Author’s response to reviews

Title: Lateral wedges with and without custom arch support for people with medial knee osteoarthritis and pronated feet: An exploratory randomized crossover study

Authors:

Michael Hunt (michael.hunt@ubc.ca)
Judit Takacs (jud.takacs@gmail.com)
Natasha Krowchuk (natasha.krowchuk@ubc.ca)
Gillian Hatfield (gillian.hatfield@ufv.ca)
Rana Hinman (ranash@unimelb.edu.au)
Ryan Chang (ryan.chang.umass@gmail.com)

Version: 1 Date: 05 Apr 2017

Author’s response to reviews:

Reviewer reports:

Editor Comments:

Please ensure the fidelity of the manuscript with the trial registration at Clinicaltrials.gov identifier: NCT02234895. For example the primary outcomes are listed as "Change in knee joint load during walking: knee adduction moment" and "Change in Knee Pain" while in the paper the primary outcome is "Self-reported knee and foot symptoms were the primary clinical outcomes of interest".

Response: Thank you for this comment. Gait data were only collected at the initial baseline data collection session. Further follow-up testing was not collected in the present cohort. This was decided after clinical trial registration based on pilot testing showing consistent changes in biomechanical data over time – it was agreed upon that we would likely not acquire any new information with a two-month gait collection in addition to what was acquired at the initial baseline data collection session (based on previous work showing the same mechanical changes at one-year follow-up collections compared to baseline with lateral wedges – Barrios et al, Journal of Orthopedic Research 31(5):659-664, 2013).

Rather, knee adduction moment and other gait data from this study at baseline are published elsewhere (Hatfield et al, Journal of Orthopedic Research 34(9):1597-1605, 2016) and with the
exception of that initial baseline testing, only clinical data were collected. Clinical data are reported in this paper and are consistent with the details provided in the clinical trials registration. FFI data were initially reported as a secondary outcome at trial registration. As a result, we have removed the word “primary” from the line in question, and simply indicate that knee and foot symptoms were the “clinical outcomes of interest” – we believe that this reflects what was initially proposed at the time of trial registration.

Reviewer #1:

Thank you for the opportunity to review this manuscript, which focuses on a very interesting and important topic area. The trial investigates an important clinical question and is generally well presented with some interesting findings reported. I do, however, feel there are some significant concerns regarding the methodology. The most concerning surrounds the sample used, which could seriously threaten the extent to which the analysis validly answers the research question. Please find below my complete list of comments:

Background:

* The first paragraph contains comments concerning Osteoarthritis in general (with a comment that it commonly affects the knee). I think some more specific detail on the prevalence and impact of knee OA would be appropriate here.

Response: Joint specific estimates of OA are rare. We have added the most up-to-date prevalence estimates for knee OA, but are unaware of any studies that have provided joint-specific estimates of the economic burden.

* I think the paragraph establishing a connection between excessively pronated or flatter feet with OA is important and presents reasonably well. I do wonder, however, if the clinical issue at hand could be more clearly explained. For example, if people have knee OA and flatter feet, is it mainly that we may need to treat painful knees and painful feet in some patients, but is it also that we may need to consider the forces we are putting on an asymptomatic but flatter/more pronated foot when we use lateral wedging insoles for the knee. On a similar note, a comment is made that rearfoot eversion in gait is associated with KAM, although the direction of this association is not stated. This could be more explicitly stated, along with the rationale for lateral wedging, and perhaps this would start to suggest the potential conundrum of using an external pronatory force to offload the knee in patients whose feet are already flatter or excessively pronated.
Response: Thank you for this comment. We agree with all points that the Reviewer has made here. The main point that we were trying to make (and expanded in the subsequent paragraph) is that there appears to be a link between the feet and knees in people with knee OA. We do not know if this is simply an association, whether there are bidirectional causative factors at play, or whether common biomechanical pathways exist between the findings. As a result, we are advocating that treatment for knee OA should consider what impacts, if any, a particular treatment has on foot biomechanics and symptoms when the primary aim is to target the knee. This is especially important in the subgroup of people with knee OA and pronated feet (given the evidence provided in this paragraph), as well as when shoe-based interventions are delivered to treat knee OA. We have expanded on this as suggested.

