Reviewer's report

Title: Cost-effectiveness of HPV vaccination regime: Comparing twice versus thrice vaccinations dose regime among adolescent girls in Malaysia

Version: 3
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Reviewer: David Bin-Chia B. C. Wu

Reviewer's report:

This is a modeling study based on Markov cohort model to evaluate the cost-effectiveness of HPV vaccination regime comparing twice versus thrice HPV vaccinations dose regime among adolescent girls in Malaysia. The model was developed to reflect the natural history of HPV infection accounting for oncogenic and low-risk HPV was adapted for 13 year old Malaysian girls cohort.

This paper in several aspects is not enough informative. First, authors attempted to estimate outcomes of infectious disease. Thus, the unknown population mixing pattern makes the analysis more complex and has limited the usefulness of Markov model. Second, although it has been mentioned that 3-dose HPV regimen has been included in National Immunization Program, while comparing 3-dose regimen with 2-dose one, the important comparator not included, i.e. no vaccination and pap screening strategy. I assumed modeling cost-effectiveness study of 3-dose regimen compared with no vaccination has not been done yet in Malaysia. Thus, it will be important to retain no vaccination in the comparator. Also, A review of cervical cancer research in Malaysia by Zaridah (2014) indicated that secondary prevention by screening is still an important aspect because even with HPV vaccination. Integrating vaccine into existing screening practices and treatment procedures in a cost-effective manner was not discussed. Finally, the scenario considered in the current analysis is quite limited. e.g. the vaccination on males is not considered. Even if all girls were vaccinated, the HPV transmission would still be maintained through men who have sex with men.

Major compulsory revisions:

1. (Line 52) As indicated by ISPOR Dynamic Trasmission Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-5 (2012), a static model e.g. Markov model used by the authors is only appropriate when addressing non-communicable diseases. When the intervention impacts disease transmission, dynamic transmission model is considered as a more appropriate approach compared to static model. The reasons of not applying dynamic model needs to be described in details. Its potential implications need to be discussed.

2. (Line 134) The current Markov model was adapted from the settings of some other countries. Authors should elaborate more on model adaption process although it has been briefly mentioned. This is to convince the readers that the current modified model could properly address country-specific setting. As per
ISPOR modeling guidelines, were multi-stakeholders e.g. clinicians, government and modelers involved to ensure the model is accurate to reflect disease process and clinical practice in Malaysia?

3.(Line 134) Did the authors carry out model validation process to ensure the model's predictability? It is encouraged that authors refer to the following paper to ensure their study adheres to CHERRS guidelines (Husereau D 2013).

4.(Line 183) One-way SA seems to be too simple and didn't capture some important parameters

5.(Line 201) Why was multivariate probabilistic sensitivity analysis not performed?

6.(Line 192) Model validation using an independent external dataset was not performed.

Minor Essential Revisions:
1.(Line 134) It is not clear whether half-cycle correction applied when running Markov model.

2.(Line 209) Would it be realistic to assume 100% vaccine coverage? What is the past experience of NIP in Malaysia?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no conflict of interest to declare.