Author’s response to reviews

Title: Foot structure, pain and functional ability in people with gout in primary care: cross-sectional findings from the Clinical Assessment Study of the Foot

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Author’s response to reviews:

Reviewer #1: Thank you for the opportunity to review the article. I enjoyed some of the new insights provided by the authors. I have a few general comments to address:

Response: Thank you for your comments, we have addressed each of these below.

Comment 1: Participant inclusion criteria - How can you truly be sure your all your participants had gout?

Response: We agree that we cannot be sure all our participants had gout, however, previous studies have demonstrated the validity of a gout diagnosis in primary care. Meier and Jick (1997) showed that a diagnosis of gout recorded in medical records in the UK had a positive predictive value of 90%. Cheng, Kao et al. (2011) have shown high agreement between gout diagnosis across two databases. Our original manuscript did discuss the validity of a primary care gout diagnosis, citing the study by Meier and Jick. We have now expanded this discussion to more explicitly highlight the validity of gout found in their study as follows (page 15 line 23-25):

“Previous studies, however, have shown that GP diagnosis is reliable [32, 33] with the positive predictive value of a recorded diagnosis of gout in UK medical records being 90% [32].”
Comment 2: With regard to the inclusion criteria can the author please comment/justify on why the 2015 ACR/EULAR criteria were not used? Reference below. This needs to be highlighted a limitation of the study


Response: The 2015 ACR/EULAR criteria were not used as they were not published at the time of data collection (2010/11). We have highlighted this as a limitation in the discussion section (page 15 line 25-26):

“New classification criteria have been published by ACR/EULAR [34], however publication took place after we completed data collection for this study.”

Comment 3: Introduction - The authors have missed a key reference that will add context to the introduction that describes gait and ankle function in gout.


Response: Thank you for drawing our attention to this article. We have now added this information in the introduction and referenced this article (page 3 line 10-15).

“Four small cross-sectional studies performed in New Zealand recruited adults with chronic gout from rheumatology clinics and found higher levels of foot-related pain and disability, reduced peak ankle joint angular velocity and slower walking speed with longer step and stride lengths, reduced range of motion in the 1st MTPJ dorsiflexion, lower peak plantar pressures in the hallux and had higher pressure time integrals in the midfoot compared to participants without gout [4-7].”

Comment 4: Disease severity and duration - You report the disease severity may be lower in your participants compared to studies cited in your introduction. How do you know the disease severity is lower in your population? Can you please provide further detail surrounding disease
severity and duration so the reader can put your data into context? This would include inclusion of:

Medications

Serum urate levels

Response: The statements in the introduction and discussion that gout severity in our study population is likely to be lower than in other studies which recruited from secondary/tertiary care populations is based on the majority of gout patients being treated in primary care, with only more severely affected cases or those failing to tolerate or not respond to standard treatments (such as allopurinol) being referred to secondary care. On this basis, it seems reasonable to assume that patients in our primary care cohort would have less severe gout than those in previous studies which recruited from secondary/tertiary care. We have revised text in the introduction as follows (page 3 line 16-18):

“However, the generalisability of these findings and whether they can be reproduced in a primary care gout population where disease severity is likely to be milder is unknown.”

This has also been summarised in the discussion (page 13 line 17-21).

“It seems likely that the differences between our findings and those of these previous studies could have arisen from our gout cases having less severe gout (which seems likely in a population recruited from primary care compared with a specialist clinic) and/or our non-gout participants also having foot-related problems.”

However, we agree that we should ideally explore this assumption in our data where possible. Unfortunately, we did not collect information about disease severity or duration, and serum urate levels were tested in a very small minority of participants during the period of time for which we had access to medical record data.

12 (46.2%) gout patients were prescribed allopurinol and this information has been added to Table 1.

Comment 5: The inclusion of ethnicity data is also important particularly when comparing UK data to US and Australasian data.
Response: The majority of participants were White UK or European, consistent with the demographic composition of the population from which the participants were recruited. This information has now been included in Table 1.

Comment 6: Subtalar joint motion - Whilst you did demonstrate that frontal plane motion in the rearfoot was reduced compared to control participants I note the mean values for the gout groups still falls within clinically accepted expected normal values. That is, 20° inversion and 10° eversion, a 2:1 ratio. Although there has been research in the last 3 years questioning the use and validity of measures related to STJ motion these measurement norms are still used clinically. Based on your data do you feel the STJ is functionally restricted being that you have demonstrated a relatively normal value for rearfoot frontal plane motion?

