Author’s response to reviews

Title: A Randomized Trial of Multivitamin Supplementation in Children with Tuberculosis in Tanzania

Authors:

Saurabh Mehta (smehta@cornell.edu)
Ferdinand M Mugusi (fmugusi@muhas.ac.tz)
Ronald J Bosch (ronbosch@sdac.harvard.edu)
Said Aboud (aboudsaid@yahoo.com)
Anirban Chatterjee (anirban69@hotmail.com)
Julia L Finkelstein (jfinkelstein@cornell.edu)
Maulidi Fataki (mfataki@muhas.ac.tz)
Rodrick Kisenge (saroriki@yahoo.com)
Wafaie W Fawzi (mina@hsph.harvard.edu)

Version: 3 Date: 19 October 2011

Author’s response to reviews: see over
Response to Reviewers v2
A Randomized Trial of Multivitamin Supplementation in Children with Tuberculosis in Tanzania

Reviewer 1: Marianne Visser

Round 2:
Thank you for addressing my previous comments. Unfortunately there are a few outstanding issues that I feel need to be addressed:

Thank you, Dr. Visser, for taking the time to review this manuscript again.

Major Compulsory Revisions:
1. Abstract: You refer to the significant increase in serum albumin among HIV-infected children and among those who received placebo. However, this finding is not presented in the results? In the discussion (para 5) you refer to the increase in serum albumin in all children?

We have removed the reference to albumin in the abstract on Dr. Paul Kelly’s (Reviewer 4) suggestion. We have also mentioned that there was no difference in the change in albumin the supplemented and the unsupplemented group in the results.

2. Results: (3rd para) you refer to the height gain among HIV-infected children between the ages of 6 months and 3 years and indicate that 79 HIV-infected children were included in the analysis. Table 1 indicates that a total number of 23+29 children were included in the 6months-3years age stratum and 10+17 children in the > 3 years stratum, respectively. Were HIV-infected infants (n=8) not included in the analysis? Please clarify.

Yes, this effect was only observed in the subgroup analyses among HIV-infected children aged 6 months-3 years. We apologize for the typo – the n is 48 in this subgroup.

3. Results: (5th para) you refer to the fact that the increase in Hb was not significant among females. What is the significance of this finding? Perhaps you were underpowered?

We do not have adequate power to make conclusive statements about results from subgroup analyses – these are hypothesis-generating at best. That said, there is an emerging body of literature that suggests that the natural history of infectious diseases and the response to nutritional supplements varies by gender.
Minor Essential Revisions

1. Abstract: when referring to a significant increase in a parameter, the effect size should preferably be included eg. "significant differences in weight gain were observed among children aged 6 months to 3 years..." (? g vs.? g ; 95% CI ?; ? p<? )

We have made this change.

2. Table 1:
Delete Number (%) in bold. Rather insert n (%) next to each categorical variable eg.
Age, n (%) HIV-infected, n (%) Delete "by Age categories" next to HIV-infected

We have made this change.

Reviewer 2: Lovett Lawson

Round 2:
I have gone through the authors reply to the reviewers comments particularly mine and the revised manuscript. I believe most of my initial comments and queries have been adequately responded to.

I have no objection in recommending the manuscript approved for publication once other reviewers are equally satisfied.

Thank you, Dr. Lawson.

Reviewer 3: Christian Wejse

Round 2:
Major:
Re comment 1. The authors explain the lack of reporting chest x-ray outcomes in their comment but has not incorporated the x-ray or mortality in the revised manuscript. The readers should be allowed to know that there were no differences in these most interesting outcomes and surely there must be room to incorporate that given the number of outcomes reported.

Thank you for your review, Dr. Wejse. We have added this information to the text.

Re comment 8: The authors should state which difference in weight it would be possible to detect with the reached sample size, ie with 255 patients how large should the weight difference be in order to be significant.

The weight difference will have to be 32.5% in order to be statistically significant with 255 children. We have added this information to the text.
Minor
Re comment 3: Even if there are no data on children with TB, surely there are data on the population level of micronutrient deficiencies also among children, and I still find this highly relevant to refer to in a trial on micronutrient supplementation.

We have added a reference in the introduction.

Re comment 4: The question was regarding success of blinding, the authors have not commented on that question.

Success of blinding was not formally evaluated.

Reviewer 4: Paul Kelly

Round 2:
I think they have dealt with most of the issues we raised.
One exception - albumin is still presented as a significant difference in the Abstract even though it has been removed from Results and is clearly not significant in Table 3. Once this is removed, I will be satisfied and do not need to re-review.

Thank you for your review, Dr. Kelly. We have removed the reference to albumin from the abstract.