PEER REVIEW HISTORY

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ARTICLE DETAILS

| TITLE (PROVISIONAL) | MPPrEP+ Study protocol: A prospective cohort study assessing the feasibility and acceptability of an HIV pre-exposure prophylaxis (PrEP) strategy for male clients of female sex workers in Kisumu, Kenya |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| AUTHORS             | Mantell, Joanne; Franks, Julie; Zerbe, Allison; Lamb, Matthew; Reed, Domonique; Omollo, Dan; Lahuerta, Maria; Naitore, Doris; El-Sadr, Wafaa M.; Agot, Kawango |

VERSION 1 – REVIEW

| REVIEWER | Price, Matthew A. |
|----------|--------------------|
|          | International AIDS Vaccine Initiative |
| REVIEW RETURNED | 29-May-2022 |

GENERAL COMMENTS

Thank you for the opportunity to review the submitted study protocol “MPPrEP+: Assessing the feasibility and acceptability of a combination PrEP and adherence support intervention for male clients of female sex workers in Kisumu, Kenya” I think this will make an interesting and important addition to the literature, though the sample size is so small, I wonder how informative this might be. Also, as the PrEP landscape is undergoing dramatic change with long acting modalities becoming available, it’s a shame there isn’t any consideration of these new offerings.

P7, line 6: consider noting that persons who engage in transactional sex are eligible for PrEP under Kenyan guidelines.

P6, eligibility criteria: Just to confirm, willing to participate means interested, willing, and able (at the time of recruitment) to take PrEP for six months, right? Participants are told, at eligibility screening, that they enrollment in the study means taking PrEP for six months?

P6, Minor point: UNAIDS recommends avoiding the term ‘hotspot’, you may wish to consider an alternative https://www.unaids.org/sites/default/files/media_asset/2015_terminology_guidelines_en.pdf

As the authors note, there isn’t much (perhaps nothing) in the published literature about male clients of FSW and offering them PrEP. As such, an important finding from this study will be the screening efforts. I would like the authors to consider, as rigorously as possible, documenting outreach, screening, and enrollment. How much effort does it take in finding these men and convincing them to join? That alone would make a worthwhile manuscript, and be a welcome addition to help us understand how suitable this population might be to this kind of intervention (i.e., even if uptake was acceptable, if you have to screen many men to enroll few, this indicates that this group will be hard to reach and an intervention of this type might not be widely taken up)
Page 7&8, apologies if I’ve missed it, but do you make it explicit that all volunteers are getting the same combination prevention intervention? I assume that is the case, but could not find the language that made this explicit.

P11, line 15: what are the “violence” and “stigma” domains? A little more explanation of data you plan to collect would be welcome. How might you integrate long acting modalities, as they become available? (e.g., a questionnaire to get at interest in new options, and/or how they might appreciate new options vs. what they’re taking under this study?)

P12, line 7: what is a ‘design effect of two’?

I may have missed this, but when do you plan (dates) to conduct this study? Is it already underway?

| REVIEWER | Graham, Susan |
|----------|---------------|
|          | University of Washington, Global Health and Medicine |

| REVIEW RETURNED | 30-May-2022 |

**GENERAL COMMENTS**

This manuscript presents the protocol for a cohort study to assess the feasibility and acceptability of a combination PrEP and adherence support intervention for male clients of female sex workers in Kisumu, Kenya. The manuscript is well written for the most part, but does not necessarily adhere to STROBE guidelines in a few places and could benefit from several clarifications, especially with respect to outcome definitions and data analysis plans. In addition, it is unclear whether the trial described is ongoing or completed, and dates should be provided.

