Author's response to reviews

Title: Hydroclimatological variability and dengue transmission in Dhaka, Bangladesh: a time-series study

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Response to referees’ comments

“Hydroclimatological variability and dengue transmission in Dhaka, Bangladesh: a time-series study”

We thank the editors and referees for their thorough reviews and useful comments. We have addressed each of the referees’ comments in sequence, and revised the manuscript accordingly. The revisions are highlighted within the manuscript. The referees’ comments are copied below in italics, with our responses to each comment in regular font.

Response to reviewer #1

The article “Hydroclimatological variability and dengue transmission in Dhaka, Bangladesh: a time-series study” presents a time series analysis using data on clinically diagnosed cases from Dhaka, Bangladesh. The analysis is based on statistically sound techniques (autoregressive poisson models) and inferences are correct. The non-linear relationship with flooding is clearly described and I think that is the major finding of this manuscript. Authors also comprehensively summarize the limitations of their study, especially the quality controls made to improve the maximum data quality possible given the constraints of the study setting.

Minor Essential Revisions

Some minor typographical corrections are in the commented draft and some suggestions about new studies on the ecology of Aedes aegypti that could be relevant to improve the discussion on stagnant ground pools and the ecology of this mosquito vector species.

We have corrected the typographical errors. We have included the suggested previous studies on the ecology of Aedes aegypti in the discussion: “Stagnant ground pools except for sewage water and septic tanks [37, 38], however, are not a common larval site for the container-inhabiting Aedes mosquito and flood water caused by overflows of river water may not be of optimal quality for the development of Aedes larvae.” (page 11, line 14-17)
Response to reviewer #2

Major Compulsory Revisions

The manuscript entitled “Hydroclimatological variability and dengue transmission in Dhaka, Bangladesh: a time-series study” aims to estimate the effect of river level and rainfall on the incidence of dengue in Dhaka while controlling for other seasonal determinants. This is pursued by statistical modeling of hospital data using mainly river level and meteorological data as explanatory variables. The authors report an association with river levels at 0-19 week lags and a causal link between river level and dengue cases is suggested.

In order to provide the reader the chance to understand the results better, a table reporting parameter estimates of the final model should be included (if too long, as supplementary information).

We have created a new Table S1 (in the supplementary online materials) that shows all the parameter estimates of the final model.

Also, 19 week lags are included in the model, it is hard to interpret the relation with dengue cases of something occurring 5 months in the past, therefore an interpretation of this result should be better discussed.

We have amended the explanation of the possible cumulative effects of low water levels in the community on dengue incidence (page 11-12): “Thousands of pieces of garbage, including plastic containers, are scattered along water bodies. When water remains in discarded containers after the increased water levels recede, breeding conditions for the Aedes mosquitoes that are capable of spreading dengue may be created. Eggs of Aedes mosquitoes are desiccation-resistant and are commonly laid above the waterline in tree holes, tires or other water-holding cavities [37]. When dry conditions prevail during the previous 6–19 weeks, water levels in the cavities gradually decrease and the eggs end up at varying distances above the waterline as a result of several ovipositions at different times. Thus, eggs laid by different female mosquitoes will accumulate in a cavity as the water level drops (and the area of the inner wall above the water increases); this is one of the cumulative effects of low water levels. The eggs will hatch
when submerged in water as a result of an increase in the level of water bodies [38]."

The causal relationship suggested between flooding and dengue transmission is at the same time the manuscript’s most interesting and original feature and its biggest weakness. The originality of the findings provide interest to the manuscript but, in my opinion, also require more than a single statistical model (a tool only capable of showing associations) to support the causal process suggested, especially in the case of a variable like river level which can clearly be correlated to other climatic variables. Even though the authors recognize that only an association is found, I still believe that more evidence suggesting causality is needed.

We agree with the reviewer’s concern that “a variable like river level can clearly be correlated to other climatic variables”. This is exactly the reason why we have incorporated all variables of rainfall, temperature and river level with same lags in the final model to adjust for potential mutual confounding. After obtaining the results using the final model, we separately estimated the relationship between the number of dengue fever cases and rainfall (or river level) adjusted for season, interannual variations, holidays, river level (or rainfall) and temperature. To make it clearer, we have added the following sentences in the statistical analysis on page 7: “We have incorporated all variables of rainfall, temperature and river level as a natural cubic spline (3 df) with the same lag period in the final model to adjust for potential mutual confounding. A detailed description of the final model is given in the supplementary material.”

We also agree that "more than a single statistical model" is required. Therefore, we have estimated whether or not the main results are sensitive to the levels of control for seasonal patterns by replacing the different number of harmonics of the Fourier terms with up to the 12th harmonic per year adding one harmonic at a time (0–10 pairs of harmonics). Furthermore, we examined indicator variables for each month instead of the Fourier terms to control the seasonality. All the results of these different models are shown in Figure S1. To investigate the sensitivity of the main results, we also repeated the analysis using the river level data from each of the four monitoring stations separately. The results are described on page 10, lines 13-17.

Furthermore, Table S1 seems to show high model selection uncertainty (#AIC values <1) between models including river level and/or rainfall. Therefore, there does not seem to be enough weight of evidence to select between the three models.
It is true that model selection is difficult when there is little difference in AIC between the models. In this study, our intention was to show the diagnostic results of each model and not to compare AIC between the models. That is why we did not choose any one model as the best model. However, to avoid any misunderstanding, we have added the sentence “The evidence is not enough to be able to select between the three models,” to the results (page 10, line 12)

In order to add more support to the results and conclusions, perhaps not an exhaustive survey, but some entomological evidence would help.

We have added the following sentences to the discussion: “Our hypothesis is supported by a previous report that a large number of Aedes albopictus was identified in a flooded area [41]. Mechanistic models to estimate Aedes mosquito abundance in response to flooding have been developed [42, 43]. Aedes albopictus is more likely than Aedes aegypti to breed and transmit dengue outside the home [40], and it is the principal vector of dengue transmission in Dhaka [44]. Dhaka has unique topographical characteristics where the low-lying land and abundant bodies of water may be related to the observed association between river level and dengue incidence. Further environmental and entomological studies are necessary to elucidate the causal pathways of these associations.”

We have also amended the following sentences in the conclusions: “Because systematic mosquito data for the study area were not available, the findings of this study do not represent a causal connection. However, this study points to the possibly important role of river levels in predicting dengue incidence in Dhaka. Further studies that incorporate entomological information are warranted.”

Another possibility would be to compare more thoroughly different candidate models including different variables reflecting different competing hypothesis using model selection techniques. Of course, it should be noted that perhaps other ways to better support the proposed mechanism can be found. Overall, it is an interesting manuscript but it needs more evidence to support its main findings.

The specific purpose of this study was to quantify the effects of river level and rainfall on dengue incidence after controlling for all possible confounders (as was described in
the manuscript) and not to identify the best predictive model of dengue fever. If the objective of the study was to select the best predictive model, then it might be a good strategy to compare more thoroughly different candidate models including different variables reflecting different competing hypothesis using model selection techniques. However, because this study had a different objective, the variables included in the model were decided a priori; this is a procedure that has been commonly used in previous studies with similar objectives. Nevertheless, as we have described above, we did create different models in seasonal control and river level data and examined whether or not the results were different from the results obtained using the final model.

We believe that the manuscript has been revised in accordance with the reviewers’ comments. Concerns have been addressed and, where necessary, explanations have been provided.

End of revisions