Author’s response to reviews

Title: The challenges of gout flare reporting: Mapping flares during a randomized controlled trial

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Author’s response to reviews:

Dear Dr Mockridge,

Thank you for the further helpful comments of the reviewers. We have made further revisions to the manuscript in response to the comments of reviewer 2. The changes are described in detail below. Page and paragraph numbers refer to the clean version of the revised manuscript.

Tristan Pascart (Reviewer 1):

No further changes needed

Unnamed Reviewer 2 (Reviewer 2)

Thank you for reviewing the comments from my previous review. Whilst the authors have responded to each of the comments addressed I still feel that the research question could be more
adequately answered with an IPD analysis. The authors suggest that this is not in the public domain. However, in systematic review terms, data can be requested from authors to undertaken IPD analyses (as happens in reality) and therefore becomes available if requested. I therefore suggest that if the authors choose not to do this, and the editorial team feel that there is sufficient information in this publication to accept the paper, then the use of an IPD analysis is documented in the Discussion section either as a limitation or as a future research suggestion. This would be beneficial.

Have changes been made: The authors have made a number of changes from Reviewer 1 and 2. However, I would suggest that these (particularly Reviewer 2’s (mine)) have not been adequately reflected in this revised paper and further comments as limitations would be beneficial.

Overall impression: The paper is an improvement from the first version but I would still question how useful this paper is compared to attempting to answer this question with a larger dataset (i.e. IPD analysis). Framing that this paper provides a signal to the results and that further study is warranted could be emphasised to get over this issue.

I would strongly recommend that these changes are made so that the reader is made explicitly aware of this. I think the paper is an improvement, but this minor amendment would also be useful.

Response: Unfortunately, the study question cannot be answered by an IPD meta-analysis currently, as individual participant level data from other trials or observational studies with this detailed information (daily flare diary data) are not available in the public domain. We have previously approached commercial companies to obtain these data, but these approaches have been unsuccessful. We hope that publication of this analysis will highlight the methodological issues involved in measurement of gout flares, and provide further opportunities to access commercial datasets that have been to date, unavailable. As suggested by the reviewer, we have added this point to the study limitations, and highlighted the potential to study other larger datasets that have daily flare diary data (page 12, paragraph 1): “This work analysed daily flare diaries of 120 study participants over a four month period. Recent larger randomized controlled trials have recorded gout flare characteristics using daily flare diaries (16), including some studies for up to one year (13, 18, 19), and an individual participant data meta-analysis of these data would be of great interest to inform measurement of flare severity in future gout studies.”
We hope this response is satisfactory to you. Thank you for your consideration of our revised manuscript.

Yours sincerely,

Nicola Dalbeth