Reviewer’s report

Title: Vaccinating children against influenza: overall cost-effective with potential for undesirable outcomes

Version: 0 Date: 24 May 2019

Reviewer: Theresa Shireman

Reviewer's report:

General comments:

This is an interesting cost-effectiveness analysis of a previously published model evaluating alternative scenarios for vaccinating children/adolescents in the Netherlands. The approach is quite thorough and well explained and the presentation includes the essential elements for reporting economic evaluations. My first major concern is how the final interpretation of the modeling is presented in the abstract, title, and discussion. The authors are over-interpreting the negative or downside impact of these polices. For example, the statement that a substantial proportion of the simulations resulted in an increase in the number of epidemics: in my mind 23% does not signal the main finding. The main finding is that across 100-23 = 77% of the simulations showed no increase or perhaps a (decrease?) in the number of epidemics. Likewise, calling out a non-negligible proportion versus stating that nearly 94% of the simulations showed a net gain in health. This is not merely a difference of opinion regarding the glass is half full or half empty: it is particularly important in this era of anti-vaxers to strike an accurate portrayal of findings especially in your abstract and title. Misrepresentation can lead to misinterpretation and ultimately a reduction in the use of an effective preventive health intervention.

My second major concern has to do with the underlying assumption about the difference in natural versus vaccine-induced immunity. The estimate, ~5 years, comes from the authors' own prior modeling and seems an essential assumption in this study. Is there any corroborating evidence for this assumption from other clinical sources? If not, I strongly recommend the authors test its impact on the modeling in sensitivity analyses: e.g., assume 1 year as for the vaccine.

Finally, the paper is exceedingly long, would benefit from a substantial shortening, e.g., 25% or more.

Specific concerns:

1. Title: would drop the part about "risk of undesirable effects" as the preponderance of evidence presented shows that vaccinating children either from 2-12 or 2-16 improves outcomes and is cost-effective at the population level.

2. Abstract: Would report the positive findings, not the negative findings as the positive clearly outweighs the negative in your analyses.
3. Page 4, line 72-73: looks like missing a word or two in this sentence

4. Page 5-6: model overview: recommend including the model (figure) with the health states in the paper, even as a supplement.

5. Methods: clearly state the comparison groups, including the current policy.

6. Page 7, line 150: spelling error…”patters"

7. Page 8: range of values from immunity should be validated by clinical data, not just your own model. And a range of values should be tested for sensitivity analysis as this is likely a very strong assumption.

8. Page 9 & throughout: there are several supplementary files, so be clear which one is being referenced in the text and be sure that all are referenced in the text.

9. Page 15: The section on number of seasons with large influenza epidemics is difficult to follow and interpret.

10. What about vaccine safety issues, adverse effects? Were those included in the costs?

11. Page 16: opening paragraph under Discussion should focus on the major findings which showed a much more positive impact of these alternatives than what is stated.

12. References: not all citations are complete, many missing page numbers for example.

13. Table 2: the incremental table should be completed more and I disagree with your stated Ext Dominance. It appears, by my calculation from your numbers, that the CP + 2-12 has Ext Dominance for the total population. Seems the same is true for values within children as well.

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

No

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

No

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

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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