Directionality of the relationship between rearfoot eversion and KAM values has been added. Additionally, the link between lateral wedging, increased rearfoot eversion, and lower KAM magnitudes has been added in the subsequent paragraph as suggested.

* In the third paragraph of the background mention is made of pronated feet being treated with orthoses that maintain subtalar neutral. There is evidence that subtalar neutral is not a valid marker to base foot function or foot orthoses prescription around and the authors should consider not using this explanation for practitioners choosing an orthoses type or design.

Response: We have removed this aspect from the statement in question. That said, we would argue that there is certainly no consensus as to the benefits (or not) of maintaining subtalar neutral. While the reviewer correctly points out that there is evidence against maintaining subtalar neutral, there is also evidence in support of this. Indeed, the two references that we provide for this statement are both expert-based opinion/clinical guidelines papers representing current best practice.

Methods:

* While 3/10 was sensibly used as a minimum pain level for the study, was there an upper limit for pain severity? Is it possible that people with very high levels of pain may not be most suitable for this intervention and require other forms or management?

Response: We did not have a maximum pain threshold for study inclusion. It is possible that those with high levels of pain would not be suitable, but a brief (unplanned and underpowered) analysis of our study data did not appear to indicate specific subgroups of people who responded or not. We would not want to speculate on the appropriateness of high-pain individuals based on our current dataset.
The biggest concern with the methodology surrounds the sample used and the definition of a flat foot. The authors have chosen a Foot Posture Index score of +4 or higher as flat foot. The published normative data have the mean FPI score at +4, with a standard deviation of over 2. This sample appears to have included those with a FPI score of 4, 5 and 6, who are people at or within one standard deviation of the mean. From table 1 it appears 6 is the 75th percentile, meaning only 25% of participants had a FPI of 7 or more. To me, this means that the sample includes mostly people with normal foot alignment and seriously threatens the validity of an analysis which is attempting to describe effects of interventions on people with flat/excessively pronated feet. The authors must respond to this issue and consider whether their data can validly answer the research question posed.

Response: Thank you for this comment. We agree with the Reviewer. There is a sufficient body of growing evidence (as presented in the Introduction) that pronated feet are more linked to knee OA than neutral or cavus feet. While the published data do report population mean values around +4, by definition any FPI score greater than 0 would indicate some signs of pronation. We specifically made a requirement that at least four items on the FPI must have been rated as +1 or +2 for study inclusion to ensure that the foot was more pronated than not. That published means are approximately +4 simply indicates that the average value is +4, and while this may be “normal” as the Reviewer suggests, it only indicates that the “norm” is some form of pronation. There should be a clear distinction between “normal” and “neutral” – in this case, we would recommend against these terms being used interchangeably. Indeed, we do not necessarily agree that a mean value is representative of normal as the Reviewer suggests (“this means that the sample includes mostly people with normal foot alignment”). As a result, we argue for simply stating that our sample is “pronated” as that is what +4 on the FPI suggests.

To avoid confusion, we have changed the wording of “flat feet” to “pronated feet” throughout this paper (including the title) to more accurately reflect the FPI data for our sample, and what the FPI data indicate about foot alignment.

The authors mention that not all participants completed the study, but more information is needed here. If 4 participants didn't complete the study (2 in the first phase), then this is a significant number in a sample of 26. The reasons for withdrawal should be stated and a justification for the decision on how to deal with the missing data should be provided. If the missing data is truly random then it may be only power that is affected, however, if these participants withdrew because they were doing poorly then the results of the analysis may be biased.

Response: Three of the four participants were lost-to-followup and did not respond to repeated email and phone communication attempts to schedule reassessment visits. The remaining participant withdrew due to mental health issues unrelated to the intervention. This information
has been added to the Results section as requested. Missing data was treated as randomly occurring, and only 6 out of 52 data points in total were lost. The number of data points for each condition has now been added to Table 2 as requested by Reviewer #2.

