Author's response to reviews

Title: Longitudinal Analysis of Antibody Responses to Trachoma Antigens Before and After Mass Drug Administration

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Author's response to reviews: see over
To The Editors, BMC Infectious Diseases
April 1, 2014

Thank you for your quick review of our manuscript “Longitudinal Analysis of Antibody Responses to Trachoma Antigens Before and After Mass Drug Administration”. We appreciate the thoughtful comments and questions that the reviewer’s provided, and to the best of our abilities we tried to incorporate these suggestions to improve the quality of the paper. We feel the data included in this paper will be very useful as trachoma elimination programs move forward in deciding the best tests for post-elimination surveillance.

Below we have included our responses to the reviewers’ comments.

Sincerely,

Diana Martin

Reviewer’s report
Title: Longitudinal Analysis of Antibody Responses to Trachoma Antigens Before and After Mass Drug Administration
Version: 1
Date: 24 March 2014
Reviewer: Phil Giffard

Reviewer’s report:
This is an interesting study that is potentially very useful for informing trachoma elimination strategies. In some ways it was negative, in that it showed that the antibody responses addressed in the study are likely not very useful for indicating the success or otherwise of mass drug administration programs. However, it is still important information.

Major Compulsory Revisions

1. What was the basis for selecting samples for inclusion in the experiments that lead to Fig 3? There seems to be a bias towards those samples that showed a medium antibody level, and so were more likely to exhibit a detectable reduction in titer after the MDA. While I am assuming that samples from trachoma negative patients were omitted with some justification (although this was not stated), the omission of some of the high IgG titer samples may have given the impression that detectable reduction in titer during the six month post MDA period was more universal than it actually was.

This analysis was done on all samples with a positive antibody response at baseline, and we have added text to clarify this (lines 194-195). We analyzed all antibody-positive samples here regardless of clinical trachoma or PCR status. We did not analyze samples antibody-negative at baseline since a
decline in the MFI would not be meaningful since they were already negative. We did not omit any high antibody titer samples from this analysis.

2. The evidence for concordance, or lack thereof between the results from the different antigens is either very weak, or the statistics are poorly explained, or both. Also, it is likely that even if the difference in concordance between responses to the different is real, it is small and of doubtful clinical/practical significance. This aspect of the analysis should be performed better and/or explained better, or omitted.

We have added additional statistical information about the concordance (lines 174-179).

3. The three month post-MDA samples referred to in the text (line 93) don’t seem to be referred to again. Were they analyzed, and if so, do the results support the conclusions of the study?

These data were briefly analyzed and showed only a slight decrease in MFI. As they did not add to the data or contradict the eventual conclusion of the lack of seroreversion, we did not include the analysis in the paper to facilitate the data interpretation. Because of that, we have removed mention of this in the manuscript (line 95).

Minor essential revisions
None
Discretionary revisions

4. The Discussion is quite long and could be edited for additional conciseness and clarity. In its current form is is difficult to determine what are the really important findings and what is peripheral.

In writing the discussion we made every attempt to be concise. This resulted in what we view as a fairly short discussion of only 4 paragraphs and fewer than 1000 words. We have added one sentence at the beginning of the third paragraph to better introduce the topic of that paragraph, but without further guidance on the source of confusion for the reviewer, we are unable to make additional changes to the discussion.

5. The Introduction has similar problems to the Discussion - it is diffuse and it is difficult to determine the central question being addressed

The Introduction has been reworded to provide more focus on the studies conducted (lines 74-80).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests.
Reviewer's report
Title: Longitudinal Analysis of Antibody Responses to Trachoma Antigens Before and After Mass Drug Administration
Version: 1 Date: 13 March 2014
Reviewer: Wilhelmina May Huston
Reviewer's report:
Minor Essential Revisions

1. Figure 2A and B are not mentioned in the manuscript text at all. The results section is very brief and in the same three paragraphs jumps between the three figures in a manner that is difficult to follow and undervalues the findings a little. Please revised the first results section to improve the wording and clearly explain each figure.

   Figure 2 was cited in the text on line 171, but the citation for Figure 3 was inadvertently omitted from the Results section. WE have added this reference and

2. Line 202 pg 9. The kinetics data is a valuable data set and however, it isn't really clear how the numbers on this line relate to the data shown in Table 1? -353.5 as a lesser decline - does this mean it didn't decline and was actually an increase? Please re-work this paragraph, especially lines 199 to 205 and clarify this data.

   We have made the requested changes (lines 202-208).

3. Line 339. Please add MFI to the abbreviations list or write in full here. Is is MFI-BG in the methods and it is MFI on this table - were the MFI or MFI-BG data used to generate these means?

   We have made the requested change to indicate that MFI-BG was used in this table.

4. Line 293 - NTD is not in the abbreviations list. Is it really necessary to have all of these abbreviations. For example, DBS, MDA and NTD are only in the text a few times. Wouldn't it better to write them in full on each occasion.

   We have removed MDA and DFID from the list of abbreviations and spelled out NTD in its two usages. We have left DBS there since it is used 5 times in the manuscript to adhere to the convention of abbreviating terms used more than 3 times in a manuscript.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language