Response: We measured inversion and eversion at the ankle/STJ with the ankle in relaxed plantarflexion with the participant supine, as described by Menadue, Raymond et al. (2006). As such, our results cannot be directly compared to the ‘traditional’ frontal plane STJ measurements commonly used by podiatrists, which generally involves placing the participant in a prone position and cupping the calcaneus to move through the frontal plane range of motion. In the original manuscript (Menadue, Raymond et al. 2006) describing the method we used, 30 healthy participants were assessed, and the mean values were 33° of inversion and 11° of eversion. As such, the values we obtained for our gout participants (21° of inversion and 10° of eversion) reflect abnormally decreased overall ankle/STJ range of motion, relative to both the non-gout participants in our study and normative values reported in the literature.

Comment 7: I feel your findings surrounding frontal plane rearfoot motion should state that you found decreased frontal plane motion in the rearfoot when compared to controls in a non-weightbearing positon. As opposed to simply stating reduced STJ motion. I feel there needs to be a clear distinction between non-weightbearing and weightbearing findings. The reason behind this is that based on provided you are able to make inferences between a static non-weightbearing measurement and dynamic function.

Response: We have added “non-weightbearing” when referring to the range of motion measurements and have reworded “subtalar joint motion” to “subtalar joint range of motion” to clarify that we are referring to static weightbearing measurements rather than dynamic foot function throughout the manuscript.
Comment 8: Ankle OA - A point that should be raised in your limitations is that you did not determine the extent to which the participants with gout were affected by OA. You state that OA could be a cause of reduced STJ ROM but it is not clear if you population had ankle OA? I find this statement to speculative based on the data provided.

Response: This point pertains to possible explanations for the limited subtalar range of motion in gout participants relative to controls. Whilst we agree with the suggestion that our subtalar joint OA explanation is speculative, we did not base this statement on the data provided but rather attempted to hypothesise potential explanations for this observation. Whilst we recognise the importance of not over-speculating, we note that reviewer 2 (comment 13) has asked us if we can suggest possible mechanisms underlying the similar observation at the 1st MTPJ. We have therefore reworded this paragraph in an attempt to suggest possible explanatory mechanisms for limited range of motion at both the 1st MTPJ and subtalar joint whilst highlighting the need for further research (page 14 line 7-16):

“The causes of limited 1st MTPJ and subtalar range of motion are unknown. Both joints are affected by gout and hence it is possible that features of gout such as synovial inflammation or tophus could play a role [7,26,27]. A possible alternative explanation for limited range of motion is OA [5], although non-traumatic OA of the subtalar joint is uncommon. First MTPJ OA is common in people with gout [3]. We could not explore these possibilities in the current study and further research is warranted.”

Comment 9: Walking Speed - You state you found no significant differences in walking speed. Could you please provide more detail on how you measured gait speed? The differing methodologies of measurement will be one of a few possible reasons for the differences found in your study versus previous study. This needs further discussion as you findings differ from numerous recent publication.

Response: Participants were instructed to walk an 8-foot course at their usual speed and each participant was timed for two walks. The faster of the two walks was used for analysis. This information has been summarised and added to page 5 line 11-16.

“Short Physical Performance Battery (SPPB): participants were observed performing a series of tests; standing balance test (based on the held side by side stand for 10 seconds, held semi-tandem stand for 10 seconds, and held full tandem stand for less than 2 seconds; 3-9 seconds and
10 seconds), time taken to rise from a chair 5 times, and gait speed test (fastest of two timed walks of an 8-foot course at the participants usual walking speed).”

The methodologies to measure speed differed between studies. Our study measured the time taken for participants to walk an 8-foot course at their own speed. Rome, Survepalli et al. (2011) and Stewart, Dalbeth et al. (2016) used electronic walkways to measure velocity of participants’ usual speed. Rome, Survepalli et al. (2011) used a longer walking course of 3.7 meters and Stewart, Dalbeth et al. (2016) used 6.1 meter course. We agree that these differing methods need to be considered when comparing findings of these studies and have acknowledged this in the discussion (page 14 line 1-3):

“However, the methods used to assess walking speed in our study and other published studies differ, requiring caution when comparing findings of these studies.”

Reviewer #2: Thank you for the opportunity to review this manuscript which assessed a number of foot characteristics (pain, structure, function) in primary care patients with gout compared to people without gout. Although the manuscript is written well, there are a number of major methodological issues which need consideration.

Response: Thank you for your comments, we have addressed each of these below.

Comment 1: Firstly, participants in both groups were derived from an existing study which included only people with foot pain (and most likely also foot problems). This is likely the reason the authors found no differences in foot pain, lower limb function and other foot deformities between the two groups. Considering the large number of variables assessed (>50), it is possible that the only two differences between the groups (STJ and 1MTP ROM) were due to type 2 error. What is the clinical importance of comparing people with gout to people with foot pain?

Response: We originally acknowledged in the discussion that type 2 errors may have occurred but this may have been unclear. We have therefore rephrased this sentence (page 15 line 15-17).

“Considering the large number of variables assessed for differences between gout and non-gout participants, type 2 errors were more likely to occur.”
Both gout participants and non-participants were originally recruited to a study of foot pain as explained in the methods section of the original manuscript on page 4, and hence both gout and control groups reported foot pain in the last 12 months. Although no differences in foot pain, lower limb function or deformities were found between the two groups, we therefore consider that gout is a plausible explanation for differences in 1st MTP and subtalar range of motion between the groups.

Comment 2: Secondly, the inclusion criteria for participants with gout included reviewing medical records 18 months after the date in which the participant attended the clinical assessment. If a participant developed symptoms of gout 18 months after the study took place, then they did not actually have gout at the time the data was collected and therefore should not be included in the gout group.

Response: We identified prevalent gout consulters within the period 18 months before and after the clinical assessment rather than newly diagnosed incident cases of gout. As the reviewer points out in comment 6 below, recruiting people aged ≥50 years means that participants were likely to have had gout for some time rather than being incident cases. Furthermore, we did not consider temporal relationships in this study but instead considered the study to be cross-sectional in design, where we compared foot and ankle characteristics between prevalent (and as the reviewer suggests, likely long-standing) gout cases identified in the three-year window and gout-free controls.

Comment 3: Thirdly, the characteristics of the participants with gout are not described (page 4, line 23). It is important to include information about disease duration, medications, flare history (including flare at time of assessment), serum urate levels and the presence of subcutaneous tophi. The authors acknowledge that joint aspiration was not performed to definitively confirm gout diagnosis (limitations section of discussion), however was this information not available in the medical records? Furthermore, no clinical criteria was used to confirm diagnosis either (i.e. the ACR/EULAR Classification Criteria for Gout). Were the patients on any urate lowering therapies? Were there any records of imaging studies (ultrasound, x-rays) available to help confirm diagnosis? (page 4, lines 16-18).

Response: Please see also our responses to reviewer 1, comments 2 and 4. The ACR/EULAR criteria were not used as they were published in 2015, some time after data were collected (2010/11). Unfortunately, we did not collect information about disease severity or duration, and
serum urate levels were tested in a very small minority of participants during period of time for which we had access to medical record data. Information about the number prescribed allopurinol has been added to Table 1.

Comment 4: Title: Consider revising the current title of the manuscript (Impact of gout on foot structure, pain and functional ability: cross-sectional findings from the CASF). You cannot determine causality (i.e. "impact of gout") from a cross-sectional design. This is particularly problematic with the current methodology which included people with gout who may have been diagnosed with gout 18 months after data collection took place.

Response: Thank you for this feedback. We have changed the title:

‘Foot structure, pain and functional ability in people with gout in primary care: cross-sectional findings from the Clinical Assessment Study of the Foot’.

Comment 5: Background: The primary justification for the study seems to be that participants with gout were recruited from primary care settings as opposed to secondary care settings. If so, this theme should be incorporated into the discussion and perhaps also the title of the manuscript. The authors may also like to include reference to these additional studies in their introduction (and discussion) which have examined foot characteristics in people with gout including joint range of motion: Journal of Foot and Ankle Research 8:41 doi: 10.1186/s13047-0150091-8; Journal of Foot and Ankle Research 10:25 doi: 10.1186/s13047-017-0207-4; Gait and Posture 44:18 doi: 10.1016/j.gaitpost.2015.11.004

Response: As indicated in our response to the previous comment, we have now included the primary care setting in the manuscript title. Comparison of our results with other studies conducted in secondary care were originally discussed from page 13 line 12 onwards.

We have referenced Stewart, Dalbeth et al. (2015) to refer to range of joint motion in the introduction (page 3 line 10-16) and discussion (page 13 line 23-25).

