Author's response to reviews

Title: Modeling the progression of swine-origin influenza A(H1N1) epidemic in Vietnam and opportunities for reassortment with other influenza viruses

Authors:

Maciej F Boni (mboni@oucru.org)
Bui Huu Manh (bhmanh73@gmail.com)
Pham Quang Thai (pqthai@nihe.org.vn)
Jeremy Farrar (jfarrar@oucru.org)
Tran Tinh Hien (hientt@oucru.org)
Nguyen Tran Hien (nthiennihe@vnn.vn)
Nguyen Van Kinh (kinhvaac@yahoo.com)
Peter Horby (peter.horby@gmail.com)

Version: 3 Date: 25 August 2009

Author's response to reviews: see over
Dear Editor(s), thank you for your prompt review of our submission “Modeling the progression of pandemic influenza A(H1N1) in Vietnam and opportunities for reassortment with other influenza viruses.” We appreciate all the reviewers’ comments and have made the necessary revisions (detailed below, in blue, next to the reviewers’ original comments in black).

In addition, we have removed the following piece of text from our model:

Role of the funding source
The sponsors of this work had no role in the study design, data collection, data analysis, data interpretation, writing of the report or the decision to submit the paper for publication.

as it seems it is not necessary for BMC Medicine. The above statement is still true, so please let us know if we should re-insert it in the main manuscript.

Reviewer’s report #1 Reviewer: Gerardo Chowell

In this paper a spatio-temporal model of the transmission dynamics of influenza that incorporates an age structured population is used to explore the potential impact of the novel swine origin influenza virus A(H1N1) in Vietnam in terms of numbers of cases and hospitalizations. The model is calibrated using demographic and transportation data from Vietnam and epidemiological characteristics reported thus far for this new virus. This is an interesting and timely paper. Overall the manuscript is clearly written and presented and recommend it for publication in BMC Medicine. I only have a few comments that need to be addressed before publication could proceed.

1. The authors use age-specific contact rates from a survey of social contact patterns conducted in 2007 in 865 members of a community in one semi-rural district of north Vietnam. Please provide the contact rate matrix in a Table in the supplement. Is these data in line with the datasets reported by Mossong et al. 2008 [Ref 8 in Supplement], Wallinga et al. 2006, Del Valle et al. Social networks.?

This is now all in the supplementary materials, on pages 2 and 3.

2. The authors mention that influenza transmission trends in Vietnam is quite irregular with more than one peak of incidence per year. An interesting question is whether these historical trends could be useful in validating the spatial patterns realized by their model. In particular, the long tail epidemics produced by the model could be due to spatial factors and levels of rurality as explained by the authors. In summary, I suggest to take another look at the historical data or justify using appropriate literature if available.

Unfortunately, these data are not publicly available yet. Vietnam’s National Institute of Hygiene and Epidemiology (NIHE) has been running influenza surveillance from 15 sentinel hospitals since 2006. These data indicate variable numbers of peaks in influenza seasons in Vietnam, and seasonality that corresponds with wet and dry seasons in the country, which can vary from region to region. We have now written “(unpublished data)” on lines 143-145 to indicate that these data are not yet available.

3. Although the movies illustrating the spatial spread of the epidemics are useful to understand the spatio-temporal spread, a plot of the peak timing as a function of distance to the most connected provinces could be useful in clarifying the spatial spread pattern.
This part is a bit tricky since the spatial resolution of our model is so coarse. What we have done is added a Figure 3 that shows the “peak delay” by province as a function of how far each province’s capital is from the closest commercial airport in Vietnam. The peaks are divided into two groups since the pandemic is predicted to have a wave in the south followed by a wave in the north. Certain provinces in this graph come out as outliers (Lai Chau in particular) where it is clear that our province-level model may not be very accurate.

4. Table 1 summarizes their simulation results. Bar plots might be easier to read for some of the results (age specific morbidity). Please consider presenting some of data in this table as graphs to ease readability.

We feel this would be somewhat unintuitive since the scales of the numbers in this table differ by many orders of magnitude. We could break this table up into 4 or 5 separate bar plots, but we feel it is best to leave the raw results in this format. If the editors feel it is necessary to change this table to several plots, please let us know and we will be happy to do so.

---

**Reviewer’s report #2**  
Reviewer: Sally M Blower
There is some confusion throughout the text and in the Figure Legends regarding which Figure is being referred to – the authors should make any necessary edits to clarify this. The main text also needs to refer to the last 2 Figures & the 2 movies that are included as Supplementary Material. I have a few minor comments regarding material that that I wish the authors to include. These are all minor essential revisions.

Apologies for the numbering mess in the original. This has all been fixed.

1) The authors predict the number of cases that could occur in humans and the numbers of chickens, ducks and pigs that are likely to be exposed to infected humans. I would like the authors to include in their discussion a paragraph on the implications of their predictions for the opportunities for reassortment of H1N1 with other influenza viruses. For example, they should discuss/speculate how many of the exposed animals are likely to become infected, what viral strains are currently circulating in pigs, chickens and swine in Vietnam etc.

This is now in lines 277-285 in the discussion.

2) In the abstract the authors should include the total number of cases they are predicting in humans.

This is now in the abstract.

3) In the introduction (and abstract) the authors should clarify that they are modeling the introduction of H1N1 into humans and the subsequent spread/exposure to chicken, ducks and swine (due to the epidemic in humans), and they are not modeling the emergence of H1N1 from swine to human. Further they should clarify that they are not modeling the dynamics of influenza epidemics in chickens, ducks or pigs.
This is now explained in the abstract and introduction (lines 99–103 and line 120).

4) In the second paragraph of the introduction do the authors mean that 60% of the worlds human and poultry population live in Asia? Or are they referring to only the poultry population?

This has now been clarified.

5) Can the authors briefly explain what they mean by a gravity model (first line in methods)?

This is now in lines 107-108.

6) SEIR needs to be defined when it is first used in the main text.


7) In the Supplementary Material the authors should show their calculations so that it may be seen how the R0 value was derived. It needs to be clarified how cross-province migration events were included in the calculations.

This is now in pages 10-11 of the supplement.

8) The authors need to explain how the relative amount of traffic on large roads to small roads was included in the model.

We had no data on this, and this number was simple varied in a reasonable range. Page 3 of the supplement now clarifies this.

9) All of the parameters that are shown in the model equations in the Supplementary Material need to be defined.

Apologies for this omission in the original submission. All the parameters are defined in the supplement now. Page 9.

10) The Blower and Dowlatabadi paper should be referenced in the supplementary material as well as in the main text.

This citation has been added.