Author's response to reviews

Title: Design of Non-Pharmaceutical Intervention Strategies for Pandemic Influenza Outbreaks

Authors:

Dayna L Martinez (d.martinez@neu.edu)
Tapas K Das (das@usf.edu)

Version: 3 Date: 2 December 2014

Author's response to reviews: see over
Response to Reviewers

Reviewer: Allison Aiello

**Reviewer's comment:** “Overall, this is a very interesting paper that addresses an important question regarding NPI application for mitigation of a pandemic. There are some question regarding the parameterization of the model. There are many assumptions, partly because data do not exist, in terms of implementation of the NPIs. The methods would have been more convincing if they included earlier NPI study data to further support the parameters that were assumed regarding NPIs and how the process may work in a real pandemic scenario.”

**Author's response:** Our parameters were, as pointed out by the reviewer, not taken from a specific NPI study data since the availability is very limited. However, our choices of parameter values were made from a broad array of pandemic literature. We went back to the manuscript and made sure all parameter values were fully supported by literature. We also added references to Table 1 (page 15).

**Reviewer's comment:** “I am not an expert in ABM. Therefore, it is not possible to comment extensively on the conclusions from the model. However, I have some moderate concerns about the assumptions used to create the intervention/model and therefore there may be ways to improve the overall model. In the limitations section, the authors should further describe the assumptions underlying the process and ways that they created the NPI's/response and whether this realistically mirrors a real way pandemic scenario.”

**Author's response:** There are many assumptions in our simulation model, which directly affect the contact and infection processes, the design of the NPIs, and the NPI responses measured from the model. Through an extensive review of influenza pandemic literature, we have provided support for our assumptions. We have also made model parameter choices based on information available in the literature from past pandemic outbreaks. Statistical analysis presented in the paper allowed us to examine the impact of parameters on various performance measures. Note that, any new influenza pandemic outbreak it’s likely to bring a new virus strain and its associated epidemiological characteristics that are different from the past outbreaks. Consequently, the actual outcomes of application of NPIs may differ from the results that are presented in this paper. However, the methodology is flexible enough to adopt the changes in assumptions and parameter values to yield NPI policy guidelines for the public health decision makers. (See page 12, starting in line 449).

**Reviewer's comment:** “The tables and figures are hard to follow with the extensive abbreviations that are used, I suggest making them clearer and spelling out abbreviations.”

**Author's response:** We added legends at the bottom of all tables and figures, where all abbreviations are spelled out.
Reviewer: Szu Chieh Chen

Reviewers comment: “P3/L60. Please delete the cited reference [19]. The working paper is not suitable for citation.”

Authors response: Citation was deleted.

Reviewers comment: “In agent-based transmission model, how to concern the interaction between two different NPIs?”

Authors response: We did a statistical ANOVA analysis using the outcomes of our simulation model to examine both the individual impact of the NPI parameters and many of the significant 2-level interactions. See, for example, Figure 4 that presents the interaction between Cases to Close a Classroom (CCC) and School Closure Duration (SCD) and it is explained on page 9 line 310. Tables 2, A-1, and A-4 also present results of 2 way interactions for different parameters of the NPIs. Some of these interactions are easy to understand and explain. For example, setting parameters for Global Threshold (GT) and Deployment Delay (DD) could affect the total number of infected (see page 10, line 360). Some other interactions are not as straightforward, and more analysis needs to be done to understand why the particular behavior has been observed. For example, interpreting two-way interactions for 3-level experiments.

Reviewers comment: “For school closure modeling, how to measure the increased number of students with their family because of the school closure?”

Authors response: One of our simulation outputs is the number of contacts. It can be seen in our simulation model description that there are different mixing groups, such as households and schools. We can track the number of contacts made each hour at every one of these mixing groups. Consequently, we can compare the number of contacts made at households in a pandemic scenario with and without school closure. Tables 4, A-3, and A-6 show the number of contacts at households and schools for three cases of interventions, a baseline (no NPI), an ad-hoc NPI, and the optimal NPI* for all three different pandemic scenarios. In all of them, the number of contacts at school is greater than the number of contacts at households for the baseline scenario (no interventions). For the ad-hoc and optimal NPI strategies, however, we can see that the number of contacts is greater in households than in schools, due to school closure and students having to stay at home with a guardian.

Reviewers comment: “Please add the cited reference for low and high level in Table 1.”

Authors response: Low and high level values of the NPI parameters were taken from papers in the literature that have studied NPIs. References have been added to Table 1. There are no references available for deployment delay (DD), classes to close a classroom (CCS), and percentage department to close a workplace (PDCW). Deployment delay has been added to our study based on our experience seeing the response to past pandemics, for example H1N1 in 2009, when even though school closure was deployed after a threshold of infected cases has been seen in some areas, there was a delay until it was fully in place. CCS and PDCW are parameters that have not been considered in other studies, since partial school and workplace closures, to the best of our knowledge, has not been studied before. This explanation was also added to the body of the paper and can be found in page 8 starting from line 272.
Reviewer’s comment: “For reasonable parameter setting, 42 days for school closure (SCD) are possible in reality scenario?”

Author’s response: We assume that the reviewer feels that 42 days of school closure is too high, and such a long closure may be impractical in reality. If so, we are in agreement with the reviewer. However our choice of 42 days of closure as an option was motivated by such considerations made earlier in the published literature. For example, Cauchemez 2008, German 2006, Kelso 2009, Milne 2008, Sypsa 2009, and Glass 2009 considered closing schools for the duration of the pandemic, which in most cases were more than 42 days. There are other papers like Carrat 2006, and Davey 2008 that closed schools until a threshold of no new infections in a certain number of days was reached, which in some cases was as long as 42 days, sometimes more. Chao 2010 closed schools for 60 days in his study. We have now added the above mentioned references in the paper (see Table 1, page 15) in support of our choices for the length of school closure parameter.