Reviewer's report

Title: Is expanding HPV vaccination programs to include school-aged boys cost-effective? A cost-utility analysis in a setting with an existing school-girl program

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Reviewer: Mark Jit

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The authors present a model-based cost-effectiveness evaluation of the incremental cost-effectiveness of including boy in an HPV vaccination programme. Such an extension is found not to be cost-effective unless the vaccine price is substantially below current HPV vaccine prices in New Zealand (and indeed anywhere in the world).

Major compulsory revisions

1. The core of the analysis is based on imputing the reduction in HPV prevalence from a transmission dynamic Canadian model to the current Markov model, interpolating between results at different coverage levels presented in the Canadian paper.

   (i) Could more be done to convince readers that the two populations are similar enough to do this kind of imputation – eg. comparing HPV prevalence, cervical cancer incidence and/or sexual behaviour in the two settings?

   (ii) Another problem with this is not the change in setting but the move from a population model to a cohort model. This necessitates taking predicted long-term HPV prevalence (i.e. 70 years after vaccination begins; page 8 of the manuscript in submission to Vaccine) from the Canadian model and assuming that this equilibrium applies to the first (and only) vaccinated cohort in the New Zealand model. It isn’t clear that this is valid since the Brisson paper indicates that it takes 20-30 years for HPV prevalence to reach a steady state. The authors argue that this is less important because the cohort has decades before cancer onset, but actually it is the time to HPV acquisition rather than cancer onset that matters, and the peak years of HPV acquisition are likely to be around 10-15 years after vaccination. Hence the first vaccinated cohort may have a very different risk of HPV acquisition from the cohort vaccinated 70 years after the programme starts.

   It isn’t clear how this would change results: the indirect benefit of vaccination would decrease if the steady state assumption is not used, but this would have two effects in opposite directions: (i) female vaccination would have less impact on disease in males, so male vaccination may look more attractive, (ii) male vaccination would have less impact on disease in general, so male vaccination may look less attractive.
(iii) Have the authors tried contacting the Brisson group for the full posterior probability distributions from their model? This would produce a more robust fit than fitting separate functions to the median and endpoints of the uncertainty interval.

2. Given that the conclusion of the article is that male vaccination is unlikely to be cost-effective, it doesn’t seem appropriate to make assumptions that bias the results against male vaccination eg. ignoring vaginal and penile cancers, RRPs and MSMs. Even if little data are available, some simple assumptions could be made (eg. rescaling figures on disease burden from other countries, assuming no herd immunity from female vaccination in MSMs).

3. On page 6, it is mentioned that lack of local data prevented building a dynamic model. What kind of data these that were lacking?

Minor compulsory revisions

1. For the benefit of international readers, it would be helpful to know the threshold in New Zealand for deciding whether an intervention is cost-effective (even if only an informal, approximate guess can be made).

2. On page 14, it should be made clear that this is the incremental amount per 12-year old girl in the relevant age cohort not per vaccinated girl (if this is indeed the case).

3. It would be useful to present the threshold price (purchase + administration) at which the different options will become cost-effective. This could include the possibility that vaccines can be purchased under a national tender for males at a cheaper price compared to for females.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests