Reviewer’s report

Title: The hidden burden of measles in Ethiopia: how distance to hospital shapes the disease mortality rate

Version: 0 Date: 16 Apr 2018

Reviewer: Matthew Ferrari

Reviewer's report:

This is an interesting analysis that tackles the important and inherently challenging problem of quantifying morbidity and mortality that occurs outside of the view of the health system.

In general, I would like to see more formalization of the models (dynamic model and statistical models) presented in the main text. It was difficult to evaluate the results without referring to the models and notation presented in the Supplement. The main text should be self-contained, with the supplement only providing additional information as necessary.

L 187 It isn't clear from the text how the authors arrived at the estimated number of cases per kebele/woreda. I presume the authors took the total estimated number of cases from the dynamic model (which was fit assuming homogenous mixing, and was not fit separately to each location) and desegregated this to the smaller spatial units — perhaps by simply assuming the same incidence rate in all locations? The assumptions here need to be clarified. If the model was fit separately to the different time series in Figure 1C, this should be clarified in the text and the parameter estimates for each fit presented.

The unobserved incidence is itself an estimated value, with a corresponding confidence interval. It is not clear if the uncertainty in that estimate was included in the accounting of the estimate of reporting rate as a function of distance. That is, in the regression described in L185, was the incidence used just the posterior mean estimate of the incidence? Or did the authors take draws from the resulting posterior distribution of incidence estimates to get a distribution of regression model fits?

L 190 The analysis of relative risk as a function of distance is not well motivated or spelled out. Here, again, I think the paper would benefit from the inclusion of some mathematical notation within the main text itself. It seems that the argument the authors are making here is that they assume that other health outcomes are not expected to have incidence rates that decrease with distance from the hospital — thus the consistent negative relationship observed in other health outcomes is evidence that measles also does not have a distance dependent incidence rate (see argument on L 294-298). This should be more clearly stated, and it also suggests the ability to quantify this formally through a statistical test; e.g. if the slope of the distance relationship for
other health outcomes is the same as for measles, then this would be consistent with a reporting issue alone. Note, for such a test, one would want to constrain the RR as a function of distance to go through the point (0,100). The fitted lines that the authors present in Figure S7 do not do this, implying, for example in the top left panel, that the RR for all patients at distance 0 is 70%, which is impossible given the definition. When fit with that constraint, it would appear that the relative risk of seeking hospitalization for measles as a function of distance is higher than for most of the other health outcomes presented.

Table 1. It is not clear how this is ordered. Given that the key pattern presented here is the rate of reporting as a function of distance, I would have expected to see this table presented in decreasing order of distance from Woliso. However, that doesn't appear to be the case — though it is clearly also neither random, nor alphabetical. I think it would be much clearer just to present this table in order of distance from Woliso.

Minor points:

L 126 — this is an estimated population size

L 127 — this level of detail on the male/female breakdown is unnecessary. It would be sufficient just to give percentages.

L 139 — the authors assume here that this coverage is homogeneous across the whole region. How valid is this assumption? See Takahashi et al 2017 Nature Communications or Utazi et al 2018 Vaccine for a recent illustration of spatial heterogeneity in vaccination coverage. The former paper also includes the necessary code make subnational estimates of coverage for other countries from the DHS surveys. This seems relevant here as both showed that coverage tends to decline with distance from major population centers.

L 171 — How was the scale parameter of the negative binomial estimated? The authors only refers to 5 estimated parameters.

L 318-319 — I think the authors mean to say that CFR increases. From 0.62% to 20%? If not, I'm not sure I understand this sentence.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

Not applicable

Are the conclusions drawn adequately supported by the data shown?
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