**Reviewer’s report**

**Title:** Design Considerations and Analysis Planning of a Phase 2a Proof of Concept Study in Rheumatoid Arthritis in the presence of possible non-monotonicity

**Version:** 1 **Date:** 07 Aug 2017

**Reviewer:** Michael Smith

**Reviewer's report:**

Thanks to the authors for making changes to the manuscript. I think it is much better structured and cohesive as a result. I appreciate the effort that has gone into making those changes. The changes made also make it clear that the conclusions of the manuscript are dependent on a priori belief in or evidence of, in this case, non-monotonicity.

I would suggest a final read through of the manuscript to check wording in some places. Also the use of brackets around IG( x, y) is inconsistent. You may also wish to expand on this abbreviation earlier in the manuscript - it doesn't appear until the last use of IG( , ).

On the subject of reproducibility: my feeling is that a third party should be able to recreate and reproduce your findings if they wish to. I think it would be good practice to provide that kind of information as supplementary material. I thought that the FACT design specification for ONE scenario + additional information from the manuscript would allow someone to extrapolate to other cases. For example, I could possibly replicate your findings using BUGS + R / MSToolkit. Most information on priors is in the manuscript, but there may be other information required to be able to exactly replicate what you've done.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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