Author's response to reviews

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

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Author's response to reviews: see over
November 8th, 2015

Dear Mr. Proel Vargas,

We wish to submit a revised manuscript entitled “Cost- effectiveness of HPV vaccination regime comparing twice versus thrice HPV vaccinations dose regime among adolescent girls in Malaysia” (MS: 1521810097159609) for consideration by the BMC Public Health.

We have considered the reviewers comments and suggestion and we have edited the paper. We have also changed the second author’s (Namaitijiang Maimaiti) affiliation as Department of Health Management, Faculty of Health Science, Necmettin Erbakan University, Konya Turkey.

Thank you for your consideration of this manuscript.

The point-to-point response to the comments by both reviewers is given in the attachment of this letter.

Thank you.

Yours truly,

[Signature]

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MS ID: 1521810097159609

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

Re: Response to reviewers’ comments/suggestion

We would like to thanks reviewers to review our paper and for comments. Here are the our response to reviewers comments;

Reviewer: Gretchen E. Ely
Comment: The paper would be strengthened with some additional editing for grammar and clarity.
Response: We have edited the paper, checked the grammar and enhance the clarity.

Reviewer: David Bin-Chia B. C. Wu
Comment 1. The reasons of not applying dynamic model needs to be described in details. Its potential implications need to be discussed.
Response: Typically, a Markov chain is a mathematical system that transitions from one state to another over time (or the State Space). Dynamics Models differ in that they typically rely on some past knowledge - that past knowledge is often used to support the definition of probability distributions that later characterize the System being modeled.

Comment 2. 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?
Response: We had Expert Group Discussion with MOH stakeholders including public health specialists and clinicians from several hospitals to make sure that this model is accurate to reflect disease process and clinical practice in Malaysia.

Comment 3. Did the authors carry out model validation process to ensure the model’s predictability?
Response: Yes, we have carried out validation on model with the experts in the Expert group discussion.

Comment 4. One-way SA seems to be too simple and didn't capture some important parameters
Response: Three most important variables were covered in this sensitivity analysis i.e. vaccine price, vaccine coverage and discount rate. For this study, our opinion is that One –way sensitivity analysis done here is adequate and easily understood by policy and decision makers. One –way SA is often enough, as researchers are interested in how a change in just one or more variable affects a final decision, both in terms of the magnitude of change and the ultimate choice.
**Comment 5.** Why was multivariate probabilistic sensitivity analysis not performed?

**Response:** In this study, we carried out the simple One-way Sensitive analysis. As in our respond on Comment 4, the main reason is to keep the output of our analysis simple and the decision makers will be able to judge the robustness of our model. In our opinion, the multivariate probabilistic SA will be have greater advantage than our one-way SA that we undertook in our study.

**Comment 6.** Model validation using an independent external dataset was not performed.

**Response:** The study was carried out using real data from hospitals in Malaysia. We do not have any independent data set of similar nature available to us to be used for model validation. The model was validated with extensive consultations with expert groups as mentioned in respond to Comment 3.

**Comment 7.** Would it be realistic to assume 100% vaccine coverage? What is the past experience of NIP in Malaysia?

**Response:** Malaysia has an excellent track record of vaccination coverage. Ministry of Health Malaysia gave high priority to immunization coverage. The current coverage of primary immunization in Malaysia is between 97.14% and 99.54%. (Ministry of Health Malaysia. Health Fact (2012). For HPV Vaccination, the immunization services are provided by two organisations under public funding i.e. Ministry of Health and Ministry of Women Affairs and Family Development since 2010. So it is realistic to assume that the coverage is 100% for the school girls. Furthermore, this is a specially captured target group and easier to be reached than other sectors of the population.