“Four small cross-sectional studies performed in New Zealand recruited adults with chronic gout from rheumatology clinics and found higher levels of foot-related pain and disability, reduced peak ankle joint angular velocity and slower walking speed with longer step and stride lengths, reduced range of motion in the 1st MTPJ dorsiflexion, lower peak plantar pressures in the hallux and had higher pressure time integrals in the midfoot compared to participants without gout [4-7].”
“This finding is similar to a previous study which found a larger reduced range of motion by 17.9° (compared to 8.7° in our study) at the 1st MTPJ in gout compared to non-gout participants [7].”

Comment 6: Methods: Page 3, line 21: the inclusion of participants older than 50 years should be discussed. As gout tends to present in the mid-third to fourth decades, it is possible that people with gout in the current study may have had the disease for quite some time.

Response: We agree gout participants are likely to have gout for a long period and we have included this on page 13 line 16-17.

“As gout tends to present itself after the third decade of life, it is possible participants have had gout for a number of years.”

Comment 7: Statistical analysis: I'm not sure that simply including a random intercept is sufficient to account for the repeated right and left foot measures. Was a random effect of foot side (right or left) also included? This paper may be helpful: Gait Posture. 2018 Jan;59:182-187. doi: 10.1016/j.gaitpost.2017.10.018

Response: Multilevel regression models were used to account for the clustering/correlation of outcomes measured in the left and right feet within the participant. This clustering was controlled by fitting a random intercept at the participant level allowing outcomes measured in the left and right feet to vary within the participant.

A random intercept at the foot level is not needed as there were no repeated measurements within the left and right feet i.e. it was not a three-level model which appears to have been used in the paper.

Comment 8: Results: Page 8, lines 13-18: obviously there will be no differences in foot pain and disability between the groups since participants in both groups were initially included only if they had foot pain. It is unclear why pain-related variables are included.

Response: Similar to reviewer 2 comment 1, both gout cases and non-gout controls were recruited from a study of people with foot pain as explained in the methods (page 4). However,
although participants in both groups had foot pain, it could not be assumed that foot pain would be of the same severity and in the same location in both groups. Hence, it was of interest to compare the severity and location of foot pain between the groups.

Comment 9: Tables 3 & 4: If the repeated right and left foot measures have been correctly accounted for in the analyses, then reporting data separately for right and left feet is not necessary. I suggest combining right and left foot data together and reporting n (%) for the number of feet rather than number of participants (Table 3). Also consider incorporating the ORs/estimated means reported in Table 4, into Table 3 (i.e. so you only have one results table). There is a lot of data presented which can be overwhelming to the reader. Also, did you consider analysing the data to determine the odds of having a feature present in one group vs having the feature present in the other group (i.e. reporting a single odds ratio per variable, rather than an odds ratio for each group)? This would further simplify the results for the reader.

Response: We thank the reviewer for these suggestions and have given them due consideration. However, after reviewing the results and tables, we respectfully disagree with the reviewer and prefer to maintain the current table structure. Two tables (tables 1 and 3) provide only descriptive data and table 2 is fairly brief and presents a relatively straightforward comparison of person-level variables between the gout and non-gout groups. Table 4 is slightly longer but presents a comparison of foot-level variables between gout cases and controls which we feel readers should be able to comprehend. The only table to present data separately for left and right foot is table 3. We note the reviewer’s suggestion to combine left and right feet together for the purposes of analysis and to report n (%) for the number of feet. However, although not uncommonly undertaken in studies of this nature, this approach would assume that observations in the right and left feet (1) have similar distributions (which may not be the case) and (2) are independent of each other within the participant (which they are unlikely to be). It was precisely for this reason that we undertook multilevel regression modelling to account for the correlation between feet (Bouwmeester, Twisk et al. 2013). We respectfully feel that the volume of data is manageable and less than that presented in many epidemiological/observational studies.

Comment 10: Discussion: Overall, the discussion could be stronger with respect to comparing the findings from the current study with existing literature. This would be a good opportunity to discuss any similarities/differences between primary care and secondary care patients with gout (i.e. the main justification for the current study).
Response: Similar to reviewer 2 comment 5, comparison of findings between the current study conducted in primary care and existing literature conducted in secondary care were originally discussed from page 13 line 12 onwards.

Comment 11: Page 12, line 6: reporting that people with gout are more likely to have HV in the left foot is a very odd way to report results. I think you should focus on the pooled right/left foot results from an accurately adjusted model (see comment above).

Response: For the reasons explained in response to comment 9 above, it would not be statistically appropriate to pool right and left feet and present the n (%) for the number of feet. However, we have removed this sentence from the discussion (page 13 line 6-8) and focused on the pooled results (page 13 line 9-11).

“This study found that people with gout recruited from a UK primary care population have reduced non-weightbearing range of motion in the subtalar and the 1st MTPJ joints compared to those without gout and were more likely to have a mallet toe deformity. In contrast, people with gout were less likely to have a claw toe deformity compared to those without gout”

“There were no consistent differences between gout and non-gout participants in foot pain location, including the 1st MTPJ and hallux, and presence of hallux valgus.”

Comment 12: Page 12, line 20: it is possible that the reason you did not find that people with gout walked slower is because both groups had foot pain. Foot pain is known to be a mediating effect of walking speed, particularly in people with gout (Gait and Posture 44:18 doi: 10.1016/j.gaitpost.2015.11.004).

Response: We thank the reviewer for this point and have added this to the discussion (page 13 line 27 – page 14 line 1).

“This may be due to both gout and non-gout participants having foot pain which is known to have a mediating effect on walking speed [25]”

Comment 13: Page 12, line 25: the authors state that 1MTPJ ROM was limited because gout commonly affects that joint. Can you be more specific - what aspects of gout contribute to
reduced joint motion? Pain? Swelling? Tophus? This paper reported a similar finding and may be helpful: Journal of Foot and Ankle Research 8:41 doi: 10.1186/s13047-0150091-8

Response: We note that this article has suggested that reduced ROM at the 1st MTPJ in gout could be due to inflammation, OA or a pain avoidance mechanism. As the reviewer suggests, tophus could also be a contributing factor. We are also mindful that reviewer 1 (comment 8) has cautioned against being too speculative about underlying mechanisms of reduced ROM at the subtalar joint. We have however revised the text in this paragraph to acknowledge these possibilities pertaining to the 1st MTPJ and subtalar joints and highlight the need for further research as follows (page 14 line 7-16):

“The causes of limited 1st MTPJ and subtalar range of motion are unknown. Both joints are affected by gout and hence it is possible that features of gout such as synovial inflammation or tophus could play a role [7,26,27]. A possible alternative explanation for limited range of motion is OA [5], although non-traumatic OA of the subtalar joint is uncommon. First MTPJ OA is common in people with gout [3]. We could not explore these possibilities in the current study and further research is warranted.”

Comment 14: Page 13: lines 1-3: The presence of secondary/concomitant OA was not measured so it is difficult to make this claim, particularly since all participants were older than 50 years, and both groups were likely to have some form of OA. Perhaps in reference to ankle joint function, the authors may find this paper helpful: Gait and Posture 63:150 doi: 10.1016/j.gaitpost.2018.04.020

Response: As highlighted in the response to the previous point, we have revised this section to highlight the need for further research into mechanisms underlying limited range of 1st MTPJ and subtalar range of motion, including a possible role for OA.

Comment 15: Page 13: lines 7-9: There are a number of studies which have assessed foot posture in people with gout (your reference #4 and: Arthritis Care & Research 64:3 doi: https://doi.org/10.1002/acr.20670; Journal of Foot and Ankle Research 8:41 doi: 10.1186/s13047-0150091-8). There is also the possibility that FPI was not accurately captured due to people adjusting their foot position to offload pain. In people with gout, there are also other variables that affect FPI such as tophus deposition which can significantly alter foot alignment.
Response: We thank the reviewer for these points which we have added to the discussion (page 14 line 23-25):

“There is also the possibility that foot posture index may not have been accurately captured as people could adjust their foot position to offload pain [29]. In people with gout, tophus deposition may significantly alter foot alignment [29].”

