Reviewer’s report

Title: Protocol for a Systematic Review of N-of-1 trial protocol guidelines and protocol reporting guidelines

Version: 0 Date: 18 Dec 2016

Reviewer: Steven Senn

Reviewer’s report:

This strikes me as being a fair proposal.

I have one concern. N of 1 trials are a minefield for statistical analysis. This is partly because the original developers of the concept, who deserve recognition for their pioneering enthusiasm, were not very knowledgeable about statistics. Hence some of the recommendations for analysis that were made originally are inappropriate. When this is added to the fact that data-structures can be very complicated (for example episodes within cycles within patients within a collection of patients or, as an alternative, designs based on Latin squares), this means that appropriate reporting of N-of-1 trials will require great care and considerable detail. I think that for your project to achieve success it will need complete up to date mastery of the statistical methodology of an evolving field with a fair amount of disagreement. You will need to make sure that you are equipped to do this. I have a strong suspicion that some of the published recommendations you will come across will be inappropriate and, indeed, that recommendations will contradict each other. You will need to exercise insight and judgement to know what to recommend. On the other hand, of course, the complexity and controversy in the field means that your review has the potential to be particularly welcome and useful.

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