Author's response to reviews

Title: History of Pap-smear in HIV-positive women in Northern Italy: A cross-sectional study

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Author's response to reviews: see over
To: Editor BMC Cancer

Re: MS: 2587129830905838 "Screening for cervical cancer in HIV-positive women in northern Italy: a cross-sectional study"

Dear Editor,

Thank you for your letter of January 13 and for the helpful reviewer’s comments. We have now revised our article according to their suggestions, and we hope it can be reconsidered for publication in BMC Cancer.

Here below is our point-by-point reply to reviewers’ remarks.

Reviewer 1 report:
This is a cross sectional study in which a self-administered questionnaire was used to determine the use of Pap smears in HIV positive women in the Emilia Romagna region in Northern Italy. The aim was to see if the use of Pap smears in HIV positive women had improved over time. The title is a little misleading as the paper is mainly a survey of Pap smear use and not screening for cervical cancer.
RE: Due to the lack of previous data from patients-based studies, our main aim was to provide representative estimates of Pap-smear history in women infected with HIV in Italy. An additional aim was to check whether the frequency of Pap-smear changed over time. The Abstract and the Introduction have been rephrased to improve definition of study aims.
We have also changed the title according to the reviewer’s suggestion “History of Pap-smear in HIV-positive women in northern Italy: A cross-sectional study”

Major revisions:
1. Details of Emilia Romagna have to be provided in the methods section such as area, population, number of HIV women.
RE: We have added a sentence to provide details of Emilia-Romagna region.

2. Only 1108 women attending the infectious disease clinics were invited to participate. Almost a third of the HIV positive women in this region were excluded. Did these women receive any care at all and in what ways were they different from the actual population studied?
RE: All HIV-positive women who underwent follow-up (recommended every 6-months) were invited to participate. To reduce the possibility of duplicate cases, we limited the
study period to one year. This means that any woman who did not attend follow-up visits between July 2006 and June 2007 was not included. We have added a reference of a previous study (Arici et al 2002), which showed that patients in the injecting drug use category, patients without AIDS diagnosis, or patients with higher CD4 counts are more likely to miss medical appointments and discontinue their follow-up. To this end, a sentence has been modified in Methods and a new sentence has been added in Discussion.

3. Without breaking confidentiality, triangulation to validate the Pap smear use needs to be done.
RE: At page 9 of the Discussion, we have highlighted study weakness due to the self-reported nature of our results. On the other hand, our goal was to obtain information directly from patients to avoid indirect reporting from the clinicians [ref. 15]. In agreement with the HIV-patients association, the study was conducted following strict confidentiality criteria and (as stated in the Discussion) “Confidentiality reasons prevented us from linking women’s reports with gynecological and cytological records …”. We are planning, however, a new study that, by means of broader confidentiality rules, could allow validation of Pap-smear use and subsequent treatment reported by HIV-positive women diagnosed with gynaecological lesions.

4. P values and confidence intervals need to be provided for all statistical tests. Even for results not presented in the tables, these details should be provided in the text.
RE: We have added 95% CIs when not reported (page 8).
In line with the recommendation for epidemiological studies (Rothman, Greenland and Lash 2008, pag. 151-157), ORs and 95% CIs were reported. OR and CIs (not p-values) permit some statement about the direction and size of a relative risk between different groups. A reference to this regard has been added, and the paragraph on Statistical analysis has been rephrased (see point 5).

5. Details of multivariate models and the results from this analysis should be provided.
RE: A column has been added in Table 1 to show ORs calculated using multivariate models. The section Statistical analysis has been updated accordingly.

6. Improvement of Pap smear use over time is difficult to assess when there is no baseline publication. We do not know if the same methodology was used.
RE: The observation is correct. We have modified sentences in the abstract and discussion.

Minor revisions:
1. Are there cervical cancer screening and treatment guidelines in Italy?
RE: No, international guidelines for screening and treatment were followed (ref. 8).

2. What were the median number of Pap smears in these women?
RE: The questionnaire did not include a specific question on lifetime number of Pap-smears for two reasons: the first is that a woman’s memory might affect self-reported data; the second is the importance of adherence to recent Pap-smears, particularly after HIV diagnosis, to prevent HPV-related advanced lesions.

3. How many of them had HPV testing, colposcopy, surgical procedures?
RE: Figure 1 summarizes data on practices after a positive Pap-smear. Additional information on HPV testing, colposcopy, and surgical procedures have been added in the Results section.
4. Check style and grammar.
RE: The text was revised by a native English speaker.

5. The discussion should refer to similar studies from other countries or regions.
RE: Very few studies were conducted on the topic. We have compared our results to similar studies from other countries expanding the first three paragraphs of the Discussion.

6. The discussion should refer to problems in the system, compliance of patients and ways to improve
RE: We added a paragraph in the Discussion section addressing this issue.

Reviewer 2 report:
This paper describes self-reported cervical cancer screening practice in HIV-positive women attending HIV-units in a large Italian region. The present study is a cross-sectional study performed in Emilia Romagna region in Italy between July 2006 and June 2007. Due to higher risk of cervical cancer in the setting of HOV, HIV-positive women should strongly benefit from regular access to cervical cancer screening. All women attending their HIV clinic answered a self-administered questionnaire on their previous Pap test and cervical follow-up. Despite a well defined question, the method used seems poorly appropriate to answer the question. In fact, in the absence of documents to confirm the answers given by the patients, the validity of answers is questioned. In order to assess the results, the authors may validate the data provided by patients at least in a drawn sample.

RE: We have recognized and discussed the limits of the self-reported nature of our study, raised also by Referee 1 (see point 3 of major revision required).
In agreement with the association of HIV-patients, the study was conducted following strict confidentiality criteria and “Confidentiality reasons prevented us from linking women’s reports with gynecological and cytological records …”. A new study is being planned, using broader confidentiality rules and written consent for follow-up, to validate self-reported Pap-smear use and to follow-up treatment in HIV-positive women diagnosed with gynaecological lesions.

We look forward to hearing from you soon.

Best regards

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