Patient Preference and Adherence

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ORIGINAL RESEARCH

"I Wish to Continue Receiving the Reminder Short Messaging Service": A Mixed Methods Study on the Acceptability of Digital Adherence Tools Among Adults Living with HIV on Antiretroviral Treatment in Tanzania

This article was published in the following Dove Press journal:
Patient Preference and Adherence

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Introduction: Digital Adherence Tools (DAT) to promote adherence to antiretroviral treatment (ART) for HIV are being increasingly adopted globally, however their effectiveness and acceptability in limited resource settings has been challenging. In this study, we examine the acceptability of DATs to improve adherence to ART.

Methods: This study was part of a three-arm randomized controlled trial (REMIND) which investigated the effect of two different DAT's: SMS text messages (SMS) or real-time medication monitoring (RTMM) on treatment adherence; compared to standard of care. Exit interviews and in-depth interviews were conducted at 48 weeks follow-up, to collect data on their experiences (successes, challenges, and barriers) and behaviours regarding the implementation of the interventions. Translated transcripts, memos and field notes were imported to NVivo software version 12. We used a thematic framework analysis which drew from Sekhon's theoretical framework of acceptability (TFA), which comprises of seven constructs (affective attitude, perceived burden, perceived effectiveness, ethicality, self-efficacy, intervention coherence and opportunity costs).

Results: Of the 166 participants enrolled, 143 (86%) were interviewed (68 in the SMS arm and 75 in the RTMM arm). Participants were highly satisfied (98%) with the DAT system and the majority of them reported it motivated them to take their medication (99%). The majority of participants reported they were confident in their ability to comply with the intervention and understood how the intervention worked (97%). Very few reported negatively about the devices (carrying the device), with only 6% reporting that they did not feel comfortable and 8% had ethical concerns with the SMS-content A few participants reported challenges with their connectivity/network and that the visits were too time-consuming. A few participants reported that they incurred extra cost for the sake of the study.

Conclusion: Overall, the acceptability of these DATs was high. However, several factors may hamper their acceptability including the content and number of SMS, carrying the devices and the network availability.

Keywords: adherence, SMS reminders, real-time medication monitoring, digital adherence tool, DAT, acceptability, ART

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http://doi.org/10.2147/PPA.S290079

Introduction

In Tanzania, the national HIV prevalence reported in 2018 was 4.6% and adults aged 15–49 years accounted for 81% of the people living with HIV (PLHIV).[1] Of those adults, 72% were on antiretroviral therapy (ART). Sustained adherence to ART can be challenging. Adherence is defined as the degree to which patients comply with treatment guidelines and medical advice.[2] In the context of HIV, good adherence means that patients should take at least 95% of their antiretroviral medication per given period,[3] although other studies have shown lower levels to be adequate.[4] Barriers to good adherence can be categorized into:[1] patient characteristics, which include illiteracy, non-disclosure of HIV status, and alcohol abuse,[2] treatment characteristics, such as complex dosing schemes and adverse effects,[3] health system-related factors, including limited numbers of health care workers, inadequate supply of drugs and long distance to the health facilities and[4] an unsatisfying patient–doctor relationship resulting in poor treatment service.[5,6] Identifying strategies to overcome these barriers is critical to ensuring adherence to ART for optimal health outcomes.

How to best support PLHIV to adhere to ART is a recurrent and clinically important question. In 2020, there were 48 million mobile subscriptions recorded in Sub Saharan Africa, representing 80% of the total population.[7] This rapid increase in the use of mobile phones across sub-Saharan Africa over the past years have opened the door to the use of Digital adherence tools (DATs), which have formed the basis of many recent interventions. There are different types of DATs; some use Short Messaging Service (SMS) texts as reminders and others use Real Time Medication Monitoring (RTMM). RTMM makes use of a pillbox that records every opening of the box as a moment of presumed drug intake. It provides real-time medication management of a patient through mobile networks by direct signal-sending of medication events (opening of the pillbox) and real-time intervening by sending SMS reminder texts.[8] Both DATs have been studied in sub-Saharan Africa to assess their effectiveness at improving ART adherence, viral load suppression and clinic attendance.[9–13] In Uganda, trials that included RTMM technology linked to SMS reminders showed high acceptability and increased positive habits towards ART adherence.[14] A study conducted in South Africa found that being monitored in real-time, motivated 80% of participants to take their ART.[15] These studies suggest a promising shift in how to leverage technology to support adherence among PLHIV.

