Author’s response to reviews

Title: The impact of multimorbidity on foot health outcomes in podiatry patients with musculoskeletal foot pain: a prospective observational study

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Author’s response to reviews:

We would like to thank both reviewers for their time and efforts in undertaking their reviews of our manuscript. We have addressed the reviewers’ comments in full and have provided a point-by-point response to each suggestion for revision below.

Reviewer 1

Major revisions

1. The response and attrition rates are troublesome. If I read your paper correctly, 1329 invitations were sent of which 193 responded (14.5% response rate), of the 154 who were eligible, 115 enrolled (74.7% response rate), of which 62 completed the FHSQ at three time-points (46.1% attrition rate). You report in your results an overall response rate of < 10%, therefore a 5% completion of all FHSQ domains. Therefore, how useful are these data? I see in the discussion that limitations are mentioned around this, but I think this could be made clearer that not only did you have a high attrition rate, but the original response rate was low, limiting your generalisability. Are you able to perform an analysis on whether the non-responders differed from the responders?

Response: Thank you for this comment. First of all we’d like to point out to the reviewers and editors that we have been open and transparent about how our data were obtained, the limitations concerning sample size, response rate, attrition and missing data, and have gone to considerable lengths to mitigate these limitations in the methods.
Perhaps the nature of the way response rate was calculated and presented initially has led to some undue concern. Given that this was not a survey where invitations were sent exclusively to eligible participants, and that interested subjects were required to contact the researcher directly to indicate willingness to hear more about the study (a condition of our ethics application approval), it is perhaps unsurprising that the initial response rate would be low. The likely reasons are a lack of interest in the study/contacting the researcher, or failure to meet inclusion criteria. As such, the response rate should be considered in light of the fact that not all of the 1,329 patients invited would have been eligible to participate. For survey research response rates of ~10% are not uncommon in studies which send invitations to eligible subjects only. The generalisability of the 10% to the 100% are considered in the context of limitations of a low response rate. We are not suggesting that 115 participants are representative of the 1,329 invitees in our study.

As mentioned in the method “Recruitment” section, potentially eligible participants were invited and willing participants were required to contact the researcher if interested in participating. The enrolment rate of 74.7% is accurate (i.e. the denominator should be n of eligible participants). We also point out that attrition differs from missing data, and so our attrition rates are accurate as presented. Missing data is addressed in full elsewhere in the manuscript. We have removed the term “response rate” which is more aligned to survey research and have replaced this with the term “recruitment rate”. We have added comment to our limitations section for clarity on this matter.

2. Why haven't you performed a between-group analysis using regression? Furthermore, the analysis may be too rudimentary to accurately describe change data in this cohort. It may be more useful to see if multimorbidity predicts a change in pain, rather than how pain changes within groups over time (particularly given your small sample size). This type of analysis will also allow for the determination of the magnitude of the difference between groups. This would also enable you to adjust for other confounding variables.

Response: Agree. We have now conducted unadjusted and adjusted (baseline FHSQ domain, age, BMI) linear regression analyses and have amended the statistical analysis, results, discussion and conclusion sections as a result.
3. It is unclear if you adjusted for baseline score in the analysis reported in Table 5 - if not, why not? Baseline score are likely going to be significant. This may be clearer to only present the change in FHSQ scores from baseline, rather than the actual scores at each time point. I would remove Table 5 - but this highlights another problem with the reporting, as you have FHSQ change data as a negative value in Table 6, where the opposite is true in Table 5. Moreover, how can change score not be significant in Table 6, but be significant in Table 5? Can you please check this?

Response: Now that we have addressed point 2 above, we have effectively addressed the issue concerning baseline scores with the addition of regression analyses. With regards to the comments concerning tables 5 and 6, table 5 presents median FHSQ domain scores at discrete time points (which can only be scored 0-100), whereas table 6 presents change scores (with negative values indicating improvement, with higher scores on FHSQ indicating better foot health). These values have been checked and are correct. It is possible that differences in change score values between groups can be statistically significant when the difference between discrete values is not statistically significant.

4. It is unusual to have four primary outcome measures. I appreciate that you used the FHSQ which reports four domains, but many authors pick one as their primary (usually pain). Are you able to justify using four, as it risks finding spurious results.

