Author’s response to reviews

Title: Parasitological impact of two-year preventive chemotherapy on schistosomiasis and soil-transmitted helminthiasis in Uganda

Authors:

Yaobi Zhang (yaobi.zhang@imperial.ac.uk)
Artemis Koukounari (artemis.koukounari@imperial.ac.uk)
Narcis Kabatereine (vcd_sci@vcdmoh.go.ug)
Fiona Fleming (f.fleming@imperial.ac.uk)
Francis Kazibwe (FKazibwe@vcdmoh.go.ug)
Edridah Tukahebwa (EdridahT@vcdmoh.go.ug)
Russell J Stothard (R.Stothard@nhm.ac.uk)
Joanne P Webster (joanne.webster@imperial.ac.uk)
Alan Fenwick (a.fenwick@imperial.ac.uk)

Version: 3 Date: 16 July 2007

Author’s response to reviews: see over
10th July 2007

Dr Annabel Phillips  
Senior Assistant Editor

Dear Dr Philips,

RE: MS: 3311412731404701: Parasitological impact of two-year preventive chemotherapy on schistosomiasis and soil-transmitted helminthiasis in Uganda

Thank you very much for your letter of 06/07/2007 together with the comments of two referees. We are very happy that both referees found the work of interest and we certainly found their comments very useful and all have been accommodated in into our revised text, a detailed description of which is attached below. We feel the manuscript has now been improved as a result and we very much hope that it is now suitable for publication as a research paper in *BMC Medicine*.

Yours sincerely

Yaobi Zhang
Point-by-point responses:

**Reviewer: Jorg Heukelbach**

**Major points:**

1. **Results:** much of the data is presented in tables and again in the text. Considering the amount of data, it would be worthwhile to reduce redundancy of presentation of data.

   We agree with the reviewer. The text has now been revised to reduce the repetition.

2. **In contrast to hookworm infection and schistosomiasis, prevalence and intensity of infection of trichuriasis and ascariasis are not presented in detail (stratified by area, sex etc). I assume that this has been done because there were no differences? Please state that in the text. Are there any areas where prevalences e.g. of ascariasis where higher, as stated in the introduction?**

   Indeed, the analysis was initially done according to different epidemiological settings. However, because of the very low infection levels of these two parasites, such analysis did not show any meaningful differences, therefore, the results were not shown in detail. This is now clarified in the text. As we mentioned in the discussion, they appear to be more focally distributed in certain parts of the country – more accurately, southwest Uganda, but infection with either of these two parasites was very low across our survey areas which are in the northwest and southeast.

3. **There are clearly too many tables and figures. Table 2 should be omitted, as the absolute values are presented in Table 1, and data of Table 2 can be deducted from this table. Similarly, Table 5 is not necessary and should be deleted. Figure 3 presents similar data as presented in Table 7.**

   Agreed and amended - Tables 2 and 5 and Figure 3 have now been removed.

4. **Discussion: similarly, in the discussion, results are repeated in detail. This is not necessary.**

   Agreed and amended – please also see response to comment 1 above.

5. **It is important to state in which areas of Uganda ivermectin mass treatment has been done in the past. Ivermectin has an excellent efficacy e.g. against ascariasis, which may explain the low prevalence of this STH in some areas.**

   A very good point – Onchocerciaisis is endemic mainly in 17 districts in the western half of Uganda, including part of north, northwest, west and southwest. Ivermectin mass distribution was mainly in these areas. However, the ivermectin distribution areas do not overlap with our study areas except in Moyo district. This is very unlikely to have major contribution to the low prevalence of ascariasis in our study areas. In the south western areas, in spite of ivermectin use, ascariasis prevalence is still high. We therefore think it’s unnecessary to discuss this in this paper.

**Reviewer Andre Roddam**

**Major points:**
1. The authors use arithmetic mean egg counts and perform their analyses on the original scales. However it is clear that the egg distribution is clearly non-normal with a large peak at 0 and a very skew distribution for positive values. The authors need to therefore justify their use of techniques such as analysis of variance which assume normality of the response or alternatively to use an appropriate transformation/alternative technique which can be justified.

The reason that we used arithmetic means and not geometric means is that the latter are considered to be biased in estimating the true mean (Fulford AJC 1994 Parasitol Today, Ref #29). We want to display the mean intensity of infection which would represent the level of the actual egg output in such populations in the epidemiological point of view, although the pattern of the egg counts in helminth infections is of severe aggregation. Also after the analyses we conducted on these data (unpublished work) we found no significant differences between arithmetic and geometric means concerning trends between the two years. We therefore maintained our arithmetic mean calculation.

2. As stated there are 4351 schoolchildren recruited at baseline but only 1704 have complete follow-up data which is used in the analysis. Whilst I appreciate the difficulties of following up children and adults in resource-limited environments I think it would be helpful to readers and provide more support for the results if there is some comparison between those who are followed-up and those who are not. For example, I was left wondering if there were differences in some key variables – like infection intensity – between those followed-up and those lost.

A good point - this information has now been added to the Methods Data management and analysis section. The baseline information in the followed-up and the dropped-out was similar in mean age, sex ratio and hookworm infection, however, the dropped-out had higher S.mansoni infection than the followed-up.

Minor points:

1. At a number of points in the manuscript it is stated that results were significantly different for a number of groups but there is no further details – please give details of the tests used in the methods section and provide p-values in the results section. Similarly for Figure 3.

We calculated and presented the 95% confidence intervals for all data we presented in the tables. Whether the difference is statistically ‘significant’ can be easily judged on whether the ranges of 95% CIs for the means are overlapping. In order to show the p-values for the three time point data of this study we would have to carry out three pairwise tests. The chance of at least one of these rejecting a null hypothesis when all three hypotheses are true is far greater than the nominal 0.05 and this is the reason why we chose to show 95% CIs rather than p-values. We think it is fair to maintain in the revised version the 95 % CIs in order to comment on the statistical significance of the results. Figure 3 has now been deleted according to the other reviewer.

2. In all the results tables there are no p-values for tests of reduction/significance nor indications of whether the 1 year follow up is different form the 2 year follow up. Although I appreciate that there are some clear and large reductions I still think it would be helpful to the reader if relevant p-values were also presented.

See above response to minor comment 1.

3. The authors regularly say “unadjusted reduction of …” which had me waiting to see what the “adjusted reduction…” was. However this was never presented. I think the authors need to choose a different description and justify why no adjustments were presented.
The ‘unadjusted’ reduction meant the reduction was calculated without consideration of other factors, e.g. age etc. The text has been revised and ‘unadjusted’ removed to avoid confusion.

4. I found the continual repetition of large portions of the results tables in the text unnecessary and distracting. The results section should be used to bring out the key highlights from the results, not to repeat what is presented in a table – readers should just be referred there.

Agreed and amended – please also see response to major point 1 of the other reviewer. The text has now been revised.