Author’s response to reviews

Title: Assessing secondary attack rates among household contacts at the beginning of the influenza A (H1N1) pandemic in Ontario, Canada, April-June 2009: A prospective, observational study.

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Author’s response to reviews: see over
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RE: Manuscript ID 6073301064814955

Assessing secondary attack rates among household contacts at the beginning of the influenza A (H1N1) pandemic in Ontario, Canada, April-June 2009: A prospective, observational study.

Dear Dr. Ibrahim Abubakar,

Thank you for sharing reviewer comments related to the above-named manuscript revision. We have carefully considered and addressed issues raised as outlined in the table below:

<table>
<thead>
<tr>
<th>Reviewer Comment</th>
<th>Revision</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>In table 1, the authors tabulate the demographic characteristics of the primary cases and household contacts. It would be useful to also have the demographic data and especially 2008/9 seasonal influenza vaccination status for the secondary cases.</td>
<td>The demographic characteristics for secondary cases (excluding co-primary and potential tertiary cases) were added as an additional column in Table 1. This information is also reported in the results section on page 10.</td>
<td>Complete. See Table 1 and text on page 10.</td>
</tr>
</tbody>
</table>
| While the authors have categorized age group into above and below 16 years of age to demonstrate a significant difference, it would be important to provide the data for different age groups (<5, 5-16, 17-25, 25-40, 40-65, >65). While the numbers in these different age groups may be too small to allow accurate statistical comparisons. | The following is now reported in the results section:  

When stratified further by age, SARs were highest in contacts aged 5-15 years (15/51 or 29.4% for ILI and 23/51 or 45.1% for ARI) and 25-39 years (5/29 or 17.2% for ILI and 8/29 or 27.6% for ARI). Rates were lowest in contacts aged 16-24 | Complete. See page 11. |
<table>
<thead>
<tr>
<th><strong>accurate statistical comparisons, nevertheless, the raw data will be important. The authors can either have a separate table or report the significant result (&lt;16 years vs &gt;16 years) in the main body of the text.</strong></th>
<th><strong>years (1/27 or 3.7% for ILI and 3/27 or 11.1% for ARI) and 65 years and above (0/8 or 0.0% for ILI and 0/8 or 0% for ARI) (data not shown).</strong></th>
<th><strong>Complete.</strong></th>
</tr>
</thead>
</table>
| **The authors should report whether there was any clustering of secondary cases in a household, if that data is available. Multiple cases in a household with differences in time of symptom onset may inflate estimates of secondary attack rate because of multiple transmission cycles.** | **This is now included:**  
**In total, 51 secondary cases were detected in 34/87 (39.1%) households; 5 households each had 2 secondary cases, 3 households had 3 secondary cases and 2 households had 4 secondary cases.** | **See page 10.** |
| **The authors report a mean of 3 household contacts per case. Clustering of secondary cases in households should be mentioned here as well.** | **See above; information is inserted in this section on page 10.** | **Complete.** |
| **Was there any difference in the serial interval for secondary cases that were ILI compared to those with ARI?** | **There was no difference in serial interval by case definition.** | **Complete.** |
| **Households with co-primary cases were not excluded. This is normally done.  
I would therefore recommend removal of households with co-primary cases.** | **We are concerned that by excluding the entire household, we may be removing households which are different in some way that we cannot understand or measure. This could, in turn, lead to biased SAR estimates. Other published pH1N1 contact studies (Papenburg J et al 2010 and Morgan O et al 2010) have similarly decided to only exclude the co-primary case,** | **Sensitivity analysis performed.**  
**A statement which explains this sensitivity analysis is included in the text on page 11.** |
not the entire household.

To test the effect of this comment, we conducted a sensitivity analysis where all households with co-primary cases (n=8) were excluded from the SAR calculations; this did not significantly change SAR estimates. For example, the overall SAR for ARI moved from 20.2% to 19.6%, and the SAR for ILI moved from 10.3 to 10.0%.

| There is variable and, in my eyes, much too long, follow-up time. A secondary case occurring 12 days after symptom onset of the primary case was hardly infected by the primary case. I recommend that you include only those households where you have equal follow-up time, e.g. 8 days. Then also cut cases that occur after that period. | In an ideal world, only cases followed up for the same amount of time would be included in the analysis. Unfortunately, as we relied on the existing public health infrastructure to collect information on household contacts, we were unable to collect detailed information on the length of follow-up and cannot make this revision. As a proxy, we obtained case investigation timelines in iPHIS which captures information on the symptom onset of the case, the date the investigation was started and the date the investigation was closed. Using this information, we have provided a description of the average follow-up period. | Data not available; however, detailed description of follow-up period has been included. |

The handling of household contacts who were symptomatic before the "primary case" seems odd. Why 3 days? If they occurred within a range of say 5 days I would simply treat them as the true primary case if they match the ILI case definition. If they did not... | In the original analysis, two contacts were excluded because they had an onset date ≥3 days before the primary case. A three day cut point was selected because in our sensitivity analysis, we looked at the impact of classifying contacts as co-primary cases. | Complete. | See text on page 8 (updated primary case definition) and page 9.
| don’t and were just symptomatic | contacts as co-primary cases if they had a symptom onset within 2 days (before or after) of the primary case, instead of 1 day. As this did not impact the SAR calculation, we decided to classify contacts as co-
| household altogether, but it may be discussable to just exclude that household contact from analysis. | primary cases if they had an onset date within 1 day (before or after) of the primary case. So, in fact, contacts were excluded if the onset date was 2 or more days before the case onset. |
| (explanation on how contacts were reclassified). | We have re-classified these two contacts as primary cases as both met the ILI case definition. This changes the study population to 87 cases and 266 household contacts. |
| | The primary case definition has been updated to reflect this change. |

| For the calculation of the serial interval I would not include potential tertiary cases because you don’t know from whom they were infected. | Symptomatic cases meeting either the ARI or ILI case definition that had a symptom onset date more than 14 days after the primary case onset were excluded in the serial interval calculation. This exclusion changed our estimate from a median of 3.4 days to 3.0 days. |
| Complete. | See text on pages 9 and 11. |

| Abstract: "range" is given for attack rates, but I suppose one is the ILI, and the other is the ARI attack rate. I would not call it a range. | Corrected. The sentence now reads as: “Secondary attack rates were estimated at 10.3% (95% CI 6.8-14.7) for secondary cases with influenza-like illness and 20.2% (95% CI 15.4-25.6) for secondary cases with acute respiratory illness.” |
| Complete. | See text on page 3. |

<p>| Page 7: what is iPHIS? (spell out) | On page 7, the last sentence of paragraph 2, iPHIS was already |
| Pending editorial decision. |</p>
<table>
<thead>
<tr>
<th>Written out in full before the abbreviation was used. Would the paper like it to always be spelt out? If so, we are happy to oblige.</th>
<th>decision.</th>
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</thead>
<tbody>
<tr>
<td>Is it really true that primary cases were not treated with oseltamivir? Was it ascertained if they were? It influences to a certain extent the results because antiviral treatment can reduce infectivity.</td>
<td>In iPHIS, antiviral treatment was only recorded for <em>hospitalized</em> pH1N1 cases. The only source of information on antiviral treatment of both non-hospitalized and hospitalized cases in Ontario is the unpublished case control study referenced on page 12 (personal communication with Laura Rosella). This study demonstrated that there was very little oseltamivir used for treatment of low-risk individuals and even the high risk individuals were often not treated or treated so late that it would make little difference). This is different from other countries.</td>
</tr>
<tr>
<td>You have not discussed the paper by Suess (AJE 2010).</td>
<td>A reference to this paper has been included on page 13 of the discussion (in the context of other studies with higher attack rates and explaining possible differences in study methodologies).</td>
</tr>
<tr>
<td>Page 13: another reason why children have higher attack rates may be their contact behaviour within the household.</td>
<td>Added to page 13.</td>
</tr>
<tr>
<td>Overall the paper seems too long for the contents, even if there is no space requirement.</td>
<td>We have tried to remove superfluous information throughout the manuscript. If you have specific suggestions to remove text, we are happy to oblige.</td>
</tr>
</tbody>
</table>
The last sentence in both the abstract and the conclusion really comes out of the blue; I don’t find it much supported are following from the study as presented.

The sentence has been removed from the abstract and modified in the conclusions.

Complete.

If there are any additional questions and comments, these may still be forwarded as before to Rachel Savage at rachel.savage@oahpp.ca or by phone at 647-260-7403.

Sincerely,

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