Author’s response to reviews

Title: The Effectiveness and Cost-Effectiveness of Three versus Six-monthly Dispensing of Antiretroviral Treatment (ART) for Stable HIV Patients in Community ART Refill Groups in Zimbabwe: Study Protocol for a Pragmatic Cluster Randomized Trial

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Author’s response to reviews:

The Editor
Trials

15 December 2017
Dear Editors

Re: Revision, TRLS-D-17-00738. The Effectiveness and Cost-Effectiveness of Three versus Six-monthly Dispensing of Antiretroviral Treatment (ART) for Stable HIV Patients in Community ART Refill Groups in Zimbabwe: Study Protocol for a Pragmatic Cluster Randomized Trial.

Thank you for considering this manuscript. We appreciate the comments provided, and the manuscript has been revised as per the reviewer’s suggestions (changes shown as tracked changes in the revised manuscript). Please find our point-by-point responses to the reviewer’s comments below. (Line numbers refer to those in the manuscript with track changes visible).

Yours sincerely,

Geoffrey Fatti, on behalf of the authors.

Reviewer reports:

Reviewer #1: This is an extremely well-written and interesting study protocol. The cluster-randomized non-inferiority design is an interesting one and appears appropriate for this setting. I have only some minor comments/requests for the protocol.

Title. Add the ART acronym in parenthesis after the word "Treatment" in the title. You may also want to modify "Stable Patients" to "Stable HIV Patients" in the title, though this is optional.

Response: Both of these changes have been made as suggested.

Abstract, line 78. Suggest outcome be stated here as "..proportion of participants alive and retained in care..." Also suggest adding the sample size (1,920 per arm) to the abstract to give abstract readers an idea of the "magnitude" of the trial.

Response: Both of these changes have been made as suggested (lines 77-78).

Methods, line 184. I would recommend changing the language "three-monthly" and "six-monthly" to something like "at three month intervals" and "at six month intervals", for clarity.

Response: These changes have been made as suggested (lines 185-190).

Line 201. Consider specifying the non-inferiority margin of 3.25% here.

Response: The non-inferiority margin has been added here as suggested.

Line 232. Perhaps clarify the "no facility or ART collection for >90 days" primary outcome here. For example, if a patient does not come in in-person for the 12 month visit (but has not
transferred to another clinic), what would be acceptable to be considered retained in care for the 12-month outcome? Would they then have to come in, in person, within the next 90 days for a "late" annual visit?

Response: Thank you for this suggestion. The definition has been clarified by adding an additional sentence: “Participants not arriving for the 12 or 24 month visit will be considered retained at these time-points if collecting ART in person within 90 days of the scheduled appointment date”. (Lines 234-236)

Line 245. I would mention again, as is stated in the Abstract, that each CARG consists of approximately 6-12 patients.

Response: This has been added as suggested (line 250).

Table 1: change "Weigh" to "Weight"

Response: This has been corrected as suggested.

Line 316: the intracluster correlation of 0.01 is per institution (not per CARG), correct? Might there be higher ICC's at institutions assigned to CARGs?

Response: It has been clarified that the intracluster correlation of 0.01 is amongst participants associated with the same health care facility (i.e. the cluster). (Line 321).

As the experimental unit is at the level of the facility (and there isn’t published data regarding ICCs with respect to retention amongst CARG participants), we elected to assume the same ICC for each of the arms.

Line 330: All of the patients within a CARG do not need to enroll in the trial, is this correct? Also, can/will patients still be in CARGs, if they are at centers participating in the control arm? If so, please clarify (if needed) how CARGs would function at the control sites compared to the 3MC and 6MC centers.

Response: Thank you for these points. It has been clarified that “It is not mandatory for all patients in a CARG to participate in the study” (Lines 336-337).

Also, it has been clarified that “Patients already in CARGs at facilities in the control arm at the commencement of the study will not be considered for recruitment, and they will continue to receive care in CARGs as per the national guidelines similar to those in the 3MC arm.” (Line 341-343).

Line 402: how is the subset of participants participating in the cost study selected?

Response: It has been clarified that “Every fifth participant enrolled consecutively per site will be selected for administration of the patient-level cost questionnaires.” (Lines 407-409).
Line 554: "Suppression" is misspelled.

Response: The spelling of this word has been corrected.