Reviewer’s report

Title: HIV Associated High-Risk HPV Infection among Nigerian Women

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Reviewer: Gary Clifford

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The authors present a cross-sectional analysis of high-risk HPV infection among women undergoing cervical screening in Nigeria, by HIV status. A number of other, larger, similar studies have been performed in other parts of Africa, so the study is not particularly powerful nor novel. However, the HPV testing methodology is good one.

Nevertheless, the data are often over-/mis-interpreted. I have a number of suggestions to the authors to improve the manuscript, to be considered largely as “Major Compulsory Revisions”:

ABSTRACT

1) The first sentence of the abstract “the incidence of cervical cancer has remained stable in HIV+ women is mis-leading and an over-simplification”. We only have good data from western countries with high-levels of screening. We know little about what is happening in areas such as Africa where cART is being rolled out far quicker than screening.

2) All HPV infections are more prevalent in HIV+ women, and increase in multiplicity of infection is a consequence, so it does make sense to focus only on multiplicity as a special outcome per se.

3) The second and third sentences of the conclusion are mis-interpretations, as there is no information in this paper on the types that cause precancer and cancer. Infact, it is known that the high prevalence of types in women without lesions (even in HIV+ women – see Clifford et al, AIDS, 2006), are not representative of those that cause cancer. This is because certain types, namely 16 and 18 are far more carcinogenic than others. See paper comparing HIV+ and HIV- cancers in Kenya and South Africa, Int J Cancer, first author de Vuyst.

BACKGROUND

4) I am not aware of any literature criticising the IARC classification of high-risk types, and certainly not the cited paper.

5) There quite a lot of data published from Africa on HPV types in HIV+ women. The meta-analysis Clifford et al, AIDS, 2006 is a good start, and there have been many more from the region since.

6) The claim that cervical cancer incidence is on average higher in Western than Eastern Africa is tenuous. The GLOBOCAN data cited are almost entirely modelled based on very few data from a couple of cancer registries in select
countries across the continent. In any case, even if such a difference is true, the hypothesis that this is due to HPV type differences is not answered by this study, that is more a comparison of HIV- versus HIV+. The West versus East Africa issue should be entirely dropped.

RESULTS

7) The prevalence of HR-type (single or multiple) positive women that were HIV+ and HIV- is purely driven by the study recruitment source. This proportion should be reported the other way round, i.e. the proportion of HIV+ versus HIV- women that were HR HPV pos. These proportions should be reported in Table 2 (see below)

8) In Table 2, overall HPV prevalence and multiple HPV prevalence can be shown. Rather than p values, which do not show the direction of the difference, prevalence ratios with 95% CIs can be shown. To make this table different to Figure 1, prevalences and prevalence ratios for individual types could be shown among HPV-positive women only, as in Clifford et al, AIDS, 2006.

9) As it stands, Figure 1 is somewhat redundant with Table 2 and could be dropped.

10) Table 3: data are too sparse to show two different models for single and multiple infection, and anyway would not be expected to be different. Hence present one column only for any HR-HPV infection. The meaning of the PRs for the risk factors (age, sexual partners, marital status, education and age at first sexual intercourse) are meaningless unless the reader knows what category is being compared to what.

11) I am surprised that no HPV35 infections were found in HIV-neg women, as this is a type that is known to be commonly found in HIV-neg women in Africa and Nigeria. The data should be checked for a technical problem.

DISCUSSION

12) Be clearer about when discussing different HPV types in Africa versus the rest of the world, and when talking about HIV+ versus HIV-ve in Africa. In general, when citing other papers, it is important not to mix HPV type distribution in the general population with that in severe lesions or cancer, which have different meanings, for the reasons explained above.

13) Drop discussion of West versus East Africa, for reasons stated above

14) Longitudinal studies of HPV infection are largely impossible due to the requirement to offer treatment and the enormity of the duration and sample size required. Rather, cross-sectional comparisons of HPV type distribution across different lesion grades up to cancer can offer a similar, but more efficient, reply to the question.

15) The last sentence about stable cervical cancer rates is not based on evidence – we badly need studies to show what is happening to cancer in HIV+ women in Africa in the cART era. There are some data (e.g. proportions of cervical cancers that are HIV-positive, see papers from Kenya and South Africa),
that suggest an increasing epidemic of cervical cancer as survival is improved with cART.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests