging in the region of the talonavicular joint; (v) height and congruence of the medial longitudinal arch; and (vi) abduction/adduction of the forefoot on the rearfoot. Each feature is scored on a five-point scale (-2 = supinated; 0 = neutral; +2 = pronated). A total score for each foot is calculated by summing each of the six items. Total scores range from -12 (supinated) to +12 (pronated).

Foot mobility	Foot mobility will be evaluated bilaterally using the Foot Assessment Platform.[34] For weight bearing (WB) measures, participants will be positioned in bilateral stance on a custom-designed platform. Total foot length will be measured, and the dorsum of the foot marked at 50% of total foot length. Midfoot height and midfoot width will be measured (in millimetres) at 50% foot length using digital calipers (Figure 2A and 2B). Participants will then be seated on the edge of a plinth to capture non-weight bearing (NWB) foot measures. With the femur horizontal, tibia vertical, and foot and ankle hanging relaxed in space, a custom-made platform will be used to measure midfoot height at 50% foot length (Figure 2C). Midfoot width at 50% foot length will be measured in the same position, using digital calipers (Figure 2D). Foot mobility will be defined in three ways: (i) midfoot height mobility, calculated as the difference between NWB and WB midfoot height; (ii) midfoot width mobility, calculated as the difference between WB and NWB midfoot width; and (iii) foot mobility magnitude (calculated as: $\sqrt{(\text{midfoot height mobility})^2 + (\text{midfoot width mobility})^2}$).  Fig 2A. WB midfoot height.  Fig 2B. WB midfoot width.  Fig 2C. NWB midfoot height.  Fig 2D. NWB midfoot width.
Weight bearing ankle dorsiflexion range of motion	Ankle dorsiflexion range of motion will be measured in weight bearing using established methods.[35] The plane of movement will be marked using a line of tape on the floor perpendicular to the wall (horizontal line), with the tape continuing vertically up the wall to approximately knee height. Participants will stand in front of the wall with the midpoint of the calcaneus and second toe of the test limb aligned on the horizontal line. Participants will be instructed to lunge forward to touch their kneecap to the vertical line on the wall, while maintaining their heel on the floor. The assessor will ensure that the heel stays in contact with the floor. The foot will be moved back gradually along the horizontal line until the point where the kneecap just touches the wall, and the heel is almost lifting off the floor (Figure 3). The distance between the wall and the longest toe will be measured (centimetres). The test will be performed three times on each limb.  Fig 3. Test position

Footwear Assessment Tool	The participant's footwear will be assessed using selected items from the Footwear Assessment Tool, which has established reliability.[36] We will evaluate one pair of shoes that they wear most frequently. Shoe fit (Item 1) will be evaluated in terms of the length between the longest toe and end of shoe (too short: < ½ thumb's width; good: 1 to 1 ½ thumb widths; too long: > 1 ½ thumb widths); width of the shoe when the upper is grasped across the metatarsal heads (too wide: excessive bunching; good: slight bunching; too narrow: taught upper unable to be grasped); and depth (adequate; too shallow). General features will also be recorded (Item 2), including age of the shoe (months); footwear type (selected from existing template [36]); and shoe weight (grams) and length (millimetres). Structural features (Item 3) will include heel and forefoot height (millimetres); and forefoot sole flexion point (at 1st metatarsophalangeal (MTP) joint; proximal to 1st MTP joint; distal to 1st MTP joint). Motion control properties (Item 4) will consist of sagittal stability of the midfoot sole (minimal >45°; moderate <45°; rigid <10°). Cushioning (Item 5) will be evaluated be measuring lateral midsole hardness (penetrometer reading). Participants will also be asked to rate how comfortable they think their shoes are on a 100mm visual analogue scale (0=extremely uncomfortable; 100=extremely comfortable).
10-metre Walk Test	Temporospatial gait parameters (e.g. walking speed, step length) will be measured using the 10-Metre Walk Test.[37] A 10-metre walkway will be measured along a level corridor. Participants will be instructed to walk at their usual comfortable walking pace from the point when they cross the starting line (0 metres) until they cross the finish line (10 metres). The investigator will start timing the trial from the moment their first foot crosses the starting line, and stop when their first foot crosses the finish line. Participants will perform three warm-up repetitions, followed by three recorded trials, ensuring that the second and third recorded trials are within 5% of the first recorded time.

REFERENCES

1. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
2. Parkes MJ, Callaghan MJ, O'Neill TW, et al. Sensitivity to Change of Patient-Preference Measures for Pain in Patients With Knee Osteoarthritis: Data From Two Trials. *Arthritis Care Res (Hoboken)* 2016;68(9):1224-31.
3. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64.
4. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735.
5. ten Klooster PM, Drossaers-Bakker KW, Taal E, et al. Patient-perceived satisfactory improvement (PPSI): interpreting meaningful change in pain from the patient's perspective. *Pain* 2006;121(1-2):151-7.
6. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.
7. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776.
8. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
9. Watson CJ, Propps M, Ratner J, et al. Reliability and responsiveness of the lower extremity functional scale and the anterior knee pain scale in patients with anterior knee pain. *J Orthop Sports Phys Ther* 2005;35(3):136-46.
10. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44.
11. Brady TJ. Measures of self-efficacy: Arthritis Self-Efficacy Scale (ASES), Arthritis Self-Efficacy Scale-8 Item (ASES-8), Children's Arthritis Self-Efficacy Scale (CASE), Chronic Disease Self-Efficacy Scale (CDSES), Parent's Arthritis Self-Efficacy Scale (PASE), and Rheumatoid Arthritis Self-Efficacy Scale (RASE). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S473-85.
12. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.
13. Areeudomwong P, Buttagat V. Reliability and Validity of the Cross-Culturally Adapted Thai Version of the Tampa Scale for Kinesiophobia in Knee Osteoarthritis Patients. *Malays J Med Sci* 2017;24(2):61-67.
14. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.
15. Busija L, Pausenberger E, Haines TP, et al. Adult measures of general health and health-related quality of life: Medical Outcomes Study Short Form 36-Item (SF-36) and Short Form 12-Item (SF-12) Health Surveys, Nottingham Health Profile (NHP), Sickness Impact Profile (SIP), Medical Outcomes Study Short Form 6D (SF-6D), Health Utilities Index Mark 3 (HUI3), Quality of Well-Being Scale (QWB), and Assessment of Quality of Life (AQoL). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S383-412.

16. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24.
17. Barton GR, Sach TH, Avery AJ, et al. Comparing the performance of the EQ-5D and SF-6D when measuring the benefits of alleviating knee pain. *Cost Eff Resour Alloc* 2009;7:12.
18. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94.
19. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198.
20. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18(6):753-8.
21. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. *J Behav Therapy Exp Psychiatry* 1972;34:257-60.
22. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.
23. Boudreau SA, Spence R, Vasov G, et al. Feature Extraction APP for Pain Profiles. *Biosyst Biorobot* 2014;7:853-54.
24. Boudreau SA, Badsberg S, Christensen SW, et al. Digital Pain Drawings: Assessing Touch-Screen Technology and 3D Body Schemas. *Clin J Pain* 2016;32(2):139-45.
25. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160.
26. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20.
27. Tampin B, Bohne T, Callan M, et al. Reliability of the English version of the painDETECT questionnaire. *Curr Med Res Opin* 2017;33(4):741-48.
28. Turner KV, Moreton BM, Walsh DA, et al. Reliability and responsiveness of measures of pain in people with osteoarthritis of the knee: a psychometric evaluation. *Disabil Rehabil* 2017;39(8):822-29.
29. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.
30. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8.
31. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.
32. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98.

33. Redmond AC. The foot posture index: easy quantification of standing foot posture. Available at https://www.leeds.ac.uk/medicine/FASTER/z/pdf/FPI-manual-formatted-August-2005v2.pdf 2005 [Available from: http://courses.ki.se/fpi_manual-formatted_august_2005v2_1_.pdf?node=202687 accessed November 8, 2017.
34. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.
35. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80.
36. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.
37. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	***1***
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	***2***
	2b	All items from the World Health Organization Trial Registration Data Set	**-**
Protocol version	3	Date and version identifier	**-**
Funding	4	Sources and types of financial, material, and other support	***25***
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	***25***
	5b	Name and contact information for the trial sponsor	***25***
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	***25***
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	***25***

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	***4-5***
	6b	Explanation for choice of comparators	***14-15***
Objectives	7	Specific objectives or hypotheses	***5-6***
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	***6-7***
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	***6-7***
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	***8***
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	***12-16***
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	***16***
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	***16-17***
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	***16***
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	***17-20***
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	***Figure 2***

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	***20-21***
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	***7-8***
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	***12***
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	***12***
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	***12***
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	***12***
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	***12***
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	***9-11, 17-20***
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	***17***

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	***21-22***
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	***22-23***
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	***22-23***
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	***22***
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	***22***
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	***22***
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	***19-20***
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	**-**
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	***7***
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	***7***

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	***8-9, 11***
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	***8-9, 11***
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	***21-22***
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	***25-26***
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	***21-22, 24***
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	***15-16***
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	***23-24***
	31b	Authorship eligibility guidelines and any intended use of professional writers	**-**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	***24***
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	***Supplementary file 1***
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	***n/a***

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis

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The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis

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ABSTRACT

INTRODUCTION: Patellofemoral (PF) osteoarthritis (OA) is a common and burdensome subgroup of knee OA, with very little evidence for effective treatments. Prefabricated foot orthoses are an affordable and accessible intervention that have been shown to reduce PF pain in younger adults. Similarities between PF pain and PFOA, as well as our pilot work, suggest that foot orthoses may also be an effective intervention for PFOA. The primary objective of this study is to compare the 3-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on knee pain severity.

METHODS AND ANALYSIS: The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a 3-month observation period (pre-randomisation) and 12-month follow-up. 160 participants with a clinical diagnosis of PFOA will be recruited from three sites in Australia, and randomised to one of two groups (prefabricated foot orthoses or flat shoe inserts). The primary outcome is worst knee pain severity during a self-nominated aggravating activity in the previous week (100mm visual analogue scale) at three months, with a secondary endpoint at 12 months. Secondary outcomes include global rating of change, symptoms, function, health-related quality of life, kinesiophobia, self-efficacy and use of co-interventions for knee pain. Blinded, intention-to-treat analyses of primary and

secondary patient-reported outcomes will be performed, as well as economic analyses.

ETHICS AND DISSEMINATION: Ethical approval has been granted by La Trobe University's Human Ethics Committee and The University of Queensland's Medical Research Ethics Committee. Study outcomes will be disseminated via peer-reviewed journals, conference presentations targeting a range of healthcare disciplines, and an open access website with clinician resources.

TRIAL REGISTRATION NUMBER: Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This multicentre study is the first full-scale RCT to evaluate simple, prefabricated foot orthoses as a treatment for patellofemoral osteoarthritis.
- The proposed project will recruit a large sample of people with patellofemoral osteoarthritis, with sample size estimates based on our pilot work.
- Outcomes will be measured at three months (primary endpoint), as well as 12 months to evaluate the longer-term efficacy of foot orthoses for this chronic condition.

- Economic analyses will provide cost-effectiveness ratios and costs per additional quality-adjusted life year, to inform clinical decision-making.
- While participants and outcome assessors are blinded, it is not possible to blind the therapists issuing the interventions, due to visual differences between the prefabricated foot orthoses and flat shoe inserts.

INTRODUCTION

Patellofemoral (PF) osteoarthritis (OA) is an important subgroup of knee OA, whose burden is becoming increasingly evident. Radiographic PFOA is more common than tibiofemoral (TF) OA in people with chronic knee pain (64 to 69% compared to 44 to 45%).[1 2] The PF joint is often the first knee joint compartment affected by OA, and increases the risk of TFOA development and progression.[3] Structural features of PFOA show greater association with knee symptoms than TFOA features. Patellofemoral osteophytes (but not TF osteophytes) are associated with knee pain (odds ratio 2.3, 95% CI 1.1 to 4.8),[4] and reduced patellar cartilage volume (but not femoral or tibial) is related to greater pain and functional impairment.[5] Importantly, compared to TFOA, PFOA tends to occur in younger people,[1] who often have greater daily physical demands due to occupational and/or childcare responsibilities. Considering the progressive nature of PFOA, the side effects of long-term medication use, and that pain and functional limitations are primary barriers to physical activity[6] and indications for total knee replacement,[7] interventions that can effectively reduce PFOA pain are urgently required.

Despite the burden of PFOA, and best-practice guidelines recommending non-surgical, non-drug interventions as the first line strategy for knee OA management,[7] there is very little evidence for effective treatments for PFOA. Although combined interventions (e.g. PF taping, knee/hip exercises, manual therapy, education)[8 9] and

knee braces[10] have some evidence of efficacy, their longer-term effects appear to be limited by poor treatment adherence.[11 12] This is particularly relevant for middle-aged adults with PFOA, whose busy lifestyles and family and work commitments are likely to influence adherence to exercise programs.[11] Issues with knee brace bulkiness and interference with clothing[12] are likely to be barriers to brace wear. For braces and orthoses to be effective, they must be comfortable and unobtrusive to daily living to ensure maximal adherence and patient outcomes.

Foot orthoses are inserts worn in everyday footwear that are contoured to match the shape of the foot. Prefabricated foot orthoses are affordable and accessible, and are an effective treatment for PF pain in young adults (aged 18 to 40 years).[13 14] Based on similarities in symptoms, biomechanics and muscle function between PF pain and PFOA,[15-17] it is plausible that foot orthoses could also have positive effects in people with PFOA. Pilot data show that people with PFOA (n=23, mean age 59±10) report immediate improvements in pain when performing a step-down task with foot orthoses, compared to shoes alone.[18] We observed high adherence and only transient, minor adverse events in our previous trial of foot orthoses in PF pain,[19] suggesting the feasibility of long-term wear. It is therefore timely to conduct a randomised clinical trial (RCT) to evaluate foot orthoses efficacy in this population. The FOOTPATH Study (FOot OrThoses for PAtellofemoral osteoarTHritis) will investigate the efficacy of prefabricated foot orthoses for people with PFOA.

OBJECTIVES

Primary objective

The primary objective is to compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts on knee pain severity in people with PFOA. *We hypothesise that, compared to flat inserts, foot orthoses will result in greater improvements in knee pain during a nominated aggravating activity at three months (H1).*

Key secondary objectives

1. Compare the three-month efficacy of prefabricated foot orthoses and flat shoe inserts in people with PFOA, on patient-reported global rating of change (GROC). *We hypothesise that, compared to flat inserts, foot orthoses will result in more participants reporting marked improvement at three months (H2).*
2. Compare the 12-month efficacy of prefabricated foot orthoses and flat shoe inserts on GROC, knee pain severity, function, quality of life, kinesiophobia, self-efficacy and use of co-interventions, in people with PFOA.

   We hypothesise that foot orthoses will yield: (i) more participants reporting marked improvement, and greater improvements in knee pain during a nominated aggravating activity, at 12 months (H3); and (ii) greater improvements in knee pain

severity, the Knee injury and Osteoarthritis Outcome Score (KOOS), Anterior Knee Pain Scale, Short-Form 12, EuroQol-5D, Tampa Scale for Kinesiophobia and Arthritis Self Efficacy Scale, and less co-intervention use at three and 12 months (H4).

3. Evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts in people with PFOA.

   We hypothesise that foot orthoses will yield better cost-effectiveness ratios and lower costs per additional quality-adjusted life year after 12 months (H5).

Other secondary objectives

Alongside primary and secondary RCT outcomes, we will investigate the following additional secondary objectives, in people with PFOA.

1. Identify factors that predict change in patient-reported symptoms over a three-month wait-and-see period.
2. Describe characteristics of people with PFOA, including patterns of pain location.
3. Investigate whether foot mobility is related to radiographic features of PF and TF joint alignment and radiographic features of OA.
4. Identify clinically applicable factors that predict poor prognosis at three and 12 months, and determine baseline values of predictor variables to facilitate clinical identification of people with a poor prognosis.

5. Determine the three-month effect of prefabricated foot orthoses on physical activity level compared to flat shoe inserts.
6. Explore factors that are associated with clinical outcomes with prefabricated foot orthoses at three and 12 months.

METHODS AND ANALYSIS

Trial design

The FOOTPATH Study is a multicentre, randomised, participant- and assessor-blinded superiority trial with two parallel groups, a three-month observation period (pre-randomisation) and 12-month follow-up. Equal numbers of participants will be randomised to each group, with the primary endpoint of GROC and pain after three months. The trial will be conducted across two university sites in Melbourne and Brisbane, Australia, with a satellite site in Hobart, Tasmania. The trial protocol was developed in consultation with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement[20 21] and the Osteoarthritis Research Society (OARSI) recommendations.[22] The trial was prospectively registered (Australian New Zealand Clinical Trials Registry; ANZCTRN12617000385347).

Ethics approval

Ethical approval has been granted by La Trobe University's Human Ethics Committee (HEC16-113) and The University of Queensland's Medical Research Ethics Committee (2017000284). In the event that a substantive modification to the study protocol is required (i.e. modifications that affect the conduct of the study), a formal protocol amendment will be prepared, and all proposed amendments reviewed by the two ethics committees. These will be reported in the ANZCTR and study publications.

Participant recruitment and eligibility criteria

Figure 1 summarises the flow of participants through the study. Participants will be recruited from the community in Melbourne, Brisbane, Hobart and regional Victoria. We will utilise a multifaceted recruitment strategy that has successfully recruited people of all ages with knee pain in our previous studies. This will include strategies such as paid and free advertisements in local newspapers, community magazines and newsletters (e.g. University staff bulletins, seniors newsletters); posters in senior citizen's centres, golf and bowling clubs, and retirement villages; sandwich boards and handouts at community events (e.g. fun runs, farmer's markets); radio and television media releases; mail-outs to health practitioners in recruitment areas (e.g. general practitioners, orthopaedic surgeons, physiotherapists); posts on university and research centre websites (La Trobe University, The University of Queensland); social media (e.g. Facebook, Twitter); and patients from the La Trobe University Health Sciences (Podiatry) Clinic, community health care centres, and hospital waiting lists.

Based on recruitment rates of 6 participants per month during our feasibility trial (single site), as well as known periods of slow recruitment (e.g. December/January), conservative estimates indicate that the duration of recruitment will be approximately 20 months. Recruitment rates across all sites will be monitored during the trial, and recruitment strategies adjusted accordingly to meet recruitment targets. There will be no incentives provided to trial investigators or participants for enrolment.

Volunteers who respond to advertisements will be screened for eligibility using a two-stage screening process. This will be conducted by an experienced musculoskeletal health professional (physiotherapist or podiatrist with a minimum of five years of musculoskeletal clinical experience). Preliminary screening questions will be asked via telephone or email. Potentially suitable volunteers will then be invited to attend a physical screening appointment at La Trobe University, The University of Queensland or a private practice (if in regional Victoria or Hobart), where a comprehensive musculoskeletal examination will be completed.

We will use a clinical diagnosis of PFOA[23], adapted from the NICE guidelines.[24] This is to facilitate generalisation of findings to clinical practice, without the need for imaging. Inclusion criteria will be: (i) age 50 years and over; (ii) predominant symptom of anterior or retropatellar knee pain aggravated by at least two PF joint loading activities (e.g. stairs, squatting, rising from sitting); (iii) pain present during these activities on most days of the previous month; (iv) pain severity of at least three on an

11-point numerical rating scale (NRS, 0-10) during aggravating activities; (v) duration of symptoms of at least three months; and (vi) either no morning joint-related stiffness, or morning stiffness that lasts no longer than 30 minutes.

Volunteers will be excluded if they have: (i) knee pain symptoms predominantly from other knee (TF joint) structures, hip or lumbar spine; (ii) knee injections or use of any shoe inserts within the previous three months; (iii) recent commencement of new physiotherapy treatment for PF pain (i.e. new intervention, or modifications to existing intervention such as therapeutic exercise); (iv) any foot condition precluding the use of foot orthoses or flat shoe inserts; (v) history of lower limb surgery involving major reconstructive procedure (e.g. anterior cruciate ligament reconstruction, osteotomy, arthroplasty); (vi) planned lower limb surgery in the following 12 months; (vii) neurological or systemic arthritis conditions; (viii) major medical conditions (e.g. cancer); (ix) contraindications to x-ray (pregnancy, breastfeeding); or (x) an inability to understand written and spoken English.

Informed consent

All volunteers who meet the study eligibility criteria will be provided with a participant information sheet. This will provide details of the first phase of the study (observation period), and outline procedures for the second phase of the study (intervention). A trained investigator will discuss the study with volunteers, and provide opportunities

for volunteers to ask any questions. The lead investigator at each university site (Melbourne: KMC; Brisbane: NJC) will be available for consultation as required. All participants will provide written informed consent prior to participation. At the conclusion of the observation period, participants will provide additional consent for the intervention phase of the study (detailed below). Participant information and consent forms for all components of the study are included in Supplementary file 1.

Baseline assessment

Participants will attend a single session at La Trobe University, The University of Queensland, or a private physiotherapy/podiatry clinic (if in regional Victoria or Hobart) for baseline assessment. Structured questionnaires and established patient-reported outcome measures will be used. These will be administered in an electronic format (via computer or tablet) to familiarise participants with the electronic platform. Participants will then nominate their preferred methods of communication (e.g. phone, email) and questionnaire completion (paper or electronic format [25]) for the duration of the study.

Participant characteristics will include age, sex, occupation, duration of knee pain symptoms, major medical conditions, other joint complaints in the past month,[26] and medication use.

Patient-reported outcome measures are outlined in Figure 2 and detailed in Supplementary file 2. Pain will be evaluated as knee pain severity over the past week (100mm visual analogue scales [VAS]),[27] PainDetect[28] and Navigate Pain.[29] The KOOS[30] and patellofemoral subscale[31] will evaluate pain severity, other symptoms, function, knee-related quality of life and patellofemoral symptoms. Other measures include the Anterior Knee Pain Scale (AKPS),[32] Short-Form-12 (SF-12) questionnaire,[33] EuroQol (EQ) 5D-5L questionnaire,[34] Tampa Scale for Kinesiophobia,[35] Pain Catastrophising Scale,[36] Arthritis Self Efficacy Scale[37], and sport and physical activity participation.

Participants will also complete a battery of clinical measures and tests (detailed in Supplementary file 3), which were selected based on their potential to predict PFOA prognosis and/or response to foot orthoses. These include height, mass, body mass index (BMI), waist circumference, presence of knee clicking and crepitus,[38] Foot Posture Index (FPI),[39] foot mobility (Foot Assessment Platform),[40] weight-bearing ankle dorsiflexion (knee to wall test),[41] Footwear Assessment Tool,[42] knee extension torque,[43] and the timed 10-metre walk test.[44]

Radiographic assessment

All participants will attend a private radiology clinic to have radiographs taken of their nominated study knee (most symptomatic eligible knee if pain is bilateral). These will

be used to characterise the cohort, and used as predictor variables in other secondary analyses. Several radiology clinics in Melbourne, regional Victoria, Hobart and Brisbane will be used to minimise participant travel time. Weight-bearing anteroposterior, lateral and skyline views will be obtained using standard clinical protocols. Radiographs will be used to grade the presence and severity of OA features in the PF and TF joint compartments. Radiographic features of joint space narrowing and osteophytes will be graded, and the presence of PF and TF OA determined using the Kellgren-Lawrence grading system[45] and a radiographic atlas.[46] Each radiograph will be graded by two experienced investigators (NJC, KMC). Anteroposterior radiographs will also be used to measure frontal plane TF alignment,[47] while lateral and skyline views will be used to measure PF alignment using established protocols.[48]

Observation period

Participants will undergo a three-month observation period, where they will not receive any treatment for their knee pain as part of the study. This is to ensure that only participants with ongoing chronic symptoms that do not improve with time are enrolled in the RCT. Participants will be informed that they will be observed for a three-month period before receiving their intervention.

During the observation period, a subgroup of participants will undergo physical activity monitoring. This subgroup will consist of the first 60 participants who have access to

the internet and a smartphone or laptop, and who agree to participate. They will be asked to wear a Fitbit® device (Flex™ / Flex 2™, Fitbit Inc., San Francisco, USA) for the duration of the three-month observation period. This is to familiarise participants with the device and to facilitate adherence with wear during the next phase of the study. Data for physical activity will be remotely extracted from the Fitbit® website.

To maintain contact during the observation period, participants will be contacted via phone or email six weeks after their baseline measures, and will be asked to rate their average and worst knee pain severity over the past week during their nominated aggravating activity (11-point numerical rating scale). Patient-reported outcome measures taken at baseline will be repeated three months after initial assessment. Participants who rate their pain during aggravating activities as less than 30mm on a 100mm visual analogue scale will not be invited to participate in the RCT. They will be offered a pair of contoured sandals (Vionic®, Arundel, Queensland, Australia), and be invited to participate in a prospective longitudinal cohort study (a separate consent process). The same battery of questionnaires administered at baseline will be completed at yearly intervals from the date of baseline assessment (up to five years), with the addition of questionnaires regarding GROC, use of co-interventions for knee pain, and adverse events). This study will occur alongside, but separate to, the RCT.

Participants who rate their worst knee pain at least 30mm on the 100mm VAS during their nominated aggravating activity will be invited to participate in the RCT evaluating the efficacy of prefabricated foot orthoses, compared to flat shoe inserts.

Randomised clinical trial

Informed consent

Participants who are eligible to participate in the RCT will provide separate informed consent for the RCT, and for the release of their Medicare and Pharmaceutical Benefits Scheme data for economic analyses.

RCT baseline measures

Three-month follow-up outcomes from the observation period will serve as baseline data for the RCT. Participants will also complete the Credibility and Expectancy Questionnaire (CEQ) to evaluate treatment expectations.[49]

Allocation, concealment and blinding

Once baseline outcome measures are completed, participants will be randomised to receive prefabricated foot orthoses or flat shoe inserts. To ensure concealed

allocation, we will use an offsite, telephone-based interactive voice response randomisation service (NHMRC Clinical Trials Centre; randomisation will be performed using a computer-generated minimisation programme with study site as a minimisation factor). Each participant's allocated intervention will be revealed to a single investigator (JMT), who will communicate this to the participant's nominated study practitioner, or to the Brisbane site research assistant (GC) who will liaise with local study practitioners. Because we are comparing two shoe inserts with different shapes, it is not possible to blind study practitioners to group allocation. As the primary outcomes are self-reported, participants are considered assessors. To ensure participant (and thus assessor) blinding, consent will involve limited disclosure. As in our recent RCT,[8] participants will be informed that they will be randomised to one of two shoe insert interventions, but will not be informed of the treatment elements or our hypotheses. Trial participants will be unblinded once data analyses have been finalised. Because we are evaluating two different shoe inserts known to have minimal associated adverse events,[19] it is anticipated that emergency unblinding will not be required.

Interventions

Forty registered podiatrists and physiotherapists with at least five years musculoskeletal experience will fit participants with their allocated intervention. All study practitioners will fit interventions for participants allocated to both groups. To

minimise participant burden, study practitioners will be located at multiple private practice clinics across greater Melbourne, Brisbane, Hobart and regional Victoria. To ensure consistency in prescription of foot orthoses and flat shoe inserts, study practitioners will undergo formal training in standardised fitting procedures for both interventions, as used in our previous RCT of prefabricated foot orthoses and flat shoe inserts for young adults with PF pain.[19 50] Study practitioners will also be provided with a comprehensive manual and video outlining study procedures, and will have email and phone access to an unblinded investigator to discuss interventions as required (Melbourne, SEM; Brisbane, BV). Participants will attend an appointment with their study practitioner within one week of baseline assessment to undergo fitting of their allocated intervention.

Participants will be asked to wear their allocated inserts as much as possible, and will be able to transfer them between footwear. This reflects current clinical practice, and will ensure maximal wear time and potential effects.

Prefabricated foot orthoses

The prefabricated foot orthoses will replicate the intervention used in our previous RCT in young adults with PF pain.[19 50] Participants will receive prefabricated foot orthoses from a commercially available range (Vasyli Medical®, Labrador, Australia) (Figure 3A, 3B). The foot orthoses are manufactured from ethylene-vinyl acetate (EVA) of high

density (hard, Shore A 70°), medium density (Shore A 55°) and low density (soft, Shore A 45°), and have an inbuilt arch support and 6° varus wedging. A variety of lengths and shapes are available to fit the shape of different footwear. At their first appointment with their chosen study practitioner, participants will bring up to three pairs of shoes that they most commonly wear (e.g. work shoes, casual shoes and sports shoes). Study practitioners will fit one pair of foot orthoses to one pair of the participant's shoes. This will be based on which of the participant's shoes are able to accommodate the foot orthoses and provide the most support, as prefabricated foot orthoses have superior effects when used with supportive footwear.[51] Where possible, the orthoses will be able to be transferred across their usual footwear. Study practitioners will ensure that the foot orthoses are comfortable, using procedures used in our previous RCT.[19 50] Figure 4 outlines the steps involved in the prescription algorithm. The first step involves selection of the type and size of orthoses based on shoe volume and foot length, respectively. Step two involves selection of the hardness of the device, based on participant comfort. If needed, study practitioners will then follow a series of sequential modifications until comfort has been achieved: (i) adding rearfoot varus wedge; (ii) adding forefoot varus to the rearfoot varus wedge; (iii) removing the rearfoot varus wedge; (iv) adding a heel raise; and (v) gently heat moulding the orthoses. Comfortable foot orthoses can effectively reduce PF pain in younger adults,[52] and are proposed to optimise adherence and potential therapeutic effects. Participants will be given written instructions for using and adapting to the foot orthoses.

