Author's response to reviews

Title: Genital warts and infection with human immunodeficiency virus in high-risk women in Burkina Faso: a longitudinal study

Authors:

Andrea Low (andrea.low@lshtm.ac.uk)
Tim Clayton (tim.clayton@lshtm.ac.uk)
Issouf Konate (kletio@yahoo.fr)
Nicolas Nagot (n-nagot@chu-montpellier.fr)
Abdoulaye Ouedraogo (ouarma74@yahoo.fr)
Charlotte Huet (charlotte_huet@yahoo.fr)
Marie-Noelle Didelot-Rousseau (mndidelot@orange.fr)
Michel Segondy (m-segondy@chu-montpellier.fr)
Philippe van de Perre (p-van_de_perre@chu-montpellier.fr)
Philippe Mayaud (philippe.mayaud@lshtm.ac.uk)

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Author's response to reviews: see over
To the editor:

Please accept our revised manuscript titled “Genital warts and infection with human immunodeficiency virus in high-risk women in Burkina Faso: a longitudinal study” for further consideration. We have tried to address all concerns of the reviewers, and we include detailed commentary below. We hope that any changes made are consistent with the reviewers’ suggestions. We look forward to hearing from you.

Sincerely,

Andrea Low and Philippe Mayaud

Reviewer 2 (LS. Massad)

We greatly appreciate the thoroughness of Dr Massad’s report and hope that the changes that we have made are consistent with his excellent suggestions. We have addressed each comment with a reply below. We would be happy to consider any further suggestions that he might have.

Results

1. In the first paragraph, note significant differences between HIV+ and HIV women (older, fewer partners, more contraceptive nonusers). Was marital status available? If so, did it differ between HIV+ and HIV- women?

We have added these points and have given detailed data on marital status in Table 1.

2. The second paragraph should reference Table 1, where these numbers are provided. To avoid redundancy, they should not be given in both places. How many women had ASCUS/ASC-H, AGC, or cancer? If no, state that. In Table 1, break out all categories--do not report LSIL/HISL (misspelled).

The reference and statement regarding ASC-H, AGC and cancer have been added, and table 1 adapted as per the recommendations.

3. In the third paragraph, give a P-value for the difference in GW prevalence between HIV+ and HIV- women. In the multivariate analysis, there should be 2 models (for all women, comparing HIV+ vs HIV- and for only HIV+ women, stratifying by CD4 count and HAART use). What factors entered the model? Are they the same as those listed in Table 2 or different?

The P-value was added. The factors included in the multivariate model have been added to the third paragraph. They are different to those in Table 2 as each model was conducted in a stepwise fashion and only included those variables which were associated with both the outcome and the variable of interest, except for those decided a priori such as age, as detailed in the methods section. If we stratify by CD4 count, there are only 3 events in women with a CD4+ count less than 200 and no events in women on HAART, leading to a fairly limited analysis. We therefore did not have the power in that aspect of the study to determine the relationship between these factors. To demonstrate this, we have added results with respect to CD4+ count to the paragraph on prevalence.
4. In the paragraph on incidence, list P value for differences across HIV/CD4 strata in the text, not just the table. In the multivariate model, again include a separate model incorporating CD4 stratum and HAART use. Was HAART use significant after controlling for CD4 count?

We have added the P-values throughout the text for clarity. We also would like to reassure the reviewer that we did in fact construct two separate models: one was comprised of HIV negative vs. HIV-1 positive women and included nadir CD4+ count. The other model was comprised of HIV-1 positive women only and examined time-updated CD4+ count and the use of HAART for the longitudinal aspects of the study. We could not include time updated plasma HIV-1 viral loads due to many missing values. We had described these models in the methods section. However, we realize that these were obviously not very noticeable. We have therefore changed table 2 to better reflect the 2 models, and have added clarifying sentences to the results.

5. Finally, in the persistence model, add another model for HIV+ women alone including HAART use and CD4 count, as above. Clarify if the results given in the last 2 sentences of the section on persistence are for univariate or multivariate analyses.

As for the incidence analysis, we had also created two models, described in the methods, to adjust for time-updated CD4+ count and HAART status. We have clarified that in the results section and have added a note about the multivariate nature of the analysis. We do not provide a separate table in the interest of brevity, as we did not identify any associations with other risk factors, which we state at the end of the paragraph.

6. The authors conclude that HPV6 but not HPV11 was associated with prevalent and incident GWs. What was their power to detect an association with HPV11 when only 13 women had HPV11? If low, then the authors should note that they did not find an association but larger studies will be required to determine if one is present.

The reviewer is certainly right that the power to detect an association with HPV-11 would be very low. We have therefore added statements to that effect in the results and the discussion section.

Discussion
6. Statements about the impact of HAART on GW prevalence/incidence/persistence should be reassessed if new multivariable models reveal new relationships.

As our analyses of the impact of HAART on GW prevalence/incidence and persistence were conducted in models comprised of HIV-1 positive women only, we have not changed the discussion. We hope that we have made sufficient changes in the methods and results to clarify that.

Tables
7. In Table 1, rather than medians, give number (percentage) of women with CD4 >500, 200-500, and <200. Also, what number (percentage) of women had undetectable HIV RNA levels?

This has been added.

Reviewer 3 (Williamson)

Thank you very much for your kind comments. We are grateful that you consider the data novel and important, and the manuscript well written. We certainly agree that the study would be
strengthened by HPV typing from the GWs themselves. We have added a statement to that effect in the discussion section.