Title: Influences on visit retention in clinical trials: Insights from qualitative research during the VOICE trial in Johannesburg, South Africa

Authors:

Jonathan J Stadler (jstadler@wrhi.ac.za)
Busisiwe Magazi (bmagazi@wrhi.ac.za)
Sinead A Delany-Moretlwe (sdelany@wrhi.ac.za)
Elizabeth Montgomery (emontgomery@rti.org)
Florence Mathebula (fmathebula@wrhi.ac.za)
Miriam Hartmann (mhartmann@rti.org)
Ariane van der Straten (ariane@rti.org)

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Author's response to reviews: see over
Dear Editors,

RE: Influences on visit retention in clinical trials: Insights from qualitative research during the VOICE trial in Johannesburg, South Africa.

Thank you for giving us this opportunity to respond to the two reviewers of our manuscript and to resubmit a revised version. We would also like to thank the two reviewers for their helpful comments, which we have carefully considered and have incorporated into the manuscript.

The following details our responses and changes made to the manuscript.

Reviewer: Keira Lowther

Discretionary Revisions
1. There is a p value cited in the description of the sample, but no description of tests used are included in the data analysis section. It would be nice to have this information if possible.

Response: on page 8, line 24 we have indicated that this was a ChiSquare test, as per the extract below:

The mean number of visits missed was lower in the VOICE-C participants, compared to those not included in VOICE-C (1.55 vs. 3.79), and more VOICE-C participants were retained at the PUEV visit compared to their non-VOICE-C counterparts (97% vs. 87%; ChiSquare test, p=0.002).

2. I wonder whether a mention of the recently published paper by Ware et al might benefit the manuscript. Their’s as a similar qualitative exploration of reasons for non attendance, but in Nigeria, Tanzania and Uganda. There are interesting similarities and differences between the two papers.

Response: Our original manuscript contained a reference to Ware et al’s paper which does raise similar issues. We have made this more obvious and include the following on Page 16, Line 4: Reference Number [16].

There are a number of complex reasons why trial participants miss visits [16]. Likewise, our findings suggest that missed visits are frequently unintentional, and due to factors outside individual participant’s locus of control.

Reviewer: Cynthia Woodsong

Minor Essential Revisions:
1. Since "serial ethnographic interviews" are not a standard methodology used in microbicide research, it would be helpful to provide a bit more information about these. For example - How does such an interview differ from an IDI, other than the interview is repeated? Why were serial ethnographic interviews conducted outside of the clinic?

Response: This is a useful comment.

We have added the following: (p6, 22-25):

The serial nature of the EIs, combined with their greater focus on the participant’s everyday life and surroundings, provided researchers with an opportunity to become better acquainted with interviewees, learn about changes to their life experience over time, and in some cases to observe their living circumstances.
2. "Mothers, daughters, partners -- social obligations to others": Since the paper subsequently discusses additional types of social obligations, the authors might consider referring to obligations in this section as "familial" obligations (Page 9, Line 5)

**Response:** We appreciate the comment, however feel that we refer here to familial relations as household members and extended kin, and moreover the heading is correct as it refers to the women’s identities rather than relationships.

Also in this section, the authors say that "...male partners also supported women's intentions..." but they do not indicate if this is all, most, or some partners.

**Response:** We have added ‘some’ as suggested (Page 10, Line 6)

Further, in this paragraph, the authors state that the outreach team contacted male partners to reach the female participant, but they do not indicate if the female participant had given permission to do so, or if this was an understanding for all participants.

**Response:** We have added the following in parenthesis (Page 10, Line 10): (she had given consent for the clinic to contact her partner)

3. The sentence "However, when planning ahead was possible" could be rephrased to make it more clear that the trial made allowances for the provision of additional study supplies.

**Response:** Thanks for pointing this out. We have added the following (Page 11, Line 10-12)

However, when participants were able to notify the trial of prolonged absences from Johannesburg in advance, women were given extra study products to cover missed visits.

4. The authors might clarify what is meant by "a doctor's note from the trial clinic," and the circumstances under which this was provided. There is a later reference to a "clinic attendance letter," but it is not clear if this is the same thing as a doctor's note.

**Response:** Agree; we have changed ‘doctor’s note’ to ‘clinic attendance letter’. Page 12, Line 6.

Moreover, employers were generally unsympathetic to requests for time off from work, even when presented with a clinic attendance letter from the trial clinic.

5. The clinic context: This section described the length of time people waited at the clinic, but it does not mention the transport time to and from the clinic. The authors might consider adding something about typical transport time.

**Response:** We agree, and explored the data set for commentary regarding travel to the clinic. Although there were very few who raised this as an issue. As a result we have added the following paragraph. Page 14 Line 3-7:

For a few participants, the absence of public transport or living far from the clinic created difficulties to visit the clinic. Participants who resided far from the clinic and reached home after dark raised additional concerns about personal safety. However, participants could notify the clinic and arrange for a pickup and drop off service to a central point from which they could catch public taxis and busses.
6. In the discussion section, the third paragraph starts off with a statement about disclosure, but the relationship of disclosure to the rest of the paragraph is not clear. Do the authors mean that informed family members and employers were more supportive of participation? What did the "negative experiences" (last sentence in this paragraph) have to do with disclosure?

Response: Agree, we have made changes to the order, and shifted the sentence about disclosure towards the end (Page 16, line 15-16). The next sentence (17-18) makes it more explicit regarding the negative experiences we are referring to:

In this regard, disclosure about trial participation was central to whether support was offered or not. In addition, despite their negative experiences of waiting for long periods of time in the clinic, women liked the benefits of the trial, and acted as responsible participants by re-scheduling visit dates, and requesting extra supplies of product.

Discretionary Revisions:
1. Abstract: It is a bit unusual to read an abstract with a methods and results section that is largely a list. The authors might consider casting this a bit differently.

Response: Agree. We have rewritten the results section of the abstract as follows:

Results: Women’s kinship, social, and economic roles shaped their ability to participate in the clinical trial. Although participants expressed strong commitments to attend study visits, clinic visit schedules and lengthy waiting times interfered with their multiple obligations as caregivers, wage earners, housekeepers, and students.

2. The authors might avoid using the word "trialist," as it is jargon that may not be understood by your wider readership.

Response: Agree. We have replaced this with the term ‘trial staff’ (Page 4, Line 15).

3. METHODS: In the first sentence, the authors should clarify that the VOICE trial site they associated with was in Hillbrow. The sentence currently reads "The VOICE trial was conducted in Hillbrow..." but earlier they stated that the VOICE trial was conducted in 3 countries (and there were multiple sites in South Africa).

Response: Agree. We have included the following: ‘The Johannesburg site for the VOICE trial was located in Hillbrow, an inner city neighbourhood’. (Page 5, Line 24-25)

Thank you