Reviewer's report

Title: Hospitalization for Human Papillomavirus -attributable disease

Version: 2 Date: 4 December 2012

Reviewer: Ruth Gil-Prieto

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Major Compulsory Revisions:
1. Abstract:
a. Conclusion about vaccination cannot be extracted from this study.

2. Methods section should be reviewed:
a. It is said that the population in the region is stable during the study period (2000-2010) and as denominator for calculating the rates 2001 population data were used. By reviewing published data the population in Veneto region an increase of 10 % from 2000 (4.5 million) to 2010 (4.9 million) can be seen. It is not a stable population. Rates should be calculated again taking into account the population variability. It can be affecting the trends reported.
b. How authors dealt with readmissions?
c. The statistics should be reviewed. “Linear regression models analysing hospitalization rates as dependent variables and year as independent variables was used to evaluate the significance of any decreasing or increasing trends” the linear regression can inform of the goodness of fit of the data to a line, but not of the significant decrease or increase of a rate during a period of time. A Poisson model should be used instead.

3. Results:
a. New rates should be reported regarding the modification in the population.

4. Discussion:
a. It is said “Our data show that the hospitalization rates dropped for women from 2000 to 2010. This decline regards cancer, and cancer of the uterine cervix in particular, and correlates with the introduction of organized screening programs in our region, that enable the detection and treatment of this disease.” Could the author give any explanation on why the screening does not seem to decrease the number of genital warts in women and why have cases of anal cancer mainly occurring in MSM also decreased? The new rates should be discussed in more detail.

Minor Essential Revisions:
1) Title should include location
2) Introduction.
a. “Human papillomavirus (HPV) represents the most frequent sexually
transmitted pathogen in the United States.” Please give epidemiologic data not only of USA, but of Europe or Global as your work is done in Italy.

b. The use of the term “burden” should be carefully checked through the manuscript

3) Methods:

a. Please define age groups to be study and its rational.

b. What proportion of the population in the Region (residents) was covered by the hospitals contributing to these study?

c. Regarding: “the fact that it was impossible to check whether more than one discharges applied to the same person (which could contribute to an overestimation of the number of cases, but not the burden due to the HPV diseases).” Can the authors access other diagnosis positions? See comment of re-admissions above.

4) Results:

a. Genital warts and cancer are very different outcomes. In terms of epidemiology, the age groups affected and the time from infection to event are completely different. It would add clarity to the text to split the analyses in two, at least in the figures (one for cancers and one for warts).

b. Please use the term “cases” or “hospitalizations” accordingly to previous comment about readmissions

c. p=n.s. Please, show value

5) Discussion:

a. “Hospital records indicate that HPV-related diseases is an important public health issue which could be prevented by vaccination strategies”. The records do not indicate that HPV-related vaccines could be prevented by vaccination. A deeper analysis in the decline of hospitalization before and after vaccine introduction could give some information. This kind of sentences should be rewritten.

6) Figures:

a. Fig 1 and 2 are entitled “HPV-related hospitalization trend”, but the trend is difficult to see due to the figure selected, that highlights the accumulative HPV-related disease and only the “total” trend is finally showed. The cumulative effect is nicely showed in figure 3, so it would add clarity to the paper to see figure 1 and 2 reporting the individual rates and its trend for each HPV-related disease. If possible separating warts.

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

**Declaration of competing interests:**

'I declare that I have no competing interests'