However, unfavourable results have been reported from digital health interventions. Studies in Kenya, Uganda, India, Tanzania and Botswana reported that some participants were concerned about unwanted HIV disclosure, others reported anticipated stigma arising from SMS content, which may mention the words medication and HIV.[10,16,17] A systematic review showed that unreliable internet connections and high purchase and maintenance costs of smart phones resulted in unsuccessful mHealth interventions in resource-limited settings.[18] Others have also reported logistical challenges; including the fact that family members often share mobile phones, the unreliable access to electricity, and issues of mobile phones breaking.[19–21] All the above-mentioned factors may limit the acceptability of DATs by both end-users and clinic staff. Given the inherent and published challenges reported in the implementation of DAT, further studies are required to explore and overcome barriers that could limit the acceptability of interventions in real-world settings.

Sekhon et al have developed a framework to guide the assessment of acceptability of innovative health interventions.[22] The Theoretical Framework of Acceptability (TFA) includes seven domains of acceptability of an intervention to be examined at three different stages. These are[1] pre-acceptability, prior an intervention's implementation,[2] concurrent acceptability, assessed during use of the intervention and[3] post-intervention after having used the intervention. We adapted the TFA to conduct a mixed-methods study among PLHIV on ART who had participated in a randomized controlled trial in Tanzania (called the REMIND-trial) to assess the post-intervention acceptability. The REMIND-trial aimed to investigate the effectiveness of RTMM and SMS on ART adherence compared to standard of care.[23] In this paper we report on the post intervention acceptability of DAT amongst trial participants.

Method

Study Design

This was a cross-sectional mixed-methods sub study nested within the REMIND trial (PACTR201712002844286; https://tinyurl.com/y98q4p3l,). The study was approved by

the Kilimanjaro Christian Medical College Research Ethics and Review Committee (CRERC) and the National Health Research Ethics Sub-Committee (NatHREC) of Tanzania. The study was conducted accordance with the Declaration of Helsinki.

REMIND-Trial

PLHIV from two specialized HIV care and treatment centers (CTC) in Moshi, Tanzania were included in this 48-week trial. The study was conducted between December 2017 and February 2020 in Moshi, Tanzania and has been reported in detail elsewhere.[23] In brief, eligible participants were adults 18–65 years of age who were on ART for at least six months, had no foreseen need to change treatment, were subjectively judged to be poorly adherent according to the study nurse, were willing to use an RTMM device and/or receive SMS, were able to read and reply to SMS, were able to come to the clinic every two months, owned an operational SIM card, lived in Kilimanjaro Region, and consented to be in the study. PLHIV were excluded if they were on co-medication for other (chronic) diseases such as tuberculosis (TB) or diabetes, were admitted to hospital, or were participating in a concurrent SMS reminder study.

Enrolled participants were randomized 1:1:1 to one of three study arms: RTMM arm, SMS arm, or a standard of care control arm. In the SMS arm, participants received SMS texts on three random days each week. One SMS text message to remind patients to take their medication was sent thirty minutes before the usual time of ART intake. Another SMS text message was sent with the question "Did you take your medication? One hour after the usual time of intake. The participant was asked to reply[1] Yes, I took it,[2] No, I did not take it, or[3] Not yet. The responses were displayed automatically on graphs for tailored feedback during consultation with a study nurse. Details about this feedback have been described elsewhere.[17]

Participants enrolled in the RTMM arm received a Wisepill device RT2000 (Wisepill Technologies®) which serves as a pillbox for ART.[24] If the device is not opened at the allocated time, which serves as proxy for no medication intake, the participant received an SMS text message with a reminder to take the medication. Adherence reports generated by the device (accessible only to authorised members of the study team) were used to tailor feedback during consultation with a study nurse. In a previous study, we have reported the flow of communication between the pillbox, central server, and the patient's phone.[25]

In both intervention arms, participants received tailored adherence counselling from the study staff as supported by the adherence reports generated from the interventions. Study nurses showed the reports to participants and discussed their adherence patterns using the stages of the model for behaviour change.[26] The contents of the tailored feedback have been described elsewhere.[17] PLHIV randomized to the standard of care arm did not receive device / SMS and were not included in this study on DAT acceptability.

Mixed-Method Study on Acceptability of RTMM and SMS

Study Procedures

Participants from both intervention arms who completed all 48 weeks of the trial were called or seen face-to-face for an exit-interview. In addition, we randomly selected ten participants from each intervention arm and invited them for an in-depth interview (IDI; n=20). This number was deemed adequate to reach data saturation.[27,28] Informed consent was obtained for all participants to take part in this acceptability study, and that this informed consent included consent to publish the participant's anonymized responses.

Data Collection

In these interviews we asked study participants to share their experience (successes, challenges and barriers) and behaviour regarding the interventions throughout the study. The interviews were conducted in Swahili in private settings based on participant 's preference and lasted approximately 45 to 60 minutes.

We used seven constructs of TFA to design the interviews to assess all seven domains (Figure A1: affective attitude, perceived effectiveness, ethicality, perceived burden, self-efficacy, intervention coherence and opportunity costs.

Exit Interviews

Exit interviews were conducted by trained research assistants (RA) as participants completed their routine clinic visits. Interviews were face to face, unless the participant preferred a phone interview. A semi-structured questionnaire was used, which was based on our previous pilot study,[29] and included issues emerging during the trial related to acceptability and adopting the TFA constructs.

Closed questions were first asked to capture the participant's general perceptions, followed by an open-ended question for each item to allow further explanation. The questions were read out loud by RA, together with the response options. Data were entered in real-time using RedCap, an open-source secure web application for building and managing online surveys and databases, which includes features for data quality assurance.

In-Depth Interviews

The in-depth interviews were conducted at an agreed upon time and space that was convenient for the participant. All interviews were conducted by the first author (KN) who is trained to conduct qualitative research including data collection and analyses. The interview guide was semi-structured and operationalized themes related to the seven mentioned constructs of acceptability in order to gain detailed insight than achieved in the more structured exit interviews. The discussion started with open-ended questions "please tell me what comes in your mind when you think back about the intervention". The participants could elaborate on the answers based on their knowledge and experience. The researcher asked follow-up questions and open probes to invite further explanation. All interviews were audio-recorded and transcribed verbatim by trained research assistants from Swahili into English. Notes and memos were also taken.

Analysis

The quantitative responses from exit-interviews were descriptively analysed using SPSSv.22 to give an overview of the frequency and percentages. Narrative explanations of the exit-interviews were listed to get better understanding of the underlying context of the quantitative answers. The qualitative responses were coded. During the process of coding, 20% of the transcripts were independently read by two authors (MSB and KN) and a list of subthemes was created based on those interviews. The interviews were discussed and agreement was achieved about the most common subthemes. A coding framework was developed based on the subthemes. Translated transcripts, memos and field notes from the IDIs were imported to NVivo software version 12 for organizing the data and coding. Narratives were then coded based on the subthemes of the coding framework. We conducted thematic framework analysis of the coded data from the transcripts. A report of coded data based on subthemes was generated and exported into Word from NVivo. The two lead authors reviewed the report and discussed and interpreted the data in regular meetings to ensure the coded data corresponded to the framework.

Results

Participant Characteristics

Of the 166 participants enrolled in the two intervention arms, 150 (90%) completed the last study visit in the 48th week. Of those, 143 were interviewed (68 participants in the SMS arm and 75 in the RTMM arm; Table A1. The median age was 43 years. Two-third of participants were female. Twenty-three participants were lost to follow up after the final study visit and could not be interviewed. Results of the exit-interview are shown in Table A2, with numbers of participants reporting the answers, including their narrative explanations.

Of the 20 participants invited for an in-depth interview, 19 (95%) participated. The twentieth participant could not be reached due to nationally imposed restrictions on research as a result of the COVID-19 pandemic. Characteristics of these 19 interviewees are shown in Table A3. There is considerable variability in demographic characteristics and adherence rates, making this a heterogeneous group of participants. The themes and Quotes are shown in Table A4.

Acceptability of the Intervention

We Present the Results According to the Seven Constructs of the TFA

Affective Attitude

In the Exit interviews, 97% of RTMM and 98% of SMS participants indicated that their general experience with the devices was either good or very good. Ninety five percent reported that the way graphs displayed their adherence level was either good or very good. In addition, 98% indicated they were happy with the interventions.

