Author's response to reviews

Title: The distribution of incubation and relapse times in experimental human infections with the malaria parasite Plasmodium vivax

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Author's response to reviews: see over
Response to reviewers – 6 August 2014

Reviewer's report

Title: The distribution of incubation and relapse times in experimental human infections with the malaria parasite Plasmodium vivax
Version: 1 Date: 3 July 2014
Reviewer: Kasia Stepniewska

Reviewer's report:
Overall, I feel that the points raised in the initial review were addressed adequately but there are still some details missing in the presentation of methods and results.

Major Compulsory Revisions

1. Methods section is a bit difficult to read – perhaps it could be rearranged to describe the datasets first, provide definitions of outcome and so on.

Authors’ response: We have reorganized and revised the methods sections to address these concerns.

2. Methods Section. It is not clear to me how the sensitivity analysis was done. In methods section it says “To examine sensitivity of the model selection procedure” while in the tables heading it says “to assess impact of data-quality on distributional fits”, which seem to me like different objectives. For the first one, I would imagine the model selection would be performed on the pseudodata, to confirm if the “best” distribution is still selected for the pseudodata. In the results only DICs are presented so does it mean that just the “best” model was fitted to the pseudodata? What models are compared with DIC?

Authors’ response: We have clarified our sensitivity analysis in both the methods and results sections.

3. Authors should justify their approach of fitting one model to the dataset with 4 sub-populations, even though the KM plots look very different between the four subsets. Figures S5 and S6, as far as I can see, show reasonably good fits in each of the subsets, and this should be commented on in the results section, but I am not convinced that this is the best fitting distribution.

Also, would it be helpful to perform fits after excluding one subset at a time? - to see if the shape of distribution does not depend on any of the subsets being included in the analysis.

Authors’ response: We greatly appreciate the reviewer bringing this issue to our attention; the primary constraint in the original analysis was computational. To address this issue we used a week of cluster time to comprehensively model...
distributions for all sub-regions individually, including sensitivity analyses. This analysis does show some differences in best-fits by subregion, which have been highlighted in new figures, and we provide both sets of distributions in this revised manuscript.

4. Page 7. Last paragraph. Third line. Not sure what is the message of this sentence - do you mean that the bimodal distribution is due to two different strains?

**Authors’ response:** We have clarified this point.

5. Figures 4 and 5. In case of bimodal distribution, when mixture models performed better than the single models, it would make more sense to present those on the graph, not the best-fitting mixture compared to the unimodal distributions.

**Authors’ response:** We have redrawn these plots to address the reviewer’s comment.

6. Results Section. Sensitivity analysis. This should form a separate section. Authors should interpret results presented in Section IV of the supplementary material. For example what disproportionally large DIC values mean, for relapse times in old world temperate subgroup.

**Authors’ response:** We have separated this section; the concern about extreme DIC differences is not an issue after refitting distributions to individual sub-regions.

7. Page 9. Third Line. “Comparison...” This statement is unclear. Does it mean that for any values of parameters from the 95% CIs, these distributions give different total number of cases?

**Authors’ response:** We have clarified this point.

Minor Essential Revisions
8. Table 3 is not referred to - should be on page 5 when describing data for the infections with long latency.

**Authors’ response:** Correct reference has been added.

9. Page 8. Line 5. Wrong figure numbering. Figure 2 does not show study populations but the studied distributions.

**Authors’ response:** This has been corrected.

10. When authors refer to supplemental information, it should be more specific,
Authors' response: We have added these throughout the manuscript.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests