PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Conducting an ongoing HIV clinical trial during the COVID-19 pandemic in Uganda: A qualitative study of research team and participants' experiences and lessons learned
AUTHORS	Muwanguzi, Patience A.; Kutyabami, Paul; Osingada, Charles Peter; Nasuuna, Esther M.; Kitutu, Freddy; Ngabirano, Tom Denis; Nankumbi, Joyce; Muhindo, Richard; Kabiri, Lydia; Namutebi, Mariam; Nabunya, Racheal; Kiwanuka, Noah; Sewankambo, Nelson

VERSION 1 – REVIEW

REVIEWER	Laher , Fatima University of the Witwatersrand Faculty of Health Sciences
REVIEW RETURNED	25-Jan-2021

GENERAL COMMENTS	This is a well-written, timely and deeply informative qualitative manuscript with extraordinary and urgent implications for HIV programmes and research. I am supportive of its publication so that it raises awareness of the difficulties that have arisen in the context of HIV while the COVID-19 pandemic restrictions are ongoing. I particularly appreciated the Tables with quotations from the study participants: it allows the reader to "hear people in their own words", adding rich context to the themes. The authors have drawn upon a wide range of issues to write the holistic Introduction, and have shown excellent insight in the Discussion. page 17 - please address the missing word (perhaps the author's name) before reference 31 is cited.

REVIEWER	Evans, Catrin University of Nottingham, School of Health Sciences
REVIEW RETURNED	06-Feb-2021

GENERAL COMMENTS	Thank you for the opportunity to review this paper. The topic is important and timely and the study overall is well described and makes some interesting points. There are a few methodological queries however which need to be addressed: TRIAL DESIGN AND RELATIONSHIP TO SAMPLING FOR QUALITATIVE STUDY AND FINDINGS Please can you add in a bit more detail about the WISE-Men

	trial? This is needed in order to make sense of the subsequent qualitative findings. For example, the paper currently states that the eligibility criteria for the trial was that men needed to be HIV negative. The participants were enrolled in Feb 2020 & the interviews were done a few months later. Yet the majority of the themes from the interview study were about difficulties accessing HIV treatment – so I am a very unclear about what happened in the mean time and how HIV testing, status, treatment and care was provided, monitored and followed up as part of the trial. So were the interviewees all HIV positive? And for how long? And what kind of in-put had they received from the study team in the meantime? This information needs to be added to the demographic information presented about the participants. Please give details related to of the 44 participants interviewed, how many were now HIV positive? However, this then begs the questions about what were the main themes and issues for those who were still HIV negative? In the paper, I can only identify one theme that relates to men who may be HIV negative (access to PREP). The paper states that the men were purposely sampled to include different age groups and employee ranks – but what about HIV status? Why was this not used as a sampling criteria? What were the challenges for those who were HIV negative? RESPONDENT VALIDATION In the methods section, it states that some study participants reviewed the categories to enhance rigour. Please state how this was done? How many participants reviewed the categories? And what were their conclusions or observations? AUTHORSHIP CRITERIA In the paper, it states that: "PAM, RN, NK, NKS are investigators on the WISe-Men trial. PK, EMN, JN, RM, FEK, CPO, LK, MN, NK, NKS critically revised the manuscript for important intellectual content." I would like to know more about what exactly PK, EMN, JN, RM, FEK, CPO, LK, MN, NK, NKS contributed to the design and execution of this study and the paper other than simply reading it which constitutes peer review rather than authorship! I feel we need to be convinced how each of these individuals who are not co-investigators on the study at all meet the ICMJE authorship criteria as outlined below: The ICMJE recommends that authorship be based on the following 4 criteria: 1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND 2. Drafting the work or revising it critically for important intellectual content; AND 3. Final approval of the version to be published; AND

	4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Fatima Laher , University of the Witwatersrand Faculty of Health Sciences

Comments to the Author:

This is a well-written, timely and deeply informative qualitative manuscript with extraordinary and urgent implications for HIV programmes and research. I am supportive of its publication so that it raises awareness of the difficulties that have arisen in the context of HIV while the COVID-19 pandemic restrictions are ongoing. I particularly appreciated the Tables with quotations from the study participants: it allows the reader to "hear people in their own words", adding rich context to the themes. The authors have drawn upon a wide range of issues to write the holistic Introduction and have shown excellent insight in the Discussion.

