Author's response to reviews

Title: How many repeated measures in repeated measures designs? Statistical issues for comparative trials

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PDF covering letter
Response to reviewers

Reviewer: Dr Schouten

Comment: Throughout the paper it is assumed that the mean correlation does not depend on the number of measures … this assumption should be mentioned.
Response: I now include the following:

It is assumed that neither the mean of the measures nor the mean correlation between measures depends on the number of measures. This will generally be the case where, for example, a decision needs to be made whether to measure the severity of a chronic condition for one or two weeks at baseline. However, care should be taken with possible exceptions. An example might be if an endpoint was measured twice a day instead of just once. In this case, correlations between measurements 12 hours apart might be higher than those taken 24 hours apart. A second possible exception is acute conditions of limited duration: measuring pain after surgery for seven days rather than four days after surgery will not improve precision if few or no patients are in pain after day four.

Comment: Typo, bottom of page 3.
Response: This has been corrected.

Reviewer: Dr Hwang

Comment: 1. It is a relevant paper that is very useful for clinical investigators who plan to conduct comparative studies with continuous outcomes. It is not necessary to limit the discussion only for randomized trials as indicated by the title, in fact, when randomization works, the baseline information is not required.
Response: The title, introduction and discussion have been changed to reflect that the study is of value for the design of comparative studies whether randomized or not.

Comment: 2. It should be clearly point out that the methods discussed here are only suitable when the question of study focus on the difference between two groups of subjects at follow-up. When the research questions are about the time course of the outcomes, different design considerations are needed.
Response: This is stated clearly in the introduction and discussion.

Comment: 2b. Most of the repeated measures studies will have some interests in longitudinal patterns, additional discussions on how to extended the proposed methods to those cases will be able to strongly strength the paper more.
Response: I feel that this is out of the scope of the current paper.

Comment: 3. Most of the formulae in Appendix 1 and 2 can be easily seen from Frison and Pocock's paper (Stat Med 1992). It may not be necessary to derive them again. Meanwhile, the paper should put the relevant references on page 6.
Response: Derivations are included for completeness; the appropriate citations are given.
Comment: 4. The discussions here are based on the "marginal change" in sample size (i.e., number of subjects) as a function of repeated measurements of r (or p). Alternatively, it will be also interesting to study the marginal change in power as a function of repeated measurements of r (or p), given a fixed sample size.

Response: This would increase the number of table from 6 to 11, which I feel would be unwieldy.