My specific comments follow:

1. Title. The title does not indicate the studies design. Please include the word “cohort.”
2. Title. The phrase “combination PrEP and adherence support” in the title is confusing, as adherence support is generally part of PrEP services.
3. Abstract. The study design should be included (i.e., “cohort study”).
4. Abstract. Use of past tense verbs makes it sound as if the intervention has been delivered and the study may be complete. Please clarify the current stage of the study in the abstract.
5. Methods. There is no information on the study setting (a research clinic?) or on dates of protocol approval, study launch, and the stage of follow-up at the time of submitting this manuscript.
6. Methods. At the top of page 6, there are said to be two interventions, but three are listed.
7. Methods, p. 6 lines 14-16. The sentence on the 2-month refill at month 1 is incomplete with no verb.
8. Methods, p. 6, lines 22-24. Measures of “values and norms related to gender and sex” are mentioned but not defined or included later in analysis plans. There are measures related to experiences purchasing sex and beliefs and attitudes about sex work that are mentioned. Is this related to the qualitative work? If so, then the quantitative and qualitative approaches need to be more clearly presented.
9. Methods, urine assay information. I would recommend striking the text on “greater sensitivity than plasma-based measures” and focusing on the urine assay and its use for self-monitoring in this section. More detail on how feedback is provided to participants.
and how they themselves use the result for self-monitoring would be helpful.

10. Methods, patient and public involvement. The word “to” is missing in the sentence starting “Interview questions at the final study visit…"

11. Methods, p. 12. The outcome definitions would benefit from a clear explanation of how the outcome will be operationalized for analysis. For example, is “PrEP adherence” a binary outcome with the cutpoint in the table? How is acceptability measured for each intervention component? A “scaled” result is mentioned but not clearly presented. Some of this information is in Table 2, but it should come earlier where the outcomes are defined and the analysis plan presented.

12. Methods, p. 12. No details are presented on the plasma assay to be used, its performance characteristics, and what a level of 0.4 ng/mL means in this context. That information is important to justify use of the plasma assay result as the primary outcome.

13. Methods, p. 13. Why was the number of paying and non-paying sex partners selected as the primary sexual risk behavioral outcome? This requires a justification.

14. As mentioned above, Table 2 does not add much since it comes too late to help understand each outcome and its analyses as presented on pages 12-13.

15. Figure Title. Determinants of “PrEP Adherence, Feasibility” is unclear – the feasibility of PrEP adherence? Determinants of feasibility?

16. Figure. The figure is generally clear and helpful, although bold subheadings would be useful under “Behavioral Skills” and the Feasibility and Acceptability Outcomes are not clear (for example what is “Feedback”?).

17. Figure. The box with “modifiable via intervention” is also placed strangely – if this is a color coding indication, it does not work well in black and white. Consider moving this specification into the Figure caption instead.

18. The manuscript would benefit from a careful check for grammar, spelling (PreP), and punctuation.

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**REVIEWER** Schaefer, Robin

**REVIEW RETURNED** 03-Jun-2022

**GENERAL COMMENTS**

Thank you for the invitation to review the protocol for this study on providing oral PrEP to male clients of female sex workers in Kenya. The article is well-written and the study will address a critical gap in the HIV response. Below are some suggestions on improving the article. I also included a few thoughts on the study procedures. While I understand that my role as a reviewer is to focus on the presented protocol, not the underlying study, the authors may still want to reflect on these.

- The authors plan to only offer daily oral PrEP to male clients of female sex workers in Kenya. While this is in line with current Kenyan national guidelines, WHO will release new guidance this July on PrEP implementation that will note that event-driven PrEP (ED-PrEP, also “2+1+1”) can be offered to all people assigned male at birth (previously just MSM). It is of course unclear when this will adopted in Kenyan national guidelines, but it could be a great option to explore in this study. ED-PrEP may be a highly suitable option for MC of FSW as they risk of HIV acquisition is likely to change considerably over time. If further information on this is needed, you can contact the WHO PrEP team.
- Related to the above, the primary outcome of the study is PrEP adherence at 6 months. However, for many of the MC, it may be unnecessary to take PrEP daily constantly for 6 months. So the authors may want to rather consider PrEP use at every visit and how this relates to actual behaviours. Given that the authors will collect information on sexual behaviour, one could even consider a measure of effective use, i.e. PrEP use during periods of risk.
- I generally suggest speaking of "effective use" rather than adherence for the reasons outlined above.
- The study will evaluate a package of multiple interventions (HIVST, urine adherence feedback, text messages). The authors should reflect on the fact that the study will not be able to distinguish between individual effects. I consider this a major limitation.
- Will there be any cost and cost-effectiveness analysis? This would be quite useful.
- FSW will act as mobilisers in this study. The authors should reflect on potential risks for them, e.g. pushback and violence from clients.
- The authors should include a timeline for the study procedures. It would also be useful to mention earlier in the main text the frequency of follow-up visits.
- What HIVST will be used in the study? Blood or oral?
- It would be useful if the authors also evaluated uptake of PrEP, not just adherence, as an outcome. This could be a qualitative supplement evaluating acceptability (among those not choosing PrEP).
- I suggest to generally just speak of sexual behaviour, not sexual "risk" behaviour (as risk behaviour can be considered stigmatising).