Results:

* Did the comparison of factors such as wear time, comfort include any statistics? If so, results of significance testing should be displayed.

Response: We ran statistical tests on comfort, but not wear time. This has been changed in-text where appropriate.

* 16 reports of adverse events seems reasonably high, even if minor, out of a total of 46 interventions trialed. Were these all separate individuals or did some report multiple adverse events in the same treatment phase? Even so, there appears to be a somewhat high percentage of people having issues with the interventions and this probably deserves more discussion time as this would have clinical implications.

Response: Thank you for this comment. While we feel that the nature of the reports were relatively minor, it is our preference to not make judgements on whether a self-reported adverse event from a participant is “real”; rather, we report all and allow the reader to determine for themselves if that is an important finding or not. This has now been addressed in the Discussion.

* Of interest, is there a cost difference between the 2 orthoses, as this may become important when considering cost-effectiveness

Response: Thank you for this excellent comment. We have added a comment to this effect in the Discussion. Prices will differ depending on the provider and location, and we have provided a likely minimum cost difference based on discussion with a number of pedorthists. Importantly, we are advocating for a cost-effectiveness analysis of the benefits (if any) of the combined insole to determine what would be the maximum justifiable price difference over and above a standard lateral wedge.

Discussion:

* In the first paragraph of the discussion there is a suggestion that the arch support insoles were more comfortable, however, this not in keeping with what is presented in the results
regarding self-reported comfort. Similarly, comfort is provided as a reason that the arch support may be more effective (in the paragraph that discusses knee pain and external loads) which again is not consistent with the results section.

Response: This has been changed to reflect the lack of statistical significance in comfort data.

* The minimum clinically important difference for the WOMAC scale was referred to reporting the size of the treatment effect found in the study. Is there a MCID available for the FFI-R, and if so, do these changes represent an effect greater than this?

Response: Unfortunately, we are unaware of any published reports of the MCID for the FFI-R.

* Limitations are included, but the type of study design itself also has limitations and should be discussed as such. This doesn't mean that it's not appropriate to use a cross-over study with a small sample as a preliminary investigation, but the limitations of this design should be outlined. On this note, it is interesting that a glance at the figures seems to highlight that the second iteration is where the differences in interventions seem most apparent. Have the authors considered reasons for this being the case? This is something that should probably feature in the discussion.

Response: We agree that a randomized crossover study has limitations. These have been briefly mentioned in the Limitations paragraph. However, as the Reviewer alludes to, these types of studies are commonly utilized between simple pre-post studies and full RCTs as a logical progression of providing evidence. We feel that the use of this study design was appropriate for this research question at this time. It is our hope that these findings may now be expanded to a full RCT that would require more time and resources.

Regarding the second iteration being responsible for the differences, we do not feel that it was the period effect; rather, it was more likely a subtle treatment effect that accounted for this visual observation of apparent differences. The lines indicate the order in which the conditions were presented, not the conditions themselves. For example, in Figure 2a, it can be seen that the group denoted by the black line did appear to experience a decrease in pain “at first glance” with their first iteration, with no apparent change in the second iteration. Individuals in this group received the combined insole first (first iteration) and the lateral wedges alone in the second iteration. In contrast, those denoted by the dotted line received the lateral wedges alone first (less apparent pain decrease in first iteration) and the combined insole second (the apparent difference that was pointed out by the Reviewer). In both instances, the larger apparent pain decrease both occurred when the groups were using the combined insole. This finding is consistent across all four graphs in Figures 2 and 3.
Reviewer #2: Thank you for the opportunity to review this article. This is a randomized crossover study investigating different types of lateral wedge insoles in individuals with medial knee osteoarthritis. The article is well written but I have some minor comments which would be useful for completeness:

Background second page - line 36. A recent paper from our group (Jones et al. 2016, JOR) has demonstrated that lateral wedges with arch supports are more comfortable and also reduce pain better than typical devices. It would be suggested that this is included in this section so that a full picture of the available literature is given.

