Reviewer’s report

Title: Childhood MMR Vaccination and the Incidence Rate of Measles Infection: A Ten Year Longitudinal Cohort Study of American Children born in the 1990s

Version: 0 Date: 01 Dec 2018

Reviewer: Walter Orenstein

Reviewer's report:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

The authors are to be commended for undertaking this study and the results should be very helpful, provided the comments below are addressed:

1. There are a number of clarifications needed to improve the quality of the analysis and overall manuscript.

2. Were the measles cases laboratory confirmed or the data were not available? This should be clarified. In other words, the authors should make clear that the diagnoses were based on clinical judgment and not on specific clinical or laboratory-based criteria.

3. In the analysis, are the authors making the assumption that both the 'exposed' group and 'unexposed' group had the same chance of exposure to wild type measles virus? If so, that needs to be made explicit.

4. In the description of the study population, there needs to be some description of the geographical area of residence of those included in the analysis. This is important to better understand the chances of exposure to wild type measles virus during the long study period (1990-2009). In addition, there should be some description of the overall number of measles cases detected by year in the area of residence of the study population. If these data are not available to the authors, then this needs to be clearly stated as a limitation in the Discussion section.

5. For each of the comparison groups, there should be a description that gives a better understanding if they are evenly clustered or distributed over the long study period. Presumably, measles cases decreased over time during 1990-2009, and likely were virtually nil after measles
was eliminated in the U.S. with the last case in 2000. Therefore, the likely chance of exposure would have been quite different in 1990 versus 2009.

6. In Table 2, the demographic summary of the persons diagnosed with measles examined in this study, it would be helpful to provide a description of the cases separately for each of the two comparison groups. Also, it would be helpful to include a variable for the 'age of onset' of measles.

7. The authors only discuss the effectiveness of a single dose of measles vaccine. However, based on Figure 1, follow-up went through 120 months (10 years of age), which suggests ample time for delivery of 2nd doses of vaccine. Can the authors calculate the effectiveness of 2 doses of measles containing vaccine (MCV) compared with one dose and 0 doses? If not, the authors should explain in the discussion and/or limitations.

8. The authors should mention in the methods how two dose recipients were handled. Were they excluded after receiving the 2nd dose?

9. In the Discussion, the authors should offer some potential reasons that they found lower VE than was found in previous studies. In the Discussion, the authors mention three "measles cases" that had been vaccinated with MMR within 30 days prior to the onset of measles. These were likely vaccine reactions, and therefore not cases. Were they excluded from the analysis? That is not clear in the text of the Figure of the study flowchart.

10. In the Discussion, lines 48-52, the authors refer to measles vaccine reactions as 'measles cases'. These should not be referred to as measles cases. And based on limitations of these date, there is a lack of evidence from this study that supports the authors calculation of a statistic and conclusion that: "The results of the present study suggest that MMR vaccine-associated measles cases are rare with a rate of 0.91 per 10,000 MMR recipients (95% confidence interval = 0.19 to 2.67) being diagnosed with a measles infection within 30 days of MMR vaccine administration."

11. Further, to remove the potential confusion of MMR reactions with measles cases, the authors should consider removing all cases of measles within 30 days of vaccination and focus the analysis only on cases occurring in unvaccinated or in vaccinated persons more than 30 days post vaccination date.

12. Could the better effectiveness associated with older age at 1st vaccination be associated with missing data on 1st vaccination (i.e., perhaps the 1st documented vaccination was really a 2nd vaccination because the 1st one was not documented). While this appears unlikely, the authors should at least mention the possibility and why they think it is or is not unlikely.

13. It would be useful to include 95% CI around VE estimates in the text and the tables.
MINOR comments

1. Abstract: In the results, two age groups are overlapping: "12-15 months" and "15-20 months".

2. Table 4 - can the authors add a footnote to the table describing the differences between Model I and Model II?

3. For Tables 3 and 4, it would be helpful to add a column for VE and also include the 95% CI's.

We overwrite this text when adding your comments to the authors.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

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