Author’s response to reviews

Title: The efficacy of foot orthoses in individuals with patellofemoral osteoarthritis: a randomised feasibility trial

Authors:

Jade Tan (jade.tan@latrobe.edu.au)
Hylton Menz (h.menz@latrobe.edu.au)
Kay Crossley (k.crossley@latrobe.edu.au)
Shannon Munteanu (s.munteanu@latrobe.edu.au)
Harvi Hart (h.hart@latrobe.edu.au)
Kane Middleton (k.middleton@latrobe.edu.au)
Anne Smith (Anne.Smith@exchange.curtin.edu.au)
Natalie Collins (n.collins1@uq.edu.au)

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Author’s response to reviews:

REVIEWER 1

This is a well-written manuscript of a carefully designed trial. I only have some minor remarks:
Response: We thank the reviewer for their positive feedback on our trial.

p. 5, line 97: provide reason for the retrospective registration
Response: Ideally we would have registered the trial prospectively. However, a quick turn around with ethics in conjunction with a sudden high interest in study involvement, resulted in the trial being registered after the first participants were recruited and randomised. Twenty-one participants were enrolled in the study before registration.

p. 6, line 114: unclear what the authors mean that the NICE guidance obviates the need for imaging, explain more explicitly
Response: We have since made this statement more clear by changing the wording as follows: “Eligibility for participation in the study was based on the NICE guidelines (https://www.nice.org.uk/guidance/cg177) [24], which stipulate that imaging is not required for a clinical diagnosis of OA.”
p. 21, line 457: why is the study protocol not available?
Response: Given that the primary aim of a feasibility study is to determine an appropriate study protocol and the feasibility for conducting a large-scale trial, it was not deemed necessary to publish a protocol paper [1]. However, the ANZCTR registration for this trial provides a detailed description of the methods used (ANZCTR number: 12616001287426).

Given the success of this feasibility study, we have since had a trial protocol accepted for publication in BMJ Open for a large-scale randomised controlled trial based on the feasibility study titled “The FOOTPATH Study: protocol for a multicentre, participant- and assessor-blind, parallel group randomised clinical trial of foot orthoses for patellofemoral osteoarthritis”.

p. 10, line 215: how did the authors decide whether the trial was feasible?
Response: A criteria for the feasibility of the trial has since been amended under the heading Primary outcome measure: feasibility of a full-scale RCT, lines 170 to 173, and now reads as follows:
“We set the following parameters to determine feasibility: one participant recruited per week, 20% (35 hours/week) adherence to the intervention [30], 50% log-book completion rate, and less than 20% drop-out rate [25, 31].”

Table 3: use generic drug names instead of brand names; what is the compound of "Difflam"?
Response: We thank the reviewer for highlighting this. The generic name of Difflam has now been added to Table 3 and is displayed as follows:
“Difflam (3% benzydamine hydrochloride topical cream)”

REVIEWER 2

Thanks to authors for their submission.

Abstract:
Method:
• First sentence is suitable for results section.
• No method of analysis was discussed.
• What results and effect estimate were reported not discussed.
• No criteria of success were discussed.
Response:
• We have since changed the first sentence to read as follows:
“This six-week, single-blinded pilot RCT randomly allocated participants with PFOA to receive foot orthoses or flat inserts.”
Participant numbers have also been moved to the first sentence of the Results section.
“Twenty-six participants (16 women; mean ± SD age 60±8 years) with PFOA were recruited.”
• Methods of analysis has been added to the Methods section within the Abstract and now reads as follows:
  “The primary outcome of feasibility was determined via the following parameters: one participant recruited per week, 20% (35 hours/week) adherence to the intervention, 50% log-book completion rates, and less than 20% drop-out, with results reported using descriptive statistics. Secondary outcomes included average and maximum pain (100mm visual analogue scale), the Anterior Knee Pain Scale, and the Knee injury and Osteoarthritis Outcome Score, analysed using analysis of covariance (ANCOVA).”
• Given the limited word count of the Abstract, we felt it appropriate to only report the feasibility results and the significant secondary outcome measures results.
• The determination of success has now been added to the Methods section and reads as follows:
  “The primary outcome of feasibility was determined via the following parameters: one participant recruited per week, 20% (35 hours/week) adherence to the intervention, 50% log-book completion rate, and <20% drop-out, with results reported using descriptive statistics.”
• We have also revised the abstract to meet the 350 word limit.