Response: Thank you for this suggestion. In this section, we are simply focusing on the apparent disconnect between insoles treatment for knee OA (predominantly lateral wedges) and how people with flat/pronated feet in the general population are commonly treated (predominantly with some form of medial arch support). Indeed, none of the references in this section pertain to people with knee OA, nor do they mention a combined lateral wedge with arch support. As a result, we have simply used the suggested reference to support the final sentence in the paragraph.

In contrast, as per your suggestion below, statements in the Discussion when we are directly comparing comfort in our cohort when using both types of insoles appear to be a better fit for this reference. Accordingly, we have added this reference in the Discussion but not the Introduction.

Methods - line 36 - +4 on the FPI is the higher range of the normal foot at rest. Were all individuals above 4. The score of 4 resembles a slightly pronated foot and I wonder if this is a 'flat foot'.

Response: Thank you for this comment. Please see detailed response to a similar comment from Reviewer #1 above.

Methods - Line 41 (starting Objective physical function ....). Why was the timed stair test chosen as an outcome measure?

Response: Stair negotiation is a recommended activity for assessment of physical function in people with knee OA (OARSI recommendation, see Dobson et al, Arthritis Care and Research 21:1042-1052, 2013). In addition to being a common activity of daily living that is reported as difficult to perform by people with knee OA, there are also suggestions that stair negotiation may be one of the most responsive outcomes of physical function assessment in this patient
population (Kennedy et al, BMC Musculoskeletal Disorders 7:100, 2006). The timed stair climb test is commonly used in many knee OA intervention studies, and represents a core objective assessment of physical function in our laboratory.

**Results**

Response: These have been added as requested.

Response: Thank you for allowing us to clarify this. We have now provided the randomization frequency (first paragraph of Results). We have also now provided a summary of the randomization order for the 17 individuals who preferred the combined insole. This was done in order to provide evidence against any period effect or recall bias when presenting preference data. Specifically, 10 of the 17 participants who preferred the combined insole received this intervention in months 0-2 (first iteration), while 7 received the combined insole in months 4-6 (second iteration). Thus, we do not believe that treatment order had any impact on self-reported preference.

Response: Thank you. This has been added. Please see response to comment above regarding our preference for discussing this reference here rather than the Introduction.

**Discussion**

Response: To our knowledge, we are unaware of any knee OA lateral wedge studies that have specifically included or excluded (“exclusion” now added to text) people based on foot type. If the Reviewer is aware of any we would be happy to reference them here.
Discussion - Line 44 (starting sample of flat foot posture...). What about other foot postures and do you think that static alignment and the FPI is responsive enough to predict biomechanical and clinical response? From previous research, it appears that rearfoot posture has more influence than more distal foot features.

Response: Thank you for bringing up this excellent point. It is likely that dynamic foot function is better able to predict clinical and biomechanical outcomes better than static measures. Indeed, Dr. Jones’ group has shown that angles obtained during a dynamic gait analysis (for example, rearfoot eversion) were able to predict which individuals with knee OA were able to reduce the knee adduction moment with the use of lateral wedges (Chapman et al, Osteoarthritis and Cartilage 23:1316-1322, 2015). Whether a static measure could do the same is unknown, though intuitively one would think that a dynamic measure would be more sensitive to changes in gait outcomes than a static measure.

The FPI was used in the present study not to predict biomechanical or clinical responses, but rather to classify foot type using measures that are available to clinicians (motion analysis systems are limited in this task simply due to a lack of access for many clinicians and patients). Therefore, while an interesting question, it is beyond the scope of this study, and we would be underpowered to do so with the current dataset.

Table 1 - The sex distribution does not match the numbers at the top of the table? The foot posture SD is 4.6, please provide the range of foot postures rather than the median. The KL4 line can be removed as this is not needed.

Response: Thank you for identifying the error in the sex distribution. This has been corrected. As previously presented, the “4,6” for the FPI pertained to the 25th and 75th percentile values. We have now provided the minimum and maximum (in addition to the group median) scores as requested. The KL4 line has been removed as suggested.

Table 2 - Put the population N in the table to reflect the numbers who completed Lateral wedge and the ones who completed lateral wedges plus arch support.

Response: These have been added as requested.