**VERSION 1 – AUTHOR RESPONSE**

REVIEWER 1: Dr. Matthew A. Price, International AIDS Vaccine Initiative Comments to the Author

Thank you for the opportunity to review the submitted study protocol "MPrEP+: Assessing the feasibility and acceptability of a combination PrEP and adherence support intervention for male clients of female sex workers in Kisumu, Kenya." I think this will make an interesting and important addition to the literature, though the sample size is so small, I wonder how informative this might be. Also, as the PrEP landscape is undergoing dramatic change with long-acting modalities becoming available, it’s a shame there isn’t any consideration of these new offerings.

7. P7, line 6: consider noting that persons who engage in transactional sex are eligible for PrEP under Kenyan guidelines.

RESPONSE: We have added text to indicate that the Kenyan government has prioritized PrEP for individuals at risk for HIV infection (Page 4).

8. P6, eligibility criteria: Just to confirm, willing to participate means interested, willing, and able (at the time of recruitment) to take PrEP for six months, right? Participants are told, at eligibility screening, that they enrollment in the study means taking PrEP for six months?

RESPONSE: Yes, this is accurate. We have added language to Page 5 to clarify that prospective participants are educated about all eligibility requirements, including ability and willingness to take study-provided PrEP for six months and to return to the study site for follow-up at 1, 3, and 6 months. At final, 6-moth visit, participants are referred to a local provider for continued PrEP if they wish.
9. P6, Minor point: UNAIDS recommends avoiding the term ‘hotspot’, you may wish to consider an alternative https://urldefense.proofpoint.com/v2/url?u=https-3A__www.unaids.org_sites_default_files_media-5Fasset_2015-5Fterminology-5Fguidelines-5Fen.pdf&d=DwIFaQ&c=G2MiLlal7SXE3PeSnG8W6_JBU6FcdVjiSsBSbw6gcR0VzYHa0heH42N3FCy53AEiz&l=Oul73CKTYW9bkV_ELATUM3TE7bOjkzXt8Hqvu5o8m1o&m=4chUaofDUGKc1GheHxCy6ELqtxCmpYNSH---rM73zWhaktUUi4j1EZGUK9v&s=ZVc1TQFkTmpm-GxoHt9fGihqXfxNLcZ7Z5hCqMCogs&e=
RESPONSE: Thank you for alerting us to the UNAIDS document on preferred HIV terminology. We have deleted the word ‘hotspot’ from the manuscript. The sentence (Page 5) now reads: “Mobilizers conduct outreach and education about the study aims and components in community-based venues such as bars and other social spaces where people sell and buy sex in the Kisumu urban area.”

10. As the authors note, there isn’t much (perhaps nothing) in the published literature about male clients of FSW and offering them PrEP. As such, an important finding from this study will be the screening efforts. I would like the authors to consider, as rigorously as possible, documenting outreach, screening, and enrollment. How much effort does it take in finding these men and convincing them to join? That alone would make a worthwhile manuscript, and be a welcome addition to help us understand how suitable this population might be to this kind of intervention (i.e., even if uptake was acceptable, if you have to screen many men to enroll few, this indicates that this group will be hard to reach and an intervention of this type might not be widely taken up)
RESPONSE: We agree with the reviewer that data to improve understanding of how to support PrEP uptake among vulnerable groups like MC are critical. We have edited the text (Page 5-6) to include additional detail on outreach and recruitment activities as well as the procedures used to document proportions of prospective participants approached who expressed interest in the study; those screened who were eligible, and those eligible enrolled. In a future manuscript these proportions will be presented as study outcomes.

