Author’s response to reviews

Title: Retention in care and virological failure among adult HIV+ patients on second-line ART in Rwanda: A national representative study

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Attn: Editor, BMC Infectious Diseases

Re: Manuscript Re-submission #2: Retention in care and virological failure among adult HIV+ patients on second-line ART in Rwanda: A nationally representative study.
Dear Editor,

We would like to thank you and the reviewers for the opportunity to resubmit the revised manuscript and have addressed all points in the enclosed documents.

We are grateful for all of your assistance in moving this manuscript forward within your journal and hope you will find these changes satisfactory.

We look forward to your response.

Yours sincerely,

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Responses to reviewers’ comments:
Overall, the manuscript is well written and good structured. However, some points merit further clarification. The majority of the issues are related to the methodology of the manuscript per se.

We thank you for the positive feedback and appreciation of this work.

1#. Could the authors clarify the study design in the methods section? Was it a retrospective cohort with prospectively collected clinic data from EMR from patients attending the 49 HIV clinics?

We appreciate your comment; This section has been rephrased to address this observation under methods section, page 4 (line 46): “A two-stage cluster sampling design was undertaken to randomly select 49 of the 340 eligible sites where all patients were considered for analysis in a retrospective observational cohort study using routinely collected program data.”

2#. It is unclear to me the start and the final time points for the observations. Do you start the evaluation after the 31st December 2016 and follow after that? What was the last time of follow-up for the cohort?

Thank you. We provided clarification on time of follow up under methods, page 5 (line 34). The section has been changed accordingly: “Our study included patients aged 15 years or older, whoever switched to second-line ART in 49 randomly selected health facilities in Rwanda since the start of second line program in 2004 until 31st December 2016.”

3#. Page 5 (line 46). The authors define virological failure as having a viral load > 1000 copies/mL after at least 12 months on first-line ART with self-reported good adherence to medication. However, as was elucidated before, the authors are interested in second-line virological failure, instead of the first-line scheme efficacy. Could the authors elaborate more on that? Was viral load ascertained considering the measurement at 12-months after the initiation of a second-line scheme?

We realized there was a typing error, indeed the viral load on second line was assessed. We therefore updated the sentence under methods, page 5 (line 46) as follow “We defined
virological failure as having a viral load (VL) > 1000 copies/mL after at least 12 months on second-line ART with self-reported good adherence to medication (>90% no dose missed) ….

3#. Could the authors describe the frequency of HIV viral load/CD4 monitoring in Rwanda setting? Is it 6-monthly? Alternatively, more frequently in high-risk patients?

Thank you. We have provided this important description in the new version of the manuscript under methods, Page 5 (line 45): “The frequency of CD4 cell count measurement was bi-annual while viral load has been measured annually for most of patients according to the national guidelines except in exceptional circumstances guided by decision from individual clinician”.

4#. Page 6 (line 7). It is unclear to me if covariates collected at the initiation of first-line ART could explain the outcomes related to the second-line ART. For instance, variables collected at the time of the switch should be included besides those at the enrollment (i.e., CD4/VL, WHO stage, etc.). If those variables at the time of switching are not available, please include this as a limitation at least.

We appreciated your observation. As per previous note; the variables presented are obtained at the time of switching from first line to second line ART. We made it clear in the section on page 6 (line17) under methods section: “The explanatory variables for this analysis were all measured at the time of switch from first to second line ART and included demographic variables (age, sex, marital status, body mass index (BMI), clinical variables (TB screening status, CD4 cell count, WHO stage, viral load, date of ART initiation, type of ART regimen)”