Response: Please note that we have not stated that we are using 4 separate primary outcome measures anywhere in the manuscript. We are not convinced that the specification of a primary outcome measure is relevant/necessary here for several reasons. The main outcome of interest is foot health, which is measured by the 4 domains of the FHSQ. The FHSQ does not have an overall summary score derived from all 4 domains. The specific identification of a primary outcome is of major importance in randomised controlled trials when it is closely linked to sample size, power calculations and the testing of a primary hypothesis/research question. This study is not a trial but an observational study. Moreover, the selection of 4 domains are clearly relevant to our objectives as specified, which are not concerned with effectiveness of an intervention, rather the influence of multimorbidity on foot health outcomes in a group exposed to podiatry.

5. Can you run an analysis on how the three groups differed at baseline for basic demographics?
Response: Yes, we have undertaken a baseline analysis on baseline demographics between groups. These are presented in table 1 and in the manuscript text under heading “Morbidity group demographic and clinical characteristics”. We have added details in the statistical analysis section, have added all p values for clarity, and had added symbols to table 1 to identify significant differences between groups at baseline.

6. The non-standardised treatments or diagnoses make drawing conclusions about multimorbidity status and response to treatment quite hard to interpret. Perhaps those with multimorbidity had more significant foot diagnoses? or were older? Or had more obesity?

Response: We agree that is it a complex issue. Specific foot diagnoses were not available but we have attempted to describe the severity and location of foot pain in table 3 in addition to foot health characteristics at discrete time points and over time. From our analyses it seems that those with multimorbidity had more severe foot pain and generally poorer foot health outcomes at baseline and throughout the study. In the regression analyses that was undertaken in response to reviewer point 2 above, we have attempted to address concerns about baseline foot health scores, age and obesity. We appreciate that the treatments are not standardised in the sense that this was not a trial of a single intervention, but an observational study of patients exposed to usual (standard care) podiatry (which we have attempted to describe in table 4). However, this arguably could be viewed as a strength for external validity of the study, in that the treatments received were delivered routinely within the NHS GG&C podiatry service.

7. In your results section, it would be more helpful to have reporting of descriptive data, rather than just the p values, which are in difficult to interpret in isolation.

Response: It is unclear to us which descriptive data are necessary here or what section of the results the reviewer is referring to. Further to checks, we can confirm that all p-values are presented with corresponding descriptive data in tables and/or figures. If there are specific descriptive data missing please do let us know and we will add it to the manuscript.

8. I'm not sure if your conclusions reflect your data. You didn't find significant between group differences in change data (Table 6), and in order to make firm conclusions on the significance of multimorbidity, I would expect more rigorous data analysis.
Response: Please see revised analyses in response to point 2, and revisions to the manuscript conclusions as a result. These analyses appear to address this point in full.

Minor revisions

9. You are reporting the IQR as a range, rather than as a single value throughout the paper. Have you used range instead of IQR? Furthermore, Line 196 reported 'inter-quartile ranges', consider changing to inter-quartile range'

Response: This seems like more of a reviewer preference than a conditional revision. We will leave this for editorial discretion. We have published IQR as a range from 25th quartile to 75th quartile with this journal previously and do not believe that this is a formal requirement.

10. Tables and figures should be at the end of the paper.

Response: Tables less than one A4 or Letter page in length can be placed in the appropriate location within the manuscript.

11. It would be useful to conclude the first paragraph with a sentence as to why this study is important.

Response: Respectfully disagree. This seems more of a discretionary revision. Information on why the study is important is provided in the abstract and throughout the background section with relevant context.

12. Line 154: self-reported height and weight?

Response: Thank you, revisions made.

13. Line 168: suggest change from '(>1 conditions)' to '(>1 condition)'

Response: This seems like more of a reviewer preference than a conditional revision. We will leave this for editorial discretion.
Response: Thank you, revisions made.