11. Page 7&8, apologies if I’ve missed it, but do you make it explicit that all volunteers are getting the same combination prevention intervention? I assume that is the case, but could not find the language that made this explicit.
RESPONSE: All participants receive the same intervention, as we now note on Page 5.

12. P11, line 15: what are the “violence” and “stigma” domains? A little more explanation of data you plan to collect would be welcome. How might you integrate long acting modalities, as they become available? (e.g., a questionnaire to get at interest in new options, and/or how they might appreciate new options vs. what they’re taking under this study?)
RESPONSE:
We have corrected this section to accurately reflect the domains assessed, and added citations as described below.
Questions assessing violence domain: This questionnaire module consists of 6 items assessing experiences of violence in the last 3 and 12 months as well as lifetime (frequency, perpetrator) and history of threats/force with sex partner. Specifically, items assess frequency of being hit, kicked or beaten in the last 12 months and by whom; frequency of being emotionally abused, such as insulted, frequently humiliated, or threatened with harm in the last 3 months and by whom; threatening to use force to get a woman to have sex when she did not want to; and forcing or pressuring a woman to have sex when she did not want to. Four of the 6 items are adapted from our work with the South African Health Monitoring Survey among FSW.1 The remaining two items (“Have you ever threatened to use force to get a woman to have sex when she did not want to?”; and “Have you ever forced or pressured a woman to have sex when she did not want to?”) were drawn from sexual assault history measures from Simbayi et al., 2006.2
Questions assessing perceived stigma related to engagement with FSW: This questionnaire module consists of 5 items assessing perceived stigma associated with purchasing sex and engagement with FSW, e.g., feeling ashamed to buy or give favours, gifts, or goods in exchange for sex; feeling ashamed to tell anyone that he buys or gives favours, gifts, or goods in exchange for sex; concern that people will treat him differently if they find out that he purchases sex; people looking down on men who go to sex workers; and people thinking that men who go to sex workers are bad people. Several of the stigma items are drawn from Pitpitan et al’s study of male clients of female sex workers in Tijuana, Mexico.

We agree that including questions related to long-acting modalities would surely generate interesting data. Unfortunately, as data collection is currently underway, we are unable to include related questions in our study tools. Long-acting injectable PrEP was not approved at the time of the initiation of this study.

13. P12, line 7: what is a ‘design effect of two’?
RESPONSE: A Design Effect is a simple number that estimates how much less efficient a non-random sample is compared to a simple random sample; a Design Effect of 2 implies that a non-random sample would need twice the number of individuals as a simple random sample to obtain the same-precision estimates. This has been clarified in the Methods section (Page 12) of the updated manuscript.

14. I may have missed this, but when do you plan (dates) to conduct this study? Is it already underway?
RESPONSE: The study is underway. It was launched in November 2021 and all participants were enrolled by January 2022. Follow-up visits are currently ongoing. Additional details have been added in various sections of the manuscript to clarify the study timeline.

REVIEWER 2: Dr. Susan Graham, University of Washington Comments to the Author
This manuscript presents the protocol for a cohort study to assess the feasibility and acceptability of a combination PrEP and adherence support intervention for male clients of female sex workers in Kisumu, Kenya. The manuscript is well written for the most part but does not necessarily adhere to STROBE guidelines in a few places and could benefit from several clarifications, especially with respect to outcome definitions and data analysis plans. In addition, it is unclear whether the trial described is ongoing or completed, and dates should be provided.

15. Title. The title does not indicate the studies design. Please include the word “cohort.”
RESPONSE: We have revised the title of the protocol to indicate the design.

16. Title. The phrase “combination PrEP and adherence support” in the title is confusing, as adherence support is generally part of PrEP services.
RESPONSE: We have revised the title of the protocol.

17. Abstract. The study design should be included (i.e., “cohort study”).
RESPONSE: This section has been revised to include the study design.

18. Abstract. Use of past tense verbs makes it sound as if the intervention has been delivered and the study may be complete. Please clarify the current stage of the study in the abstract.
RESPONSE: The study is currently ongoing. The Abstract has been edited to reflect the appropriate tense. We have adjusted the tense to reflect present tense and included additional language describing the status of the study.
19. Methods. There is no information on the study setting (a research clinic?) or on dates of protocol approval, study launch, and the stage of follow-up at the time of submitting this manuscript. 
RESPONSE: Additional details related to the study setting have been added to the Methods section (Page 6). Further details related to the dates of protocol approval and study launch have also been added to the Abstract and Method sections (Page 15).

20. Methods. At the top of page 6, there are said to be two interventions, but three are listed. 
RESPONSE: Thank you for pointing out this discrepancy. We have noted there are 3 adherence support interventions: (1) use of a validated point-of-care (POC) urine tenofovir (TFV) assay, UrSure, with real-time feedback and tailored self-management counseling; (2) HIV self-testing; and (3) weekly one-way text messaging on Page 7 in the updated manuscript.

21. Methods, p. 6 lines 14-16. The sentence on the 2-month refill at month 1 is incomplete with no verb. 
RESPONSE: Thank you. We have corrected that sentence to include a verb (Page 7).

22. Methods, p. 6, lines 22-24. Measures of “values and norms related to gender and sex” are mentioned but not defined or included later in analysis plans. There are measures related to experiences purchasing sex and beliefs and attitudes about sex work that are mentioned. Is this related to the qualitative work? If so, then the quantitative and qualitative approaches need to be more clearly presented. 
RESPONSE: After careful consideration, we opted not to include measures about values and norms related to sex in this study. This text has been removed from the updated manuscript.

We do not plan to conduct qualitative interviews. Instead at the final interview (Month 6), we will ask several open-ended questions about the acceptability of PrEP and the intervention and conduct a content analysis of the responses. These questions elicit participants’ perceptions of the good and bad things about taking PrEP and reasons for continuing or discontinuing taking PrEP after the study is over; whether they disclosed study participation and to whom; reasons for disclosure or non-disclosure; and the best and worst part of being in the study.

23. Methods, urine assay information. I would recommend striking the text on “greater sensitivity than plasma-based measures” and focusing on the urine assay and its use for self-monitoring in this section. More detail on how feedback is provided to participants and how they themselves use the result for self-monitoring would be helpful. 
RESPONSE: We have deleted the phrase: ‘greater sensitivity than plasma-based measures’. All study staff were trained to describe the assay as an experimental way to inform counseling for daily oral PrEP use. Staff were further trained to coach participants to reflect on and discuss the Ursure results in the context of their own life, with the goal of strengthening their ability to reflect on and manage their adherence behavior.

24. Methods, patient and public involvement. The word “to” is missing in the sentence starting “Interview questions at the final study visit…” 
RESPONSE: Thank you for pointing out this omission. This sentence has been edited.

25. Methods, p. 12. The outcome definitions would benefit from a clear explanation of how the outcome will be operationalized for analysis. For example, is “PrEP adherence” a binary outcome with the cut point in the table? How is acceptability measured for each intervention component? A “scaled” result is mentioned but not clearly presented. Some of this information is in Table 2, but it should come earlier where the outcomes are defined and the analysis plan presented. 
RESPONSE: The text has been revised to describe acceptability assessed at one-, three-, and six-month follow-up assessments.
26. Methods, p. 12. No details are presented on the plasma assay to be used, its performance characteristics, and what a level of 0.4 ng/mL means in this context. That information is important to justify use of the plasma assay result as the primary outcome.
RESPONSE: Thank you for highlighting this important point. We have added detail to the outcome description on page 13 and referenced the assay on page 7.

27. Methods, p. 13. Why was the number of paying and non-paying sex partners selected as the primary sexual risk behavioral outcome? This requires a justification.
RESPONSE: Thank you for this question. After discussion with the study team, updates to this section have been made to indicate that the outcome assesses number of partners, which is a risk factor for HIV acquisition (Pages 13-14).

