Reviewer's report

Title: HIV and pre-neoplastic and neoplastic lesions of the cervix in South Africa: a cross-sectional study

Version: Date: 17 February 2006

Reviewer: Gary M Clifford

Reviewer's report:

General

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

The question concerning to what extent HIV increases the risk for cervical cancer is especially important in sub-Saharan Africa given the size of the HIV epidemic. Indeed, some previous studies from HIV endemic regions show a lack or little excess of cervical cancer in HIV positive patients (Hawes el, Sitas et al, Mbulaiteye et al). This is in contrast to the much larger excess seen in developed settings.

The described study is a very well powered case:control study for assessing risk of cervical cancer in South Africa and particular concerning HIV as a risk factor. However, this important message is lost by an inappropriate analysis of the case:control data. The authors have stratified the large set of matched controls by PAP results, substituting women with normal cytology as a reference group and turning controls (e.g. ASCUS/LSIL/HSIL) into cases, which presumably ruins all the careful matching that was done. Unfortunately, this approach is highly confounded by HPV prevalence. It is well established, and shown also in the present article that HIV greatly increases HPV prevalence, and that SIL is a largely (but not entirely) HPV related phenomena. Thus, controls with normal cytology will, by definition, have very low rates of HIV, and are not the correct comparison group.

The correct, and powerful, matched case:control study should compare HIV prevalence in cases (6.0) with that in ALL matched population controls (5.7%). This would give an OR of not much more than one and a confirmation that there is little excess risk for cervical cancer in this population. I personally believe that this lack of excess is largely due to co-AIDS-mortality in the absence of widespread HAART treatment, but this is an issue for the discussion.

While it is of interest to see the proportion of HIV+ve stratified by PAP result, for issues of screening as the authors rightly note, this is not the principal power of the case:control study design. Many previous cross-sectional studies from Africa and elswhere have established the association of HIV and SIL. I recommend the authors to focus more on cancer risk as few such studies exist.

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

At multiple points in the paper the authors speak of their study providing "information on the prevalence and risk of SILs among HIV positive women". This is not strictly true. We cannot really estimate the prevalence or risk of SIL among HIV positive women from this case:control study, but we can accurately estimate the risk of cervical cancer for HIV positive women.
The authors themselves draw the caveat that the prevalence of SIL among HIV positive women is higher than other studies - this is maybe because the controls were matched to look like cervical cancer cases.

Discretionary Revisions (which the author can choose to ignore)

I recommend that the authors try to gather information on HPV type distribution among the 29 HIV+ve cases if possible, and even do a larger comparison with that in a selected number of HIV-negative cancer. There are suggestions that HIV positive women are infected with a broader range of types than the general population, but there are no data to show if this is also the case in cervical cancer. This study would be one of the very few that could shed light on this issue.

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

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests