Author's response to reviews

Title: A Dynamic Estimation of the Daily Cumulative Cases during Infectious Disease Surveillance: Application to Dengue Fever

Authors:

Pei-Hung Chuang (d49307013@ym.edu.tw)
Jen-Hsiang Chuang (jhcchuang@cdc.gov.tw)
I-Feng Lin (iflin@ym.edu.tw)

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Author's response to reviews: see over
Dear Editors,

We would like to thank again for all your valuable comments for our previous revised manuscript. A point-by-point response to the editors and two reviewers' comments is enclosed in this cover letter and the second version of the revised manuscript will be uploaded accordingly. The major changes in our revised manuscript are briefly summarized as follows:

1. We have added or revised sentences in the main texts according to the reviewers’s suggestions. All changes have been tracked marked in the revised manuscript. (Please see details on the point-by point response bellows)

2. Table 1 has been changed to cover two seasons 2005-2007.

3. We have moved figure 4 and the description about the data in the “Discussion” section to the “Result” section.

4. Table 2 and its related texts have been removed from the manuscript.

5. The legend “daily observed” of Figure 2 was renamed as “daily confirmed” and the colors of the lines were changed in consistent to Figure 3.

We hope that you find these changes satisfactory for possible publication. All authors have reviewed and agree with this work and the response to comments and criticisms of the reviewers. We all have learned so much from your comments. We are looking forward to a favorable response from you.

Sincerely yours,
I-Feng Lin
Response to the referees' comments
Manuscript “A Dynamic Estimation of the Daily Cumulative Cases during Infectious Disease Surveillance: Application to Dengue Fever”

Below, please find point-by-point response to the referees’ comments. Referees' comments appear in italic.

Reviewer: Hirofumi Ishikawa
Reviewer's report:
General:
The manuscript is much improved. However, there still remain some major modifications.

Major compulsory revisions:
1. The authors should describe an explanation of Fig.4 in “Result section”. The sentences in page 17, lines 2-5 should be moved to “Result section.”

Answer:
Thank you. We have moved the explanation of Fig 4 to the Results section as suggested.

2. The authors should explicitly indicate grounds, such as results in Figures or Tables, for the affirmative in comparison between a parametric approach based on gamma distribution and non-parametric approach (page 15, line below2-page 16, line 5).

Answer:
Thank you for the comments. We have added statements referring Figure 2 (for daily new cases), Figure 3 and Table 1 (for cumulative cases) for the affirmative in comparison between a parametric and non-parametric approach in the revised manuscript (changes marked).

Minor essential revisions:
3. Does “the daily new cases observed on date c” show “purple dashed line in Fig. 2”? If so, “the daily new cases observed on date c”, unlike “the daily new cases estimated”, was fixed value without regard of different dates’ viewpoint. If not, this description may confuse readers (page 12, lines 12-13).

Answer:
The “the daily new cases observed on date c”(purple dashed line) in Figure 2 was
confirmed new cases observed on date $c$ without using the proposed models. Therefore this number was not fixed daily. We have changed the legend for the purple dashed line in Figure 2 from “daily observed” to “daily confirmed”. We hope this will avoid confusion.

4. About “a valid estimation” pointed out in No.8 previously, the revised manuscript is much improved. The reviewer hopes more accurate description on the basis of Table 1 (page 15, lines 4-8).

**Answer:**
We have added more descriptions based on Table 1 right before the sentence “This proposed method… provided more accurate estimates…” as suggested (changes marked).

5. The description in page 19, lines 2-5 seems the repetition of the sentences in page 16, lines 5-8.

**Answer:**
We have rewarded the last sentence in the Discussion to avoid the repetitions.

**Discretionary revisions:**
6. The authors should improve English expressions in page 13, lines below 1-2, page 14, lines 1-2, and page 15, lines below 1-2.

**Answer:**
We have sent our manuscript for English editing by a English native speaking colleagues to improve English expressions.
Reviewer: Laura Forsberg White

Reviewer's report:

Major Compulsory Revisions:

1. I still have concerns about the simulations that the authors describe. It is really not clear what they are going to show given that they do not actually seem to represent epidemic data. Sampling with replacement, but without regard for the dependence in the data is a bit odd and does not seem to show anything. I would suspect that the datasets generated from this sampling scheme are so similar to the original data that they are not very meaningful. The authors only say that they use some sort of bootstrap technique to preserve the shape of the data but it is not clear what they are doing. I just can’t tell if these simulations are appropriate and actually adding to the result by the information given. It the authors could simulate some actual seasonal disease data that is not necessarily based on an existing dataset or is guaranteed to have enough randomness to it so as to be information, that would be more meaningful. It is not clear from the information given that this is the case.

Answer:
Thank you for the valuable comments. While we intended to report sampling variation on the analyzed data and used somewhat inappropriate terms of simulation-like measures, the information added was limited. In order not to introduce confusions, if the editors and reviewers agree, we would like to remove the table 2 and its related texts. The changes were marked on the revised manuscript.

2. I am still concerned about the change in protocol at the Taiwan CDC and how that will impact implementation of this method in the future. What the change seems to mean is that the OC time will now decrease somewhat. So using data from before the policy change to estimate the OC curve (as is required in the method) will tend to overestimate the OC distribution for calculating $P_i(c)$ until sufficient data has been accumulated under the new procedure to outweigh the data from the old procedure.

Answer:
We agree that the $P_i(c)$ may be overestimated using the data crossing different protocols in laboratory diagnosis. Actually, the epidemic curves of the two seasons 2005-2007 (Please see the new Figure 1) and the distributions of the OC times were not the same even using the same protocol. However, the estimates using the information within one year before the estimation date still performed not bad. These information serves like a “prior” in estimating the daily cases. With a new protocol with shorter OC time, a proper “moving window” only including the cases with new
definition until more data accumulated could be chosen.

Minor Essential Revisions:
1. pg 6. The last sentence of the Background is a bit ambiguous. The authors should be clear that they are developing a new method to estimate the number of daily cumulative cases and that this method will be applied to dengue fever in Taiwan, as an example. As it is currently stated, it reads that the method is both applied to dengue as an example and was also developed for the sole purpose of analyzing dengue in Taiwan.

Answer:
We have revised the last sentence of the Background as suggested.

2. pg. 6, first sentence of Methods. It is not clear why May 1 is chosen. What does that have to do with the dengue fever season spanning two years?

Answer:
Since there are almost no dengue fever cases during the winter in Taiwan, we chose May 1 as the beginning of the dengue epidemic season. We have deleted the unclear sentence and revised the first sentence of the Methods.

3. pg 7, next to last sentence of Data sources section. The authors mention the Gamma distribution here without any prior information on what this is referring to. This is a bit confusing to a reader.

Answer:
In order not to confuse readers, we deleted the sentence next to the last one of Data sources section, and inserted a statement “As mentioned in the previous section, the mean and standard deviation of the OC-time were different between positive and negative cases,…” in the last paragraph of the Proposed method section.

4. pg 7, last sentence of Data sources. Why do the authors not provide a curve of the 2005-2006 season. It is not the season being studied, but is very important to the implementation of the method. It would be important to see how that season compares in shape to the 2006-2007 season.

Answer:
We have added the curve of the 2005-2006 season in Figure 1 as suggested.
5. pg 8, line 12. In parenthesis it says $O_i \geq c$. Should this be $D_i \geq c$?

**Answer:**
We have corrected it as suggested.

6. pg. 8, eqn (1). For the second line of the equation, how can $E_i(c) = Y_i + P_i(c)$ when $Y_i$ is unknown in this case? I suspect that it should just be $P_i(c)$, unless I am missing something.

**Answer:**
We have corrected it as suggested.

7. pg. 9. The definition of $t_i(c)$ in the equation is not really the OC time for those that are censored. $t_i(c)$ should be given a different name, since $T_i$ is already given the name of the OC time.

**Answer:**
If the editors and reviewers agree, we would like to keep the notation simple. We have redefined the $t_i(c)$ as the OC-time or censored OC-time for the $i^{th}$ suspect case as of date $c$. (page 9, lines 5-6)