Reviewer’s report

Title: Assessing Correlates of Protection in Vaccine Trials: Statistical Solutions in the Context of High Vaccine Efficacy

Version: 1 Date: 02 Jan 2019

Reviewer: Dean Follmann

Reviewer’s report:

My comments have been adequately addressed. I have a few comments on the revision.

Page 7 lines 45-57 describe a new simulation, but not enough detail is given, e.g. distribution of the surrogate, the parameters generating the data, number of simulations.

Also Table 3 is referenced as Table 2. Also, Table 3 has a VE with a hat on it. Is the hat appropriate? I think you mean true VE which should be labeled as such.

Also the rest of this section (lines 6-44) is about the relationship between alpha_hat and beta_hat. Table 3 is about the estimated VE under different methods, so how does this simulation "confirm these results" (as you say on line 46) i.e. confirm conclusions from the scatterplots of Figure 1? What model do you estimate here?

The results of Table 3 deserve comment. With the logistic model, as VE increases 1, the method messes up more and we see mean(VE) getting more and more biased; the method is blowing up more and more. Firth and WIP show similar VE estimates even as VE increases. I wonder why that is. Can you speculate? Is the number of subgroups with 0 vaccine events similar across the various high VEs?

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

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