Author's response to reviews

Title: Patterns of geohelminth infection, impact of albendazole treatment and re-infection after treatment in schoolchildren from rural KwaZulu-Natal/South-Africa

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Author's response to reviews: see over
Response to the comments regarding the manuscript “Patterns of geohelminth infection, impact of albendazole treatment and re-infection after treatment in schoolchildren from rural KwaZulu-Natal/South-Africa”

Dear Reviewers, dear Editorial Team

thanks a lot for the helpful suggestions of the reviewers and for your efforts reviewing the manuscript. Below please find my responses (in blue) to the reviewers suggestions. I have incorporated most of the suggested changes into the new version of the manuscript and explained the few cases where I would prefer not to change the text.

Yours sincerely

Elmar Saathoff

Reviewer: John Horton

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)  
None apparent. However there are some items that should be noted and corrected if possible (see below)  

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)  
None noted.

Discretionary Revisions (which the author can choose to ignore)  
1. It would be helpful to know which of the human hookworm species is involved in this area. There are some differences in the sensitivity of Necator and Ancylostoma to albendazole, although not as marked as with mebendazole.
   - Necator is the predominant hookworm. Changed (p.9, § 2).

2. Although it is stated when treatments and assessments were conducted, it would be helpful if these were placed together and perhaps using a graphic which showed them together with the months. This would make assessment of questions like the seasonality of hookworm easier to understand.
   - Table 3 which is concerned with re-infection was changed so that it now provides all the information about the timing of treatments and assessments.

3. a rationale for the timing of follow-up for reinfection would be useful (constraint by school terms?). 16 weeks is probably too short for hookworm, especially if it is seasonal.
- True, we were constrained by school terms and holidays. Clarified in manuscript (p.6, § 1)

4. Reading of Kato-Katz: the text reads as if slides were read twice, once for hookworm, and once for the other helminths. I suspect that this is not the case - consider revision of the wording to make clear what was done.

- Slides were indeed read twice. Clarified in manuscript (p. 6, § 3)

5. CR and ERR were presumably done at the 3 week post treatment follow-ups, although it is not specifically stated.

- True, they were calculated for the surveys 3 weeks after treatment. Clarified in text (p. 5, last §; p.8, §2; Table2)

6. In looking at the re-infection data (page 8) it would be useful to include here the months when the assessments were made (see point 2), so making linkage with Fig 3 easier.

- Changed, see 2.

7. Discussion: it is worth stating that since the baseline data and those from Schutte are little different despite the passage of 20 years, transmission and epidemiology would appear to have changed little. It makes the case that without intervention, helminths will remain a problem in rural communities.

- Good point. Changed (p.13 §3)

8. Treatment: Trichuris remains a problem for treatment, and the authors are right to highlight it. Not only does there appear to be effects of intensity resulting in variable CR/ERR, but also there is some evidence of geographic variation. It is unfortunate that the prevalences are not high enough to do further investigations, but it might be worth while looking to see if the higher baseline subjects did less well.

- Changed (p.11, §2)

9. Although it is noted that resistance was not a factor, and that albendazole has not been used, is there any evidence that mebendazole has been used, since cross resistance is possible as both are benzimidazoles?

- It is also highly unlikely that any other benzimidazoles were used on a bigger scale. Clarified in text (p.11, §1)

10. Re-infection discussion. This would be easier to understand with the graphic suggested above.

- Changed, please refer to 2.

11. Figure 1 could be included in figure 2 as a small window. Figure 2, although very interesting may be a little overdetailed. Since the individual participating homes are shown, one might expect that some reference to this would occur in the text. Similarly, the geology is interesting, especially that most homes are not on the aluvial soils (presumably because they are either subject to flooding or used for crops), no specific use is made of the data. Would a simpler map be possible?
- If this point is not insisted upon, I would prefer to leave the map as it is because I think it provides a relatively informative overview of the study area. For additional reasons please refer to my answers regarding Point 6 of Prof Crompton.

12. Please use words for the months in figure 3. They can be written vertically using 3 letter abbreviations. It makes reading text and comparing with the figures easier.

- Changed.

