Author’s response to reviews

Title: Equity in adherence to and effect of prenatal food and micronutrient supplementation on child mortality. Results from the MINIMat randomized trial, Bangladesh

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Version: 3 Date: 18 November 2013

Author’s response to reviews:

November 19, 2013

Dear Editors, BMC Public Health,

We once again thank the reviewers for their inputs and the insights that they have added in our manuscript. Please find below point by point response to the reviewers.

Also, please find attached the revised manuscript (version November 19, 2013) and figure 1 (version November 19, 2013) as separate files.

On behalf of all authors

Thanking you

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Response to reviewers – Equity in adherence to and effect of prenatal food and micronutrient supplementation on child mortality. Results from the MINIMat randomized trial, Bangladesh.

Reviewer 1 – Malavika Subramanyam.
1. Need to include a sentence on the specific methods used to address the research question in the abstract.
Response – addressed, please see the last sentence under methods in the abstract.

Background:

2. “Other efforts may show variation in equity effects in different settings due to design as well as the historical and political trajectories of the local health system [5].”

This sentence is still not very clear to me. The response in the letter to the reviewers was: “Many propose to target the group most in need. This is the straightforward way. However, other efforts for examples if we depend on the existing health system and its personnel will take care that distributions are equal and both poor and relatively rich will use that equally then there can actually be variations. This is because the design of the intervention and the history of development of health system in that particular country and also the way the political trajectory has evolved may not allow equal distribution let alone equal effect. This has been addressed now in the manuscript.

I now understand based on the explanation given in the letter in response to reviewers’ comments. However, I don’t think this has been addressed in the manuscript. There needs to be a little more explanation here.

Response- now addressed in the manuscript, please see background in the main text, line 8 and thereafter.

3. “Other efforts may show variation in equity effects in different settings due to design as well as the historical and political trajectories of the local health system [5]. These attributes of the local health system may not always allow delivery of services equally to the rich and the poor. Economic growth does not automatically lead to improvement in health, e.g., in prevalence of child malnutrition [6].”

There needs to be a better flow from one sentence to another. Currently the sentences start too abruptly. I can guess what the authors are trying to say based on the explanation given in the letter to the reviewers. However, we cannot expect the readers to guess. Please make the links between one sentence to the next more explicit.

Response – now addressed in the manuscript in the lines following the response covered under point 2.

4. “In this paper we analyzed the adherence to and the effect of prenatal food and micronutrient supplementations in rural Bangladesh from an equity perspective.”

Please clarify the outcome on which “the effect of prenatal food and micronutrient supplementations” are examined.

Response- addressed. Please see the first sentence of the last paragraph in the introduction

5. “We used level of maternal education as the main stratifying variable and tested the robustness of the analysis by using household asset scores as the stratifying variable, and interpreted the results considering that these variables
reflect different aspects of resources.”
This language is more suited to the methods section. Please re-word such that you avoid terms such as “stratifying variable” and “variables”. In the background section it would be better to present hypothesis or research questions using terminology that is conceptual or theoretical. For instance, “In order to investigate whether interventions differed in their impact on reducing social inequalities, we examined differences in adherence to and etc etc…. between children of mothers with lower versus higher level of education.” Also please include a theory based reason for additional stratification by household assets.

Response – now addressed in the manuscript. Please see from the second line in the last paragraph under background. The word variable is replaced by ‘indicator’ in this section.

Methods:

6. “The robustness of the analysis was tested by use of the other main socio-economic variable, asset scores dichotomized value, which is a measure of family wealth.

Please give details about what is meant by “robustness of the analysis was tested.” Do you mean a test of whether the results were robust if a different socio-economic variable was chosen?

Response- by testing robustness of the analysis we meant whether the results were consistent when another SES variable is used. We have now addressed the issue and used the word consistency instead of robustness. Please see page 5 in the revised manuscript.

7. “Presence of daily wager in the family and reported income/expenditure status were also used as descriptive statistics, as well as maternal age, parity, body mass index (BMI, kg/m2) at entry into the intervention, and haemoglobin in early pregnancy.”