14. Table 2: Can you justify why you didn't consider obesity as a comorbidity?

Response: Current multimorbidity research largely, but not exclusively considers (rightly or wrongly) obesity to be a risk factor as opposed to a specific long-term health condition (Duffield et al, 2017). In a practical sense, obesity is not currently included in the self-administered comorbidity questionnaire which we used to assign morbidity group. As per our response to reviewer comment 2 – we have used BMI in our adjusted regression model and it was not a significant independent predictor for any FHSQ scores at 3 or 6 months. We also (in response to reviewer 2) have provided details in the discussion concerning the definition of multimorbidity which acknowledge differences in the literature.


15. Line 373-376: Why didn't you look at these data in your cohort to determine if this was indeed the case?

Response: Those data analyses would be addressing a different aim and are therefore outwith the scope of the current study. We also note that the article is already rather long and data heavy.

16. Fig 2 and Fig 3: I don't think both of these are necessary. Fig 3 graphics would need improving if you decide to keep it

Response: Thank you, we have deleted figure 3 from our submission and have revised fig 2 accordingly.

17. Table 2:
Response: Thank you, revisions made.

Reviewer 2

1. Foot pain prevalence citations: reference #2 is a systematic review which includes references 1, 3 and 4, so there's no need to cite them all.

Response: Thank you, revisions made.

2. Generalisability: the overall response rate was very low (8.65%). This is acknowledged by the authors as a key limitation of the study. However, it would also be helpful for readers (particularly those outside the UK) if the authors could provide some explanation as to what the criteria are for patients to be referred to 'podiatric biomechanics' clinics (as opposed to other types of NHS podiatry clinics) as this influences the sample denominator. In addition, are there any data that can be extracted from the TrackCare management system (eg. age, sex) that could provide insights as to how respondents differed to non-respondents?

Response: We would like to refer the reviewer to our response to reviewer 1 comment 1, which identifies a similar issue concerning low response rate. Briefly, we acknowledge that the term response rate as initially presented was not accurate as this suggested that all subjects invited to participate were eligible. Whereas, the recruitment rate (or conversion/enrolment rate) from the number of eligible participants invited is far more favourable (74.7%).

With regards to the criteria for referral, or rather allocations of referrals to specific clinic types: referrals (either self-referral by phone or clinician referral letter) are vetted by the NHS podiatry team. Referral allocations to podiatric biomechanics clinics are at the discretion of vetting podiatrists, but are largely comprised of complex MSK foot pathology. We have amended the Participants and Setting section of the Methods accordingly to acknowledge this.
While age and sex values for non-responder analysis would have been available – TrakCare is not yet ideally set up for extraction of this data and as such it remains cumbersome and time consuming. We did not have sufficient resources in place to cover the admin time required for extracting this data for analysis. Screening of clinic lists via TrakCare was conducted by an NHS GG&C podiatrist with TrakCare clearance and not by an immediate member of the research team.

3. **Accuracy of self-report:** can the authors provide any data on the accuracy of self-reported conditions using the Self-Administered Comorbidity Questionnaire? Previous studies of self-reported medical history checklists have found that they are reasonably accurate, except for some conditions such as arthritis [1, 2].

Response: We have added a section to the limitations section of the discussion concerning the construct validity of the SCQ which appears to vary according to index condition. We do not believe this would have been a significant vulnerability to our study given the role of the SCQ in group allocation only.

4. **Definition of multimorbidity:** there is some inconsistency in the literature in relation to the definition of multimorbidity (see: [3]). The authors have used 2 or more conditions, which is consistent with the WHO definition (World Report on Ageing and Health, 2015). It would helpful to state this, but also to mention in the discussion that the application of different definitions of multimorbidity will influence study findings.

Response: Thank you, we have added our definition to the methods and have acknowledged the variety of definitions in the discussion.

5. **Total number of conditions:** it would be helpful for the authors to report the median and range of total conditions in the sample rather than just the percentages in each of the three groups.

Response: Thank you, revisions made.
6. Adjustment for confounders: the paper reports comparisons in FHSQ scores between the three groups (Table 5), however the data presented in Table 1 suggests that age and BMI are positively associated with the number of conditions. Would the authors consider age and BMI (and possibly sex) to be confounders of the association between multimorbidity and FHSQ scores? If so, should these comparisons be adjusted?

Response: We thank the reviewer for this comment and refer to our earlier response to reviewer 1 comment 2 which led to revision of our statistical analysis and the addition of multivariate linear regressions with adjustment for confounders.