Author’s response to reviews

Title: Maximizing adherence and retention for women living with HIV and their infants in Kenya (MOTIVATE study): study protocol for a randomized controlled trial

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Author’s response to reviews:

Dear Editorial Board of Trials,

RE: RESPONSES TO REVIEWER COMMENTS

We would like to sincerely thank you for reviewing our manuscript, and for providing important comments. We have taken all of the referees’ comments into consideration, and have revised the manuscript accordingly. Below, please find our point-by-point responses to the referees’ comments.

REVIEWER #1

Comment 1:

Line 8: if the guideline was referred to as option B, what is it now referred to?

Response:
We appreciate the reviewer’s comment. In response, we have deleted the word “previously,” given that the new guidelines are still popularly referred to as “Option B+” in practice.

Comment 2:

Please describe the mobile coverage and accessibility in the regions to be studied. Can all persons afford cell phones? Is this a source of selection bias and/or confounding? Is cell-phone access income-dependent and could this be a reason for poor adherence?

Response:

We appreciate this comment. In Kenya, a country of 43 million people, there are currently 37.8 million active mobile phone subscriptions, representing about 88% of the population. We have included this statement in the manuscript (lines 354-355). While mobile phone access is high, we acknowledge that not all persons can afford cell phones, and agree that this may be a source of selection bias and/or confounding. In addition, we agree that cell phone access may be income-dependent. Socioeconomic status itself however is not conclusively associated with adherence as shown in a systematic review of this topic by Falagas et al. 2008 BMC. Our study will collect data about phone ownership/access that will enable us address these questions (and any limitations) at the point of data analysis and reporting.

Comment 3:

The participant selection criteria is biased. Access to phones discussed above. Willingness to have home visits and visit a counsellor could be a source of selection bias. Whilst this bias is present at each sites, what efforts are considered to either estimate, minimize or measure this.

Response:

We appreciate this comment and acknowledge that willingness to have home visits and visit a counsellor could be sources of bias. In response, we have attempted to design this trial to approximate real-world conditions. As such, we view the ability for study participants to decline home visits as something that would be expected under routine care conditions. Thus, while this potential source of bias could be seen as limiting the study’s internal validity, we view it as an opportunity to maximize external validity and enhance the potential of our study interventions to be implemented with fidelity if found to be efficacious.

Comment 4:

What risks are there for participants (eg involuntary disclosure)? How are these to be managed?

Response:
Thank you for this comment. Potential risks to participants in this study are detailed in the informed consent form and thus were excluded from this manuscript. These risks include social harm if information participants reveal about their sexual behavior, HIV status, or other personal details were to be disclosed outside of the research. This study approach takes into account these potential risks, as well as suggestions for the most acceptable delivery of the interventions revealed in our preliminary research in this rural Kenyan setting. For example, community mentor mothers are trained by staff who have extensive experience in the community on maintaining confidentiality, avoiding inadvertent disclosure, and couples counselling in order to minimize risk during home visits. Our own formative research and that in similar settings suggests that home-based visits can be conducted in a safe and acceptable manner in rural East Africa.

Patient anonymity may be compromised by the text messaging intervention since the phone numbers to which messages are sent are essentially personal identifiers. However, the computer on which these phone numbers will be stored will be accessible only to specifically designated study staff. Every effort will be made to safeguard subjects from future contact. Text messages are based on content preferences expressed by study participants. In our prior text messaging study, participants preferred to receive general messages that did not specifically mention HIV or anti-retroviral drugs. This approach will be maintained, thereby minimizing risk of disclosure.

Research has shown that pregnant women with HIV face stigma and discrimination at home, in the community, and also within health care facilities. This study directly addresses this institutional discrimination by providing stigma reduction training to all study facilities.

Comment 5:

Who will be recruiting participants at each site? How will selection bias be managed by recruiters?

Response:

Participants at each site are recruited by study nurses. To address this comment, we have modified line 117 to read, “HIV-positive pregnant women attending ANC at one of the study sites will be recruited by a study nurse at presentation to clinic or referral from the community.” Selection bias will be managed by recruiting all eligible women based upon study eligibility criteria. If there is any residual bias, we will acknowledge this limitation when we report study outcomes.

Comment 6:

Why is a VL <1000 cpm considered virally suppressed, when the international norm is <400 or <50 cpm?

Response:
Thank you for this comment. The VL cut-off used here is based upon the Kenya national guidelines for antiretroviral therapy management which use 1000cpm as the lower limit of detection and is consistent with current World Health Organization recommendations.

Comment 7:

Is there a defined study period / limit? What happens if sample size is not achieved in that time?

Response:

The study is expected to be completed within 5 years of initiation based on the duration of funding (through April 2019). If sample size is not achieved in that time, and depending upon funding availability, we will apply to the institutional review board for an extension of the recruitment period.

REVIEW #2:

Comment 1:

Alternate measures of adherence: Is there a sensitivity analysis planned using an alternate measure of adherence such as the percentage of attended visits of those scheduled?

Response:

We appreciate this comment. Indeed, a sensitivity analysis that uses alternate measures of adherence would be an important complement to our pre-specified analysis. We will include this in our revised data analysis plan.

Comment 2:

Are only scheduled texts/calls planned or will there also be unscheduled calls following missed appointments/visits?

Response:

Thank you for this comment. We do not plan to have unscheduled calls following missed visits. Instead, women who do not attend scheduled clinic appointments will be followed up by their health care providers based on existing routine care guidelines.

Once again, thank you for your consideration of our manuscript for publication in Trials.

Sincerely,
Thomas A. Odeny
On behalf of the authors.