To reflect current clinical practice, and to provide sufficient opportunity to ensure adequate comfort and prescribe additional foot orthoses, participants will attend up to six appointments with the study practitioner in the first six weeks of the study. Appointments will be scheduled as follows, where appropriate for individual participants: two appointments in week one; one appointment in week two (with an additional appointment in the same week as needed); one appointment in week three or four; one appointment in week six. Participants will be provided with up to four pairs of foot orthoses, fitted to multiple pairs of commonly worn shoes, in order to maximise wear time.

To maximise outcomes of wearing a comfortable, contoured device, participants will receive one pair of sandals (Shore A 50°) from the Vionic range (Vionic®, Arundel, Queensland, Australia). Participants will be encouraged to wear these during times that they do not normally wear enclosed footwear that accommodates foot orthoses (e.g. at home or during warmer weather). Feedback from our previous RCT in young adults with PF pain[19] indicated that participants often chose to wear sandal-type footwear in warm weather, for a large proportion of the year. The Vasyli® sandals offered as an adjunct to foot orthoses were well received by participants in our previous RCT, and increased the time that participants wore a contoured device.

Participants with a high BMI (≥30 kg/m^2) will be invited to attend a follow-up appointment at six months post-randomisation, to receive new foot orthoses. This will not be necessary for those with a BMI <30 kg/m^2, as the pressure-redistributing properties of prefabricated foot orthoses are maintained after 12 months.[53] However, participants will be offered an additional appointment at six months and/or nine months if they are having any issues with the foot orthoses (e.g. increase in pain, excessive wear of orthoses).

Flat shoe inserts

Flat shoe inserts will be used as the comparator intervention (Figure 3C). This is because the contour and wedging of the foot orthoses are proposed to exert mechanical effects on the foot and lower limb, which is thought to be the basis for symptom improvement. Participants will be informed that the study aims to compare two different types of shoe inserts. The flat inserts will be described as an intervention designed to enhance sensory feedback, supported by findings from our previous RCT in PF pain, where those who received flat inserts also experienced improvements in pain over 12 months.[19] The flat inserts will be the same as those used in our previous RCT, with identical covering fabric to the foot orthoses. To control for gradual contouring that occurs with repeated wear of low-density inserts (a limitation of previous studies), the flat inserts will be made of high-density EVA (Shore A 70°). Standardised guidelines for fitting and follow-up of the flat inserts will aim to ensure

these are perceived as a credible intervention (Figure 5). As with the foot orthoses, participants will be provided with up to four pairs of flat inserts fit to multiple pairs of commonly worn shoes. To address the potential influence of therapist contact, those randomised to this group will also attend an initial appointment with a study practitioner for fitting of flat inserts, and up to two follow-up appointments to ensure adequate comfort and fit. At six months post-randomisation, a follow-up appointment will be made with the study practitioner to issue new flat inserts, to minimise the effects of cumulative contouring with repeated wear.

At the conclusion of the study, if prefabricated foot orthoses are found to be more efficacious than flat inserts, those randomised to the flat insert group will be offered one pair of foot orthoses and one additional appointment with one of the study practitioners at no cost to them.

Criteria for discontinuing or modifying allocated intervention

The occurrence of adverse events will be monitored throughout the duration of the RCT by study practitioners, participant logbooks, and three-monthly telephone calls to participants. In the event of minor adverse events (e.g. rubbing, blisters) associated with either intervention, study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms described above. This may include replacement of foot orthoses with a softer device. If participants still report

discomfort, they will be encouraged to halve their foot orthoses or flat insert wear time for a period of two weeks, and then gradually increase wear time as tolerated. If comfort is unable to be achieved, the intervention will be ceased, as this reflects current clinical practice.

In the event of a sustained increase in knee pain, or aggravation of another area of pain (e.g. low back pain), study practitioners will review the prescribed device and modify accordingly, based on the prescription algorithms. If this does not relieve the participant's symptoms immediately, then intervention will be ceased. Participants who cease their allocated intervention will be encouraged to remain in the trial to enable follow-up data collection at all nominated time points.

Strategies for improving and monitoring adherence to interventions

Study personnel will maintain regular communication with participants over the study period (e.g. email, phone), and will encourage adherence to the interventions at each time of contact. Adherence to foot orthoses or flat insert wear will be monitored using a variety of strategies. Study practitioners will record attendance at each appointment. To reduce participant burden associated with daily diary entries, participants will report their adherence at three-monthly intervals during the RCT. This will be recorded as the average days per week and hours per day that they wore the foot orthoses or flat inserts over the preceding four weeks.[54]

Concomitant care and interventions

During the observation and intervention periods, participants will be able to continue with stable medication doses and exercise programs, and use some concomitant interventions (e.g. analgesics, heat/cold, general exercise).[55] New physical therapies (e.g. exercise, manual therapy, taping, bracing), intra-articular injections and surgery will be discouraged. If participants have problems with their allocated intervention or wish to seek additional treatment outside the trial, they will be asked to contact the unblinded investigator at their trial site to discuss this (Melbourne, Hobart, JMT/SEM; Brisbane, BV). Use of concomitant interventions will be recorded during the intervention period using monthly logbooks (issued at RCT baseline) and structured questionnaires at three-monthly intervals.

Participant retention

Study personnel will utilise established methods to maximise participant retention. Following enrolment in the study at the commencement of the observation period, participants will be contacted at regular intervals throughout the study period to collect outcome data, ascertain any issues with the intervention, and maintain communication. We have endeavoured to minimise participant burden by utilising an online data collection platform, and limiting the number of appointments that

participants are required to attend in-person (one screening/baseline appointment; one x-ray appointment; maximum of seven practitioner appointments over 12 months). Although financial incentives will not be provided, financial reimbursement for travel costs will be available for participants if required. Participants who discontinue use of the intervention will be encouraged to complete outcome measures for the duration of the study to minimise missing data.

Outcomes

Outcome assessment will occur at three, six, nine and 12 months. Three months is the *a priori* primary end-point of interest, as early improvement in symptoms is likely to influence ongoing adherence with foot orthoses or flat inserts. Twelve-month follow-up will evaluate longer-term effects and economic efficiency of foot orthoses, which is important given the chronic nature of PFOA, and reflects clinical practice.

At entry into the study, participants will be asked their preferred method of receiving and completing outcome measures. Where possible, outcome data will be collected using an internet-based platform, which has equivalent measurement properties to paper-based completion.[25] This strategy was used in our pilot studies on people with PFOA,[56] ensuring feasibility of online data collection in this population. However, for participants who do not have internet access or would prefer to complete outcome measures in paper format, paper versions and reply-paid envelopes will be mailed.

Outcome measures of GROC, pain and function have been selected based on international recommendations for knee OA.[57] These are listed below and detailed in Supplementary file 2.

We have selected patient-reported outcomes over imaging and surgical endpoints, aligning with international recommendations highlighting the importance of patient-centred outcomes.[22 57] Considering the financial cost and participant burden of repeated magnetic resonance imaging (MRI), and the lack of correlation between symptoms and imaging,[58] it is important to first determine whether prefabricated foot orthoses improve pain and function. This will ensure continued adherence and greater potential for longer-term effects on joint structure. Whilst total knee replacement is usually recommended for end-stage joint disease, severe pain and functional limitations,[7 55] other factors such as race, ethnicity, socioeconomic status and patient preferences can also influence decisions for surgery.[59] Thus, patient-reported outcomes are, at present, the ideal method to evaluate foot orthoses outcomes for PFOA. Indeed, regulatory agencies such as the United States Food and Drug Administration require the use of patient-reported outcomes in the development of medical products to support labelling claims.[60]

Primary outcome (three months)

Knee pain is the predominant symptom of PFOA and the primary indication for undergoing total knee replacement.[7 55] Pain will be evaluated as *worst knee pain severity during a self-nominated aggravating activity in the previous week.*[8 10] Participants will nominate one of three everyday activities that they experience the greatest pain severity (rising from sitting, squatting or stair ambulation). Pain severity will be measured on a 100mm VAS (terminal descriptors 0=no pain, 100=worst pain possible). VAS measures of pain severity have well-established reliability and validity, including in PF pain.[27] This will be measured at baseline, six weeks, three months (time of primary interest), and six, nine and 12 months.

Secondary outcomes

Secondary outcomes will be administered at baseline, six weeks (knee pain severity and GROC), three months, six and nine months (knee pain severity and EQ-5D-5L), and 12 months (Figure 2).

- Knee pain severity over the past week (100mm visual analogue scales).[27]
- GROC (7-point Likert Scale: 'much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'; dichotomised to 'improved' ('much better, 'better') *vs.* 'not improved' ('a little better' to 'much worse').
- KOOS subscales: symptoms, pain, function in daily activities, function in sport/recreation, knee-related quality of life, patellofemoral symptoms.[30 31]

- AKPS.[32]
- SF-12.[33]
- EQ-5D-5L.[34]
- Tampa Scale for Kinesiophobia.[35]
- Arthritis Self Efficacy Scale.[37]
- Use of co-interventions for knee pain.[61]

Physical activity will be monitored in the subgroup of participants who received a Fitbit® physical activity monitor during the observation period. Data relating to physical activity levels (e.g. steps, distance) will be extracted weekly for each participant, for the first three months after randomisation. Data will be analysed in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) for total step count and time spent in low, moderate and high-intensity activity bands (defined as step count per 15-minute epoch). All physical activity data will be remotely downloaded from the Fitbit® data server using a freely available R package (Fitbit Scraper), and imported into Microsoft Excel for analysis.

Other outcomes

Treatment adherence and adverse events: Every three months, participants will complete a short questionnaire for physical activity, footwear worn and foot orthoses or flat insert wear time, and adverse events.[54] Evaluation of 12-month adherence is

vital to determine whether frequency of wear is maintained long-term. This will assist with translating outcomes into clinical practice guidelines. Study practitioners will record attendance, prescription notes and adverse effects during fitting and follow-up.

Treatment credibility and expectations: The CEQ will be completed again at three and 12 months.[49]

Economic outcomes

Data on direct health costs will be sourced from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. Direct and indirect health costs (e.g. medication use, hospital admissions, other co-interventions such as physiotherapy, time off work due to PFOA or treatment) will be captured from the following sources: (i) monthly participant logbooks; (ii) 3-monthly telephone interviews; and (iii) the Institute for Medical Technology Assessment (iMTA) Productivity Costs Questionnaire (iPCQ).[62] The EQ-5D is a reliable and valid measure of health-related quality of life, and considers mobility, self-care, usual activity, pain/distress and depression/anxiety.[34 63] EQ-5D will be measured at baseline, and at three, six, nine and 12 months, and used to calculate quality-adjusted life years.

Long-term follow-up

After completion of the RCT 12-month follow-up, participants will be asked to complete the same battery of patient-reported outcome measures at yearly intervals, up to four years after completion of the RCT (five years from baseline). This will allow us to conduct prognostic analyses to identify pain trajectories and predictors of long-term outcome, as in our previous RCTs.[64]

Sample size

Treatment efficacy will be evaluated by between-group comparisons on the primary outcome measure, which is worst knee pain severity during a self-nominated aggravating activity in the previous week, measured on a 100mm VAS). The minimal clinically important difference for pain on a VAS is 15mm.[65] Sample size calculations are based on an analysis of covariance (ANCOVA) adjusting for baseline of the outcome variable, and assume a between-person standard deviation of 30mm (based on pilot data in people with PFOA) and baseline to three-month correlation of 0.5. A sample of 160 (80 per group) provides a minimum 90% power (α=0.05) to detect significant between-group differences, and allows for ~20% dropouts.

Observation period: In people with chronic knee pain, pain severity has been shown to improve naturally over three months when people are being monitored by a general practitioner.[66] Thus, to ensure that participants in the RCT have sufficient levels of pain at baseline, and that any observed improvements in pain during the three-month

time of primary interest are attributable to the intervention, we will include a three-month observation period prior to randomisation. Based on previous findings, it is anticipated that some participants will experience natural improvement in their pain severity during this time.[66] Thus, we will continue to recruit participants into the observation period until we have recruited the required sample size into the RCT (n=160). Based on conservative estimates that approximately two thirds of participants will qualify for the RCT at three months, it is anticipated that a total of ~230 participants will be recruited. This will be revised throughout the study period.

Data management and storage

The majority of outcome data will be collected electronically, facilitating simultaneous data entry. For paper-based data collection, data will be entered by a single trained investigator (JWD). A second investigator will check a random subset of manually entered documents to ensure accuracy. Once data entry is finalised, quality checks will ensure that all data points are within expected values. Only named investigators will have access to the full dataset.

Personal data, including informed consent forms, participant names, contact details and date of birth will be stored on a password-locked computer hard drive, separately from patient-reported or other study data, in order to ensure data de-identification. All subsequent study data will be identified by participant number only, and will be stored

on the La Trobe University server Research Data Storage, which is only accessible only by the research team through secure means. All project documentation will be stored on a secure, password locked external hard drive, overseen by an external company (DS PRIMA, Port Melbourne, Victoria, Australia). No persons external to the research team will have access to information stored on this server. Appropriate ethical procedures will be followed for all data (e.g. participant coding, data file encryption, storage in locked filing cabinets). Any paper containing participant details, such as baseline questionnaires, will remain in the locked filing cabinet and will not be accessible outside the premises. Data pertaining to participant characteristics, questionnaires and clinical tests will be preserved for possible future use by the investigators. De-identified data will be stored in an Excel spreadsheet. If researchers other than those listed as investigators wish to use the data, prior approval will be sought from the La Trobe University human ethics committee. Participants will be made aware of this in the Participant Information Statement, ensuring that they are aware of the possibility that their data will be used for future studies, and are able to provide written informed consent.

Due to the minimal known risks associated with the interventions being evaluated, this study will not require a formal data monitoring committee or planned interim analysis.

Statistical methods

Primary and key secondary objectives

Intention to treat analyses will be performed, with all randomised participants included regardless of protocol adherence. Blinded analyses of primary and secondary patient-reported outcomes will be performed. The dichotomised measure of GROC will be expressed from blinded analyses as relative risk (RR) and number needed to treat (NNT), with 95% confidence intervals, to facilitate clinical guidelines.[19 67] For the primary outcome and continuous secondary outcome measures, linear mixed models (with baseline value as a covariate and treatment condition as a fixed factor) will be used to evaluate the treatment effect and 95% confidence interval at three months and 12 months ($p<0.05$). Linear mixed models utilising repeated measures at all time-points will allow non-biased estimates of treatment effect in the presence of any potential missing cases. This likelihood-based estimation procedure results in non-biased estimates, providing data are missing at random and models are adjusted for any imbalance between groups in potential confounders at baseline (age, sex, weight, symptom duration, PF/TF OA radiographic severity). Relative risk (95% confidence intervals) will be calculated for use of co-interventions and adverse events.

Economic evaluation

Blinded economic analyses will be conducted to evaluate the 12-month economic efficiency of prefabricated foot orthoses compared to flat shoe inserts, from the

societal perspective. Hospitalisations will be converted to costs using the National Weighted Activity Unit costing model. Incremental cost-effectiveness analyses will use the formula $[(DC_{foot\ orthoses} + IC_{foot\ orthoses}) - (DC_{flat\ inserts} + IC_{flat\ inserts}) / (E_{foot\ orthoses} - E_{flat\ inserts})]$, where DC=mean direct health costs, IC=mean indirect costs, E=effect, $_{foot\ orthoses}$= foot orthoses group, and $_{flat\ inserts}$=flat insert group. Effect for the primary economic evaluation will be the proportion of participants who 'improve' (measured on the GROC) within each group at 12 months. Thus, the cost-effectiveness ratio will reflect the marginal cost per additional 'improved' participant from the societal perspective over a 12-month time horizon. Uncertainty in this ratio will be examined by constructing a 95% confidence ellipse on a cost-effectiveness plane, and transforming these to cost-effectiveness acceptability curves using non-parametric bootstrap resampling of primary data. Sensitivity analyses will be conducted, varying the threshold of 'improvement' on the GROC to reflect increasingly higher thresholds. Quality-adjusted life year scores for each participant (calculated as area under the curve applied to utility measures calculated from EQ-5D) will be substituted for GROC scores as the effect measure, creating an incremental cost-utility ratio to determine the marginal cost per additional quality-adjusted life year for the more effective intervention.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not directly involved in the development of the research question, study design or selection of outcome measures. Patients will not be directly involved in the recruitment to or conduct of the study, except as participants if they meet the eligibility criteria and provide informed consent. At the conclusion of the study, overall study findings and individual participant data will be provided to study participants on request.

ETHICS AND DISSEMINATION

This study complies with the Declaration of Helsinki, and has been approved by ethics committees at La Trobe University and The University of Queensland. All participants will provide written informed consent prior to baseline data collection and enrolment in the three-month observation period. Participant information and consent forms for each phase of the study are included in Supplementary file 1. Participants will undergo knee radiographs at a single time point as part of this trial, ensuring that the amount of ionising radiation is consistent with standard clinical exposure. When prescribed by trained health practitioners, prefabricated foot orthoses and flat shoe inserts are associated with minimal and transient adverse events.[19] Thus, there are minimal ethical and safety considerations associated with this trial.

Study outcomes will be widely disseminated through a variety of sources. Primary and key secondary objectives will be submitted to a high-impact peer-reviewed journal in

the field. Because study outcomes are applicable to a broad range of health professionals, we will target a general medical journal to facilitate wider dissemination of findings to key stakeholders (e.g. general practitioners). Each of the other secondary objectives will be addressed in separate publications, and submitted to appropriate journals in the field. Authorship will be in accordance with guidelines provided by the International Committee of Medical Journal Editors [68]. We will also submit articles to key professional magazines to enhance dissemination to clinicians. Our publication strategy will be complemented by submission of abstracts to key national and international conferences, covering multiple discipline groups (e.g. physiotherapy, podiatry, general practice), as well as OA conferences. We will also develop an open access website and resources for clinicians, including videos detailing how to prescribe foot orthoses, and run workshops on PFOA and foot orthoses for registered health professionals. This will facilitate translation of findings to clinical practice, especially practitioners located in rural or remote areas.

DISCUSSION

PFOA is a major public health problem, and has no cure. Pain and stiffness experienced during daily activities, occupational tasks and exercise can reduce active participation. Importantly, PFOA in middle-aged adults can affect productivity and contribution to society, and result in more years of knee pain and disability across the lifespan. Along with direct personal and economic costs of PFOA, indirect costs

associated with consequences of physical inactivity are a major burden on health expenditure.

This RCT will be the first to evaluate patient-reported benefits of foot orthoses – a simple, low-cost, low-risk intervention that is widely accessible to people with PFOA. Findings of efficacy and cost-effectiveness of prefabricated foot orthoses could represent a turning point in the effective long-term management of PFOA. When worn in everyday and exercise footwear, foot orthoses have the potential to reduce pain every time the foot hits the ground, substantially increasing an individual's capacity and motivation to be physically active. This has important implications for maintenance of general and mental health with increasing age. Importantly, the ease of daily use of foot orthoses, with minimal patient burden, is likely to maximise adherence, enhance outcomes, and reduce reliance on health practitioner resources.

AUTHORS' CONTRIBUTIONS

NJC, KMC, HBM, TGR, AJS, RSH, BV and TPH conceived the study and obtained funding. NJC, KMC and HBM designed the trial protocol with input from TGR, AJS, RSH, BV, TPH, SEM and JMT. AJS and TPH provided statistical expertise. AJS will conduct primary statistical analysis. NJC drafted the manuscript with input from KMC, HBM, TGR, AJS, RSH, BV, TPH, SEM, JMT, HFH, BEP, GC, JWD and LRM. All authors have read and approved the final manuscript.

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COMPETING INTERESTS STATEMENT

Professor Vicenzino reports non-financial support from Vionic®, outside the submitted work. He is a member (non-paid affiliation) of the Vasyli Think Tank™, which was founded in 2011 to foster collaboration and cooperative thought among a leading group of health professionals specialising in the field of lower limb biomechanics. All other authors have no conflicts of interest to declare.

DATA SHARING

The trial protocol and anonymised individual participant data underlying the results reported in the article will be made publicly available (mediated access) immediately after publication, with no end date. Data will be available through institutional data repositories (La Trobe University:http://arrow.latrobe.edu.au:8080/vital/access/manager/Index). Access to the data will be granted to researchers who provide a methodologically sound proposal, and sign a data access agreement. Proposals should be directed to Professor Kay Crossley (k.crossley@latrobe.edu.au).

REFERENCES

1. Hinman RS, Lentzos J, Vicenzino B, et al. Is patellofemoral osteoarthritis common in middle-aged people with chronic patellofemoral pain? *Arthritis Care Res (Hoboken)* 2014;66(8):1252-7. doi: 10.1002/acr.22274

2. Duncan RC, Hay EM, Saklatvala J, et al. Prevalence of radiographic osteoarthritis--it all depends on your point of view. *Rheumatology (Oxford)* 2006;45(6):757-60. doi: 10.1093/rheumatology/kei270 [published Online First: 2006/01/19]

3. Duncan R, Peat G, Thomas E, et al. Incidence, progression and sequence of development of radiographic knee osteoarthritis in a symptomatic population. *Ann Rheum Dis* 2011;70(11):1944-8. doi: 10.1136/ard.2011.151050 [published Online First: 2011/08/04]

4. Kornaat PR, Bloem JL, Ceulemans RY, et al. Osteoarthritis of the knee: association between clinical features and MR imaging findings. *Radiology* 2006;239(3):811-7. doi: 10.1148/radiol.2393050253 [published Online First: 2006/05/23]

5. Hunter DJ, March L, Sambrook PN. The association of cartilage volume with knee pain. *Osteoarthritis Cartilage* 2003;11(10):725-9. doi: S1063458403001602 [pii] [published Online First: 2003/09/18]

6. Hendry M, Williams NH, Markland D, et al. Why should we exercise when our knees hurt? A qualitative study of primary care patients with osteoarthritis of the knee. *Fam Pract* 2006;23(5):558-67. doi: 10.1093/fampra/cml022 [published Online First: 2006/05/30]

7. Carr AJ, Robertsson O, Graves S, et al. Knee replacement. *Lancet* 2012;379(9823):1331-40. doi: 10.1016/S0140-6736(11)60752-6 [published Online First: 2012/03/09]

8. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64. doi: 10.1016/j.joca.2015.04.024

9. Quilty B, Tucker M, Campbell R, et al. Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol* 2003;30(6):1311-7. doi: 0315162X-30-1311 [pii] [published Online First: 2003/06/05]

10. Callaghan MJ, Parkes MJ, Hutchinson CE, et al. A randomised trial of a brace for patellofemoral osteoarthritis targeting knee pain and bone marrow lesions. *Ann Rheum Dis* 2015;74(6):1164-70. doi: 10.1136/annrheumdis-2014-206376

11. Campbell R, Evans M, Tucker M, et al. Why don't patients do their exercises? Understanding non-compliance with physiotherapy in patients with osteoarthritis of the knee. *J Epidemiol Community Health* 2001;55(2):132-8. [published Online First: 2001/01/12]

12. Squyer E, Stamper DL, Hamilton DT, et al. Unloader knee braces for osteoarthritis: do patients actually wear them? *Clin Orthop Relat Res* 2013;471(6):1982-91. doi: 10.1007/s11999-013-2814-0

13. Crossley KM, van Middelkoop M, Callaghan MJ, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br J Sports Med* 2016;50(14):844-52. doi: 10.1136/bjsports-2016-096268

14. Barton CJ, Lack S, Hemmings S, et al. The 'Best Practice Guide to Conservative Management of Patellofemoral Pain': incorporating level 1 evidence with expert clinical reasoning. *Br J Sports Med* 2015;49(14):923-34. doi: 10.1136/bjsports-2014-093637

15. Crossley KM, Hinman RS. The patellofemoral joint: the forgotten joint in knee osteoarthritis. *Osteoarthritis Cartilage* 2011;19(7):765-7. doi: 10.1016/j.joca.2011.05.005 [published Online First: 2011/06/21]

16. Wyndow N, Collins N, Vicenzino B, et al. Is There a Biomechanical Link Between Patellofemoral Pain and Osteoarthritis? A Narrative Review. *Sports Med* 2016;46(12):1797-808. doi: 10.1007/s40279-016-0545-6 [published Online First: 2016/05/05]

17. Crossley KM, Schache AG, Ozturk H, et al. Pelvic and Hip Kinematics During Walking in People With Patellofemoral Joint Osteoarthritis Compared to Healthy Age-Matched Controls. *Arthritis Care Res (Hoboken)* 2018;70(2):309-14. doi: 10.1002/acr.23261 [published Online First: 2017/04/25]

18. Collins NJ, Hinman RS, Menz HB, et al. Immediate effects of foot orthoses on pain during functional tasks in people with patellofemoral osteoarthritis: A

cross-over, proof-of-concept study. *Knee* 2017;24(1):76-81. doi: 10.1016/j.knee.2016.09.016 [published Online First: 2016/11/09]

19. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735. doi: 10.1136/bmj.a1735 [published Online First: 2008/10/28]

20. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158(3):200-7. doi: 10.7326/0003-4819-158-3-201302050-00583 [published Online First: 2013/01/09]

21. Chan AW, Tetzlaff JM, Gotzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586. doi: 10.1136/bmj.e7586 [published Online First: 2013/01/11]

22. McAlindon TE, Driban JB, Henrotin Y, et al. OARSI Clinical Trials Recommendations: Design, conduct, and reporting of clinical trials for knee osteoarthritis. *Osteoarthritis Cartilage* 2015;23(5):747-60. doi: 10.1016/j.joca.2015.03.005

23. van Middelkoop M, Bennell KL, Callaghan MJ, et al. International patellofemoral osteoarthritis consortium: Consensus statement on the diagnosis, burden, outcome measures, prognosis, risk factors and treatment. *Semin Arthritis Rheum* 2018;47(5):666-75. doi: 10.1016/j.semarthrit.2017.09.009 [published Online First: 2017/09/23]

24. National Institute for Health and Care Excellence. Osteoarthritis: care and management 2014 [Available from: https://www.nice.org.uk/guidance/cg177 accessed 8 July 2018.

25. Gudbergsen H, Bartels EM, Krusager P, et al. Test-retest of computerized health status questionnaires frequently used in the monitoring of knee osteoarthritis: a randomized crossover trial. *BMC Musculoskelet Disord* 2011;12:190. doi: 10.1186/1471-2474-12-190 [published Online First: 2011/08/20]

26. de Klerk BM, Willemsen S, Schiphof D, et al. Development of radiological knee osteoarthritis in patients with knee complaints. *Ann Rheum Dis* 2012;71(6):905-10. doi: 10.1136/annrheumdis-2011-200172

27. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.

28. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20. doi: 10.1185/030079906X132488

29. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160. doi: 10.1186/s12891-017-1521-5 [published Online First: 2017/04/20]

30. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.

31. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776 [published Online First: 2017/03/05]

32. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.

33. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.

34. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33(5):337-43. [published Online First: 2001/08/09]

35. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.

36. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.

37. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44. [published Online First: 1989/01/01]

38. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8. doi: 10.1016/j.joca.2014.02.008

39. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98. doi: 10.1016/j.clinbiomech.2005.08.002 [published Online First: 2005/09/27]

40. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.

41. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80. [published Online First: 2001/10/26]

42. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.

43. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.

44. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30. doi: 10.1519/JPT.0b013e318248e20d

45. Kellgren JH, Jeffrey MR, Ball J. The Epidemiology of Chronic Rheumatism: Atlas of Standard Radiographs. Oxford: Blackwell Scientific 1963.

46. Altman RD, Hochberg M, Murphy WA, Jr., et al. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995;3 Suppl A:3-70. [published Online First: 1995/09/01]

47. Moyer R, Wirth W, Duryea J, et al. Anatomical alignment, but not goniometry, predicts femorotibial cartilage loss as well as mechanical alignment: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2016;24(2):254-61. doi: 10.1016/j.joca.2015.08.016

48. Macri EM, Stefanik JJ, Khan KK, et al. Is tibiofemoral or patellofemoral alignment or trochlear morphology associated with patellofemoral osteoarthritis? A systematic review. *Arthritis Care Res (Hoboken)* 2016;68(10):1453-70. doi: 10.1002/acr.22842

49. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.

