

## REVISIONS TO UCHOOSE MS

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**RESPONSE:** Thank you for this comment. We have checked the manuscript and have ensured that all major sections are set at level 1 heading, are bolded and set at 18pt font. We have further checked the format for levels 2 and 3 headings are set at the correct font. Finally, we have ensured that the rest of the manuscript meets PLOSONe style requirements.

2. We note that the grant information you provided in the 'Funding Information' and 'Financial Disclosure' sections do not match. When you resubmit, please ensure that you provide the correct grant numbers for the awards you received for your study in the 'Funding Information' section.

**RESPONSE:**

This study was designed and implemented by the Microbicide Trials Network (MTN) funded by the National Institute of Allergy and Infectious Diseases through individual grants (UM1AI068633, UM1AI068615 and UM1AI106707), with cofunding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health (NIH)

3. Thank you for stating the following in your Competing Interests section: "The work presented has not been published and is not under consideration in any other peer-reviewed media. The listed authors have all contributed significantly to the design, analysis, and written work, and all authors have given final approval for the version to be published. To the best of our knowledge, no conflict of interest, financial or other, exists." Please complete your Competing Interests on the online submission form to state any Competing Interests. If you have no competing interests, please state "The authors have declared that no competing interests exist.", as detailed online in our guide for authors at <http://journals.plos.org/plosone/s/submit-now>

This information should be included in your cover letter; we will change the online submission form on your behalf.

**RESPONSE:** Thank you. We have ensured that the cover letter contains the above information regarding competing interests.

**Additional Editor Comments**

The paper offers a comprehensive overview of the advancements made in HIV prevention, focusing on a subject of great interest from the perspective of the beneficiaries. Nonetheless, to increase the manuscript's quality, I believe the authors should heed the suggestions provided by the reviewers. Moreover, I'd like to emphasise the following points:

4. It's crucial for the authors to provide a scientific rationale for the sampling techniques employed and clarify the basis for determining the final sample size. Which specific criteria or references from prior studies influenced this decision?

**RESPONSE:** We revised the methods section and have included a paragraph stating the rationale of the sampling techniques employed and clarifying the basis for determining the final sample size. Specifically, we cite existing literature and our own previous work in similar studies as having guided the sampling techniques used. We then state that ‘our sample size is advised by ‘information power’ where our recruitment reflected specificity in areas of inquiry (e.g., choosing a product, or choosing neither or those experiencing unique challenges, and, collecting data at specific periods during the study’ as key determinants of the sample size ( see pages 4-5, lines 110-136)

5. For clarity, I suggest the results section include a well-organized table detailing the characteristics of the FGDs. This table should outline the number and origin of participants for each FGD, address potential biases due to participant demographics (e.g., all participants of the same age? younger (16) vs older (21)), and specify the FDG locations (e.g., healthcare facility name, county, or neighborhood). Upon examining Table 2, it's challenging to differentiate between FGD and IDI participants.

Response: We have created the table as seen below, but we felt that it did not add much to the findings. We also seem to have many tables and figures, in this paper. So, we appreciate your thoughts on this. Should you review the table below and feel that it is important to add, let us know and we will include in the findings.

**Table 4: Characteristics of FGDs and FGD participants**

FGD Number and site	Number of participants per FGD	FGD composition by age range	FGD Composition by product use	Product adherence category	Site/Country
FGD1(DTHF)	3	16, 17, 18	Mixed (Ring, Neither)	High	Cape Town, South Africa
FGD1(MUJHU)	3	16, 20, 19	Mixed (Ring, Pill)	High	Kampala, Uganda
FGD1(WRHI)	3	18, 19, 19	Ring	High& medium	Johannesburg, South Africa
FGD1(UZCHS)	4	16, 16, 18, 19	Ring	High	Harare, Zimbabwe
FGD2(DTHF)	5	17, 18, 18, 19, 20	Mixed (Ring, Pill, No product)	High-low	Cape Town, South Africa
FGD2(MUJHU)	5	19, 19, 19, 19, 20	Mixed (Ring, Pill)	Mixed	Kampala, Uganda
FGD2(WRHI)	4	16, 18, 18, 20	Mixed (Ring, Pill)	High-Medium	Johannesburg, South Africa
FGD2(UZCHS)	3	17, 17, 18	Mixed (Ring-pill)	Medium	Harare, Zimbabwe

FGD3(DTHF)	3	19, 19, 21	Mixed (Ring, Pill)	High-medium	Cape Town, South Africa
FGD3(MUJHU)	4	16, 18, 19, 19,	Ring	High	Kampala, Uganda
FGD3(WRHI)	4	17, 20, 18, 21	Mixed (Ring, pill)	High-Medium	Johannesburg, South Africa
FGD3(UZCHS)	3	18, 18, 17	Ring	High	Harare, Zimbabwe
FGD4(DTHF)	5	16, 16, 18, 18, 19	Mixed (No product, Ring)	Mixed	Cape Town, South Africa
FGD4(MUJHU)	6	18, 18, 19, 19, 20	Ring	High-Medium	Kampala, Uganda
FGD4(WRHI)	4	16, 19, 19, 19	Mixed (Ring, Pill)	High	Johannesburg, South Africa
FGD4(UZCHS)	3	17, 17, 18	Mixed (Pill, ring)	Medium	Harare, Zimbabwe
Total					

6. To prevent confusion, the term "private place" inside the healthcare facility needs to be defined precisely

**RESPONSE:** This has been changed in paper. We have changed this from private settings to 'private rooms' at the clinical trial site

7. I've noticed the authors refer to "tablet" while interviewees say "pills." The authors should either choose one for uniformity, which is, in my opinion, a better option, or maintain this distinction throughout for consistency. Thank you for your observation, we have ensured that paper refers to 'Pills' and not 'tablet'

**RESPONSE:** Thank you for your observation, we have ensured that text in the paper refers to 'Pills' and not 'tablet'

8. Based on the findings, the discussion and/or conclusion sections should include more specific recommendations about the implications and continued implementation of HIV programmes in the study sites. Adding more detail to this would improve the paper's clarity and comprehensiveness.

**RESPONSE:** This is well noted; however, given how different the discussion points are, we opted to include a recommendation/implication under each discussion point as much as possible. We preferred this method to avoid repetition and maintain coherence in the discussion section. We want to draw the reviewer's attention to areas that highlight specific recommendations/implications under particular discussion points. In lines 490 to 505, we share our recommendations based on our discussion point on 'product triability.' Lines 508 to 510 describe recommendations that pertain to the type of counselling that might be important in programmatic settings. Lines 531-534 share our advice regarding product switching observed during the study and how this is achievable in a real-world setting. Finally, in lines 540-543, we provide our thoughts and suggestions regarding what is possible in terms of support strategies that might be most relevant in real-world settings, suggesting that drug-level feedback is not plausible.

### **Reviewers Comments to the Author**

**Reviewer #1:** This is a very well written paper on a highly relevant topic

**Major:**

**Intro:**

9. Please spell out more clearly how the study is novel compared to previous studies. The argument “However, research examining product preference and choice using active products is still lacking” seems to contradict with the previous sentences (“found that discreetness and longer duration of protection to minimize user-burden were favored, along with products that did not interfere with intimate relationships, and provided HIV prevention for unanticipated situations (18). Furthermore, previous experience with a long-acting contraception (e.g., implants) influenced choice of product”) showing factors that inform decision-making

**RESPONSE:** Thank you for this comment and for the opportunity to clarify. We start by arguing that previous research testing preference used placebo products. Using placebo products means that a participant experiences a product that has no side effects, and yet we know that side effects play a significant role in product choice decisions. To make it clearer, we have stated that ‘research examining product preference and choice using products with active HIV prevention drugs is still lacking, and this is the first of its kind testing preference for oral PrEP containing Emtricitabine/Tenofovir Disoproxil Fumarate and the vaginal ring containing Dapivirine, by offering participants the option to experience both products before choosing their preferred HIV prevention product’.

### **Methods:**

10. What determined the number of FGD and IDI? Was any interim analysis conducted?

**RESPONSE:** This comment is well noted, and we have clarified this in point four above. We have added a section titled ‘Qualitative Study Sample’ in which we describe how we determined the sample size (see p5, lines 116-119)

11. How did you validate? Was any triangulation (e.g., of data obtained from different stakeholders) done?

**RESPONSE:** This comment is well received. As stated in the paper on page 8 lines 186-192 of the manuscript, FGD data was our primary data for this paper. Once the analysis was complete and themes developed, we utilized IDI data (which used similar questions) to validate and confirm that data generated on each theme presented information identical to that obtained from FGDs. We also ensured that the development of the FGDs and IDIs guides was robust, having been generated by a team of senior social scientists and researchers at study sites who understand the context better. We further ensured that staff trained in qualitative research and were not part of the staff complement involved in the REACH trial conducted the interviews. All this information is presented in the paper. We have also added a section in the methods section (see page 9) that describes our code development processes, actual coding, and how we measured inter-coder reliability.

12. Table 2: check the formatting of lines.

**RESPONSE:** Thank you for this observation. We have ensured that lines are formatted correctly.

### **Results:**

13. A table describing the characteristics of qualitative study participants next to those included in the trial but not in the qualitative study would be relevant.

**RESPONSE:** We have reviewed the characteristics of the entire REACH sample and compared it to the qualitative choice period sample, and we have yet to find a difference. We suspect that the lack of difference in the characteristics may be partly due to the fact that participants selected for the qualitative also had to reflect the age inclusion criteria, and the mean age of both samples was 19 years. Therefore, such a sample would have similar characteristics around education completion, with few earning an income. The majority of 19-year-olds are not married but have main partners. The majority also chose the ring as their preferred HIV prevention option, as already published elsewhere. We have provided these references in the paper.

Given the information presented in Table 2, adding another column representing the entire REACH sample clutters the table. It overwhelms the reader without adding information different from what is currently shown in this table. Because of this, we have opted to omit to add this information, but should but should the reviewer or editor require this addition, we could add the full sample information as a supplementary table.

14. Emphasize novelty of findings shown, if any. The first paragraph is a good place to do this

**RESPONSE:** The Novelty of these findings is explained by the fact that they are drawn from participants taking part in the first of its kind, 18-month MTN-034/REACH trial that allowed participants to experience both the ring and the pill for six month and then offered them an opportunity to choose their preferred option during the last six months of the study. We have now clearly started this in the first paragraph of the discussion section. See page 24, lines 449-451

15. 441-461: few references – reads like the results section.

**RESPONSE:** Additional references in this section have been added

16. 14. Discuss drug level feedback: how could this (or another approach aiming at the same type of info “yes, you ‘re doing well”) work in a programme?

**RESPONSE:** We note this comment; however, our take-home message is that DLF did not directly inform choice, and, therefore, we find it difficult to make suggestions/recommendations of an alternative approach that could deliver a similar message if it was not a driving factor. In addition, DLF would be hard and costly to implement in real-world settings. That said, client-centered discussions may be more important than DLF, offering a more subjective experience that participants appreciated more. For example, participants preferred to talk more about getting information on how to engage their families to support their PrEP use., or how to manage side effects

17: Limitations: reflexivity is recommended: how did the experiences and views of the researchers and moderators affect data collection and analysis? Any other bias? Recall bias? Social desirability in a trial on new PREP methods?

**RESPONSE:** We have added in the limitation section several points about the limitations of qualitative research methods, in general, and how we have addressed both recall, social-desirability and other sources of bias in this research context. (If you want you can add the paragraph once cleaned up that we have at the end of the discussion).

16. Abstract: “use,”: comma should be point

**RESPONSE:** This has been corrected.

17. Intro: “understand how the use of active products may pose different challenges compared to prior findings in placebo trials” could be “how the comparison of active products” and “placebo-controlled”?

**RESPONSE:** Thank you for noting this and for the suggestion made. After reviewing the sentence again, we opted to remove that line and have re-written it as follows: *“We specifically aimed to understand how experiencing a product first, informed choice, and future roll out of multiple prevention options, using the REACH data”*

**18. Reviewer #2:** Firstly, thank you for the opportunity to review this manuscript. It is very well-written, the research design itself is clear (coming from part of a well-structured, well-known larger study) and the findings are helpful and have an operational relevance to many different contexts. One of the most interesting parts of the study design is the ‘crossover’ period and I think that is something readers can really learn from, so would like to see more made of this in the results.

**RESPONSE:** We very much appreciate this comment. We have rewritten the section and have made it clearer than before and have cited some of our primary papers that comprehensively describe the cross-over design for the REACH trial. See lines 85-96 on page 4 of the manuscript. For this paper, however, we wanted to focus more on the qualitative data collection methods conducted in the choice period than the trial itself.

19: Can the authors offer a definition of what is meant by 'modern contraceptives'?

**RESPONSE:** When we reviewed and revised the paper, we took this statement and the sentence out entirely because it didn't provide needed information to the reader and had no impact on the findings presented.

20. This is an interesting study design which clearly a lot of thought and expertise went into - well done! I have made a few comments and suggestion for clarification below.

**RESPONSE:** The authors state that a total of 16 FGDs were conducted, and if I understand the table correctly, a total of 62 participants were involved. This means that each FGD only had between 3 and 4 participants in it. These low numbers pose a methodological challenge as the group dynamic would not be large enough for the benefits of a focus group, which should typically be around 8-10 people if carried out according to qualitative research guidelines. Please can the authors include these low numbers of participants as a limitation and explain what was done to mitigate this, reflect on why there were so few participants, and whether group interviews were considered instead?

**RESPONSE:** In the limitations section, we added why the number of participants in FGDs was lower than usual. We also indicate that we collected IDI data. We describe in the analysis how the two data sets were used as follows, “Our analysis followed a stepwise approach and a consensus process (through regular meetings and discussions), prioritizing the FGDs as the primary data source on choice, as the timing of the FGDs allowed

participants to reflect on their decision-making process for the choice period, including influential factors that contributed to choose. IDI data were then used to confirm themes from the FGD or identify variations and nuances. We focused on themes that directly spoke to participants' decision-making processes at entry into the choice period and reasons underlying their options".

