Author's response to reviews

**Title:** Optimizing early child development for young children with non-anemic iron deficiency in the primary care practice setting (OptEC): study protocol for a randomized controlled trial.

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**Version:** 2

**Date:** 22 February 2015

**Author's response to reviews:** see over
February 22, 2015

Editor-in-Chief,
Trials.

Re: Re-submission of manuscript (MS: 1011551628152862) with point-by-point response to reviews

Dear Dr. Altman,

We had submitted our manuscript titled “Optimizing early child development for young children with non-anemic iron deficiency in the primary care practice setting (OptEC): Study protocol and an internal pilot for a pragmatic randomized controlled trial” to your journal on the 8th of December, 2014 for consideration of publication. On the 2nd of February, 2015 we received your mail asking us to revise and resubmit the manuscript with a point-by-point response to the comments. Please see below our point-by-point response to the concerns that were sent to us. We are submitting the revised manuscript based on the comments/changes that were asked to be made.

Please let me know if there is any more information or concerns that need to be addressed. Thank you for considering our manuscript for your journal, Trials.

Regards,
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Our response has been included after each reviewer comment.

Response to reviewer:

1. Perhaps the authors could include the SPIRIT checklist as an appendix

   We have included the SPIRIT checklist as an appendix

2. The background section is possibly rather too long and includes an overview of IDA which appears to be less relevant than the detail about NAID – the background could more effectively focus on the research context around childhood NAID and move more quickly to the rationale for this treatment trial.

   The evidence related to IDA and child development forms the foundation for building evidence related to NAID and child development. Hence we feel it is necessary to include this information in the background. However, in the current draft we have condensed the information in this section (page 6).

3. One query I had about the rationale and flow of background literature was whether in fact the links between NAID and developmental problems have been definitively established or whether the data from this treatment trial will also contribute data on whether there is a connection between NAID and poorer outcomes, thus building a case for screening.

   Our trial will contribute to understand whether there is an association between NAID and poorer developmental outcomes in young children and the effectiveness of iron interventions to improve the development of children with NAID. We have established in the background that there is significant lack of evidence in relation to the effect of NAID on children’s development. Performance of high quality, adequately powered clinical trials in developed country setting will begin to establish an evidence base for screening for iron deficiency with an aim to improve developmental outcomes. (See page 7, line 207-211)

4. The first sentence of the trial objectives and hypotheses section could be more clearly written so it is clear that the trial is a comparison of oral iron plus dietary advice versus placebo plus dietary advice. At the moment it says the trial will assess oral iron plus advice with placebo and advice which is confusing.

   We have changed the trial objectives and hypotheses as follows -

   The primary objective of this trial is to assess the effectiveness of 4 months of oral iron plus dietary advice versus placebo plus dietary advice, in children with NAID aged 12-40 months to improve their developmental outcomes. We hypothesize that children receiving 4 months of oral iron plus dietary advice will have better developmental outcomes than those who receive placebo plus dietary advice (page 9).
Response to editorial request:

1. Please ensure the title conforms to journal style for study protocol articles. The title should follow the format ?__________: study protocol for a randomized controlled trial.?

   The title has been changed according to the journal style as below-
   
   “Optimizing early child development for young children with non-anemic iron deficiency in the primary care practice setting (OptEC): study protocol for a randomized controlled trial.”

2. Please move your statements of consent and ethical approval to the Methods section.

   Consent and ethical approval section has been moved to the Methods section (page 22).

3. Please mention each author individually in your Authors' Contributions section. We suggest the following kind of format (please use initials to refer to each author's contribution): ?AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript?

   Author’s contribution has been changed as instructed -

   KA and PP was responsible for the design and conception of the study, development of study protocol, nutritional guidance and data collection instruments, drafting and reviewing the manuscript for important intellectual content, and approved the final manuscript. KT ensured the accuracy of the statistical analysis and sample size calculation and approved the final manuscript. JM, CB, AH, DF, EM, CM, SZ was responsible for critical review of the manuscript and approved the final draft.

4. Please move the additional file section below the reference list.

   The additional file section has been moved below the reference list (page 34) and another file has been included as appendix 3, the SPIRIT checklist.

5. Please include a figure title and legend section after the reference list.

   A figure title and legend section has been added after the reference list on page 34.