Reviewer’s report

Title: Long-term consistency of vaginal gel use among HIV-1 sero-discordant couples in a phase III double blind trial (MDP301), in rural SW Uganda

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Reviewer: Richard Haaland

Reviewer’s report:

This manuscript provides an assessment of several potential long-term correlates of consistent vaginal microbicide use by women in HIV serodiscordant couples during a clinical trial in rural southwest Uganda. This study uses self-reported adherence data from the large multi-site MDP301 clinical trial of the anti-HIV microbicide gel PRO2000 to identify factors that may influence usage of future microbicide products in a population of women in Masaka, Uganda. This study made the important observation that consistent microbicide usage was associated with both a woman’s age and the number of sleeping rooms in a woman’s residence.

Major Compulsory Revisions:

1. The use of the terms “consistent” and “inconsistent” was originally used by MDP301 to divide the participants from multiple study sites into two equal groups along the median value of reported gel use at last sex act for behavioral studies. However, in the context of the study by Abaasa et al., the term “consistent” is a bit misleading as it categorizes participants according to criteria established under different circumstances. By the authors’ definition, consistent use of the vaginal gel is “reported use of the gel at the last sex act for 92% of the actual visits” (Methods 3rd paragraph). This appears to be a somewhat arbitrary determination to continue using the MDP301 criteria of the median value from the entire clinical trial at all 6 sites and should be rethought as to whether or not it is reflective of the intended meaning of “consistent gel use” in this context.

2. The authors need to address the limitations of only using self-reported adherence for a measure of “consistent” gel usage while several other studies have indicated that self-reported adherence in clinical trials of HIV prevention is unreliable and typically over-inflated. Additionally, “consistent” gel usage is defined as use of gel at the last sex act, however, it does not account for all or even most sex acts during the previous month. For example, a woman may report 5 sex acts as well as using the gel during each sex act yet return only 1 used applicator resulting in a classification as a “consistent” user.

3. It is unclear why median gel usage during the trial at last visit was 92% (Methods 3rd paragraph) and the “proportion of women reporting to have used the gel at their last sex act was over 90%” (Results paragraph 5), yet the “overall reported consistent gel use was 67.8%” (Results paragraph 5). The authors
should address the apparent discrepancy between the overall reported consistent gel use and the much higher other reported numbers. This discrepancy likely results from using the 92% cut-off value from the MDP301 trial. Perhaps it would be more accurate to use the median value for Masaka as the determining line between “consistent” and “inconsistent” usage for comparisons.

4. The authors need to address how consistent usage is affected by women completing smaller numbers of visits (eg. 13) compared to larger numbers (eg. 26) using their 92% criteria for consistent gel usage. For example, a woman who only attended 13 visits and reported gel usage for last sex act in 11 of those visits would be categorized as non-consistent. However, if the same woman were to complete the remainder of her visits, as well as the associated counseling sessions, and reported gel usage for last sex act in 12 of the final 13 visits, she would be considered consistent.

Minor Essential Revisions:
1. Both Figure 1 and Figure 2 need detailed Figure Legends so they can stand alone without the text.
2. In Figure 2, an “n” value for the number of women attending each visit would be helpful for the reader to see how visit attendance changes over time especially from week 52 to week 104. Additionally, it may help to have equally spaced visit values as time from week 4 to week 12 is 8 weeks, but 12 to 24 is 12 weeks and 100 to 104 is 4 weeks.
3. The text of the entire manuscript should be edited for small mistakes, such as the “LRT P-value<0.15” (Methods Statistical Analysis paragraph) should read “LRT P-value<0.05). Other instances exist of incorrect word usage. A more accurate writing style would make the manuscript easier to follow and convey the message more clearly.
4. The iPrEx and HPTN 052 trials (Background 2nd paragraph) are probably not good references for consistency as they were not microbicide trials.
5. The authors need to explain in the Methods section how things like condom use, family planning use, employment status and pregnancy status were given a yes/no or positive/negative status. These values are things that likely change over 104 weeks and the criteria for these designations should be clearly stated.

Discretionary Revisions:
1. Data regarding the correlations (or lack thereof) between self-reported gel usage and applicator usage may provide useful information about the reliability of their self-reported gel usage at last sex act.
2. The finding that number of sleeping rooms in residence may impact gel usage could be very important for future microbicide trials as well as future implementation and probably could serve as the focus of the manuscript, including the title.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.