Abstract:

Results:
• How the sample size was calculated?
Response: Respectfully, given abstract word limits stipulated by the journal, we did not add details of the statistical analyses used to calculate the sample size to the abstract. Details of how the sample size was calculated can be found within the main body of text under the Proof of concept paragraph, lines 239 to 242:
  “The estimate of effect size between groups for the key secondary outcome of maximum knee pain severity during an individual’s most aggravating activity of either ‘rising from sitting’, ‘going up and down stairs’, or ‘squatting’ in the previous week was 21.9mm (95% CI -2.1 to 46.0). The SD of this outcome at baseline was 24.6 (19.2 to 35.2), with the correlation between baseline and six-week measures being 0.72 (0.46 to 0.88). This confirms that a sample size calculation based on an ANCOVA adjusting for baseline value, assuming a between-person SD of 30mm and baseline to three-month correlation of 0.5, is appropriate. A sample size calculation using these parameters determined that a sample of 160 (80 per group) would be needed. Allowing for ~20% drop-outs, this provides a minimum 90% power (α=0.05) to detect a clinically meaningful between-group difference of 15mm or more in maximum knee pain severity over the preceding week during one of three self-nominated aggravating activities (rising from sitting, stair ambulation, or squatting).”
Main body:
Background:
Line 84: 'The aim of this feasibility study was to evaluate the efficacy of foot orthoses in reducing pain and improving function in individuals with PFOA'. But the authors said this was a feasibility trial for a larger trial.

Response: We thank the reviewer for picking up this lack of clarity within our manuscript. We have since changed the wording of the manuscript to read as follows: “The aim of this feasibility study was to explore the key methodological issues for a future large-scale randomised controlled trial (RCT) to estimate the efficacy of foot orthoses in reducing pain and improving function in individuals with PFOA. This was addressed via three key objectives: (i) to determine the immediate comfort levels of foot orthoses versus flat inserts in individuals with PFOA; (ii) to evaluate proof-of-concept for a clinically meaningful benefit in pain and function for foot orthoses compared to flat inserts over six weeks; and (iii) to determine whether foot orthoses and flat inserts are credible and acceptable interventions for PFOA.”

Main body:
Method:
• What were the criteria of success?
• How the missing data were handled?
Response:
• Our assessment of feasibility was primarily driven by recruitment rate, along with adherence to the intervention and log-book completion, and loss to follow-up. We have now defined the criteria for success and amended the Primary outcome measure: feasibility of a full-scale RCT paragraph, lines 170 to 173, to read as follows: “We set the following parameters to determine feasibility: one participant recruited per week, 20% (35 hours/week) adherence to the intervention [30], 50% log-book completion rate, and less than 20% drop-out rate [25, 31].”
• Data were analysed on a “complete case basis” as described in the main body of text under Statistical analyses, line 232. No imputation of missing data was undertaken given the minimal number of cases missing (n = 1 in the foot orthoses group and n = 2 in the flat inserts group).

Main body:
Results: table 1: What were reported for continuous outcome?
Response: Continuous outcome measures were primarily reported as means and standard deviations as per the legend at the bottom of Table 1.

This manuscript is not acceptable in the current form. I would recommend the authors to follow the consort statements for pilot and feasibility trials and prepare the manuscript accordingly.
Response: We have since re-reviewed the CONSORT statement for reporting randomised pilot and feasibility trials when revising this manuscript. An updated CONSORT checklist for this trial has been attached.
REFERENCES