28. As mentioned above, Table 2 does not add much since it comes too late to help understand each outcome and its analyses as presented on pages 12-13.
RESPONSE: After consideration of Reviewer feedback, we have removed Table 2 and instead, made additions to the outcome definitions (#25 above).

29. Figure Title. Determinants of “PrEP Adherence, Feasibility” is unclear – the feasibility of PrEP adherence? Determinants of feasibility?
RESPONSE: Thank you for this. We have revised the Figure title for clarity.

30. Figure. The figure is generally clear and helpful, although bold subheadings would be useful under “Behavioral Skills” and the Feasibility and Acceptability Outcomes are not clear (for example what is “Feedback”?).
RESPONSE: The Figure has been edited to include bold subheadings and expanded descriptions as suggested.

31. Figure. The box with "modifiable via intervention" is also placed strangely – if this is a color coding indication, it does not work well in black and white. Consider moving this specification into the Figure caption instead.
RESPONSE: We appreciate this feedback. We have now included “modifiable via intervention” in the key and the related elements are indicated with asterisks.

32. The manuscript would benefit from a careful check for grammar, spelling (PreP), and punctuation.
RESPONSE: We have reviewed the manuscript for grammatical, spelling and punctuation errors.

REVIEWER 3: Robin Schaefer, Comments to the Author
Thank you for the invitation to review the protocol for this study on providing oral PrEP to male clients of female sex workers in Kenya. The article is well-written and the study will address a critical gap in the HIV response. Below are some suggestions on improving the article. I also included a few thoughts on the study procedures. While I understand that my role as a reviewer is to focus on the presented protocol, not the underlying study, the authors may still want to reflect on these.

33. The authors plan to only offer daily oral PrEP to male clients of FSW. While this is in line with current Kenyan national guidelines, WHO will release new guidance this July on PrEP implementation that will note that event-driven PrEP (ED-PrEP, also “2+1+1”) can be offered to all people assigned male at birth (previously just MSM). It is of course unclear when this will adopted in Kenyan national guidelines, but it could be a great option to explore in this study. ED-PrEP may be a highly suitable option for MC of FSW as they risk of HIV acquisition is likely to change considerably over time. If further information on this is needed, you can contact the WHO PrEP team.
RESPONSE: We acknowledge that ED-PrEP may be an effective HIV prevention strategy for male clients of FSW. Unfortunately, as the study was already launched in November 2021 prior to the new recommendation by WHO, we are unable to consider this option, but hope to develop a larger trial of MC and certainly would explore this prevention strategy in such a study.

34. Related to the above, the primary outcome of the study is PrEP adherence at 6 months. However, for many of the MC, it may be unnecessary to take PrEP daily constantly for 6 months. So the authors may want to rather consider PrEP use at every visit and how this relates to actual behaviours. Given that the authors will collect information on sexual behaviour, one could even consider a measure of effective use, i.e. PrEP use during periods of risk.

RESPONSE: As far as we are aware, this pilot study is the first to offer PrEP to MC of FSW. We assess PrEP use and condom-protected sex at our 1, 3 and 6-month follow-ups. This study will enable us to ascertain the frequency with which study participants purchase sex from FSW in Kisumu and provide some indication as to whether ED-PrEP would be beneficial to our small sample of men. We know that 117 of the 120 participants (97.5%) returned for their one-month visit which included PrEP refill and an interview. Findings from this study may inform the development of larger trial-in which we could consider looking more closely at the issue of PrEP use during periods of risk.

35. I generally suggest speaking of “effective use” rather than adherence for the reasons outlined above.

RESPONSE: We appreciate this distinction and agree that terminology and support frameworks linking PrEP use closely to periods of heightened vulnerability are essential. The manuscript has been edited to highlight that study staff were trained and supervised to follow current national guidelines, which define PrEP as daily oral medication. Accordingly, providers counseled and supported participants to adhere to a once-daily pill-taking schedule.

36. The study will evaluate a package of multiple interventions (HIVST, urine adherence feedback, text messages). The authors should reflect on the fact that the study will not be able to distinguish between individual effects. I consider this a major limitation.

