Reviewer's report

Title: Systematic review of models estimating the cost-effectiveness of routine varicella and herpes zoster vaccination in high-income countries

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Reviewer: Alena M. Pfeil

Reviewer's report:

Summary: The authors performed a systematic review of the cost-effectiveness of varicella and herpes zoster vaccination in high-income countries with a special focus on modelling methods. The literature search was conducted in PubMed and compromised 351 hits of which 38 were included after screening full-texts. Varicella vaccination in patients aged less than 19 years was cost-effective from a payer perspective and cost-saving from a societal perspective not taking into account the impact on herpes zoster incidence. The majority of the studies concluded that herpes zoster vaccination is cost-effective depending on the age at vaccination and the applied cost-effectiveness threshold.

Major compulsory revisions:

1: The background section is very long. I would recommend shortening the section, including a statement about the economic impact of varicella zoster virus infection, and excluding paragraph 7. In my opinion, this information would be more suitable in the discussion than in the background section.

2: The aim of the study does not include any information about the comparator. Most of the studies examined the cost-effectiveness of varicella or zoster vaccination compared to no vaccination and I would state this already here. I think that the aim should not include a potential strength of the study. Therefore, your sentence “To our knowledge, this is the first systematic review covering...” should be included in the discussion section where you talk about strengths of your study.

3: Regarding the methods, were references of the included studies screened to potentially identify further articles? Was the critical appraisal conducted by two independent reviewers? What was the primary outcome measure if there was only one? I would recommend to state which outcome measure(s) was/were assessed. Why were the costs inflated to 2010 values and not 2013 values? If it is possible to provide more actual price levels, I would recommend updating the values.

4: Please provide main reasons for exclusion of identified studies either in the text (results, paragraph1) or Figure 1.

5: The authors state in the methods section that they critically appraised the included studies, but they do not present the results of the “quality assessment”. I would suggest including this. It could either be added to one of the numerous tables, if possible or at least a general statement could be included in the text
that most studies/few studies were of good/moderate/bad quality according to the framework the authors used.

6: I suggest that the authors revise the study characteristics section. The section is very long due to the fact that the text was divided according to varicella and HZ vaccination and several tables were prepared. For example, the data on the model approach (static or dynamic) is provided in paragraph 2 of the results, but also in Tables 1 and 4. I think it is very helpful for the reader to get an overview of the characteristics of the included studies, but details can be assessed in the tables. Therefore, I would recommend shortening paragraph 1-3 in the section study characteristics, varicella vaccination. For example, state that the majority of the studies included considered European countries or state that 13 studies were included using a dynamic approach and 10 using a static modelling approach, but leave out the details in this place.

7: In my opinion, the number of provided tables is too high. Tables 1 and 4 could be collapsed with the corresponding tables 2/3 and 5/6. Data such as country, model type, time horizon and funding source should be provided in the same table as type of economic evaluation, perspective, and other model characteristics. Data such as impact of varicella vaccination on HZ incidence and herd protection should be included in the same table as vaccine characteristics. Some data are presented twice in different tables. For example, age at varicella vaccination is provided in Tables 2 and 7. Further, age at vaccination, dose schedule, and comparator are included in the table on economic results. But these are characteristics of the underlying models. Therefore, I would suggest including it in tables on general study characteristics or model characteristics.

8: The second paragraph of the discussion repeats the findings of the results. I would suggest restructuring it in text format and only include the most important findings summarised in 2-4 sentences. The section on ‘comparison with previous reviews’ should be shortened. Please state which studies were included in this systematic review, but not in previous reviews by providing references after the statement. If findings from other systematic reviews are in line with your findings, shortly state this. Otherwise, explain why there could be a difference. But I would not suggest discussing every previous review in detail.

9: Transferability/Generalisability of the studies should be discussed in the limitations of the study, and not before. The authors should also mention in the limitations section that the validity of the findings of the systematic review depends on the underlying studies that have been included.

10: The conclusions should convey key messages of the systematic review and provide further implications for future studies or research. In my opinion, this section is too long at the moment and I would recommend shortening it.

Minor essential revisions:
- Background, paragraph 3/4: Please include references. State in which country(ies) the observational studies were performed. Provide further information about the meta-analysis. Meta-analysis including RCTs, observational studies or both? State in which country the post-marketing study was conducted.
- Background, paragraph 4: Please delete brackets around statistically non-significant.
- Methods, paragraph 2: Please provide a reference for the World Bank data.
- Methods, paragraph 3: Please provide a reference for the OECD data.
- Results, paragraph 1: Finally, 38 studies ‘were’ included instead of ‘remained to be’ included.
- Discussion, paragraph 3: Please state how many studies identified HZ vaccination to be cost-effective instead of writing ‘nearly no study’.
- Discussion, paragraph 4: Please use ‘spread of infection’ instead of ‘force of infection’.
- Discussion, paragraph 14: Please write ‘taken into account’ instead of ‘taken account’.
- Conclusions, paragraph 1: Please use ‘magnitude’ instead of ‘height’ of the cost per QALY threshold.
- References: Please provide access dates when you refer to websites, e.g. references 26, 27, 29, etc.
- References: Reference 52 is missing.

Discretionary revisions:
- Background, paragraph 4: References are missing or not optimal.
- Background, paragraph 5: The extensive listing of countries with recommended routine childhood varicella vaccination can be shortened.
- Methods, paragraph 1: I would recommend updating the search because it has been conducted one year ago.
- Results, paragraph 1-8: If possible, please provide references.

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 have co-authored a systematic review of the cost-effectiveness of herpes zoster vaccination, which has been supported by an unrestricted educational grant from Sanofi Pasteur MSD (provider of the herpes zoster vaccine).