Reviewer: David W Crompton

Reviewer's report:

1 The paper is timely and the work appears to have been well done. The 54th World Health Assembly passed a resolution urging member states to have essential drugs for schisto and STHs (geohelminths) accessible for school-age children in areas where the infections are endemic. This report is in line with WHO policy and adds to the growing body of experience about deworming school children.

2 I advise using "geohelminth" throughout; no need to switch to "soil borne ..." (see Introduction).

- Changed.

3 The first para of the Introduction is common knowledge and could be dropped.

- Changed (p.3)

4 I suggest that claiming children..."most vulnerable to the effects of worm disease" does not always stand up. What about hookworm infections in already iron-stressed pregnant women?

- Changed (p.3, §2)

5 The authors refer to morbidity. However the authors do not offer any evidence of the reduction/prevention of morbidity. I think the strength of the paper is as a solid piece of operational research - I would not get into morbidity unless some data are available.

- It is true that we did not investigate morbidity in this study. This is the reason why we can not and do not say anything about the health impact of helminth infections and of anthelmintic treatment in this population. However, the only reference to morbidity in the text is in the introduction where we say that prevention of serious morbidity is an aim of helminth control programmes in general. I think it does make sense to mention it in this context and have therefore not changed it.

6 Do we really need Figs 1, 2 and 3?

- All three Figures provide information that might be interesting to readers of this article. Figure one indicates where in South Africa the study area is situated, Figure 2 gives an – admittedly very detailed – overview of the area and Figure 3 provides climatic information which might be interesting with regard to the possibly seasonal transmission of hookworm. Having said that I must admit that only figure 1 would have featured in a print version of the article. But because 1. web-space is (nearly) unlimited, 2. Readers can disregard the figures if they want because in the web-
version they would only be dominant if readers choose to click on them, and 3. As mentioned above the figures do provide information which might be of interest at least to some readers, I would prefer to leave them in the article.

7 Since treatment at school for schisto and STHs can be given at the same time to the same children - why not include the results of that work in this paper? Otherwise delete all reference to schisto?

- Because the timelines and treatment approach for schisto differed, I found it rather confusing to deal with geohelminths and schisto in the same article. However, an article regarding schisto is presently being reviewed at this journal (MS: 2079768049408718)

8 The clearance/ consent section is reassuring. I suggest the authors include a statement about the consent of the staff. If deworming at school becomes widespread, school staff co-operation will be essential. Were the staff paid?

- The staff were only informed and asked for their co-operation, but they were neither formally consented nor were they paid. This is now clarified in the manuscript (p.5, §3)

9 Re Kato Katz - how do we know the egg counts were accurate? Was there any form of "quality control" over the counting? Who "read" the slides?

- Egg counts were done by trained microscopists. Repeat counts for quality control purposes were done on a subsample of about 5% of slides. Clarified in manuscript (p.6, §3)

10 Is Fig 4 depicting a Frequency Distribution? I am confused over Prevalence on the y axis.

- Figure 4 does indeed show a frequency distribution. The graph and legend have been changed and are hopefully less confusing now.

11 Unless stated otherwise by the authors, ascariasis, trichuriasis and hookworm disease are usually reserved for disease/morbidity. I suggest stick to A.lumbricoides infection etc etc throughout.

- Changed throughout.

12 Regarding Trichuris - if difficult to make conclusions about re-infection, why is it "however remarkable that prev. and inten...decreased...? (Perhaps rephrase?)

- Changed (p.9, §1)

13 If CR and ERR are "notoriously unreliable indicators" why should we be concerned about the authors' results concerning Trichuris? (Perhaps rephrase?)

- Changed (p.11, §1)

14 "Mild side effects" are mentioned. Can some qualitative and quantitative detail be mentioned? This aspect is important.

- The sentence was: “...when - according to the opinion of school staff - pupils and their parents had realised that treatment was beneficial and had only mild side effects.” We believe that the observed side effects (mainly lower abdominal pain in a few children) were due to treatment for schistosomiasis with Praziquantel in children
with heavy schisto infections, and that they were not due to albendazole. Because both were given on the same day it was impossible to differentiate the effects of the two drugs, but in the second round of treatment, when only albendazole was given, there were no more complaints. However, because the sentence is confusing and we do believe that the complaints had nothing to do with the geohelminth treatment the text was changed (p.12, §2)