50. Vicenzino B, Collins N, Crossley K, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: a randomised clinical trial. *BMC Musculoskelet Disord* 2008;9:27. doi: 10.1186/1471-2474-9-27 [published Online First: 2008/02/29]

51. Barton CJ, Menz HB, Crossley KM. Clinical predictors of foot orthoses efficacy in individuals with patellofemoral pain. *Med Sci Sports Exerc* 2011;43(9):1603-10. doi: 10.1249/MSS.0b013e318211c45d

52. Mills K, Blanch P, Dev P, et al. A randomised control trial of short term efficacy of in-shoe foot orthoses compared with a wait and see policy for anterior knee pain and the role of foot mobility. *Br J Sports Med* 2012;46(4):247-52. doi: 10.1136/bjsports-2011-090204 [published Online First: 2011/09/21]

53. Cronkwright DG, Spink MJ, Landorf KB, et al. Evaluation of the pressure-redistributing properties of prefabricated foot orthoses in older people after at least 12 months of wear. *Gait Posture* 2011;34(4):553-7. doi: 10.1016/j.gaitpost.2011.07.016 [published Online First: 2011/08/23]

54. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198. doi: 10.1186/s13063-017-1936-1 [published Online First: 2017/04/30]

55. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008;16(2):137-62. doi: 10.1016/j.joca.2007.12.013 [published Online First: 2008/02/19]

56. Wyndow N, Crossley KM, Vicenzino B, et al. A single-blinded, randomized, parallel group superiority trial investigating the effects of footwear and custom foot orthoses versus footwear alone in individuals with patellofemoral joint osteoarthritis: a phase II pilot trial protocol. *J Foot Ankle Res* 2017;10:19. doi: 10.1186/s13047-017-0200-y [published Online First: 2017/04/30]

57. Bellamy N, Kirwan J, Boers M, et al. Recommendations for a core set of outcome measures for future phase III clinical trials in knee, hip, and hand osteoarthritis. Consensus development at OMERACT III. *J Rheumatol* 1997;24(4):799-802.

58. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord* 2008;9:116. doi: 10.1186/1471-2474-9-116

59. Gossec L, Paternotte S, Maillefert JF, et al. The role of pain and functional impairment in the decision to recommend total joint replacement in hip and knee osteoarthritis: an international cross-sectional study of 1909 patients. Report of the OARSI-OMERACT Task Force on total joint replacement. *Osteoarthritis Cartilage* 2011;19(2):147-54. doi: 10.1016/j.joca.2010.10.025 [published Online First: 2010/11/04]

60. Health USDo, Human Services FDACfDE, Research, et al. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* 2006;4:79. doi: 10.1186/1477-7525-4-79 [published Online First: 2006/10/13]

61. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94. doi: 10.1136/bjsports-2014-093845 [published Online First: 2014/09/24]

62. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18(6):753-8. doi: 10.1016/j.jval.2015.05.009

63. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24. doi: 10.1002/acr.20640

64. Collins NJ, Bierma-Zeinstra SM, Crossley KM, et al. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med* 2013;47(4):227-33. doi: 10.1136/bjsports-2012-091696 [published Online First: 2012/12/18]

65. Salaffi F, Stancati A, Silvestri CA, et al. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004;8(4):283-91.

66. Kastelein M, Luijsterburg PA, Belo JN, et al. Six-year course and prognosis of nontraumatic knee symptoms in adults in general practice: a prospective

cohort study. *Arthritis Care Res (Hoboken)* 2011;63(9):1287-94. doi: 10.1002/acr.20522

67. Crossley K, Bennell K, Green S, et al. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med* 2002;30(6):857-65.

68. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication. 2010 [Available from: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html accessed 23 November 2017.

FIGURE CAPTIONS

Figure 1. Flow of participants through the study.

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

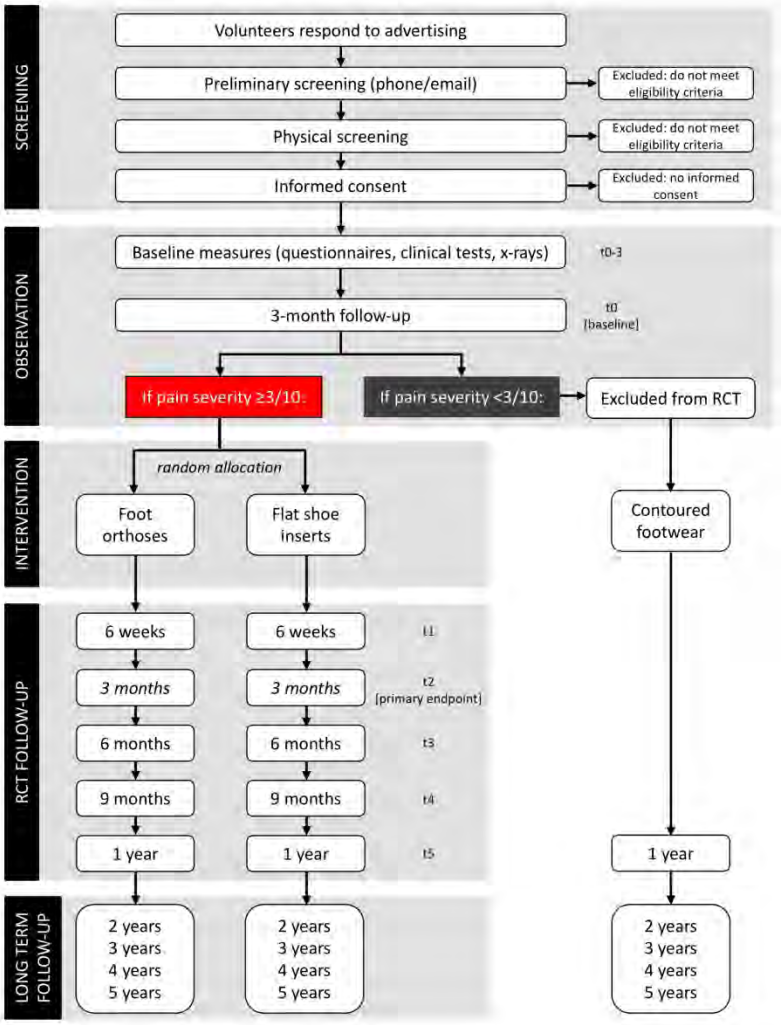

Figure 1. Flow of participants through the study.

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	STUDY PERIOD						
	Enrolment / Baseline		Post-allocation				Close-out
TIMEPOINT*	t0-3	t0	t1	t2	t3	t4	t5
ENROLMENT:							
Eligibility screen	X						
Informed consent	X	X					
Allocation		X					
INTERVENTIONS:							
Contoured shoe inserts		◆	—	—	—	—	◆
Flat shoe inserts		◆	—	—	—	—	◆
ASSESSMENTS:							
Participant characteristics	X						
Knee pain severity	X						
Navigate Pain	X						
PainDetect	X						
Pain Catastrophising Scale (PCS)	X						
Sport and physical activity participation	X						
Anthropometric measures	X						
Knee clicking and crepitus	X						
Knee extension torque	X						
Foot Posture Index (FPI)	X						
Foot mobility	X						
Weight bearing ankle dorsiflexion range of motion	X						
Footwear Assessment Tool	X						
10-metre Walk Test	X						
Primary outcome measure:							
Worst knee pain severity during self-nominated aggravating activity in the previous week	X	X	X	X	X	X	X
Secondary outcome measures:							
Patient-reported global rating of change (GROC)			X	X			X
Pain visual analogue scales	X	X	X	X	X	X	X
Knee injury and Osteoarthritis Outcome Score (KOOS)	X	X		X			X
Anterior Knee Pain Scale (AKPS)	X	X		X			X
Arthritis Self-Efficacy Scale (ASES)	X	X		X			X
Tampa Scale for Kinesiophobia (TSK)	X	X		X			X
Short-form 12 (SF-12)	X	X		X			X
Euroqol-5D-5L (EQ-5D)	X	X		X	X	X	X
Other outcomes:							
Use of co-interventions for knee pain				X	X	X	X
Adverse events				X	X	X	X
Direct health care costs				X	X	X	X
iMTA Productivity Cost Questionnaire (iPCQ)				X	X	X	X
Credibility and Expectancy Questionnaire (CEQ)		X		X			X

* t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months; t3 = 6 months; t4 = 9 months; t5 = 12 months

Figure 2. SPIRIT diagram of enrolment, interventions and assessments for the FOOTPATH Study.

275x397mm (300 x 300 DPI)

Figure 3. Prefabricated foot orthoses in full length (A) and three-quarter length (B); and flat inserts (C).

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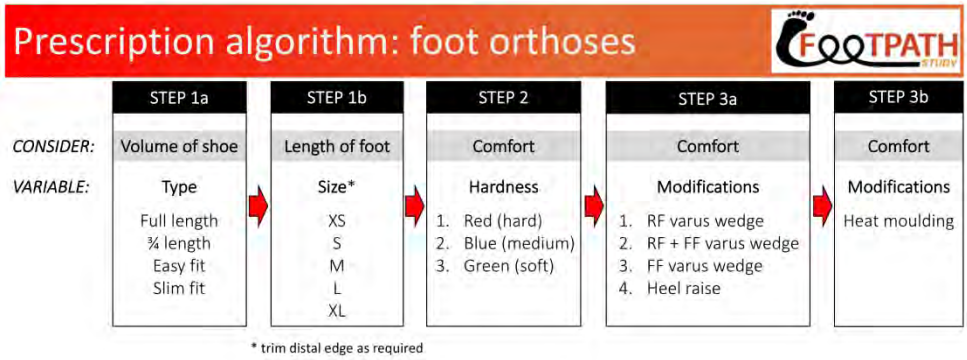

Figure 4. Prescription algorithm for fitting prefabricated foot orthoses. Steps 1 to 3 are to be followed sequentially. Numbered options within each variable are to be trialled sequentially (e.g. red orthoses, then blue orthoses, then green orthoses). XS, extra small; S, small; M, medium; L, large; XL, extra large; RF, rearfoot; FF, forefoot.

338x190mm (300 x 300 DPI)

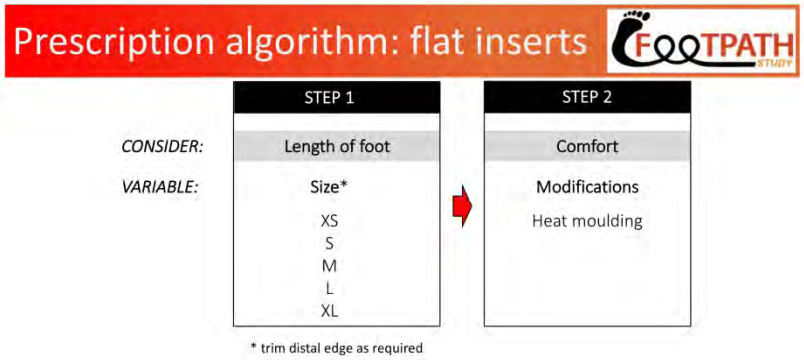

Figure 5. Prescription algorithm for fitting flat inserts. XS, extra small; S, small; M, medium; L, large; XL, extra large.

338x190mm (300 x 300 DPI)

Supplementary file 1. Participant information and consent forms.

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PARTICIPANT INFORMATION STATEMENT: PART A

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

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We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether footwear interventions can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether specific footwear interventions are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

If you are potentially eligible for the trial, you will be screened via telephone, and attend La Trobe University for a knee examination. If you are included in the trial, you will undergo baseline assessment at the same venue as your knee examination. For the first 3 months of the trial, we will monitor your knee condition using questionnaires. You will then be provided with a footwear intervention to take home and wear for 1 year, and be asked to complete a series of questionnaires online or via mail.

All assessments and footwear interventions will be provided at no cost to you.

At baseline, you will be asked to complete:

- Questionnaires, including:
  - Age, gender, occupational and sporting history, mechanism of injury, symptom duration, rehabilitation, medication use, and family history of arthritis
  - Your expectations and values regarding your condition and its management
  - Physical activity (type, frequency and dosage)
  - Knee-related pain, symptoms, function and quality of life
  - General health and self-efficacy
- Physical testing, including:
  - Height, weight and waist circumference
  - Movement and palpation of your knee
  - Foot and ankle mobility measures
  - Knee strength: The maximal strength of your leg muscles will be measured using a special device. The examiner will ask you to push against it, as hard as you can, in one direction.
  - Functional performance tests, including walking and hopping
  - Measures of pressure pain onset: The examiner will apply a pressure stimulus with a probe to 4 points around your knee, and one point at your elbow. As the pressure increases, you will be asked to press a button to indicate the precise moment that the pressure sensation changes to one of pressure and the first onset of pain. At this point the pressure will cease. Three measures will be taken at each site, and repeated on both knees and elbows.
- X-rays of your knee:
  - You will undergo the x-rays at a private radiology clinic that is convenient to your home or workplace. This will take approximately 30 minutes.

You will be invited to attend the La Trobe University Health Sciences Clinic, at the Bundoora Campus of La Trobe University, to undergo the baseline assessment. This will take approximately 2 hours of your time. You will first complete a series of questionnaires about your knee pain, as outlined above. You will then undergo the physical tests described above, including measures of foot and ankle motion, knee strength, and functional performance. For the physical tests, you will be asked to change into shorts. You may either bring your own shorts or we can provide some for you.

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During the telephone screening, you may be asked if you would like to participate in a sub-study that will monitor your physical activity with a Fitbit™ device for 3 months. If you choose to participate in the sub-study, you will be issued a Fitbit™ device to wear on daily basis for 3 months. Your decision to take part or not in the sub-study will not impact on your participation in the main study. For this sub-study, you will be required to have access to the internet (home, public library etc.) and a smartphone/laptop. During the baseline assessment, the Fitbit™ application will be installed on your device to ensure that the researchers at La Trobe University can remotely extract the data from your Fitbit™.

Your knee condition will then be monitored for 3 months, during which time you will receive no intervention. This is a novel and important part of this study, to learn more about the natural course of kneecap arthritis. At the conclusion of the 3-month observation period, you will be asked to repeat the same questionnaires that you completed at baseline.

You will then be contacted by a member of the study team, regarding your footwear intervention. At this time, they will explain in more detail what is involved, and will ask you to provide consent. You will then be given a footwear intervention to take home and wear for a period of 1 year. This may involve a sandal, or a special insole to wear in your own shoes. These be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the footwear intervention in safely. You will be encouraged to use the footwear intervention as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At the conclusion of the 3-month observation period, you may be invited to participate in the sub study which will require you to continue to wear your Fitbit™ device for the duration of the main study. Your decision to take part or not in the sub study will not impact on your participation in the main study.

During this time, you may be provided with a diary where you can record your physical activity, how often you wear the footwear intervention, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the footwear intervention, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the questionnaires outlined above (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. You may ask for a copy of your assessment results. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years.

