Reviewer’s report

Title: C-reactive protein as a potential biomarker for disease progression in dengue: A multicountry observational study

Version: 1 Date: 01 Nov 2019

Reviewer: Michael Hawkes

Reviewer's report:

I thank the authors for their revised manuscript and responses. Most of my comments have been satisfactorily addressed.

I do remain unsatisfied with the authors' responses to the following, but leave these as discretionary revisions, which the authors may choose to ignore:

6. Exclusion of patients with high CRP

Authors' Reply: "The accuracy of an arbitrary value outside the upper limit of detection of the assay, we decided, was unacceptable."
Equally or more unacceptable is disregarding these patients entirely from the analysis!

"The numbers were 19 and therefore would not affect the overall results."

Please provide a sensitivity analysis, including and excluding these patients to show that the overall results are not affected. Can use arbitrary level above cutoff or multiple imputation when including the patients with CRP above upper limit of detection.

8. Table 3, and indeed entire non-linear analysis of CRP as prognostic marker, not easy to understand
The authors vigorously defend their intricate statistical approach, and oppose a ROC analysis and dichotomization of the CRP.

Accepting their statistically grounded arguments, I maintain that this comes at the expense of clarity and simplicity. Clinicians will have difficulty applying the results to their clinical practice.

I continue to urge the authors to report, in addition to their complex analysis, a single OR for CRP above a certain cutoff as a dichotomous predictor of intermediate/severe dengue.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.
I declare that I have no competing interests.

**Statement on potential review bias**
Please complete a statement on potential review bias, considering the following questions:

1. Did you co-author any publication with an author of this manuscript in the last 5 years?

2. Are you currently or recently affiliated at the same institution as an author of this manuscript?

If you can answer no to all of the above, write 'I declare that I did not publish with these authors in the last 5 years and also meet the affiliation criteria’. If your reply is yes to any, please give details below.

I declare that I did not publish with these authors in the last 5 years and also meet the affiliation criteria.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.