PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Implementation of a peer support intervention to promote the detection, reporting and management of adverse drug reactions in people living with HIV in Uganda: a protocol for a quasi-experimental study
AUTHORS	Kiguba, Ronald; Ndagije, Helen; Nambasa, Victoria; Katureebe, Cordelia; Zakumumpa, Henry; Nanyonga, Stella; Ssanyu, Jacquellyn; Tregunno, Phil; Harrison, Kendal; Merle, Corinne; Raguenaud, Marie-eve; Kitutu, Freddy

VERSION 1 – REVIEW

REVIEWER	Adenuga, Babafunso A. Adex Medical Consult
REVIEW RETURNED	10-Oct-2021

GENERAL COMMENTS	Implementation of a peer support intervention to promote the detection, reporting and engagement of adverse drug reactions in people living with HIV in Uganda; a protocol for a quasi-experimental study General appraisal of the study protocol Authors were able to fully describe the objectives of the study, which are in line with the title and presumed results that are sought from the study. Specifics The dates of the study were not included in the abstract. Also, the authors stated the trial registration number (Trial Registration: ISRCTN75989485) in the abstract, however, the actual authority who issued this registration number was not mentioned.

REVIEWER	Karwa, Rakhi Purdue University
REVIEW RETURNED	10-Nov-2021

GENERAL COMMENTS	Thank you for the opportunity to review this study protocol. To my knowledge, the utilization of peer supporters for ADR detection has not previously been published in the literature with such a robust study design. The results of this study will be very interesting to read. Comments on the manuscript:

	Introduction, third paragraph: This paragraph lacks direction. It starts with the roll out of DTG and IPT, touches upon anecdotal evidence and then goes into the incidence of ADRs in general or with DTG. I think that you could be more intentional about this paragraph. Are you trying to say that there is a high incidence out there or a low incidence based on the data included? are you trying to say that you don't know the incidence for your population? I think you could state that these ADRs have been observed and to what incidence and then make those connections so that the reader knows the message you are conveying. Methods, Intervention, 2nd paragraph: 1. "mentored PLHIV in the intervention arm will identify with the peer supporters whom they will rely on to improved..." This sounds confusing. It sounds like the PLHIV are allowed to choose their peer supporter. Is that true? The next paragraph sounds like they will be assigned based on age, gender, etc. 2. Do you have education minimum standards for peer supporter? 3. Why exclude PLHIV on ART for < 6 months? Many ADRs happen when first starting medications. 4. Please explain the retrospective assessment of "occurence of ADRS during the 4-month period preceding study enrolment" - under exclusion criteria. Please explain why you are doing this and how you plan to conduct it. 5. Please explain why feasibility is the primary outcome and not the detection of ADRs. I am aware that the goal is to improve the detection through a new method of integrating peer supporters into the process. 6. What is the plan to address any serious ADRs that are detected? How will you triage patient care so that PLHIV are able to connect to clinicians? How do you plan to include clinicians to ensure that there is buy in and that information is shared in a reasonsable time frame to improve patient care?

VERSION 1 – AUTHOR RESPONSE

BMJ Open.
Re: Response to Reviewers' Comments
Thank you for reviewing our manuscript titled "Implementation of a peer support intervention to promote the detection, reporting and management of adverse drug reactions in people living with HIV in Uganda: a protocol for a quasi-experimental study". A point-by-point response to the reviewers' comments are presented below.
Reviewer 1
Comment 1: The research protocol was well written and concise.
Response 1: Thank you!

Reviewer 2

Comment 2: Thank you for the opportunity to review this study protocol. To my knowledge, the utilization of peer supporters for ADR detection has not previously been published in the literature with such a robust study design. The results of this study will be very interesting to read.
Response 2: Thank you!
Comment 3: Introduction, third paragraph: This paragraph lacks direction. It starts with the roll out of DTG and IPT, touches upon anecdotal evidence and then goes into the incidence of ADRs in general or with DTG. I think that you could be more intentional about this paragraph. Are you trying to say that there is a high incidence out there or a low incidence based on the data included? are you trying to say that you don't know the incidence for your population? I think you could state that these ADRs have been observed and to what incidence and then make those connections so that the reader knows the message you are conveying.
Response 3: The text is revised with some text removed to improve on clarity in the paragraph. Thank you.
Comment 4: Methods, Intervention, 2nd paragraph: "mentored PLHIV in the intervention arm will identify with the peer supporters whom they will rely on to improved..." This sounds confusing. It sounds like the PLHIV are allowed to choose their peer supporter. Is that true? The next paragraph sounds like they will be assigned based on age, gender, etc.
Response 4: The text is revised to eliminate confusion as follows; “Peer supporters in the intervention arm will guide the mentored PLHIV to report ADRs to NPC and improve the latter’s healthcare-seeking behaviour.”
Comment 5: Do you have education minimum standards for peer supporter?
Response 5: We have added text, “… peer supporters will be screened by the research team to gauge their ability to be peer supporters e.g. the ability to use the Med Safety App/USSD, ability to read and write in English and good interpersonal skills. Satisfactory peer supporters will give written informed consented”.
Comment 6: Why exclude PLHIV on ART for < 6 months? Many ADRs happen when first starting medications.
Response 6: Text added, “Many ADRs happen when starting ART although such PLHIV tend to be unstable on treatment. The priority of this pilot is to understand first the dynamics (feasibility and acceptability) of the peer support intervention when introduced to a stable group of PLHIV on ART (for >=6 months). If found to be feasible, the peer support intervention will be tested in the unstable group of PLHIV on ART (for <6 months).”
Comment 7: Please explain the retrospective assessment of "occurrence of ADRs during the 4-month period preceding study enrolment" - under exclusion criteria. Please explain why you are doing this and how you plan to conduct it.
Response 7: These details have been removed from the exclusion criteria sub-section and transferred to the Data collection and management sub-section. The following revision is added: “Participating PLHIV will be asked at enrolment if they experienced suspected ADRs in the 4-months preceding the study. The self-reported suspected ADRs will be corroborated with additional information on documented suspected ADRs from retrospective clinical chart review of the 4-month period prior to study enrolment. The clinical charts will be accessed by the health facility staff.” The aim is to compare the level of documentation of ADRs in the clinical charts with self-reported ADRs by PLHIV on ART.
Comment 8: Please explain why feasibility is the primary outcome and not the detection of ADRs. I am aware that the goal is to improve the detection through a new method of integrating peer supporters into the process.
Response 8: Both feasibility and number of suspected ADR reports are primary outcomes.
Comment 9: What is the plan to address any serious ADRs that are detected? How will you triage patient care so that PLHIV are able to connect to clinicians? How do you plan to include clinicians to ensure that there is buy in and that information is shared in a reasonable time frame to improve patient care?

Response 9: Added to the data collection and management sub-section; “PLHIV who experience serious ADRs will be linked directly to the health facilities where they receive ART for ADR management. Peer supporters will refer serious ADR cases to peer supervisors who will, in turn, refer these cases to focal clinical staff assigned to the study by the health facility administration; usually stationed at triage to connect the cases to clinicians.”
Note: Three co-authors from World Health Organization withdrew from the publication, namely; Ayako Fukushima, Noha Iessa and Pal Shanthi (see attached email).

VERSION 2 – REVIEW

REVIEWER	Karwa, Rakhi Purdue University
REVIEW RETURNED	23-Jan-2022

GENERAL COMMENTS	The endpoints/outcomes that are being measured should be included in the abstract.

VERSION 2 – AUTHOR RESPONSE

Reviewer 2

Comment 1: The endpoints/outcomes that are being measured should be included in the abstract.

Response 1: Thank you! The endpoints/outcomes have been added to the abstract.

Regards,

Ronald Kiguba

Corresponding Author.