Response: *Thank you so much for the encouraging comments and for helping us to improve on the quality of our manuscript.*

1. Comment: page 17 - please address the missing word (perhaps the author's name) before reference 31 is cited.

Response: *We have now corrected this to include the author's names (Block and Erskine) before citing reference 31 on page 20. Thank you for this observation.*

Reviewer: 2

Dr. Catrin Evans, University of Nottingham

Comments to the Author:

Thank you for the opportunity to review this paper. The topic is important and timely and the study overall is well described and makes some interesting points. There are a few methodological queries however which need to be addressed:

Thank you so much for helping us to improve our manuscript, it reads so much better now, and the methodological quality has been greatly strengthened.

TRIAL DESIGN AND RELATIONSHIP TO SAMPLING FOR QUALITATIVE STUDY AND FINDINGS

1. Comment: Please can you add in a bit more detail about the WISE-Men trial? This is needed in order to make sense of the subsequent qualitative findings. For example, the paper currently states that the eligibility criteria for the trial was that men needed to be HIV negative.

Response: *This comment is especially important and will help to give the reader some context for this current study. We hade added a sub-section titled 'WISe-Men Clinical Trial' at the beginning of the methods section on page 5. This is presented below;*

> **WISe-Men Clinical Trial**
>
> This was a two-arm cluster randomized trial (CRT) involving men employed in private security companies. The clusters were private security companies each employing more than 50 men. The trial was conducted in two Ugandan districts: Kampala and Hoima. Through randomization, Kampala district was allocated to the intervention arm and Hoima to the control arm. The clusters in the intervention arm received HIV Self-testing while those in the control arm received standard HIV testing services. Men who worked at private security companies were eligible to participate in the trial if they were 1) 18-60 years old, 2) Employed >6 months within the security industry 3) Not tested for HIV before or attained Negative test results for HIV ≥ one year prior to enrolment. The participants in each arm received either an HIV test or an HIV test kit with planned follow-up at 1month, 3 months and 12months to assess linkage to care or prevention services.

2. Comment: The participants were enrolled in Feb 2020 & the interviews were done a few months later. Yet the majority of the themes from the interview study were about difficulties accessing HIV treatment – so I am a very unclear about what happened in the meantime and how HIV testing, status, treatment and care was provided, monitored and followed up as part of the trial. So were the interviewees all HIV positive? And for how long? And what kind of in-put had they received from the study team in the meantime? This information needs to be added to the demographic information presented about the participants.

Response: *Thank you so much for flagging this. We have included details about the trial participants HIV status in the table of the demographic characteristics (Table 1). We have also included a statement in the results section of the paper on page 9.*

> The trial participants in this study (n=32) had all received HIV testing services as part of the clinical trial and 10 (31.2%) were newly diagnosed as HIV positive.

We have also provided further information regarding what in-put they received from the study team during this time. (Page 11)

Mitigation measures for trial participants challenges in accessing HIV treatment, care or prevention services

As a result of the challenges experienced by study participants, the trial team implemented some mitigation measures to ensure that the participants received their treatment or had access to prevention services. The measures included

i. Home delivery of ART by study counsellors for participants who needed refills, these visits were also useful for follow-up assessments, and counselling for study participants and their partners.

ii. Delivery of ART to community pick-up points for participants who were not willing to receive the study team members in their homes.

iii. Follow-up phone calls from the study counsellors and nurses for participants who returned reactive HIV self-test kits and needed further counselling for ART initiation. During these counselling sessions, further information was provided regarding COVID-19.

iv. Home and community delivery of condoms for all study participants.

v. Active linkage of participants to clinics for further counselling and initiation of PrEP.

vi. Provision of letters and health information to health facilities that enabled the participants to link to HIV care and treatment at new facilities.

3. Comment: Please give details related to of the 44 participants interviewed, how many were now HIV positive? However, this then begs the questions about what were the main themes and issues for those who were still HIV negative? In the paper, I can only identify one theme that relates to men who may be HIV negative (access to PREP).

Response: *Thank you so much for this key comment, we have now re-written some portions of the results section to highlight that these challenges were faced by both groups especially in the categories titled 'difficulties accessing research sites', 'fear of exposure to COVID-19', and 'misinformation'. The accompanying participant narratives have also been included in Table 2.*

Transport difficulties (Page 13)

Following enrolment into the trial, all participants each participant were meant to return for follow-op visits after 1 week, one month and then at three months. This was for participants who tested HIV positive and HIV negative. Unfortunately, the stay-at-home orders made this impossible and those who tested HIV negative were unwilling to spend their money and face the inconvenience to travel to the research sites. The research team then changed to follow-up phone calls; however, some participants had poor telephone network connectivity and therefore missed these calls.

