Reviewer’s report

Title: Persistence of Cervical High-Risk Human Papillomavirus in Women Living with HIV in Denmark – the SHADE

Version: 0 Date: 17 May 2019

Reviewer: Gary Clifford

Reviewer’s report:

The authors present a prospective study of HPV natural history in HIV-positive women in Denmark, based upon the linkage of various medical databases that is possible in few places outside Denmark. This includes linkage with the national cervical cancer screening database, although this database does not contribute to the main analysis of HPV persistence.

Principal findings are the confirmation, in Denmark, that HPV persistence (with CD4 count) and detection of cervical HSIL (with AIDS diagnosis) are linked to severity of immunosuppression in this population.

Some suggestions for the authors:

I don't think it is appropriate to claim that "most frequent persistent genotypes were HPV52, 33 and 31" in the abstract. This suggests that these types were more persistent than others, which was not shown (nor even statistically tested given the small samples size).

"a high rate of persistent hrHPV infections with predominantly non-16/18 hrHPV genotypes" also suggests some particular dangerosity of these types in HIV-positive, but that was also not shown in the paper, as numbers were too small to link even with HSIL outcomes. Maybe linking HPV persistence to outcomes is a future objective of this study ? But the data is not there yet, and we know from larger studies and meta-analyses that HPV16 and 18 remain the most carcinogenic types in cervical cancer even in HIV-positive persons - but this message has been somewhat lost in the tendency to focus on the nonHPV16/18.

Also in the abstract, it seems that the conclusion "With the current HIV guidelines aiming at early identification of PLWH and initiation of ART upon diagnosis, numbers of HPV-related cancers may decrease in WLWH.", has little link to the data presented in the current study

Results, line 233 - perhaps replace "showed up" with "participated" ?

Table 4 - The meaning of the p-values is unclear. What are the comparison groups ?

Discussion - Whilst there is a lot of valuable discussion about the issue of HPV natural history and cervical cancer prevention in HIV-positive women, there needs to be a stronger link to how this study informs the picture.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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No

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