Author’s response to reviews

Title: Is expanding HPV vaccination programs to include school-aged boys likely to be value-for-money? A cost-utility analysis in a country with an existing school-girl program

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Author’s response to reviews: see over
Dear Nathaniel Nazareno,

Thank you very much for the opportunity to make further revisions on this manuscript. Please note that we have changed some terminology in the paper, for clarity and consistency with our other recently published manuscript on the cost-utility of HPV vaccination for girls in New Zealand [1]. Please note this change in the Methods section:

“We adapted a previous Markov model on the cost-utility of girls-only HPV vaccination (manuscript under review), to estimate quality-adjusted life-years (QALYs) gained and net health system costs, for girls-only and girls and boys vaccination. The QALY metric captures both years of life lost from premature death, and loss of quality of life through morbidity. To value this health loss, we used disability weights (DWs), as outlined below. We formally use the term QALY^{DW} in this paper’s Methods and Results, but shorten it to QALY in other sections.”

As such, we made revisions to the Abstract, Methods, Results, Discussion, Tables and Figures. We also included an additional supplemental figure (Supplemental Figure 2) to accommodate the request of Reviewer 1.

We also responded to the reviewer comments, point by point, in the text below.

Reviewer 1 Comments:

The analyses and comments that the authors have conducted have gone a long way towards addressing my concerns with the first version of the manuscript. I’m not totally convinced by the limited Canada-New Zealand comparison but given the limited data on sexual behaviour in New Zealand, I agree that adequate sensitivity analyses are the best way to capture potential differences in HPV reduction between New Zealand and Canada. Similarly, the additional sensitivity analysis where herd immunity benefits for males are excluded in a female-vaccination only programme is an important step towards incorporating the potential reduction in herd immunity benefits as a result of much of male HPV disease being in MSM.

Minor essential revisions

While the additional sensitivity analyses are useful, the assumptions are only varied one at a time, and with the sole consideration of whether changing them increasingly could change the overall conclusion. They are also buried at the bottom of a table or in the appendix. It is worth considering a scenario most in favour of male vaccination (i.e some attenuation of the reduction in male cancers due to female vaccination due to both MSM and changes in sexual behaviour) and exploring what kind of vaccine prices would make male vaccination cost-effective. This would be helpful for public health messaging: while at current prices male vaccination is highly unlikely to be cost-effective, there is likely to be some low price (perhaps close to the GAVI price) at which male vaccination could become cost-effective under favourable assumption.

Our response: We have now included a cost threshold analysis for the scenario most in favour of male vaccination (the scenario excluding herd immunity benefits related to anal and oropharyngeal cancers for males when only females are vaccinated). Please see New Supplemental Figure 2. We also added the following to our Results,
“In a cost threshold analysis for the most favourable and extreme scenario for boys’ vaccination (excluding herd immunity benefits related to anal and oropharyngeal cancers for males when only females vaccinated), we found that the combined cost of the vaccine and administration would need to be $167 per dose or lower (i.e., 34% less than best model expected price of $254 and 34% higher than best model’s cost-effectiveness threshold price of $125) for vaccination to be considered cost-effective at a willingness-to-pay threshold of NZ$45,000/QALY\textsuperscript{DW} (see Supplemental Figure 2).”

**Discretionary revisions**

If anything the adjustment for MSM is overly conservative, and it may be better to reduce the herd immunity benefit by a fraction representing the likely proportion of male cancers that are in MSM (there are relative risks for cancer in MSM compared to MSW in the literature albeit not for New Zealand).

**Our response:** We agree that our adjustment is conservative. We intentionally tested for the maximum favourable circumstances that would best favour boys’ vaccination moving in the direction of becoming cost-effective.

**Reviewer 2 Comments:**

**Minor Revision.**

I am satisfied with the revision, the authors did a good job.

The only sentence in the abstract that is confusing is:

"In fact, increases in vaccination coverage of girls led to higher health gains for boys, due to herd immunity".

This is not clearly stated in the results section of the Abstract nor in the results section of the main body. I also do not like the wording "In fact" because the total indirect benefit from increasing the uptake among girls (herd immunity) strongly depends on the model.

I agree that increasing the uptake among girls is a better method for preventing cervical cancer than including boys in the program, but I find it hard to believe that it is also more beneficial for preventing disease among men (do I interpret the sentence correctly?).

**Our response:** We removed this sentence in the Abstract to avoid confusion.

**Final comments:** We thank the editor and the reviewers for thoughtful comments that have helped us to further improve the manuscript through clarification and justification.

**Reference**