Fear of exposure to COVID-19 (Page 14)

Participants were concerned about the likelihood of exposure to the coronavirus at the research site. They requested for a significant risk allowance for in-person visits during

the pandemic. This was expressed more among participants who returned negative test results. They felt that there was no need to put themselves in danger of exposure to COVID-19 since they had already tested HIV negative.

Incorrect information about COVID-19 (Page 12)

Some participants reported that they received wrong information from their peers. For example, some participants were informed that PLWHA who were on ART were more likely to get infected with COVID-19. Therefore, some participants stopped taking their medication. Other participants who tested HIV negative were initially unwilling to follow the COVID-19 guidelines. They reported that their peers informed them that only people with underlying disease conditions were at risk for infection with the Corona virus. The WISe-Men trial had also involved blood pressure, blood glucose and syphilis tests. Therefore, some of the participants who tested negative for all the tests, were misinformed regarding their ability to contact COVID-19.

We have also provided details about the HIV status of the participants in table 1.

4. Comment: The paper states that the men were purposely sampled to include different age groups and employee ranks – but what about HIV status? Why was this not used as a sampling criteria?

Response: *The inclusion of the HIV status as one of the sampling criteria was erroneously overlooked during the writing of the manuscript. We have now included it in the 'in-depth interviews' sub-section of the methods section. (Page 7)*

Participants were purposefully sampled to include men from different employee ranks, age categories (18-25, 36-35, 36-45 and 46-64) and HIV status (positive and negative).

5. Comment: What were the challenges for those who were HIV negative?

Response: *The challenges for those who were HIV negative are highlighted in the response to a previous comment. (Number 3).*

RESPONDENT VALIDATION

6. Comment: In the methods section, it states that some study participants reviewed the categories to enhance rigour. Please state how this was done?

Response: *We have now included some more information on how the respondent validation was done. (Page 8)*

To ensure trustworthiness and credibility of the data, a sample of the study participants reviewed the categories and subcategories. The sample (n=7) included one participant from each of the different employee ranks, different age groups, different HIV status and 3 members from the research team. The reviewers read through the identified categories and sub-categories validate them as a true representation of their perspectives of participating in an ongoing clinical trial during a pandemic.

7. Comment: How many participants reviewed the categories? And what were their conclusions or observation

Response: *The participants felt that that categories and subcategories represented their perspectives. This is now further highlighted in the manuscript on page 8. Thank you for highlighting this.*

The participants corroborated most of the categories and sub-categories, except one category 'Wrong information' which was changed to 'misinformation'.

AUTHORSHIP CRITERIA

8. Comment*: In the paper, it states that: "PAM, RN, NK, NKS are investigators on the WISe-Men trial. PK, EMN, JN, RM, FEK, CPO, LK, MN, NK, NKS critically revised the manuscript for important intellectual content."*

I would like to know more about what exactly PK, EMN, JN, RM, FEK, CPO, LK, MN, NK, NKS contributed to the design and execution of this study and the paper other than simply reading it which constitutes peer review rather than authorship! I feel we need to be convinced how each of these individuals who are not co-investigators on the study at all meet the ICMJE authorship criteria as outlined below:

The ICMJE recommends that authorship be based on the following 4 criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Response: Thank you for raising this critical question on authorship and authorship criteria. We have now re-written this section to point out each one's individual contribution in line with the ICMJE criteria. It now reads as follows on page 22;

PAM is the Principal Investigator of the WISe-Men clinical trial and was involved in data collection, analysis and drafting the manuscript. RN is the WISe-Men trial manager and was involved in data collection, analysis and drafting the manuscript. NK and NKS are both co-investigators and supervisors on the WISe-Men trial, were involved in designing the study and critically revised the manuscript for important intellectual content. TDN is a co-investigator on the WISe-Men trial and was involved in conceptualizing the study and drafting the work. PK made substantial contribution to the conception of the study, and critically revised the manuscript for important intellectual content especially around IRB and ethical issues. EMN made substantial contribution to the design of the study and was involved in data analysis and drafting the work. JN and FEK were critical in inductive content analysis of the findings from IDI and FGD's and critically revised the manuscript for important intellectual content. CPO was involved in the early conception of the study, generation of study themes and drafting the work, LK and MN were critical in data

collection from both trial team members and study participants and critically revised the manuscript for important intellectual content, specifically the methods section.

All the authors gave final approval of the work to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

VERSION 2 – REVIEW

REVIEWER	Evans, Catrin University of Nottingham, School of Health Sciences
REVIEW RETURNED	27-Mar-2021

GENERAL COMMENTS	All comments have been addressed