Author's response to reviews

Title: The impact of anthelmintic treatment intervention on malaria infection and anaemia in school and preschool children in Magu district, Tanzania: An open label randomised intervention trial.

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Author’s response to reviews: see over
Re: Response to reviewer’s comments

Dear Editorial Team

On behalf of my co-authors, I would like to thank you for considering our manuscript MS: 6153411251477281 for publication into your journal: I am hereby resubmitting the revised manuscript in which I have addressed all reviewers comments which were put forward to the first submission manuscript (see areas marked with yellow color in the revised manuscript). The following is a point by point response to the reviewers’ comments:

Reviewer # 1 (Mathieu Nacher).

Methodology:

Comment 1: The design is inappropriate to answer the question because there was no arm without treatment. Assuming that 50% in the single treatment arm would get re-infected makes it difficult to detect a difference. I understand this was guided by the ethical committee. In the end there might have been serious power problems leading to difficulties in the interpretation of results. The authors have been very rigorous in their writing and presentation of the data. but for the main question asked I think it is not possible to conclude that anthelmintic drugs increase or decrease or do nothing to malaria incidence or severity. Perhaps these limitations due to the comparisons made should be emphasized more in the discussion.

Author’s response: This reviewer’s comment is quite fair and we have emphasized this limitation in the discussion section (see areas marked yellow). Since this limitation was due to national ethics guidelines, the research team had no other options apart from following the guidelines.

Reviewer # 2 (Cecilia V. Holland).

MAJOR COMPULSORY REVISIONS

Results:

Comment 1: The prevalence, density and means reported in Table 2 are not independent of each other and therefore cannot be analysed by Chi-square, t-tests and ANOVA. It is necessary to use statistics that take account of this for example repeated measures ANOVA. Such an approach is reported in Kirwan et. al., 2010.
Author’s response: All concerns regarding data reported in table 2 have been addressed and the data management and analysis section have been revised. It is important however to note that for each survey point (when only one survey round is considered), it was correct to compare prevalence of *P. falciparum* infection and prevalence of anaemia between the intervention and control group using the chi-square test because this is simply a cross-sectional comparison. Likewise, for each survey round, it was correct to compare mean intensity of *P. falciparum* infection and mean haemoglobin levels between the intervention and control group using the t-test because only two groups were compared cross-sectionally. On the other hand, in line with the reviewers comments, the repeated measures ANOVA was the appropriate test to compare mean intensity of *P. falciparum* infection and mean haemoglobin levels when the three survey points (baseline, 12 months follow up and 24 months follow up were considered together longitudinally.

MINOR ESSENTIAL REVISIONS

Introduction:

Comment 1: The authors refer to the fact that no longitudinal randomised studies have been undertaken but see Kirwan et. al., 2010 BMC Infectious disease; also the review paper by Nacher (2011) and the paper by Brutus et. al., 2006 should also be discussed and referenced.

Author’s response: These are fair comments and have been addressed in the relevant sections of the manuscript (see areas marked with yellow). As suggested by the reviewer, references by Kirwan et al 2010, Nacher 2011 and Brutus et al 2006 have been cited in the manuscript and discussed in the discussion section as appropriate. Other related references such as Murray et al 1978 and Brutus et al 2007 have been cited as well and discussed as appropriate.

Methodology:

Comment 1: I wonder if the mixing of both pre-school and school-aged children has a possible diluting effect on the observed results due to reduced malaria prevalence in older children - did the authors take account of age in their analysis?

Author’s response: The effect of age was taken care of during analysis and there was no diluting effect of observed results (reduced prevalence of malaria in older children) resulting from mixing pre-school and school children. Unfortunately baseline prevalence of malaria by age group is not shown in the current manuscript but it was 27.6% in pre-school children (3-5 years) (n=333) and 30.3% in school children (6-13 years) (n=1,213) (p>0.05). Further, it is expected that randomization of both pre-school and school children into intervention and control groups (table 1) would take care of any age related and other effects if any.
Results:

Comment 1: In Table 1, Does S. mansoni/S. haematobium denote a mixed infection? It is not quite clear.

Author’s response: Yes, S. mansoni/S. haematobium means mixed infection or co-infections of the two parasites. This has now been clearly shown in the table.

Comment 2: T. trichiura is mentioned in the text but not the table?

Author’s response: T. trichiura is mentioned in the text but not in the table because out of the 589 children whose data were analyzed, only 3 children (0.5%) were infected by T. trichiura hence the prevalence was very low and as such no further analysis was possible for this parasite.

Kind regards,

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