This is a list of variables and not a list of descriptive statistics. Please clarify.

Response – now clarified in the text. Please see the sub-section, Variables, page 10.

8. “The variables are now listed under a new section called variables.”

This is a quote for the letters written by the authors in response to the reviewers. However, I was unable to find the section called variables. The list of variables (see point number 7 above) needs more details as well. In my previous review of this manuscript I have requested for greater detail regarding these variables. I am unable to find it in the revised manuscript.

Response – Now addressed in the manuscript, page 10.

Reviewer 2 – Lieven Huybregts.

1. The authors have now clearly stated what their hypothesis was (i.e. effect modification by maternal education as proxy for equity, of intervention on adherence and mortality). My previous remark suggested to take a closer look at the <6y and the #6y groups. The authors rightfully identified that mothers with
less education were significantly older, had a higher parity and lower BMI at 8 weeks of pregnancy. These observations suggest that the effect modification by maternal education could actually be an effect modifications of higher parity (in case of mortality!), age (adherence!), and BMI at 8 weeks (mortality?!). Therefore, it is imperative that the authors present the results from the analysis adjusted for these confounders (table 2 and 3), or present the unadjusted and adjusted analysis. Basically, we want to know if the education effect is still present adjusting for age, parity, BMI.

Response - addressed in the manuscript – table 2 and 3 are revised and adjusted analyses are presented, pages 25 and 26.

2. I regret to insist again on the accuracy of your trial data. I believe a paper cannot be published if the data is not consistent.

From the trial profile I deduce 3591 (602+604+591+598+608+588) deliveries available, which is tantamount to 3625 (608+610+595+605+612+581) total live births and 3560 (597+599+587+592+604+581) singleton live births. So I fail to understand from your methods how you were able to obtain 3659 live births (first line study site and participants) and 3627 children that were included for analysis”. It does not match up with your trial profile and the previous publication. In case further analysis demonstrated that your estimates are correct and the previous were not correct, I propose the reason why is added to the methods.

The JAMA paper mentions in the first § of the results section 3625 live births, which corresponds to what you have shown in your trial profile (also in the tables). I would rewrite the first § under ‘study site and participants’:

A total of 4436 pregnant women were randomized resulting in 3591 recorded deliveries. This number was associated with 3625 live births of which information on maternal school attendance was available for 3591.”

Response - addressed and incorporated in the text under methods under the sub-section study sites and participants, page 6.

3. Figure 1: I would replace ‘birthing women’ by ‘deliveries’. Also change ‘Live’ to ‘live’ (lower case) in the first box.

Response- now addressed – corrections have been made in the figure.

4. Table 2, drop examination (two times) in the text below the table. Also, correct ‘significant’.

Response- addressed – table 2 is now corrected and adjusted results are presented.

5. Table 2: I must add that the table is still not so clear. I would remove the results from the interactions and put these in the text (results section). It is written two times that UF60 (<6 years) was different with EMMS (one time with P=0.0001, one time with P=0.98). I guess this is a typo.

Response – now addressed – a new table 2 is now provided as mentioned under point 1 and the interactions are now moved to the text. Errors are corrected.

Related changes are also made in the abstract and statistical analysis section under methods, page 11.
6. Abstract: you mention that HR from the JAMA study under ‘results’, however, they belong to the background section, since they were already published. Under ‘results’ one can only enlist results from this particular study.

Response- addressed, results from JAMA paper are now removed from abstract.

7. Study limitations: The strengths and limitations are those of the main intervention study. However, the present study entails a secondary analysis (subgroups). So it might be more useful to focus on the real limitations. I don’t believe that the addition of a real control group (with no intervention) would allow the authors to conduct an adherence analysis. I suggest to add following limitations: (1) that the adherence was not until childbirth in the case of the food supplements which might hamper external validity. (2) in your rebuttal you wrote that you add differential reporting by educational level as a limitation, however, I cannot retrieve this sentence. Please add the latter (you can indeed argue that at the start compliance was more easy to measure).

Response - addressed in the manuscript, page 15.