21. The tool used for FGDs is described as an interview guide - should this be 'focus group guide', as the questions were amended to reflect the group context, and weren't identical to the interview questions. The distinction between the two guides is made in the table, but not in the narrative

**RESPONSE:** Thank you for these suggestions. This has been amended and now reads, *"All interviews and FGDs were conducted in private rooms at the clinical sites by trained in-country interviewers using a semi-structured IDI and FGD guide..."*

22. The process for recording interviews is mentioned, but there is no parallel mention of recording the FGDs and how they were transcribed/translated.

**RESPONSE:** Thanks for noting this. We have added FGDs in the sentence describing the data collection, transcription and verification because both IDIs and FGDs followed the same process.

23. Similarly, informed consent is mentioned for interviews but not FGDs.

**RESPONSE:** This to has been revised and now reads *"Written informed consent for the qualitative component was obtained as part of the overall informed consent process at enrollment and was verbally reconfirmed before conducting IDIs and FGDs"*

24. Could you further clarify the different roles of the authors in the methodology section? There is mention of a QDMT and analysts as well as data being 'transcribed directly into English locally by one staff member' but whether or not there are overlaps in these roles is unclear.

**RESPONSE:** We have clarified on page 6 lines 153-7, the Qualitative Data management team was based in the US and worked closely with the staff at study sites based in southern Africa. In the analysis section, we also state that QDMT coded data working the staff at study sites.

25. Could you provide more details about what the 'card statements' are in the methods section? These are mentioned in the table but not described in detail

**RESPONSE:** During focus group discussions, we used card statements on the adherence support questions to allow participants to confirm whether the support strategies employed in the study assisted them to be useful or not. This was an activity conducted as part of the interview. We have removed the word card statement from the manuscript to stop the confusion. Describing it does not add anything to the paper.

26. In the results table, can you clarify if respondents could state if they were living with more than one adult household member, such as both their mother and father, for example? It would be interesting to see how many lived with more than one parent/guardian in terms of risk factors,

particularly as there are mentions of losing family members and living with family members who have HIV.

**RESPONSE:** We have added a footnote in the table with this information.

27. The quotations are lost a little in the table at times and I would have liked to have seen them integrated more into the narrative, but I realize that this may also be due to word count limitations, and that a restructuring is likely not possible at this point!

**RESPONSE:** We agree with your observation.

28. The manuscript is well-written, but there are several typos and grammatical errors throughout, particularly in the quotations which would benefit a thorough revision and edit for punctuation, typos, apostrophes and clarity. I recognise the importance of keeping the voice of each individual in a study like this and not editing their language to lose their individuality, but editing for clarity/typos will make their voices more powerful and help the reader be able to fully engage with their words. My comments apply to the quotes throughout, but some specific examples are: ‘anthing’, ‘when she is seeing’, ‘What made to go a ring’ and ‘What made me to leave’.

**RESPONSE:** Thank you for this observation. We have reviewed all the quotes and corrected these.

29. The word ‘yoh!’ is used in quotes - this appears as 'yho' and 'yoh'

**RESPONSE:** We have amended this in all our quotes. The correct version from these study settings is ‘Yoh’

30. In the table ‘preferred both equally’ would read better as ‘had no preference’

**RESPONSE:** Thank you. This has been amended

31. The side-effect of vaginal fluid is mentioned several times - this is clarified as ‘discharge’ in some of these mentions, but it may be worth explaining more what it means in the quotes as well as reflecting more on the scientific evidence/known side-effects relating to this so that the reader can understand how commonly this is reported and seen in other contexts.

**RESPONSE:** The issue of vaginal discharge was not commonly reported, although our qualitative women reported it as something they did not like when they were using the ring. We added a few lines in the discussion section (515 to 519) showing how women described this. We also indicated that about 10% of the women in REACH mentioned this, which is reported in other published papers. I hope this is sufficient.

31. I was interested by the phrasing used on line 429 - is poor persistence the same as poor adherence and/or retention?

**RESPONSE:** Persistence is a component of adherence (1). However, adherence comprises of initiation, execution and implementation but persistence means regularly coming for regular visits, collection of products

32. Overall, this is a very solid manuscript and the suggestions I make above are minor. Thank you again for the opportunity to review.

**RESPONSE: Thank you for the constructive feedback**

**Additional Editor Comments:**

1. van der Straten A, Montgomery E, Hartmann M, Minnis A. Methodological Lessons from Clinical Trials and the Future of Microbicide Research. Current HIV/AIDS reports. 2012;10.