Reviewer's report

Title: The United States and Canada as a coupled epidemiological system: an example from hepatitis A

Version: 2 Date: 4 October 2007

Reviewer: Kimberly Thompson

Reviewer's report:

General:

Overall this is an interesting and well-written study. I believe that the authors have done a good job on the modeling and that they have integrated relevant data available from the literature and from some unpublished sources. I think that the paper has a lot of merits and I hope that my comments are helpful to the authors.

I find it remarkable to think that such a study is required to help Canadian public health officials appreciate the role of the US with respect to risks from infectious disease importation. The authors appear to be making the case that public health officials in Canada should consider travel to the US as a potential risk factor, and I would have assumed that this is in fact already considered. From a policy perspective, the authors explore the impact of the introduction of vaccine in the US on Canada, but it would seem to me to be an even more interesting question to explore the impact of introducing universal vaccination in Canada, given that the US is now vaccinating Canada has targeted vaccination.

I appreciate why the authors chose the formulation for this model (i.e., 2 countries), but I would be interested in the seeing the authors do more to consider risks from other countries. To paraphrase, the risks of importation are related to both the number of trips to/from a country and the risk of infection in that country. The authors make the case that the relatively high frequency of travel to the US means that even though the risks of infection are relatively small, the contribution from the US may be larger than currently appreciated. However, without seeing what the epidemiology looks like, it's difficult for me to know if the authors assumptions here are really OK. I'm also concerned that with respect to hep A, foodborne illnesses are important and it is not trivial to ignore them (in my opinion). It's also odd to me for the paper not even mention the role of food service workers in the spread of hep A and how the disease spreads within a country. I appreciate that the authors want to demonstrate that travel to the US is probably a source of some cases of hep A in Canada, but the paper does not ask or answer the big question for me, which is how big is the contribution relative to all of the other sources?

Also, putting on a policy hat, why would the authors find it valuable to look at the disease incidence as a function of volume of travel? Do they think that this
volume of travel can be controlled? I am particularly concerned with speculative statements like the last one in the Results part of the abstract. I believe that the authors need to think through what they are taking as endogenous and exogenous and how those framing assumptions might be influencing what they see from their modeling. What about the existence of important risk groups (i.e., subpopulations) within each country - the authors mention them on page 5 (MSM), but do not explicitly model them. I noted that Health Canada provides information (http://www.phac-aspc.gc.ca/hcai-iamss/bbp-pts/hepatitis/hep_a_e.html) about relative risks for different groups, and presumably the authors are suggesting that this website should include as a group people who travel to/from other countries including the US. What is the policy outcome that should result from this work?

I appreciated the Tables provided a lot of information and I liked the comprehensive nature of Table 1. I ask that the editors not cut the tables, since they are very helpful. However, I had a difficult time determining the sources for some of the information presented (notably, what is the data source for Fig. 1)? Can the authors say more about the actual cases in the US and Canada? Was there a large outbreak in Canada in the mid-1980's that can be attributed to a particular source, is there clear evidence of importation between the US and Canada and what about clear evidence of importation from other parts of the world? In this regard, I also think the authors should review more of the relevant literature (e.g., why not cite the study by Teitelbaum: Teitelbaum Peter (2004) An Estimate of the Incidence of Hepatitis A in Unimmunized Canadian Travelers to Developing Countries Journal of Travel Medicine 11 (2), 102–106?). I'm asking all of these questions because I believe that the authors should think about the broader context. They have an elegant model, but I think that more thought is required since the model is basically showing what the authors have set it up to show. They have not shown that the US contributes significantly to the burden of hep A disease in Canada relative to the contributions from other countries. What they show is that given the amount of interaction between the US and Canada, we should expect the US to be a potential source of hep A into Canada. That seems obvious to me, but I defer to the authors about what is known.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

I have relatively few compulsory revisions, mainly because I believe that the authors have been very clear in explaining their model. That said, it makes no sense to have results reported as years in the 100s. What does year 120 mean? I know that the authors needed to run their model long enough to reach equilibrium, did it take 100 years? What are the implications of this? The authors need to talk about the dynamics of the model so that it is clear to the reader what they take as time zero (the initial start time of the model), and what happens over the entire time period. I'm not convinced that the time period that they've used is appropriate, but I suspect that this is mainly a reflection of my ignorance about what the authors have done. In any case, the results are essentially meaningless
to me since I have no idea what the time axis means in all of the figures with Year on the x-axis.

I'm also not sure that it is appropriate to assume that the risk of importation from Canada into the US is very small just due to population size differences. As the US vaccination increases and the risks drop in the US, it seems possible that the risks could be non-negligible. How large would they have to be to matter?

With respect to the Canadian Vaccination Parameters, given a policy of targeted vaccination to high-risk groups, does it make sense to assume equal coverage in all age groups? It may not make a difference, but it I think that the authors need to say more about heterogeneity in the population.

My review is already late and I have not checked the equations carefully, so someone should do this. The authors should also say more about what it means to assume that things are in equilibrium.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.