Reviewer's report

Title: Prevalence of Human Papillomavirus cervical infection in an Italian asymptomatic population

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Reviewer: Marc Baay

Reviewer's report:

General

This paper reports the prevalence of HPV in an Italian asymptomatic population. Although several studies have been published from a number of countries, it would appear that this is the first report from Italy. However, the first question that comes to mind is why did it take 12 years to prepare the data for publication. Furthermore, does this time lapse have an impact on the PCR method used? Although the MY09/11 primer pair is still used, several adaptations have been made (the use of AmpliTaq Gold in stead of AmpliTaq, the use of PGMY primers, the use of PCR-EIA or line blot, rather than dot blot).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The Methods section is not sufficiently detailed and does not adhere to the general rules for description, especially in the case of the PCR method. Concentration of the primer is generally reported in pmol/reaction, dNTPs in mM or µM. It would also be interesting to know the supplier of the Taq polymerase. Where suppliers are given, they are wrong; it is Amersham not Hamersham or Hamensham. A reference for the Bethesda system would be appropriate since several revisions have taken place. The section on statistical analysis does not mention the actual statistical test used, or what the significance level was.

The discussion section, in my view, is meant to discuss the results obtained in the light of the existing literature. However, in the whole of the discussion only 3 references are given. This is an especially important flaw in the part where the authors state that the HPV positivity found in this study is low compared to other studies. Only one reference is given which dates back to 1991. However, multiple studies with lower prevalences are available. In a study from the Netherlands on 3,305 cytologically normal smears from the general female population, 3.3% of the women were found to have a HR-HPV infection (1). In Germany, 8466 women attending routine cervical screening were tested for HR-HPV by HC2. Of the 7832 women with a cytologically normal smear, 460 (5.9%) were HPV positive (2). In a Swedish study on women aged 32-38, 417 women out of 6123 were HR-HPV positive (6.8%) (3). Finally, HR-HPV was found in 257 out of 3089 (8.3%) women with normal cytology from a routine cervical screening population in Scotland (4). Although all of these women have a normal smear, the number of women in the Italian study with an abnormal smear was only 3/503, so this would not be expected to have a serious impact on HPV prevalence in the overall population. Furthermore, in a non-selected female population from Belgium, the prevalence was 10% (5). All of these data suggest that rather than being too high, the prevalence found in the Italian population matches well with prevalences found in other European countries.

A little further in the discussion the authors again refer to other studies, referencing only one. Moreover, I do not believe that the fact that infections are transient is an explanation for the difference in prevalence with age. Infections will be transient in most women of all ages, and in fact, clearance may take longer in older women. On the other hand, built-up immunity towards the virus(es), due to exposure earlier in life, may explain the difference. Finally, in univariate analysis schooling was found to be significantly associated with HPV positivity. Although this finding is no longer significant in logistic regression, it should be discussed, especially since it is strikingly different from the findings in literature on this aspect. All in all, I feel that the discussion should be substantiated by further reference to the literature.

In the abstract, the authors state that their results confirm a link between this infection and one of the main risk factors for cervical carcinoma. Surely, infection with HPV is the most important risk factor for CaCx development. If the authors feel otherwise, at least they should state to which main risk factor HPV infection is linked. Finally, I do not agree with their conclusion that the prevalence found is too low, as discussed above.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discussion: the words sisters (line 2) implies a genetic relationship, I believe the authors mean nuns. Furthermore, a reference would be in place, especially since it was first suggested by a fellow Italian.

Table 2: It is unclear what the G stands for, under HPV+.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

none