Author's response to reviews

Title: Patterns of Schistosoma haematobium infection, impact of praziquantel treatment and re-infection after treatment in a cohort of schoolchildren from rural KwaZulu-Natal/South Africa

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Author's response to reviews: see over
Dear Reviewers, dear Editorial Team

thanks a lot for your helpful suggestions and for your time and efforts spent on reviewing this manuscript. Below please find my responses 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: Lani S Stephenson

1. Abstract: suggest add to end of last sentence in 1st paragraph: ‘in a cohort of children followed (grade 3).’ (to clarify which children were actually studied)
   
   R: Changed (Abstract, §1)

2. Results, line 1: ‘already’ is awkward; suggest delete or replace with ‘at’.
   
   R: Changed (p.3 §1)

3. Results, line 3: insert: ‘apparent’ overall cure rate [because non-viable ova were counted as viable ova, therefore the cure rate was only an apparent one and likely to be larger than it seemed]
   
   R: Changed (p.3 §1)

4. p. 4, line 3: ‘serious chronic disease’ – such as? List at least a few important conditions. There is no mention anywhere in the ms. of why schisto is bad for children, or people, yet the ms. is being submitted to a general biomedical publication with no space constraints! Many potential readers will not know or care much about schisto, and the introduction to this ms. doesn’t help them care.
   
   R: Changed (p4, §1)

5. p. 4, 2nd para, line 3: change ‘this group’ to ‘all children in participating schools’ because it is sometimes unclear whether the ms. is discussing all children in the schools vs. just the ones examined for this ms.
   
   R: Changed (p.4, §2)

6. p. 4, 2nd para, lines 5-6: rearrange to ‘keep infection intensities low in this vulnerable age group’
   
   R: Changed (p.4, §2)

7. p. 5, line 3: change to ‘school routine to a minimum and because’
   
   R: Changed (p.5, §2)

8. p. 5, 2nd para, lines 2-3: ‘only children who had been treated with praziquantel were included in the analysis’: what %’s of the total number seen pre-treatment are these?
   
   R: This information was added and discussed (p.9, last§ and p.11, last§)
9. p. 6, Specimen collecting, line 1: insert ‘1998 in the study population only to assess’ to clarify the survey was not done in all children
R: Changed (p.7, §2)

10. p. 7, line 2: rearrange to: ‘are used only’
R: Changed (p.7, §3)

11. p. 7, lines 4-9: How many microscopists were there examining the slides? Was any consideration given to quality control or assessment of inter-observer error? This is also where the ms. should first state that egg counts included viable and non-viable ova in the same category.
R: Changed (p.8, §1)

12. p. 9, ‘considerably underestimates the total prevalence’: would prefer ‘considerably underestimated the total prevalence in this population’ because that may not be equally true for all populations with schisto [or all laboratories].
R: Changed (p.10, §3)

13. p. 9, ‘For reasons which will be discussed below’: this is very confusing to the reader. Results are given before how they were arrived at is explained. Better to state in Methods under egg counts that non-viable eggs were also counted and delete the ‘for reasons…’ phrase here.
R: Changed (p.10, last § and p.8, §1)

14. p. 10, line 2: suggest add to end of sentence: ‘and were 12 to 13 years old at the end.’
R: Changed (p.11, §2)

15. p. 10, Treatment line 2: ‘already’ is awkward English; ‘as soon as’ would sound better.
R: Changed (p.10, §2)

16. p. 10, Treatment line 4: ‘less than satisfactory’ – that’s for sure. One expects over 90% or even over 95%!
R: Changed (p.12, §2)

17. p. 11, lines 7-9: ‘an unreliable tool’: this is too strong a statement, even with a reliable and prestigious reference. If the tool is truly unreliable, it’s useless and we cannot advocate its use for medical purposes. If one urine specimen from a group gives a prevalence of 30%, a second taken under similar conditions could increase the prevalence to 35-40 % perhaps, but not 80 or 90, and it couldn’t decrease the prevalence to 10%… In addition, some labs produce better quality data than others…
‘A less than optimal tool’ would be a safer and more accurate statement.
R: Changed (p.13, §1)

18. p. 12, middle of pg: rearrange to ‘Bulinus globosus snail hosts’
R: Changed (p.14, §2)

19. Fig 5: there is no mention on the figure of the number of girls or boys in each of the age categories. This makes it difficult to interpret the statements about the age pattern of reinfection in the ms., since some categories [eg, over 15 yr] probably have very small n’s.
R: Changed (Figure 5)
**Reviewer:** Simon Brooker

However, the analysis ignores untreated individuals, and so is not a true evaluation of programme effectiveness. Rather the paper reports treatment efficacy of praziquantel and reinfection after treatment, which is already well-described in the literature, and as such, does not warrant publication. Furthermore, many of the epidemiological patterns by age and sex are expected and therefore of limited interest to the international audience. If the paper can be substantially re-worked to assess programme effectiveness, it would be a useful contribution to the literature. Otherwise, it remains of limited interest.

**R:** I do agree with Dr Brooker that it would be interesting to include untreated individuals in the analysis but obviously I disagree with his assessment regarding the relevance of the manuscript as it is. Instead I believe that the much more positive judgement of Professors Stephenson and Crompton is correct and that the paper merits publication. It is unfortunately impossible to do the re-analysis that Dr Brooker suggests because we did not collect the necessary data. However, in order to provide more insights into the effectiveness of the entire intervention the revised version states the proportion of children who were treated and also discusses this issue (p.9, last§ and p.11, last§), something which was also suggested by Prof. Stephenson. Furthermore I have changed the wording in those parts where it might suggest that the manuscript evaluates programme effectiveness and not just treatment efficacy in the population under study: effect to impact (p.2, “Background”); effective to efficacious (p.3, §1); effective to efficacious (p.14, last§).

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**Reviewer:** David W Crompton

1 I have started to labour this point: people are infected with S, haematobium and NOT with schistosomiasis. Schistosomiasis is better reserved for the disease and to be used in conjunction with morbidity.

**R:** changed throughout if not used in conjunction with morbidity

2 If you have space for Figs 1 and 2 so be it, but I do not think these are needed. There will be other ways of identifying the place.

**R:** As argued before I think for web-based journals space is not a consideration of major importance. Another argument against the maps could be the distraction of the reader they might cause, however, readers who are not interested in the geographical setting do not have to open the map windows. Although I agree with Prof. Crompton that there are other ways of identifying the place, I think for those readers who are interested the two maps are a good source of information. I would thus prefer to leave them in the article, but would not want to insist on that point if others also deem it important to take the maps out.

3 On page 5 - I should stress that the drugs were given as single oral doses (with water?). I should describe what was done to be sure the drugs were actually swallowed and I should explain if anything was done about side effects. How was the PZQ dose calculated? [These points can help others working on helminth control programmes].

**R:** This information was added (p.6, §2)

4 Given the merits of using primary schools as treatment centres - I would welcome a statement about how permission/collaboration was obtained with the educational authorities.

**R:** Changed (p.4 §2)
5 Egg counts give an indirect measure of intensity. Perhaps mention that on page 8. We never know what the worms are up to if - as happens to all of us - we have to count eggs in excreted material.

R: Changed (p.8, §1)

6 The authors raise the point that PZQ might not be particularly effective against juvenile schisto. I wonder if that has any relevance to the argument at the bottom of page 10. As far as I recall, not every expert is convinced about this matter.

R: The point whether or not praziquantel is effective against juvenile schistosomes is really not important for the argument and because this also seems to be unclear I have left it out and recalculated the respective re-infection periods (p14, §2)

7 In practice during public health programmes, all this egg counting is not possible in many places; the resources to do it - cash and technicians - are not available. I hope the thoroughness of this study will not make health professionals decide that schisto is too difficult to tackle.

R: A sentence was added for clarification (p.15, §2)

8 On page 12 - I would be inclined to write "Our data indicate that in the study area S. haematobium transmission occurred MAINLY during the...

R: Changed (p.14, §2)

9 On Fig 4 - do we still use "centilitres"?

R: I think we can. The “litre” part is covered by the journals instructions for authors which state that “SI Units should be used throughout (litre and molar are permitted, however).” although the corresponding Systeme Internationale unit would be m$^3 \times 10^{-5}$. “centi” is an SI prefix as per the ‘Bureaux Internationale des Poids et Mesures’ website (http://www1.bipm.org/en/si/prefixes.html). Apart from that the amount in ml is also stated in the text, and centilitres are mainly used here because “EPC” is a relatively handy acronym for “eggs per 10ml".