RESPONSE: We acknowledge that this is a limitation of our study. The aim of this study is to assess the feasibility and acceptability of providing PrEP along with adherence support services. Disentangling the independent contributions of the 3 components is not the intent of this study and would be a better fit for a larger implementation science study.

37. Will there be any cost and cost-effectiveness analysis? This would be quite useful.

RESPONSE: We agree that this is an excellent idea. However, due to the resource limitations of this study, we are unable to include a cost and cost-effectiveness component. If we are able to design and implement a larger trial, we would certainly include such analysis.

38. FSW will act as mobilisers in this study. The authors should reflect on potential risks for them, e.g. pushback and violence from clients.

RESPONSE: We agree that a recruitment strategy that supports the safety of staff working in the field is essential. For this study, the FSW acting as mobilizers for the study site are trained conduct outreach in sex work settings. They are highly experienced, having recruited earlier cohorts of FSW and MCs for formative work and a related RCT. They also receive close supervision to ensure that they are safely and effectively conducting outreach and engagement with prospective HIV-related research participants, including MC. There were no reports of hostile or challenging responses to recruiters, or any violence experienced during recruitment activities.

39. The authors should include a timeline for the study procedures. It would also be useful to mention earlier in the main text the frequency of follow-up visits.
RESPONSE: We have made edits across both the Abstract and Methods section to include language that provides additional detail related to the expected timeline of the study. In addition, we have included further description of participant follow-up period and number of study visits in the Methods section (Page 5).

40. What HIVST will be used in the study? Blood or oral?
RESPONSE: We have edited the text to specify that OraQuick® HIV Self-Test kits are being provided in this study.

41. It would be useful if the authors also evaluated uptake of PrEP, not just adherence, as an outcome. This could be a qualitative supplement evaluating acceptability (among those not choosing PrEP).
RESPONSE: Thank you for the comment. We note that willingness to initiate PrEP at time of enrollment is an eligibility criterion for this study. As part of the informed consent process, potential participants are informed that the study will provide PrEP for a six-month period. We will be able to ascertain how many participants do not use PrEP over the six-month study period.

We agree that a qualitative supplement would generate interesting findings related to acceptability but are unable to add this component due to resource limitations of this small study.

42. I suggest to generally just speak of sexual behaviour, not sexual “risk” behaviour (as risk behaviour can be considered stigmatising).
RESPONSE: We agree with this suggestion and have replaced ‘sexual risk behavior’ with ‘sexual behavior’ throughout the manuscript.

1. University of California San Francisco, Anova Health Institute, Institute WRHaHR. South African Health Monitoring Study (SAHMS), Final Report: The Integrated Biological and Behavioural Survey among Female Sex Workers, South Africa 2013-2014. San Francisco, CA: University of California San Francisco; 2015.
2. Simbayi LC, Kalichman SC, Jooste S, Mathiti V, Cain D, Cherry C. HIV/AIDS risks among South African men who report sexually assaulting women. Am J Health Behav 2006; 30(2): 158-66.
3. Pitpitan EV, Strathdee SA, Semple SJ, et al. Perceived stigma of purchasing sex among Latino and non-Latino male clients of female sex workers in Tijuana, Mexico. J Immigr Minor Health 2015; 17(1): 172-80.

VERSION 2 – REVIEW

| REVIEWER          | Price, Matthew A. |
|-------------------|--------------------|
|                   | International AIDS Vaccine Initiative |
| REVIEW RETURNED   | 16-Sep-2022        |

GENERAL COMMENTS: All the comments have been answered satisfactorily.

| REVIEWER          | Graham, Susan |
|-------------------|---------------|
|                   | University of Washington, Global Health and Medicine |
| REVIEW RETURNED   | 12-Aug-2022   |

GENERAL COMMENTS: The authors have addressed the reviewer comments, and this protocol is now suitable for publication.

| REVIEWER          | Schaefer, Robin |
| REVIEW RETURNED          | 09-Aug-2022 |
|-------------------------|-------------|
| **GENERAL COMMENTS**    | Thank you for this opportunity to review the revised manuscript. I am fully satisfied with the authors’ responses to my comments and have no further feedback. I am looking forward to seeing the results of this interesting study. |