Author's response to reviews

Title: A comparison of customised and prefabricated insoles to reduce risk factors for neuropathic diabetic foot ulceration: a participant-blinded randomised controlled trial.

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Author's response to reviews: see over
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Dear Editorial Team

Re: A comparison of customised and prefabricated insoles to reduce risk factors for neuropathic diabetic foot ulceration: a participant-blinded randomised controlled trial
# 1802018718533641

Thank you for the review of our paper. We appreciate the clarity of your review and the addition of the relevant recommended articles. We have responded to the reviewers comments and have resubmitted a revised manuscript (see below).

This article provides new and important information regarding insole provision for the neuropathic diabetic foot. We thank you for your interest in publishing our manuscript and hope that you will now find it suitable for inclusion in the Journal of Foot and Ankle Research.

Yours sincerely

Dr Joanne Paton and colleagues.

DATA HANDLING AND STATISTICAL ANALYSIS

1. We sought further assistance from a statistician colleague (DZ) to help with the re-analysis of the data and to further check all analyses. DZ has been added as a co-author.

2. We agree with the editors that intention to treat analysis is considered the ‘gold standard’ analysis for randomised controlled trials. As requested by the editors we have only included an intention to treat analysis and removed the secondary analysis.

3. In recognition of the high drop-out and missing data rates and at the editors’ request we performed multiple imputation rather than last observation carried forward.

4. We acknowledge that ANCOVA could be considered as an alternative analysis for this study and read with interest the supporting articles referenced. However we remain confident that slit plot ANOVA is appropriate for the analysis particularly given that 1) the baseline values between groups is similar, 2) we
continue to feel it is more appropriate to look at mean levels of change pre and post intervention rather than absolute scores. We have however amended our limitations section as requested to read:

Some suggest that we should have used ANCOVA rather than split plot ANOVA. The majority of previous work into the effect of insoles on kinetic measures reports on mean levels of change pre and post intervention rather than looking at the difference between mean levels in the groups post intervention adjusted for baseline scores. In addition, the threshold below which insoles must maintain peak pressure to prevent ulceration is as yet unknown, instead the evidence suggests that the lower peak pressure the lower the ulceration risk. We do not think that using an ANCOVA would actually make any difference to our conclusions given that the baseline values for each group were similar.

5. We have removed the p-values when reporting reductions in pressure and increases in contact area.

PEAK PRESSURE VERSUS PRESSURE TIME INTEGRAL

1. As requested by the editors we have incorporated the following two papers into our discussion.


Total peak pressure was selected as the traditional measure of footwear and insole efficacy to ease comparison of results between studies. Forefoot pressure time integral was selected to reflect the increased risk of ulceration over the forefoot area and to give consideration to the possible effect of the functional foot orthosis on the timing of dynamic gait. Moreover in pilot work for our study we concluded that forefoot pressure time integral gave additional potentially important information not provided by peak pressure [12].

It has been reported that peak pressure and pressure time integral are interdependent and that within clinical trials significant differences in patterns found
between the two parameters are generally minimal [20,21]. Thus opinion has begun to question the value of routinely reporting both measures of insole efficacy [20,21]. Whilst one study concluded that peak pressure and pressure time integral were interchangeable when testing the efficacy of offloading footwear, this work was not extended to include functional devices [21]. The functional foot orthosis may differ in its mode of action from other footwear and insole modifications because rather than simply offloading a high pressure area, it attempts to improve gait efficiency by altering the loading pattern and timing of the stance phase of gait. Thus in this instance, we selected the parameter forefoot pressure time integral to more closely reflect the aims and principles of the functional foot orthotic design, that is to adjust the timing and order of events to improve gait efficiency. However, we acknowledge that future studies may conclude that forefoot peak pressure is an equally suitable measure and accept that our findings may have been the same if forefoot peak pressure had been selected.

OTHER ISSUES

1. We have added that the trial was registered with Clinical Trial.gov after completion of the data collection and understand the relevance of this information.

   Trial registration: Clinical trials.gov (NCT00999635) Note: This trial was registered on completion.

2. The word longitudinal has been removed from page 4 line5.

3. CO128 tuning fork has been replaced with 128 Hz tuning fork. Mid-foot has been changed to midfoot (page 5).

4. The paragraph heading has been changed to ‘Primary outcome measures’ to avoid over capitalising. The following references have been inserted to support the validity and reliability of the F-scan (page 7).


5. As requested by the editors we have added information regarding the method used to check for consistency of velocity.
Gait velocity of each run was timed to check for consistency in the event variation was found the data was discarded and the test repeated. Participants were asked to walk between two chairs placed at either end of a walkway. Between the chairs, two marks were placed on the floor with a distance of ten meters between them. Using a stop clock, the time taken for the participant to walk the ten meter distance was recorded. Gait velocity could then calculated in metres per second.

6. The word 'demographics' has been removed from page 10 participants and follow up section, last line.

7. As requested by the editors the group results for the blind testing have been included in addition to the overall results for the entire sample (page 11).

To assess for bias and breaking the blind process, participants were asked at completion of the study to guess their intervention group assignment. Of the 45 respondents receiving the prefabricated insole, 25 (56%) thought they had been given the custom-made functional insole, 4 (8%) thought they had the prefabricated insole and 16 (36%) did not know. Of the 46 respondents receiving the custom-made functional insole, 30 (65%) thought they had been given the custom-made insole, 4 (9%) thought they had been given the prefabricated insole and 12 (26%) did not know. A total of 34 (37%) participants chose the intervention received, 29 (32%) guessed incorrectly and 28 (31%) were unable to decide which insole they had been provided. Participants remained blind to the intervention allocation for the trial duration.

8. Details of the adverse event experienced by the person in the custom insole group have been added. In addition the inappropriate statistical finding presented has been removed.

Five (4%) of the 119 recruited participants developed adverse effects whilst participating in the RCT. Four of the five had been randomly allocated the prefabricated insole: One suffered a Charcot joint, the other three developed plantar ulcers, one of which was apparently caused by a sock being inadvertently left in the toe of a shoe while worn. One further participant suffering an adverse effect had received the custom-made insole. At follow-up, a 1st interphalangeal joint ulcer was discovered in conjunction with suspected osteomyelitis. The participant was withdrawn from the study with immediate effect and placed in an offloading walker.
9. The type of study has been added to the reference Mohamed and colleagues (page 12).

10. The word ridged has been changed to rigid on page 13. The same correction has been amended on page 14.
11. Page 16. ‘most cost effectiveness’, has been corrected to ‘most cost effective’.
12. Page 16. The term neuropathic patient has been replaced with participants with diabetic neuropathy. The manuscript has been checked for consistency of terms.