Reviewer’s report

Title: Impact of HPV vaccination with Gardasil® in Switzerland

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Reviewer: Lone Petersen

Reviewer's report:

The paper "Impact of HPV vaccination with Gardasil® in Switzerland" by Martine Jacot-Guillarmod, Jérôme Pasquier, Gilbert Greub, Massimo Bongiovanni, Chahin Achtari and Roland Sahli deals with very important issues - the population based effect of HPV vaccination and the effect of vaccination in relation to adjustments in the cervical screening programmes.

Two swiss populations are studied. Group I consists of 18 years old girls, who were invited the national HPV vaccination programme at the age of 12-14. The second group consists of women admitted for cervical cancer screening abnormalities. The results demonstrate a very convincing decline in incidence of positive HPV tests for those types covered by the Quadrivalent vaccine (HPV 6,11,16,18) among the 324 women tested in group I.

In group II an important decline of HPV 6,11,16, and 18 positive samples is demonstrated among the youngest patients below 26 years of age.

Despite the reduction in vaccine related HPV types among young women vaccinated before sexual debut with only 2.8% positive for HPV 6, 11.16 or 18 a total of 39 women are tested positive for HPV 16, 18, 31, 33, 45, 52 and 58 by a self sampling test according to figure 1A and a total of 95/324 are positive for any of the 28 HPV. As this accounts for 12% and 30% of the 324 women actually tested, I do not agree to the conclusion that primary screening by HPV test should now be introduced in Switzerland as far to many women have to be secondary screened by cytology.

The reduction in HPV 16 and 18 infections is demonstrated in both vaccinated and nonvaccinated young women in group 1. In my opinion the number of women in the two subgroups does not allow firm conclusions. Especially as the number of women tested accounts for only 8.8% of the entire population invited and selection bias may be present.

The study has some limitations which should be addressed more deeply.

Group II represents a subpopulation selected because of cervical cytology abnormalities. It is mandatory that this group represents a high risk group with an abnormal incidents of HPV infections compared to the normal population. This issue and the influence on the results obtained and the evaluation of the results must be addressed in the paper.
The response rate to the self sampling test in group I is only 8.8%. I need more arguments to justify general conclusions on the hole group based on such a small proportion.

The two study groups are tested by different HPV tests and two different methods (self test/PAP smear). The potential influence on the results should be addressed.

I would recommend that the phrase vaccinal HPV is replaced by "vaccine against HPV (6,11,16,18)" - especially as headline in figures.

In figure 1 I suggest that the number of patients included is given - f ex in the headline. This will make the reader able to evaluate the results in more details.

When these issues above is addressed I do recommend publication.

**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.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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I have been PI on GardaSil and GardaSil9 investigations in Denmark.

Have been talks about HPV vaccines for MSD and Sanofi Pasteur

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