Comment 16: Page 13, lines 10-12: This does not make sense. Do you mean "consistent", not "inconsistent". This study found that people with gout had more HV: Journal of Foot and Ankle Research 8:41 doi: 10.1186/s13047-0150091-8

Response: We apologise for the confusion here. Reference 26 in the submitted manuscript was incorrect and should have been: Roddy et al. Gout and nodal osteoarthritis: a case-control study. Rheumatology 2008;47:732-2. This study and the article by Stewart, Dalbeth et al. (2015) highlighted by the reviewer both found that people with gout had more hallux valgus than controls without gout. Hence, our finding that people with gout were less likely to have hallux valgus in the left foot is indeed inconsistent with the findings of these previous studies. We have corrected the reference and added the paper by Stewart, Dalbeth et al. (2015) reporting these findings as follows (page 15 line 1-3):

“People with gout were less likely to have hallux valgus in the left foot, which is inconsistent with previous studies where hallux valgus was more prevalent and more severe in people with gout [7,30].”

Comment 17: Page 13, line 14: HV is not always painful.

Response: We recognise that hallux valgus is not always painful. However, hallux valgus is more common in people with foot pain (Roddy, Zhang et al. 2008) and therefore the fact that our control group comprised individuals with foot pain might explain why our findings about the association between gout and hallux valgus was inconsistent with previous studies.

Comment 18: Page 13, lines 15-17: HV can actually be asymmetrical
Response: Similarly, we recognise that hallux can be symmetrical, and in fact is more commonly bilateral than unilateral (Roddy, Zhang et al. 2008). We made the point that hallux valgus would not be expected to affect the left foot more or less commonly than the right to emphasise that our finding that people with gout were less likely to have hallux valgus in the left foot but not the right may be a spurious finding. We have revised this sentence to make this point clearer (page 15 line 6-9):

“However, there is no pathophysiological reason to expect hallux valgus to preferentially affect the left foot less commonly than the right in people with gout, and this association disappeared when examining hallux valgus across both feet, suggesting a possible spurious finding.”

Comment 19: Page 14, lines 5-7: the authors state a limitation was the inability to distinguish which foot was affected by gout. By this do the authors mean by an acute flare of gout? Also note, that neither foot may have had a history of acute involvement. Also, research has shown that even during asymptomatic periods, people with gout still report pain and disability and exhibit structural and functional impairments (Journal of Foot and Ankle Research 8:41 doi: 10.1186/s13047-0150091-8)

Response: We recognise that some impairments may persist during asymptomatic periods. However, it is not uncommon for patients with gout to report ever having symptoms in only one foot and therefore knowing the laterality of involvement would be ideal when exploring foot-level characteristics such as range of motion or foot posture. For this reason, we acknowledged not knowing which foot had been affected by gout as a limitation.

Comment 20: Page 2, line 17 and line 22: be consistent with abbreviation of metatarsophalangeal joint. I.e. use either MTPJ or MTP.

Response: We have changed the wording from MTP to MTPJ throughout the manuscript.

Comment 21: Page 3, line 4: change "…resulting in severely painful acute attacks" to "which may result in severely painful acute attacks". MSU deposition can be subclinical and asymptomatic and does not always cause acute symptoms of gout.
Response: We have changed this as requested on page 3 line 2-5.

“The causal risk factor is hyperuricaemia, leading to the formation of monosodium urate (MSU) crystals in and around the joints, which may result in severely painful acute attacks and a chronic arthropathy”

Comment 22: Page 3, line 6: change "commonly affects the…” to "commonly affecting the…”

Response: We feel this sentence reads well with the original wording and therefore respectfully decline this suggestion.

Comment 23: Page 3, line 9: what do you mean by "chronic effects of gout”’?

Response: To be more clear we changed ‘chronic effects of gout’ to ‘chronic effects of MSU crystal deposition’ on page 3 line 8-10.

“Whilst the predilection of attacks of gout for the foot and ankle is well-recognised, the chronic effects of MSU crystal deposition on foot structure and function have been under-researched.”

Comment 24: Page 3, line 12: this is incorrect. These studies found shorter step and stride lengths in people with gout compared to healthy controls (not longer step and stride lengths).

Response: We have corrected the sentence to ‘shorter step and stride lengths’ on page 3 line 13.

“Four small cross-sectional studies performed in New Zealand recruited adults with chronic gout from rheumatology clinics and found higher levels of foot-related pain and disability, reduced peak ankle joint angular velocity and slower walking speed with shorter step and stride lengths, reduced range of motion in the 1st MTPJ dorsiflexion, lower peak plantar pressures in the hallux and had higher pressure time integrals in the midfoot compared to participants without gout [4-7].”

Comment 25: Page 5, line 4: need to state abbreviation MFPDI in full at first use
Response: We stated the MFPDI stands for the Manchester Foot Pain and Disability Index at first use on page 5 line 7-8.

“Foot function and foot pain: calculated from the Manchester Foot Pain and Disability Index (MFPDI) function and pain subscales [9].”

Comment 26: Page 5, line 12: include more information on the 'gait speed test' and how it was performed

Response: Similar to reviewer 1 comment 9, participants were instructed to walk an 8-foot course at their usual speed and each participant was timed for two walks. The faster of the two walks was used for analysis. This information has been summarised and added to page 5 line 11-16.

“Short Physical Performance Battery (SPPB): participants were observed performing a series of tests; standing balance test (based on the held side by side stand for 10 seconds, held semi-tandem stand for 10 seconds, and held full tandem stand for less than 2 seconds; 3-9 seconds and 10 seconds), time taken to rise from a chair 5 times, and gait speed test (fastest of two timed walks of an 8-foot course at the participants usual walking speed).”

Comment 27: Page 5, line 25: this is incorrect. The FPI is scored between +12 and -12 (not +2 and -2)

Response: We have amended page 6 line 3 to correct for this error.

“Foot posture index: consisted of a six-item assessment of foot posture, with each item scored between -2 to +2, which was then transformed into a single score using Rasch analysis”

Comment 28: Page 6, line 10: what is meant by "deformity" at the 1st MTPJ? What kind of deformity?

Response: Participants were examined for 1st MTPJ and interphalangeal joint hyperextension deformity. We have added this to page 6 line 13-16.
“Deformity: assessed on physical examination, the palpable presence or absence of deformities on all toes, 1st MTPJ, and lesser toes. MTPJ and interphalangeal joint hyperextension were examined at the 1st MTPJ. For the lesser toes, the type of deformity examined were mallet, hammer, claw and retracted toes [19].”


Response: Skin lesions were defined as either having hyperkeratotic lesions and ulcers (plantar and dorsal aspect). This has been added to page 6 line 17-18.

“Skin lesions: assessed by observation (both plantar and dorsal) of each region of the foot (midfoot, greater toe, and lesser toes) for hyperkeratotic lesions and ulcers.”

Comment 30: Page 6, lines 17-18: remove ".. assessment of both feet was performed..". It is already stated above that feet were assessed bilaterally. Also, how was STJ ROM measured? Goniometry?

Response: We have removed ".. assessment of both feet was performed..". Subtalar joint range of motion was measured using a goniometer (page 6 line 22-24).

“Subtalar joint non-weightbearing range of motion eversion/inversion: a standardised assessment measuring the participant’s subtalar joint eversion and inversion in degrees using a goniometer [21]”

Comment 31: Page 7, line 19: why adjust for BMI? What effect might BMI have on the variables measured? Include reference to relevant literature reporting on the association between BMI and foot problems.

Response: We adjusted for BMI as we considered it to be a true confounder of the association between gout and foot characteristics. Obesity is an independent risk factor for gout and has been reported to be associated with several foot problems including foot pain (Dufour, Losina et al. 2017), midfoot OA (Thomas, Peat et al. 2015), plantar pressure (Walsh, Butterworth et al. 2017), and plantar heel pain (Butterworth, Landorf et al. 2012), but may be protective against hallux
valgus (Nguyen, Hillstrom et al. 2010, Menz, Roddy et al. 2011). It therefore appeared to a potential confounding variable that it was appropriate to adjust for.

Comment 32: Page 8, line 1: change "26" to "Twenty six".

Response: This has been changed on page 8 line 5.

“Twenty-six gout participants were identified and then individually matched to four non-gout participants, although two gout participants could only be matched to three non-gout participants each.”

Comment 33: Page 8, lines 7-8: this data is not presented in any tables - perhaps report the data in the text here (i.e. n (%) of participants in each group categorised as being overweight). Also provide BMI cut point definition of "overweight".

Response: We have added this information to table 1.

Comment 34: Page 12, line 21: this is the incorrect reference

Response: The reference for the systematic review has been corrected to ‘Stewart S, Dalbeth N, Vandal AC, Rome K. The first metatarsophalangeal joint in gout: a systematic review and meta-analysis. BMC Musculoskeletal Disorders. 2016; 17:69’ (page

“A previous study [4] and a systematic review [2] also found participants with gout reported higher levels of pain and foot disability than those without gout.”

Comment 35: Page 13, line 12: check that this is the correct reference.

Response: Similar to comment 16, the incorrect reference was used. This has been corrected using two references:


References


