Author's response to reviews

Title: Making clinical trials more relevant: improving and validating the PRECIS tool for matching trial design decisions to trial purpose

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Author's response to reviews: see over
The Editor
Trials

26th March 2013

Dear Doug Altman,

With reference to the e-mail received 25th March, I am pleased to submit a revised copy of the protocol Making clinical trials more relevant: improving and validating the PRECIS tool for matching trial design decisions to trial purpose to be considered for publication in Trials.

Attached is a point-by-point response to the comments from the reviewer, Janice Pogue and the editorial team.

This manuscript, in whole or part, is not being considered by others for publication.

I look forward to hearing from you in due course when the protocol is likely to be published.

Yours faithfully,

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Response to Reviewer: Janice Pogue

1) Authors have taken on an important task and addressing validity and reliability of the PRECIS-2 tool will represent an important advance. The authors should consider that they are not really demonstrating improvement between PRECIS-2 and the original PRECIS, but rather perceived improvement. To demonstrate improvement would involve the same trials being rated using the old and new tool, and compared.

We thank the reviewer for this encouraging comment on what we believe is an innovative and important project to improve and validate the most promising tool available.

We have edited the protocol to cover this comment regarding perceived improvement. On page 5 we have entered the following comment “PRECIS has never been formally validated but a diverse group of methodologists and trialists have used the tool - it is interesting to note who has used the PRECIS, as it was developed for all trialists to make design decisions Thorpe et al [10].

Also on page 17, under Discussions, we have added: “This study will involve a large number of trialists, methodologists and others to obtain suggestions for how the original PRECIS tool can be improved; we will then validate a modified version of this tool, PRECIS-2.”

2) There are a few minor omissions. Although I am sure the authors intend to use the matching of the pragmatic and exploratory trials in the analyses planned in phase 4, the statistics section do not mention this pairing.

Page 16 under Sample size and statistics, we have entered the following comment to clarify the matching mentioned previously “Phase 4 will involve matched (by intervention) pairing of pragmatic and explanatory trials.”

3) It would be useful to know what is the specific hypothesis that will be tested using the Cochrane risk of bias score? Is it that pragmatic trials should have greater risk of bias? This should be stated within the protocol.

Page 16 under Sample size and statistics, we have entered the following comment to clarify the Cochrane Risk of Bias scores will be compared for the matched explanatory and pragmatic trials to assess internal validity, in particular: sequence generation, allocation sequence concealment; blinding of participants, personnel and outcome assessors; incomplete outcome data; selective outcome reporting; other potential threats to validity like publication bias. We will test the hypothesis that pragmatic trials have a greater risk of bias than trials that take a more explanatory approach.
4) Also what is the purpose of the prognostic model to be built through multivariate regression?

Page 16 under **Sample size and statistics**, we have added “We will also perform multivariate regression in to attempt to further explain variation in effect (e.g. **are** topic of trial, risk of bias, sample size, degree of pragmatism etc. **predictive of intervention effect size**).

**Response to Editors:**

*Please remove the conclusion section from the abstract*

This has now been removed.