Reviewer’s report

Title: Assessing the cost-effectiveness of HPV vaccination strategies for adolescent girls and boys in the UK

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Reviewer: Michaela Hall

Reviewer's report:

In this paper, the authors provide cost-effectiveness estimates for including males in the existing HPV vaccination programme in the UK, which currently targets 12-13-year-old girls. The authors utilise a SIRS-V style epidemiological model of HPV transmission and vaccination to simulate the epidemic dynamics of 9 common HPV types (16, 18, 6, 11, 31, 33, 45, 52 and 58); stratified by age (10-50 years), sex (male, female), sexual preference (heterosexual, homosexual and bisexual) and sexual activity profile in the UK. The outcomes from this model are used to inform a separate economic model, which simulates the incidence and the costs associated with HPV-related diseases (CIN, cervical cancer, vaginal cancer, vulvar cancer, anal cancer, penile cancer, oropharyngeal cancer, genital warts and recurrent respiratory papillomatosis). The authors assess a range of HPV vaccination scenarios, varying the type of vaccine used (bivalent, quadrivalent and nonavalent), vaccine coverage and eligibility (girls only vaccination versus gender-neutral vaccination). The main finding of this paper is, while girls-only HPV vaccination at currently observed uptake rates in the UK is extremely cost-effective compared to a limited vaccine effect scenario (i.e. vaccination programme is ceased), the incremental cost-effectiveness of adding males to the programme is reduced.

Comments:

1. In the introduction (p3 lines 27-29), the sentence "In 2007, Australia targeted a wider range of girls/women aged 12-26 years" is misleading. It should be clarified that the older age group was targeted as part of a limited catch-up programme.

2. Regarding p4 line 29, it should be explicitly stated what male vaccination in Australia had a limited impact on. I.e. the sentence could be re-worded to read "Research in Australia also showed a limited impact of boys' vaccination on HPV infections and related cancers in males ([45]), although …"

3. In the final paragraph of the introduction (p 5 lines 5-12), only the epidemiological model is introduced (lines 7-9). However, the sentence starting on line 9 refers to "the above models" (i.e. the plural). The economic model should be introduced after the epidemiological model.
4. Regarding p7 line 5, the wording "to which to fit" does not read well.

5. Regarding p7 lines 25-27, the number of simulations required should be stated here.

6. I found the statement (p8 lines 11-12) that for "most but not all strategies, girls only for 2008-2016 was always in place" to be confusing. The strategy assumptions would be clearer if the 2008-2016 vaccination assumptions were stated for each one. For example, in the halted vaccination scenario, the authors could state that female vaccination ran from 2008-2016 (state what coverage was assumed) but that the vaccination programme was stopped. This change is not necessary and at the discretion of the author.

7. It would be nice to see a "no vaccination" scenario added as an additional strategy to this analysis. The use of the halted vaccination scenario as the baseline comparator is difficult to interpret, as a halted vaccination programme does not necessarily mean the absence of any vaccine impact. This change is not necessary and at the discretion of the author.

8. Regarding p11 line 1. What are the vaccine dose assumptions surrounding the 2-dose schedule? That is, is there any vaccine-derived benefit applied for individuals who receive the first dose only, and is the cost of this one dose counted? Or, is it assumed that the effectiveness and cost of both doses are applied at once?

9. If possible, it would be interesting and informative to provide additional HPV prevalence charts with population stratification (even if just in an appendix). For example, HPV prevalence over time by sex may illustrate the herd-protection conferred to males via a female-only HPV vaccination programme. Additionally, age-group stratification and stratification by HPV type (e.g. 16/18, 6/11, 31/33/45/52/58) would be interesting to see, especially when comparing the bivalent, quadrivalent and nonavalent vaccines. This change is not necessary and at the discretion of the author.

10. Regarding p14 line 13, please state the number of replicates rather than using the phrase "a considerable number".

11. Regarding p18 lines 25-27, can the JCVI 2018 statement be included in the reference list?

12. Not accounting for cervical screening should be stressed as a limitation of this analysis (while it is mentioned in the discussion section, it deserves a little more emphasis). A change from a cytology-based programme to an HPV-based programme is likely to impact rates of CIN and cervical cancer, and therefore the results of the presented cost-effectiveness analysis. Castanon's 2017 paper quantifies the predicted impact that a transition to HPV-based cervical screening may have on cervical cancer incidence England (1).

13. Suggest adding "per lifetime" to the sentence ending p20 line 15.
14. Regarding p 31, lines 19-20. The assumption that vaccination effectively treats infected individuals should be stated as a limitation, as it may affect cohorts where catch-up vaccination programmes are offered.

15. Please confirm the simulated age-range in the economic model. This information should be included in the main text and also Appendix S2. Simulating up to age 50 may be appropriate in the transmission model, however, such an early end age is not appropriate for simulating cancer incidence as there are still plenty of cervical cancer cases diagnosed in women aged 50+, with 11% of cases diagnosed in women over 75 years (2).

References


Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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