We may also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period
During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?
You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy) or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research
Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

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X-ray: You will be asked to have an x-ray of your knee. This involves exposure to a very small amount of radiation from x-ray imaging. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from the x-rays of your knee is less than 0.015 mSv. At this dose level, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be very low.

It is important to be aware that with any imaging investigation, there is a small chance of a previously unknown medical condition being detected. In the unlikely event that this occurs, we will contact you directly and inform you of the findings. Should you require further medical review, we will also organise a referral to your chosen GP. It must be emphasized that the purpose of this study is to investigate your knee pain and not to identify other potential medical conditions. While we will ensure that you are made aware of any incidental findings reported on by the consulting radiologist, neither the investigators, the radiologist, nor the Universities involved, will be held accountable if a medical condition exists that is not detected during the process.

Physical testing: The physical tests are routinely performed by Physiotherapists and Podiatrists, and are not associated with any risks. You may experience a small amount of discomfort in your joints or muscles during the physical examination or testing procedures. Please report to the researcher any undue discomfort or pain experienced during the testing. If the pain or discomfort is deemed to be excessive by yourself or the investigators, testing will cease.

If required, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

Footwear intervention: You may feel some discomfort in your feet or knees when starting to use the footwear intervention. Occasionally, footwear interventions can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the footwear intervention and/or wearing time.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

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What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part A

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator: Date:

Name and phone number of contact person in case of an emergency:

Name: Phone:

Family Doctor: Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature: Date:

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PARTICIPANT INFORMATION STATEMENT: PART B

Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
Prof Hylton Menz	School of Allied Health, La Trobe University	h.menz@latrobe.edu.au
Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
Prof Trevor Russell	School of Health and Rehabilitation Sciences, The University of Queensland	t.russell1@uq.edu.au
A/Prof Anne Smith	School of Physiotherapy and Exercise Science, Curtin University	anne.smith@curtin.edu.au
Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au
Dr Harvi Hart	School of Allied Health, La Trobe University	h.hart@latrobe.edu.au
Ms Brooke Patterson	School of Allied Health, La Trobe University	b.patterson@latrobe.edu.au

We invite you to participate in our research project "Efficacy of shoe inserts for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple shoe inserts are an effective treatment for kneecap arthritis. The aims of this project are to: (i) determine whether shoe inserts can reduce pain and improve outcome in people with kneecap arthritis over 1 year; and (ii) evaluate whether shoe inserts are a cost-effective treatment for kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a shoe insert intervention to take home and wear for 1 year, and ask you to complete a series of questionnaires online or via mail.

All assessments and shoe insert interventions will be provided at no cost to you.

You will be randomly allocated to receive one of two different shoe inserts, to wear in your own shoes. Although they are slightly different in design and possible mechanism of effect, both of these inserts have been shown to reduce kneecap pain in younger adults. These will be fitted by an experienced Podiatrist or Physiotherapist, and may require you to attend up to six appointments at a clinic that is convenient to your home or workplace. We will give you instructions on how to break the shoe inserts in safely. You will be encouraged to use the shoe inserts as much as possible (e.g. around 8 hours per day), whenever you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

During this time, you will be provided with a diary where you can record your daily physical activity, how often you wear the shoe inserts, what other type of footwear you have used, whether you have experienced any adverse effects from wearing the shoe inserts, and whether you have had any other medical issues. At regular intervals during the 1-year intervention period, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. We will continue to monitor your knee symptoms, using the same questionnaires, at yearly intervals for 5 years. You may ask for a copy of your assessment results.

You may also be provided with a FitBit to record your physical activity. This is a simple device worn on your wrist, which records your daily step count. If you do receive a FitBit, we will provide you with information and instructions on how to use the device.

We will also ask your consent to obtain data about your health care from Medicare and Pharmaceutical Benefits Scheme (PBS) databases. This data is important for us to determine which footwear intervention is most cost-effective. You will be asked to fill out a consent form authorising the study to access your complete Medicare and Pharmaceutical Benefits Scheme (PBS) data as outlined on the back of the consent form, and in Appendix A of this information statement. Medicare collects information on your medical visits and procedures, and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to the Department of Human Services who holds this information confidentially. You will also receive a phone call from one of the study personnel at 3-monthly intervals, who will ask you questions about how your knee is going (e.g. time off work, impact on daily activities, use of other interventions, hospital admissions). This type of analysis is commonly

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conducted alongside intervention studies such as this. We will provide you with a separate information sheet specifically outlining details of this process.

During the study, you may be eligible for reimbursement of a proportion of your travel costs.

Use of pain-relieving medications and other forms of treatment during the trial period

During the 1-year trial period, we recommend that you use paracetamol (e.g. Panadol®), up to 4 grams/day, as a pain-relieving medication if it is necessary. You must attempt to not use any other treatment for your knee pain during the study period. However, if you do not obtain sufficient pain relief with this approach, you are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies (with the exception of Medicare and PBS data). Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

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What are the possible risks of participating in this project?
You may feel some discomfort in your feet or knees when starting to wear the shoe inserts. Occasionally, shoe inserts can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to the shoe inserts and/or wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?
Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?
The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under guidelines set out by the *National Health and Medical Research Council*. Electronic data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of consent forms and questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for 15 years after completion of the project in the Health Sciences storage vault, Building 3, level 1. After 15 years, hard copies will be shredded and placed in a secure document disposal bin, and computer files will be permanently deleted.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

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Funding
Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?
Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints
If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,
Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart *(on behalf of the research team)*

Appendix A. Medicare and Pharmaceutical Benefits Scheme data fields

Medicare Benefits Schedule (MBS)	
Date of service	Date that the service was rendered by the provider, to the patient
MBS Item number	Items Numbers as per the Medicare Benefits Schedule
MBS Item description	Describes the service as per the Medicare Benefits Schedule
Provider charge	The dollar amount the provider charged for the service
Benefit paid	The benefit paid to the patient
Patient Out of Pocket	The dollar amount the patient is out of pocket
Hospital Indicator	Indication of whether or not the service was provided in hospital
Pharmaceutical Benefits Scheme (PBS)	
Date of supply	Date the prescription was supplied by the pharmacy
PBS Item Number	Items Numbers reflected in the PBS
PBS Item Description	The item description as noted in the PBS
Patient contribution	The contribution paid by the patient
PBS Net Benefit	Amount paid by the Government
Form category	Original or repeat prescription
ATC Code	The ATC Code is defined by the Commonwealth Department of Health which may be different to the code allocated by the WHO Collaborating Centre for Drug Statistics Methodology
ATC Name	The group the drug falls under in the Anatomical Therapeutic Chemical (ATC) classification system

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): PART B

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan, Dr Harvi Hart, Ms Brooke Patterson

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐
I consent to participate in the sub-study measuring physical activity with Fitbit™	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:

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Investigator:	Date:

Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

	Yes	No
I am willing for the study investigators to arrange a referral to my nominated medical practitioner in the unlikely event of a previously unknown medical condition being discovered during radiological imaging	☐	☐

Participant's signature:	Date:

Participant ID:

PARTICIPANT CONSENT FORM

Consent to release of Medicare and/or Pharmaceutical Benefits Scheme (PBS) claims information for the purposes of the FOOTPATH Study

Important Information

Complete this form to request the release of personal Medicare claims information and/or PBS claims information to the FOOTPATH Study.

Any changes to this form must be initialled by the signatory. Incomplete forms may result in the study not being provided with your information.

By signing this form, I acknowledge that I have been fully informed and have been provided with information about this study. I have been given an opportunity to ask questions and understand the possibilities of disclosures of my personal information.

PARTICIPANT DETAILS

1. Mr ☐ Mrs ☐ Miss ☐ Ms ☐ Other ☐

Family name: _____ First given name: _____

Other given name (s): _____

Date of birth: DD/MM/YYYY

2. Medicare card number: _____

3. Permanent address: _____

Postal address (if different to above): _____

AUTHORISATION

4. I authorise the Department of Human Services to provide my:

☐ Medicare claims history OR

☐ PBS claims history OR

☐ Medicare & PBS claims history

for the period* DD/MM/YYYY to: DD/MM/YYYY to the FOOTPATH Study.

*Note: The Department of Human Services can only extract 4.5 years of data (prior to the date of extraction), The consent period above may result in multiple extractions.

DECLARATION

I declare that the information on this form is true and correct.

5. Signed: _____ (participant's signature) Dated: DD/MM/YYYY **OR**

6. Signed by _____ (full name) _____ (signature) on behalf of participant

Dated: DD/MM/YYYY

☐ Power of attorney* ☐ Guardianship order*

* Please attach supporting evidence

APP 5 – PRIVACY NOTICE

Your personal information is protected by law, including the Privacy Act 1988, and is collected by the Australian Government Department of Human Services. The collection of your personal information by the department is necessary for administering requests for statistical and other data.

Your information may be used by the department or given to other parties for the purposes of research, investigation or where you have agreed or it is required or authorised by law.

You can get more information about the way in which the Department of Human Services will manage your personal information, including our privacy policy at humanservices.gov.au/privacy or by requesting a copy from the department.

Power of attorney – A power of attorney is a document that appoints a person to act on behalf of another person who grants that power. In particular, an enduring power of attorney allows the appointed person to act on behalf of another person even when that person has become mentally incapacitated. The powers under a power of attorney may be unlimited or limited to specific acts.

Guardianship order – A Guardianship order is an order made by a Guardianship Board/Tribunal that appoints a guardian to make decisions for another person. A Guardianship order may be expressed broadly or limited to particular aspects of the care of another person.

A sample of the information that may be included in your Medicare claims history:

Date of service	Item number	Item description	Provider charge	Benefit paid	Patient out of pocket	Hospital indicator
20/04/09	00023	Level B consultation	$38.30	$34.30	$4.00	N
22/06/09	11700	ECG	$29.50	$29.50		N

A sample of the information that may be included in your PBS claims history:

Date of supply	PBS item code	Item description	Patient contribution (this includes under copayment amounts**)	Net Benefit (this includes under copayment amounts**)	Form Category	ATC Code	ATC Name
06/03/09	03133X	Oxazepham Tablet 30 mg	$5.30	$25.55	Original	N05 B A 04	Oxazepam
04/07/09	03161J	Diazepam Tablet 2 mg	$30.85		Repeat	N05 B A 01	Diazepam

** Under co-payments can now be provided for data after 1 June 2012

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PARTICIPANT INFORMATION STATEMENT: PART C

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)

Investigators:

Prof Kay Crossley	School of Allied Health, La Trobe University	k.crossley@latrobe.edu.au
Prof Hylton Menz	School of Allied Health, La Trobe University	h.menz@latrobe.edu.au
Dr Natalie Collins	School of Health and Rehabilitation Sciences, The University of Queensland	n.collins1@uq.edu.au
Prof Trevor Russell	School of Health and Rehabilitation Sciences, The University of Queensland	t.russell1@uq.edu.au
A/Prof Anne Smith	School of Physiotherapy and Exercise Science, Curtin University	anne.smith@curtin.edu.au
Prof Bill Vicenzino	School of Health and Rehabilitation Sciences, The University of Queensland	b.vicenzino@uq.edu.au
Prof Terry Haines	Department of Physiotherapy, Monash University	terrence.haines@monash.edu
Prof Rana Hinman	Department of Physiotherapy, The University of Melbourne	ranash@unimelb.edu.au
Dr Shannon Munteanu	School of Allied Health, La Trobe University	s.munteanu@latrobe.edu.au
Ms Jade Tan	School of Allied Health, La Trobe University	jade.tan@latrobe.edu.au

We invite you to participate in our research project "Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH)", collaboration between La Trobe University and The University of Queensland. We would like to give you some background information on why we think this project is important, and what we would like you to do if you decide to participate.

What is this project about and why is it important?

Kneecap arthritis is a leading cause of knee-related pain, disability and health expenditure in the Australian community, and has no cure. Compared to general knee arthritis in elderly people, kneecap arthritis can also affect middle-aged adults, impacting on productivity and contribution to society, and resulting in more years of knee pain and disability across the lifespan. At this time, we know very little about effective treatments for kneecap arthritis. This project is investigating whether simple footwear interventions are an effective treatment for kneecap arthritis. The primary aim of this project is to determine whether footwear can reduce pain and improve outcome in people with kneecap arthritis. This knowledge may provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis.

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What does the research involve?

You are being invited to participate in this study based on your responses to questionnaires that you completed recently, as part of the FOOTPATH Study. We will provide you with a footwear intervention to take home and wear, and ask you to complete a series of questionnaires online or via mail at yearly intervals for the next 5 years.

All assessments and footwear interventions will be provided at no cost to you.

You will be contacted by one of the study personnel (who is an experienced Podiatrist or Physiotherapist) to confirm your shoe size. They will determine the best method of prescribing the footwear intervention to you. This may require you to attend an appointment at La Trobe University. We will give you instructions on how to break the footwear in safely. You will be encouraged to wear the footwear as much as is comfortable for you, when you are moving around (e.g. daily tasks such as cleaning, or exercise such as walking).

At yearly intervals, for a period of 5 years, you will be asked to complete the same questionnaires that you have completed previously (via email or postal mail), as well as how your knee condition has changed overall since commencing the trial. This will take approximately 20-30 minutes to complete each time. At the conclusion of the trial, you are free to keep the footwear intervention that you received. You may ask for a copy of your assessment results.

Use of pain-relieving medications and other forms of treatment during the trial period

You are free to use other treatments or take other medication as you require. It is possible that limiting the amount of (or altering) pain medication or treatment may cause an increase in your knee pain.

Why were you chosen for this research?

You can participate in this project if you are 50 years of age or older, and have experienced symptoms indicative of kneecap arthritis for at least 3 months. This may include a gradual onset of knee pain that is aggravated by activities that load the knee (e.g. stair climbing, squatting, prolonged sitting).

You are not eligible to participate in this project if you: (i) are not fluent in written and spoken English; or (ii) have another significant knee, hip or lower back condition; or (iii) have had recent treatment for your knee pain (e.g. knee injections or shoe inserts within the previous 3 months); or (iv) have recently commenced physiotherapy treatment for your knee pain; or (v) have any foot condition precluding the use of footwear interventions; or (vi) have had any major surgery to your knee or hip (e.g. total joint replacement or osteotomy), or are planning to have surgery to your knee or hip; or (vii) have any neurological or systemic arthritis conditions; or (viii) are not suitable to have an x-ray of your knee (e.g. pregnancy, breastfeeding).

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Consenting to participate in the project and withdrawing from the research

Before you can participate in the project, you will be asked to read this participant information statement and sign a consent form indicating you have understood what the project is about and that you agree to participate. You have a right to withdraw from further participation at any stage without disadvantages, penalties or adverse consequences. You may also request to have your data withdrawn from the project by contacting the investigators, or by sending a withdrawal form within 4 weeks of completing the project. This will not impact upon any relationships with La Trobe University and/or affiliated clinics or sporting clubs.

You will also be asked to indicate if you agree to your data being used for future studies. Your data would identify you only by a code (and not your name), but your data would be potentially identifiable (i.e. we could break the code to access your name and personal details in case we needed them. An example of when this might arise would be if we needed to contact you at any stage).

What are the possible risks of participating in this project?

You may feel some discomfort in your feet or knees when starting to wear the footwear. Occasionally, footwear can cause some skin irritation, pressure points under the feet, or an increase in knee pain. If you experience any continued pain or discomfort in your knee or leg muscles, please contact the researchers. These problems are usually quickly and easily resolved with modifications to wearing time.

If you are attending La Trobe University, emergency procedures will be used to deal with any medical event that arises during the testing. The La Trobe University Health Sciences Clinic and on-call security have documented procedures for emergencies. This includes annual St John's ambulance CPR training and appropriate management of fire for all staff.

What are the possible benefits of participating in this project?

Although you may experience some improvements in your knee pain after wearing the footwear intervention, there may be no direct benefits in completing this project. However, your participation will provide evidence for a simple, effective, non-invasive treatment for kneecap arthritis, and inform researchers and clinicians regarding optimal design of footwear interventions for kneecap arthritis.

What will happen to the results?

The results of this project may appear in journal publications and in conference presentations, but you will not be able to be identified in any of these reports. Data may also be used by members of this research team in future projects to compare with results from similar studies that have used the same testing procedures.

Results from the project will be confidential and only accessible by the researchers named above. No one other than the investigators will have access to the data. No findings that could identify you will be published and access to individual results is restricted to the investigators. All data and results will be handled in a strictly confidential manner, under

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guidelines set out by the *National Health and Medical Research Council*. Data will be kept in a password protected computer located at La Trobe University Health Sciences 3 building, gait laboratory. Hard copies of questionnaires will be kept in a locked filing cabinet in the office of Prof Kay Crossley (room 521; 5th Floor, Health Sciences 3) at La Trobe University. Data will be stored for at least 5 years after completion of the project in the Health Sciences storage vault, Building 3, level 1.

At the conclusion of the project, results of the project and your personal data will be made available to you upon request. This may entail mailing your results to your home residence, or if you prefer, a discussion with one of the investigators in person. Please direct requests for this information to Prof Kay Crossley (Phone: 03 9479 3902; Email: k.crossley@latrobe.edu.au).

Funding

Funding for this project has been kindly provided by the *National Health and Medical Research Council of Australia (NHMRC)*.

Who can I contact if I have any questions?

Questions concerning the procedure and/or rationale used in this investigation are welcome at any time. Please ask for clarification of any point, which you feel is not explained to your satisfaction. Your initial contact is the person conducting the experiment (Professor Kay Crossley, 03 9479 3902 or k.crossley@latrobe.edu.au).

Complaints

If you have any complaints or concerns about your participation in the project that the researcher has not been able to answer to your satisfaction, you may contact the Senior Human Ethics Officer, Ethics and Integrity, Research Office, La Trobe University, Victoria, 3086 (Phone: 03 9479 1443, Email: humanethics@latrobe.edu.au). Please quote the project reference number S15/286.

Thank you,

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Dr Shannon Munteanu,

Ms Jade Tan

(on behalf of the research team)

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LA TROBE UNIVERSITY HUMAN ETHICS COMMITTEE PARTICIPANT CONSENT FORM

Efficacy of footwear for patellofemoral osteoarthritis (FOOTPATH): Part C

Investigators:

Prof Kay Crossley, Prof Hylton Menz, Dr Natalie Collins, Prof Trevor Russell, A/Prof Anne Smith, Prof Bill Vicenzino, Prof Terry Haines, Prof Rana Hinman, Dr Shannon Munteanu, Ms Jade Tan

I, _____, have read and understood the **participant information statement and consent form**, and any questions I have asked have been answered to my satisfaction. I understand that even though I agree to be involved in this project, I can withdraw from the study at any time, up to four weeks following the completion of my participation in the research. Further, in withdrawing from the study, I can request that no information from my involvement be used. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

	Yes	No
I am willing to have photographs and/ or videos taken during the testing session and consent for these de-identified images or videos to be used solely for education and research purposes at physiotherapy schools at other universities in Australia and when presentations are made at conferences / workshops in National and International Settings.	☐	☐
I consent to my data being included in other research projects. I acknowledge that my data will be coded, but can be potentially identified.	☐	☐

Last Name:		Given Name:
DOB:	Age:	Contact Phone number:
Address:		
Signature:		Date:
Witness name:		Date:
Investigator:		Date:

School of Allied Health
College of Science, Health and Engineering
La Trobe University

Name and phone number of contact person in case of an emergency:

Name:	Phone:
Family Doctor:	Phone:

Participant's signature:	Date:

Supplementary file 2. Outcome measures used in the FOOTPATH Study.

	Description	t0-3	t0	t1	t2	t3	t4	t5
Primary outcomes								
Worst knee pain severity during self-nominated aggravating activity in the previous week	Participants nominate one of three everyday activities that they experience the greatest knee pain severity with (rising from sitting, stair ambulation, squatting). Pain severity during this activity is measured on a 100mm visual analogue scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). Pain visual analogue scales are reliable, valid and responsive in people with patellofemoral pain.[1] Pain severity associated with a self-nominated aggravating activity is sensitive to change in people with PFOA and knee OA.[2]	•	•	•	•	•	•	•
Secondary outcomes								
Self-reported global rating of change (GROC)	Participants will respond to the question 'overall, how has your knee pain changed since the start of the study?' on a 7-point Likert scale ('much better, 'better', 'a little better', 'same', 'a little worse', 'worse', 'much worse'). This will be dichotomised to 'improved' ('much better, 'better') and 'not improved' ('a little better' to 'much worse'). GROC has been used in previous PF pain RCTs to calculate relative risks and number needed to treat for clinical guidelines.[3 4] This is a clinically relevant and stable concept for evaluating an individual patient's perspective on meaningful improvement.[5]			•	•			•
Pain visual analogue scales	Participants will complete a series of pain visual analogue scales, rating the severity of their knee pain on a 100mm scale (terminal descriptors: 0 = no pain, 100 = worst pain possible). This will include: (i) usual pain over the past week; (ii) worst pain over the past week); (iii) maximum pain when walking; (iv) maximum pain when sitting for one hour; (v) maximum pain when rising from sitting; (vi) maximum pain when going up and down stairs; (vii) maximum pain when squatting; and (viii) maximum pain when running. Reliability, validity and responsiveness of pain visual analogue scales have been established in patellofemoral pain.[1]	•	•	•	•	•	•	•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Knee injury and Osteoarthritis Outcome Score (KOOS)	The KOOS consists of 42 items across five subscales: (i) symptoms; (ii) pain; (iii) function in daily activities; (iv) function in sport/recreation; and (v) knee-related quality of life.[6] Participants will also complete the 11-item KOOS-PF, a subscale developed to be used in people with patellofemoral pain conditions in conjunction with the original KOOS.[7] Participants respond to each item using a 4-point Likert scale, and a normalised score from 0-100 is calculated for each subscale (100 = no knee problems, 0 = extreme knee problems. The KOOS and KOOS-PF are reliable and valid in people with patellofemoral pain and osteoarthritis.[7]	•	•		•			•
Anterior Knee Pain Scale (AKPS)	The AKPS, or Kujala Patellofemoral Score, consists of 13 items describing common symptoms and functional impairments associated with patellofemoral pain conditions.[8] Weighted scores from each item are summed to give an overall score (100 = no disability, 0 = maximal disability). The AKPS is reliable, valid and responsive to change in people with patellofemoral pain.[1 8 9]	•	•		•			•
Arthritis Self-Efficacy Scale (ASES)	The ASES consists of 20 items across three subscales: (i) self-efficacy for managing pain; (ii) self-efficacy for physical function; and (iii) self-efficacy for controlling other symptoms.[10] For each item, participants rate on a 10-point scale how certain they are that they can perform specific tasks or manage their knee pain symptoms. Item scores are summed to provide an overall score from 10-100, where higher scores represent greater self-efficacy.[11] The ASES has adequate reliability, validity and responsiveness for research use.[11]	•	•		•			•
Tampa Scale for Kinesiophobia (TSK)	The TSK evaluates fear of movement and re-injury.[12] Participants use a 4-point Likert scale to rate their agreement with 17 items (1=strongly disagree, 4=strongly agree). Items 4, 8, 12 and 16 are reverse scored, and a total score calculated ranging from 17 to 68, where higher scores indicate greater fear of movement and re-injury. While evaluation of psychometric properties has not been performed in people with patellofemoral pain, the Thai language version of the TSK demonstrated adequate measurement properties in people with knee osteoarthritis .[13]	•	•		•			•

	Description	t0-3	t0	t1	t2	t3	t4	t5
Short-form 12 (SF-12)	The SF-12 (version 2) comprises 12 items across eight domains: bodily pain (BP), physical functioning (PF), role limitations due to physical health problems (RP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH).[14] A physical component score (PCS) is calculated from the BP, PF, RP and GH subscales, and a mental component score (MCS) calculated from the VT, SF, RE and MH subscale. Transformed scores for each subscale range from 0 (worst health state) to 100 (best health state). The SF-12 is valid for reproducing the PCS and MCS of the Short-form 36 (SF-36).[15]	•	•		•			•
Euroqol-5D-5L (EQ-5D)	The EQ-5D consists of five items encompassing five dimensions: mobility, self-care, usual activity, pain and discomfort, and anxiety and depression. Participants select the best of five possible responses. The EQ-5D Index is calculated from a predefined algorithm, with a score of 1 representing the best imaginable health state, 0 representing death, and negative scores indicating a state worse than death.[16] Participants will also complete the EQ-5D visual analogue scale evaluating self-reported health state (0=worst imaginable health state, 100=best imaginable health state). EQ-5D has been validated in knee pain cohorts.[17]	•	•		•	•	•	•
Use of co-interventions for knee pain	The number of participants who report using co-interventions specifically for their knee pain (e.g. medication, allied health services such as physiotherapy, complementary medicines such as osteopathy, topical medicines, or taping/bracing) will be recorded from a number of sources (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[18]				•	•	•	•
Adverse events	Adverse events (e.g. new pains in the body, rolled ankles, blisters, swelling) will be recorded from a number of sources specifically designed for this study (e.g. participant log-books, 3-monthly questionnaires, 3-monthly telephone interviews).[19]				•	•	•	•

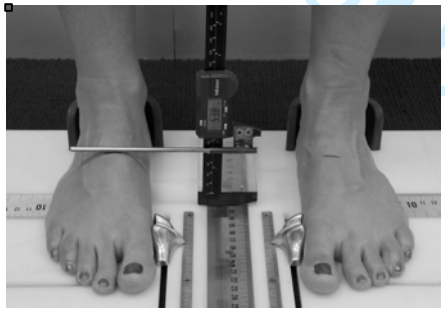
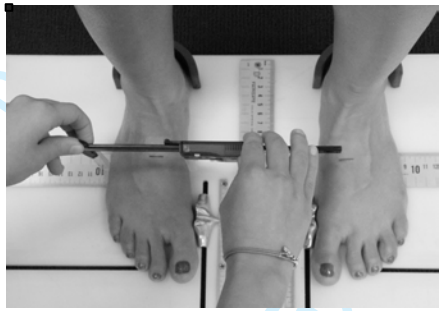
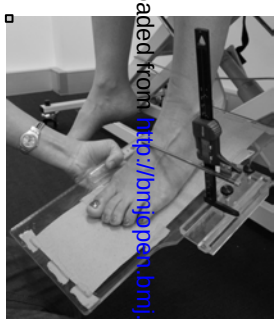
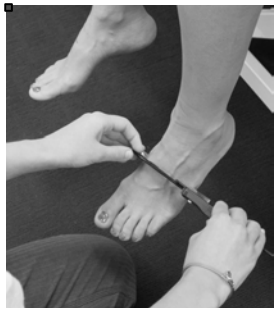
	Description	t0-3	t0	t1	t2	t3	t4	t5
Direct health care costs	Direct health costs will be captured from multiple sources, for use in economic analyses: (i) Medicare Australia and Pharmaceutical Benefits Scheme (PBS) databases; (ii) participant self-report (monthly log-books; 3-monthly telephone interviews); and (iii) costs associated with delivering the study intervention.				•	•	•	•
Institute for Medical Technology Assessment (iMTA) Productivity Cost Questionnaire (iPCQ)	The iPCQ will be used to capture indirect / productivity costs, for use in economic analyses. It consists of 18 questions and three modules: (i) productivity loss due to absence from paid work; (ii) productivity loss during paid work due to health reasons; and (iii) productivity loss of unpaid work.[20] The iPCQ will be administered via telephone interview.				•	•	•	•
Credibility and Expectancy Questionnaire (CEQ)	The six-item CEQ was used to evaluate the credibility and expectancy of treatment received.[21 22] Items 1, 2, 3 and 5 are scored on a nine-point Likert scale, while items 4 and 6 are scored from 0-100%. Higher scores indicate greater perceived credibility and benefit. The CEQ has demonstrated adequate internal consistency and test-retest reliability.[22]		•		•			•
Other measures								
Knee pain severity	Participants will respond to the question "how bad would you say your knee pain is now?" by selecting one of four responses: 'no pain', 'mild', 'moderate', 'severe'.	•	•	•	•	•	•	•
Navigate Pain	Participants will record the location of their knee pain on a high-resolution 3D schema of the lower limb, using a custom application (Navigate Pain, Aalborg University, Denmark)[23 24] on a personal computer tablet (Samsung Galaxy, Samsung, Seoul, South Korea). Pain areas will be individually extracted and expressed as total pixels by the software, and visually classified for location.[25] The touch screen interface has high agreement with paper-based pain maps.[24]	•						

	Description	t0-3	t0	t1	t2	t3	t4	t5
PainDetect	PainDetect will be administered to identify neuropathic pain components.[26] Nine items evaluating gradation of pain, pain course pattern and pain radiation are summed to give an overall score from -1 to 38. The presence of neuropathic pain is likely if the total score is ≥19, while a score ≤12 suggests that pain is unlikely to have a neuropathic component.[26] PainDetect is reliable[27] and recommended as a screening measure for neuropathic pain.[28]	•						
Pain Catastrophising Scale (PCS)	The PCS is a 13-item questionnaire used to evaluate pain-related catastrophising.[29] Participants use a 5-point Likert scale to indicate the degree to which they experienced each thought/feeling when they have pain. An overall score is calculated by summing all 13 items (range 0-52), as well as three subscale scores for rumination, magnification and helplessness. Higher scores indicate higher degrees of pain catastrophizing. The PCS has sufficient reliability and validity for use in adults.[29]	•						
Sport and physical activity participation	Participants will complete a standardised questionnaire about their current and previous physical activity. Items include: (i) current regular physical activity (>30mins duration); (ii) other physical activity or competitive sport prior to knee pain onset; (iii) whether they have changes their physical activity because of their knee pain, and why; and (iv) whether they plan to return to sport if they have modified their physical activity.	•						

t0-3 = 3 months prior to randomisation; t1 = 6 weeks; t2 = 3 months (time of primary interest); t3 = 6 months; t4 = 9 months; t5 = 12 months (close out)

Supplementary file 3. Clinical tests performed prior to commencing the observation period (t0-3).

Test	Description
Anthropometric measures	Height will be measured using a stadiometer. Body mass will be measured using digital scales. Body mass index (BMI) will be calculated as mass (kg) / height (m)^2. Waist circumference will be measured with a tape measure, at the narrowest point or midpoint of the lower costal border (10th rib) and iliac crest.
Knee clicking and crepitus	The presence of knee clicking and crepitus will be evaluated bilaterally using methods described by Schiphof et al.[30] Participants will be seated comfortably on a standard chair. The tester will rest their hand over the participants' patella of the test limb, and ask the participant to actively extend their knee from 90° of knee flexion to 0° of knee extension (if possible) 3 times. Crepitus will be defined as an audible grinding noise and/or palpable vibrations in the knee during active movement.
Knee extension torque	Knee extension force will be measured bilaterally using previously described methods .[31] Participants will sit comfortably on a high stool, with their knees in 90° flexion, and their thighs secured to the chair with a seatbelt (Figure 1). Participants may hold the seat of the chair with their arms in full extension. A strain gauge will be secured to the posterior aspect of the chair and strapped around the test ankle, at a point 10cm above the lateral malleolus. Participants will be instructed to extend their knee to end of range and push maximally for three seconds. Three trials will be performed on each side. To calculate knee extension torque, force will be multiplied by leg length (distance between the lateral femoral epicondyle and lateral malleolus).  Figure 1. Test position.
Foot Posture Index (FPI)	The FPI is a valid and reliable method of quantifying weight bearing static foot posture.[32] Methods are detailed in the user guide and manual (available online).[33] Participants will stand in relaxed bilateral stance, with their arms by their side and looking straight ahead. Six aspects of static foot posture are evaluated on each foot: (i) talar head palpation; (ii) supra and infra malleolar curvature; (iii) calcaneal frontal plane position; (iv) bulging in the region of the talonavicular joint; (v) height and congruence of the medial longitudinal arch; and (vi) abduction/adduction of the forefoot on the rearfoot. Each feature is scored on a five-point scale (-2 = supinated; 0 = neutral; +2 = pronated). A total score for each foot is calculated by summing each of the six items. Total scores range from -12 (supinated) to +12 (pronated).

Foot mobility	Foot mobility will be evaluated bilaterally using the Foot Assessment Platform.[34] For weight bearing (WB) measures, participants will be positioned in bilateral stance on a custom-designed platform. Total foot length will be measured, and the dorsum of the foot marked at 50% of total foot length. Midfoot height and midfoot width will be measured (in millimetres) at 50% foot length using digital calipers (Figure 2A and 2B). Participants will then be seated on the edge of a plinth to capture non-weight bearing (NWB) foot measures. With the femur horizontal, tibia vertical, and foot and ankle hanging relaxed in space, a custom-made platform will be used to measure midfoot height at 50% foot length (Figure 2C). Midfoot width at 50% foot length will be measured in the same position, using digital calipers (Figure 2D). Foot mobility will be defined in three ways: (i) midfoot height mobility, calculated as the difference between NWB and WB midfoot height; (ii) midfoot width mobility, calculated as the difference between WB and NWB midfoot width; and (iii) foot mobility magnitude (calculated as: $\sqrt{(\text{midfoot height mobility})^2 + (\text{midfoot width mobility})^2}$).  Fig 2A. WB midfoot height.  Fig 2B. WB midfoot width.  Fig 2C. NWB midfoot height.  Fig 2D. NWB midfoot width.
Weight bearing ankle dorsiflexion range of motion	Ankle dorsiflexion range of motion will be measured in weight bearing using established methods.[35] The plane of movement will be marked using a line of tape on the floor perpendicular to the wall (horizontal line), with the tape continuing vertically up the wall to approximately knee height. Participants will stand in front of the wall with the midpoint of the calcaneus and second toe of the test limb aligned on the horizontal line. Participants will be instructed to lunge forward to touch their kneecap to the vertical line on the wall, while maintaining their heel on the floor. The assessor will ensure that the heel stays in contact with the floor. The foot will be moved back gradually along the horizontal line until the point where the kneecap just touches the wall, and the heel is almost lifting off the floor (Figure 3). The distance between the wall and the longest toe will be measured (centimetres). The test will be performed three times on each limb.  Fig 3. Test position

Footwear Assessment Tool	The participant's footwear will be assessed using selected items from the Footwear Assessment Tool, which has established reliability.[36] We will evaluate one pair of shoes that they wear most frequently. Shoe fit (Item 1) will be evaluated in terms of the length between the longest toe and end of shoe (too short: < ½ thumb's width; good: 1 to 1 ½ thumb widths; too long: > 1 ½ thumb widths); width of the shoe when the upper is grasped across the metatarsal heads (too wide: excessive bunching; good: slight bunching; too narrow: taught upper unable to be grasped); and depth (adequate; too shallow). General features will also be recorded (Item 2), including age of the shoe (months); footwear type (selected from existing template [36]); and shoe weight (grams) and length (millimetres). Structural features (Item 3) will include heel and forefoot height (millimetres); and forefoot sole flexion point (at 1st metatarsophalangeal (MTP) joint; proximal to 1st MTP joint; distal to 1st MTP joint). Motion control properties (Item 4) will consist of sagittal stability of the midfoot sole (minimal >45°; moderate <45°; rigid <10°). Cushioning (Item 5) will be evaluated be measuring lateral midsole hardness (penetrometer reading). Participants will also be asked to rate how comfortable they think their shoes are on a 100mm visual analogue scale (0=extremely uncomfortable; 100=extremely comfortable).
10-metre Walk Test	Temporospatial gait parameters (e.g. walking speed, step length) will be measured using the 10-Metre Walk Test.[37] A 10-metre walkway will be measured along a level corridor. Participants will be instructed to walk at their usual comfortable walking pace from the point when they cross the starting line (0 metres) until they cross the finish line (10 metres). The investigator will start timing the trial from the moment their first foot crosses the starting line, and stop when their first foot crosses the finish line. Participants will perform three warm-up repetitions, followed by three recorded trials, ensuring that the second and third recorded trials are within 5% of the first recorded time.

REFERENCES

1. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85(5):815-22.
2. Parkes MJ, Callaghan MJ, O'Neill TW, et al. Sensitivity to Change of Patient-Preference Measures for Pain in Patients With Knee Osteoarthritis: Data From Two Trials. *Arthritis Care Res (Hoboken)* 2016;68(9):1224-31.
3. Crossley KM, Vicenzino B, Lentzos J, et al. Exercise, education, manual-therapy and taping compared to education for patellofemoral osteoarthritis: a blinded, randomised clinical trial. *Osteoarthritis Cartilage* 2015;23(9):1457-64.
4. Collins N, Crossley K, Beller E, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ* 2008;337:a1735.
5. ten Klooster PM, Drossaers-Bakker KW, Taal E, et al. Patient-perceived satisfactory improvement (PPSI): interpreting meaningful change in pain from the patient's perspective. *Pain* 2006;121(1-2):151-7.
6. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28(2):88-96.
7. Crossley KM, Macri EM, Cowan SM, et al. The patellofemoral pain and osteoarthritis subscale of the KOOS (KOOS-PF): development and validation using the COSMIN checklist. *Br J Sports Med* 2017 doi: 10.1136/bjsports-2016-096776.
8. Kujala UM, Jaakkola LH, Koskinen SK, et al. Scoring of patellofemoral disorders. *Arthroscopy* 1993;9(2):159-63.
9. Watson CJ, Propps M, Ratner J, et al. Reliability and responsiveness of the lower extremity functional scale and the anterior knee pain scale in patients with anterior knee pain. *J Orthop Sports Phys Ther* 2005;35(3):136-46.
10. Lorig K, Chastain RL, Ung E, et al. Development and evaluation of a scale to measure perceived self-efficacy in people with arthritis. *Arthritis Rheum* 1989;32(1):37-44.
11. Brady TJ. Measures of self-efficacy: Arthritis Self-Efficacy Scale (ASES), Arthritis Self-Efficacy Scale-8 Item (ASES-8), Children's Arthritis Self-Efficacy Scale (CASE), Chronic Disease Self-Efficacy Scale (CDSES), Parent's Arthritis Self-Efficacy Scale (PASE), and Rheumatoid Arthritis Self-Efficacy Scale (RASE). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S473-85.
12. Kori SH, Miller RP, Todd DD. Kinisiophobia: a new view of chronic pain behaviour. *Pain Management* 1990:35-43.
13. Areeudomwong P, Buttagat V. Reliability and Validity of the Cross-Culturally Adapted Thai Version of the Tampa Scale for Kinesiophobia in Knee Osteoarthritis Patients. *Malays J Med Sci* 2017;24(2):61-67.
14. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220-33.
15. Busija L, Pausenberger E, Haines TP, et al. Adult measures of general health and health-related quality of life: Medical Outcomes Study Short Form 36-Item (SF-36) and Short Form 12-Item (SF-12) Health Surveys, Nottingham Health Profile (NHP), Sickness Impact Profile (SIP), Medical Outcomes Study Short Form 6D (SF-6D), Health Utilities Index Mark 3 (HUI3), Quality of Well-Being Scale (QWB), and Assessment of Quality of Life (AQoL). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S383-412.

16. Gignac MA, Cao X, McAlpine J, et al. Measures of disability: Arthritis Impact Measurement Scales 2 (AIMS2), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), The Organization for Economic Cooperation and Development (OECD) Long-Term Disability (LTD) Questionnaire, EQ-5D, World Health Organization Disability Assessment Schedule II (WHODASII), Late-Life Function and Disability Instrument (LLFDI), and Late-Life Function and Disability Instrument-Abbreviated Version (LLFDI-Abbreviated). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S308-24.
17. Barton GR, Sach TH, Avery AJ, et al. Comparing the performance of the EQ-5D and SF-6D when measuring the benefits of alleviating knee pain. *Cost Eff Resour Alloc* 2009;7:12.
18. Munteanu SE, Scott LA, Bonanno DR, et al. Effectiveness of customised foot orthoses for Achilles tendinopathy: a randomised controlled trial. *Br J Sports Med* 2015;49(15):989-94.
19. Munteanu SE, Landorf KB, McClelland JA, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis (the SIMPLE trial): study protocol for a randomised controlled trial. *Trials* 2017;18(1):198.
20. Bouwmans C, Krol M, Severens H, et al. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health* 2015;18(6):753-8.
21. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. *J Behav Therapy Exp Psychiatry* 1972;34:257-60.
22. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31(2):73-86.
23. Boudreau SA, Spence R, Vasov G, et al. Feature Extraction APP for Pain Profiles. *Biosyst Biorobot* 2014;7:853-54.
24. Boudreau SA, Badsberg S, Christensen SW, et al. Digital Pain Drawings: Assessing Touch-Screen Technology and 3D Body Schemas. *Clin J Pain* 2016;32(2):139-45.
25. Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18(1):160.
26. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22(10):1911-20.
27. Tampin B, Bohne T, Callan M, et al. Reliability of the English version of the painDETECT questionnaire. *Curr Med Res Opin* 2017;33(4):741-48.
28. Turner KV, Moreton BM, Walsh DA, et al. Reliability and responsiveness of measures of pain in people with osteoarthritis of the knee: a psychometric evaluation. *Disabil Rehabil* 2017;39(8):822-29.
29. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation. *Psychol Assess* 1995;7(4):524-32.
30. Schiphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22(5):631-8.
31. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003;83(3):237-52.
32. Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: the Foot Posture Index. *Clin Biomech (Bristol, Avon)* 2006;21(1):89-98.

33. Redmond AC. The foot posture index: easy quantification of standing foot posture. Available at https://www.leeds.ac.uk/medicine/FASTER/z/pdf/FPI-manual-formatted-August-2005v2.pdf 2005 [Available from: http://courses.ki.se/fpi_manual-formatted_august_2005v2_1_.pdf?node=202687 accessed November 8, 2017.
34. McPoil TG, Vicenzino B, Cornwall MW, et al. Reliability and normative values for the foot mobility magnitude: a composite measure of vertical and medial-lateral mobility of the midfoot. *J Foot Ankle Res* 2009;2:6.
35. Bennell KL, Talbot RC, Wajswelner H, et al. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother* 1998;44(3):175-80.
36. Barton CJ, Bonanno D, Menz HB. Development and evaluation of a tool for the assessment of footwear characteristics. *J Foot Ankle Res* 2009;2:10.
37. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 2013;36(1):24-30.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	***1***
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	***2***
	2b	All items from the World Health Organization Trial Registration Data Set	**-**
Protocol version	3	Date and version identifier	**-**
Funding	4	Sources and types of financial, material, and other support	***25***
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	***25***
	5b	Name and contact information for the trial sponsor	***25***
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	***25***
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	***25***

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	***4-5***
	6b	Explanation for choice of comparators	***14-15***
Objectives	7	Specific objectives or hypotheses	***5-6***
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	***6-7***
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	***6-7***
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	***8***
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	***12-16***
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	***16***
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	***16-17***
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	***16***
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	***17-20***
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	***Figure 2***

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	***20-21***
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	***7-8***
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	***12***
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	***12***
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	***12***
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	***12***
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	***12***
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	***9-11, 17-20***
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	***17***

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	***21-22***
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	***22-23***
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	***22-23***
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	***22***
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	***22***
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	***22***
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	***19-20***
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	**-**
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	***7***
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	***7***

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	***8-9, 11***
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	***8-9, 11***
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	***21-22***
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	***25-26***
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	***21-22, 24***
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	***15-16***
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	***23-24***
	31b	Authorship eligibility guidelines and any intended use of professional writers	**-**
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	***24***
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	***Supplementary file 1***
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	***n/a***

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.