Author's response to reviews

Title: Cost-effectiveness of invitation to food supplementation early in pregnancy combined with multiple micronutrients on infant survival: Analysis of data from MINIMat randomized trial, Bangladesh

Authors:

Rubina Shaheen (Rubina.Shaheen@kbh.uu.se)  
Lars Ake Persson (Lars-Ake.Persson@kbh.uu.se)  
Shakil Ahmed (shakila@unimelb.edu.au)  
Peter Kim Streatfield (pkstreatfield@icddrb.org)  
Lars Lindholm (Lars.Lindholm@epiph.umu.se)

Version: 4  
Date: 1 May 2015

Author's response to reviews:

May 1, 2015  
Dear Editors, BMC Pregnancy and Childbirth,

We have addressed the reviewers’ comments. Please find below our point by point responses addressing the comments. Corresponding changes are made in the manuscript.

Reviewer: Stephan Litschig

Major Compulsory Revisions:

1. The authors mention that the highest-cost figures between NGO- and government-run community nutrition centers (CNCs) were used in the analysis but the footnotes in Tables 1, 2, and 3 state that reported costs come from NGO-run CNCs. Which is it?

I agree with the authors’ choice to use the highest-cost estimates for the main results of the paper as this is the most conservative. Nonetheless, this scenario does not reflect an actual mode of delivery.

I would therefore like to see the incremental cost effectiveness (ICE) analysis under three cost scenarios: (actual) NGO-run CNC, (actual) government-run CNC, and (hypothetical) highest cost scenario, combining highest cost items from either mode of delivery. The cost sensitivity analysis could be added to the existing tables. Results could be discussed in a separate section in the paper.

Response:

We have addressed the suggestions made by the reviewer, and presented ICERs under NGO run community nutrition centres (CNCs), government run
CNCs and under a hypothetical highest cost scenario. In the last option we used highest costs selected from the first two options and highest proportions used by pregnant women so that the cost estimates reflect the possible highest cost. In the previous version though highest costs were used, the proportions used by pregnant were from NGO run CNCs that yielded lower cost and ICER estimates than those presented in the current version. The cost estimates are added to the existing tables.

2. My second suggestion is to additionally report the ICE analysis based on the limit points of the 95% confidence interval for the intent-to-treat effect of moving from UFe60F to EMMS. The goal would be to quantify the uncertainty regarding the true ICE and facilitate comparison with existing studies.

The analysis should be done separately for each cost scenario above if it turns out that the cost scenarios matter a lot. Again, the ICE estimates based on the limit points of the 95% confidence interval could be added to the existing tables. Results could be discussed in a separate section in the paper.

Response:

We have addressed the suggestions by the reviewer, and presented ICERs using the limit points of the 95% confidence interval (HR, 95% CI of HR) from the intent-to-treat analysis of moving from UFe60F to EMMS. These have been done separately for each of the cost scenario and the resultant estimates are added to table 3. Corresponding changes are made in the results and discussed in a separate section in the discussion.

Minor Issues not for Publication

p.6 line 14: extra space in front of period sign.
Response: addressed.

p.8 line 10: “There were…”
Response: addressed.

p.8 line 12: I was unsure why 29.36 was used instead of 24.22.
Response: Because even though pregnant women consumed more food, they probably received similar services as the children and therefore we assumed services per person, not per adult equivalent. This resulted in using 29.36 instead of 24.22 when we calculated the use of working time. Clarified in the text, page 9 lines 22 to page 10 lines 1 to 2.

Table 2, footnote a: “to prenatal” repeats.
Response: addressed.

Table 2, line 7: “number 15” not numbers.
Response: addressed.
Table 2, footnote b: “women” not woman.
Response: addressed.
Table 2, footnote e: this should be c instead.
Response: addressed.
Table 2: The cost per 1000 women with UF60F is sometimes written as 42878 and sometimes as 42,878. Idem for the other cost and Table 3. Using the comma throughout might be preferable.
Response: addressed, used comma throughout.
p.11 line 22: missing period sign and omission of “the” in “Hossain et al. questioning the…”
Response: addressed.
p.13 line 4: missing per cost and LY saved: “our estimate of US$31 cost per LY saved”
Response: addressed.
Table 3, footnotes b and c: what group does “iron folic acid” refer to exactly? Was there a treatment arm that was only offered iron folic acid without food supplementation?
Response: those were errors from a previous version of the manuscript, now corrected.
Reviewer:Bharati Kulkarni
1. Page 7, line 8 : please explain the term ’ discounted at 3% and 5%’ in case of average life years. This term is not very familiar to all health researchers.
Response: addressed. The explanation of why discounting of life expectancy at birth has now been given. Page 8, line 11 to 13.
2. Page 8, line 9: The sentence is not clear. Please clarify that total was equal to 24.22 adult equivalents.
Response: addressed. Explanations are given, page 9 lines 18 to 20.
3. Page 11, lines 17-18: The sentence is not meaningful.
Response: addressed. Combining information from the next sentence we have now clarified the line. Page 15, lines 18 to 20.
4. Page 12, line 14: Please clarify that the figure represents per capita GDP.
5. Page 13, lines 1,2: The authors have compared the cost of per IM averted with
their intervention with the cost of community based management of acute malnutrition. This comparison is not appropriate. Acute malnutrition requires complex interventions and the costs are bound to be high.

Response: addressed. Removed related lines acknowledging the complexities the reviewer raised.

We have added the trial registration date just after the abstract, and added the full name of the ethical review board, page 7 line 20.

In addition, we corrected English. We have added the words “the effect of” in abstract page 3 line 2, replaced “we showed” with “we have shown” on page 5 line 6, added the word “arms” after EMMS page 8 line 2, replaced “represent” with “represented” page 8 line 21, removed the words “and health care” page 9 line 3-4, and added an “and” before recurrent cost, and added “NGO run” line 15, page 17 line 11 added “actual” before show up and line 12 replaced the world balancing with “reasonable”, and page 19 line 10 removed “(NNP)”.

Since now three cost situations are presented, there are changes related to plurals, “CE analysis show” replaced with “CE analyses have shown” page 15 line 2, “our analysis also shows’ with “our analyses have also shown” page 15 line 3 to 4, “estimate” replaced with “estimates” page 16 line 14, “is” replaced with “are” page 16 line 16, “is” replaced with “are” page 17 line 1, “estimate” replaced by “estimates” page 17 line 2, “iron-folic acid” to “UFe60F” page 17 line 3, table 2 “week nine” replaced by “week 9” to remain consistent with “week 9” in other places, added “because of rounding, some estimates are same”, under table 3,Footnote a.

Since the cost scenarios and sensitivity analyses are now presented we have added a section called “Analyses” at the end of the methods section.

Because of use of figures up to forth digit after decimal and because of rounding the person days used by pregnant women was 7981 on page 8 line 10 now we have changed it to the exact figure, 7579, page 9 line 20.

We have replaced reference number 24 with the recent and specific CE paper of the relevant study cited as reference number 24 before. Reference number 17 and corresponding gross domestic product figures all through the manuscript have been changed based on latest information available providing figure for 2013. Since a new reference justifying discounting of LYs gained in now added (reference number 18) and reference number 27 is now removed (Puett et al.,) thus the numbering of references after reference number 18 has now increased by one digit.

We sincerely thank the reviewers for their comments which we believe improved our manuscript substantially.

Thanking you
Sincerely
On behalf of all authors
Rubina Shaheen
Doctoral Student
Department of Women’s and Children's Health
Uppsala University
Uppsala, Sweden