Reviewer’s report

Title: Vaccination against 2009 pandemic H1N1 in a population dynamical model of Vancouver, Canada: timing is everything

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Reviewer: Chris Bauch

Reviewer’s report:

This paper uses a deterministic compartmental model to evaluate crucial questions regarding use of vaccines to mitigate the 2009 H1N1 pandemic. The contact matrix of the model is parameterized from Vancouver-based contact network data, and other parameter values are populated from the relevant pH1N1 literature wherever possible. The authors compare the effectiveness of the actual age distribution of vaccine coverage (AC) to a hypothetical distribution that vaccinates all age groups at a uniform rate (UC) and a hypothetical distribution that only vaccinates parents and children (PC). The authors find some interesting differences between the strategies (in particular, PC significantly reduces total morbidity despite lower overall coverage although its impact on total mortality is less clear), but the dominant message of the study is how program effectiveness can be strongly compromised due to delays in program implementation.

It is clear that much thought and effort has gone into the development of this high-quality model. The authors are obviously very experienced at this have been very careful in how they formulated and parameterized the model. The topic they address is also highly relevant since many jurisdictions are seeking to understand what they could have done differently/better in 2009. The paper is well written, and the appendix includes full details of the model as well as significant supporting information in the form of sensitivity analyses. I think this paper represents a very valuable addition to the literature and the handling editor may even want to consider requesting it to be featured on the journal homepage, once it has gone through appropriate revisions. As a result, I only have one potential major revision regarding how the PC strategy was formulated, along with a few minor changes:

Major Revision

1. How the Parent and Child (PC) strategy is formulated is crucial since the more interesting results of the paper emerge from that strategy. However, the rationale for many aspects of the PC strategy is not clear to me. For instance, why would the vaccine not be given to children under 5 years of age, as Table 2 states? Also, since the strategy presumably should not target 30-39-year-olds without children, why does the strategy include the entire 30-39 age class? It seems like it would be easy to estimate what percentage of individuals aged 30-39 in Vancouver/BC/Canada have children and then to only vaccinate that proportion
of that age class. The same goes for 20-29 and 40-49 year-olds. A third thing that confused me about the PC strategy is that it does not allow for any other individuals to be vaccinated, even though the vaccine coverage is lower than AC or UC and hence vaccine would presumably still be available once all parents and children received it. This would amount to individuals outside the PC classes actually being refused the vaccine. Many Canadian jurisdictions in the 2009 pandemic practiced sequencing whereby high-priority groups received the vaccine first but the vaccine was later made available to everyone. Hence, a more realistic way to formulate the PC strategy would be to allow other groups to be vaccinated once the target coverage had been reached in PC groups, such that the eventual coverage matches the 47% of the UC and AC strategies. This would be particularly interesting in light of Figure 2 showing that the 5-17 age class was the first to be “hit” by the pandemic. Hence, my major revision to suggest is that the authors should either (1) rethink and reformulate the PC strategy in response to the above comments, and/or (2) keep the PC strategy as is but also add a fourth sequencing strategy (such as 0-17 and 65+ year-olds first and then everyone else). As I mentioned in my opening, I think the paper is a valuable addition to the literature as it currently stands, but clearing up these questions around the PC strategy would make it considerably more useful for evaluating the 2009 pandemic and preparing for future pandemics, and hopefully with all the modelling machinery in place it will not create too much extra work to run these additional vaccine coverage scenarios.

Minor Revisions:

2. Abstract: the abstract describes the model as a city level contact network model that captures transmission network dynamics. This implies it is a true network model but actually it is a compartmental model that has been parameterized with contact network data (which the authors do make clear elsewhere). Information is lost when using contact network data to parameterize a compartmental model and so it is important to be clear that this is actually a compartmental model, parameterized with contact network data. Wording should be changed to reflect this.

3. Abstract: results are described in terms of morbidity, but morbidity is never defined.

4. Page 4: “The commencement of this second wave… depending in part upon prior first wave experience, demographic and environmental factors”. Is this speculation/expert opinion or is there a reference the authors could cite supporting the dependence on these three factors?

5. Page 7: please be more explicit about what type of sensitivity analysis was conducted. It sounds like a univariate analysis.

6. Table 1 reports ranges for some parameter values. Please clarify how these are used in the analysis.

7. For Vancouver, would there be grounds to include in the sensitivity analysis pre-existing immunity for those younger than 55 years? There may have been some due to previous H1N1 vaccines or the spring wave, naturally.
8. Discussion: It would be interesting to add a comment on how specific the results may be to the contact patterns in Vancouver. For instance, with a large Asian population, I suppose that intergenerational households are common and thus herd protection effects from a PC strategy would be more significant than for a place like Winnipeg or Halifax for example.

9. References: The URL references may not be formatted according to BMC guidelines, which probably requires things like accession dates and document titles.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have been a co-author with some of the authors of this manuscript in recent years. I have also received research contracts from GlaxoSmithKline, which manufactures a pandemic flu vaccine.