Reviewer's report

Title: Rubella immunity among prenatal women in Ontario (2006-2010)

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Reviewer: Antonietta Filia

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This is an interesting paper regarding rubella immunity among prenatal women in Ontario, an important issue in the context of congenital rubella elimination.

Major Compulsory Revisions

1) Background, second paragraph. More details regarding the two-dose MMR vaccination program in Ontario would be useful, e.g. At what ages are each of the two doses administered? Is MMR a recommended or compulsory vaccination? Is MMR vaccination a requirement for school entry? Have any adolescent and adult supplementary immunization activities been performed?

2) Background. Targets established for pregnant women and postpartum should also be mentioned.

(< 4% rubella-negative primigravida women; vaccination of 99% susceptible women postpartum)

3) Background. The authors should provide some data on rubella and CRS cases reported in Canada and in Ontario in the examined time period. When were the last confirmed endemic rubella and congenital rubella cases reported in Ontario?

4) Methods. The type of information collected from each patient at the time of screening should be stated. This appears to include only patient name, date of birth and city of residence. Was any information collected regarding other risk factors associated with non-immune rubella titres, such as race/ethnicity, country of birth, parity, gravidity? If so, further analyses should be performed to measure susceptibility rates in these subgroups.

5) Methods. Additional information should be given regarding the geographic distribution of health regions in Ontario and any major differences between northern and southern health units. Are northern health units mainly urban or non-metropolitan? How is the Ontario population distributed across the province? Are there any major cities in Northern Ontario? Is there a large immigrant population?

6) Discussion, first paragraph, 2nd sentence (“In comparison, achieving 97% vaccine coverage…rubella-containing vaccine”). The significance of this statement should be stated. Are the authors implying that VC is probably higher than 97%? In this paragraph the authors should mention that the 4.4% rate is slightly higher than the established target of 4% for certification of elimination. Also, in some areas of northern Ontario susceptibility is as high as 9.7%.

7) Discussion, first paragraph. The last sentence seems to be out of context in
this paragraph and should be moved, perhaps to Paragraph 6 “In this study, 18.5%....”

8) Discussion, second paragraph. This paragraph should be revised. It is difficult to make a comparison of rubella susceptibility rates obtained in the present study and those in the cited studies since some of the latter are much more dated (Quebec study conducted in 1994-1996, Alberta study 2002-2005, Toronto study 2002-2007). The authors should mention this. Also, were the same cutoffs used in all studies to define seronegativity/susceptibility? For example, in the study conducted in Alberta, seronegativity was defined as a level < 10 IU/mL. On the contrary, in the present study women with antibody titres 5.0 - 9.9 IU/mL were considered to have “Indeterminate” immune status and the percentage of women with indeterminate status is non-negligible, ranging from 5% to 7%. Finally, the authors state that the immunity demonstrated is greater than the modeled threshold of rubella elimination for the US. However, the present study only evaluates immunity in women and the proposed elimination threshold may not apply to current conditions and to the Canadian/Ontario population.

9) Discussion, third and fifth paragraphs. These two paragraphs are somewhat repetitive and should be merged. In paragraph 3, the authors state that “the significant increase in immunity with increasing age may be attributable to the increasing n. of women who have been targeted for immunization through assessment during their childbearing years”. The cited reason may account in part for this result but other factors may have also played a role and should be mentioned e.g. older women have more chance of having been exposed to natural infection but also through postpartum vaccination (this is actually mentioned in paragraph 5 and should be moved here). In the first sentence of paragraph 5, the higher susceptibility among adolescents and young women could also be due to failure to vaccinate (according to information given in the Background, vaccination coverage appears to be quite low:71%) or to vaccine failure.

10) Waning immunity is cited as a possible factor leading to higher seronegativity in adolescents and young adults. This should be further discussed, also with reference to the number of vaccine doses received and to the prevention of congenital rubella.

11) Discussion, third paragraph. Are any data available on the percentage of Ontario hospitals that have adopted standing orders for in-hospital postpartum vaccination of rubella-susceptible women?

12) Limitations of the study are not fully discussed. For each limitation, the authors should discuss how it may have affected study results. Also, some limitations are not mentioned e.g. serosurveys have the limitation of not distinguishing between vaccine-induced and disease-induced immunity; besides demographic factors, other risk ctors for rubella susceptibility (such as country of birth, parity, gravidity, religion) were not examined; postpartum rubella vaccination status was not examined.

13) Conclusions. The statement that rubella susceptibility is lower than in other jurisdictions in North America is not entirely supported by the study findings (see
also comment n. 9) Also, it is not clear why the focus should be solely on post partum women since ideally women should be vaccinated before their first pregnancy.

Minor Essential Revisions

1) Background, second paragraph, first sentence. Substitute “young adults” with “adolescents”. The authors should specify that the goals are to reach 97% one-dose immunization coverage for children by their second birthday and 97% two-dose coverage amongst 7-year-olds and adolescents.

2) Discussion, second paragraph. The references given at the end of the second sentence should be Ref 11-13.

3) Discussion, second paragraph, first sentence: “Rubella susceptibility demonstrated in this analysis is slightly lower…”. Remove “slightly”.

4) Discussion, fourth paragraph. The reference given at the end of the second sentence is incorrect (Ref. 11 study was conducted in Quebec).

5) Discussion, fifth paragraph, first sentence. Remove “older” before adolescents, replace “younger” with “young”

6) Abstract. The first sentence of the abstract “Countries of the Americas have been working towards the goal of eliminating rubella and CRS since 2003.” is somewhat misleading since it implies that rubella transmission has not been interrupted. As reported in the manuscript and the cited reference, it should be further stated in the abstract that endemic rubella transmission appears to have been interrupted in the Americas since 2009.

Discretionary revisions

1) Throughout the manuscript, whenever possible, it would be preferable to use the terms seropositive and seronegative rather than immune /susceptible.

Minor Issues not for publication:

1) Materials and methods. First sentence. Sentence should read “ In Ontario, prenatal specimens, as well as those for…” (add “as” after “well”)

2) Discussion, first paragraph, first sentence. Change 5% to 4.9%

3) References. Ref 3 and 6, authors of these studies should be added.

I agree that my signed report be posted on the website along with the article, if the manuscript is accepted for publication.

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