Similar results were found in the in-depth interviews in which participants indicated to feel happy with the intervention, particularly concerning the reminders to take the medication. Nearly all the IDI participants were satisfied with the graphs showing their adherence status. Participants were happy to see the adherence percentages of opening the devices as well as the number of SMS that they had replied to. Those whose graphs showed a low adherence, indicated they were pleased to discuss their findings with the nurses and to explore how best they could improve their adherence in the coming clinic visits. When they were asked how they felt after completing their

last 48-week study-visit, the majority indicated to be disappointed that the study was over.

Additionally, respondents elaborated that they will miss the extensive counselling and support received from study nurses during the clinic visits. At the end of the trial, patients preferred not to return the device nor to stop receiving SMS despite being informed that this was part of the study protocol at the beginning of the study. The size and appearance of the device were positively valued. Participants said it was easy to carry, and to keep in their pocket and it was not easily identifiable as a pill box containing ART.

> For me to be enrolled in the project, it was something that made me feel very happy and I would say it was a good opportunity for me … especially when I was given the device which helped me to store my medications, which I could open at any place and take my medications without any stress. 35-year-old female participant

> What I would request is for the project to put … or continue with the system of reminding people, even after the project has ended, messages could remain on the phone so that people could still be reminded. 39-year-old male participant

> I wished they [read SMS] were coming every day because they motivated me to remember taking medications. 40-year-old female participant

"I was keeping the device in my pocket, and sometimes I could hold it in my hands and nobody could ask me because it almost resembles my phone handset" … "I found the device was very useful to me because I could be taking it anywhere I went. It was easy to store my medicines in there, more than keeping into a container whereby when you open it, you draw everybody's attention.

If I travel, I put it into my bag also. I used to store it in a can container, but if I travel that container makes noises, so different from device. I do refill my medicines in the device nobody knows what I am carrying." 54-year-old-male participant

Perceived Effectiveness

Several participants agreed that the interventions had increased their motivation to take their medication every day. In the exit interviews, 142 (99%) mentioned the intervention improved their adherence to treatment, 90% appreciated the SMS content and 80% reported they wished to receive the more than one messages every day.

IDI participants suggested that before the intervention, they had difficulties adhering to treatment especially in front of people. Many appreciated the SMS content "don't forget medication". Participants whose clinic files indicated a high viral load prior to the study, felt the study had assisted to reduce their viral load, with some mentioning how it fit within their regular lifestyle.

> I was given the device, it was very helpful which gave me a motivation to remember that I had not taken my medication. 50-year-old female

> Before, it was very difficult for me to take my medications in the place with many people, but with the device, I could just open it, take my medications without anybody noticing what I have just done. 45-year old female

> The messages rescued me as I have already opened a red card by nurses at the clinic [meaning having bad treatment outcomes], but after the project, I was removed from the red card and opened another file. 45-old-female

Perceived Burden

In the exit interviews, a number of patients reported to have difficulties using the intervention; nine (6%) responded it was not appropriate to receive the SMS, 23% responded to experience related HIV stigma, 2% reported the device was difficult to use, 5% considered it was a burden to keep the device at home, and 22% mentioned the SMS did not arrive on time.

IDI participants reported facing difficulties in having the device or replying to the SMS during the intervention period. They reported to be concerned with several aspects of the intervention. One participant found the feedback session during clinic visits too long (average of one hour per session). Another participant felt that there were too many SMS coming per week and preferred to be sent less often or weekly. One participant preferred the SMS reminders to be sent without any questions that required a response. Some participants were worried about losing the device or having it stolen and one respondent felt the device was too big to fit in his trouser pocket.

> The interview with nurses at the clinic was too long until I get tired. May be the interview should be made shorter in future studies. Also, that nurse's tablet was somehow giving trouble to operate. 45-year old female

> Yes, it is big, and if I travelled, I used to put it into my bag because to put it in my pockets, its size is bigger than the

> touch phone. So, to carry this device in my pockets plus the phone, really looks a big load in my trouser pockets. That is why many times I carried it in my bag. 33-year old female

Some participants also raised the issue of stigma; stigma which was primarily based on their own HIV status rather than taking part in the interventions. However, a few participants did raise the concern that taking part in the intervention may have increased the risk of their HIV status being inadvertently disclosed owing to the appearance of the device or because they may receive an SMS with the word "medication" included in the text.

> I try to hide it, my mother forced me to give it [the phone] to her to read, saying she must see the message, I told her it is the message regarding the medications, then she was asking me what kind of medications ….if the word medicine could be removed it should be replaced with another word. Let's say the message could be saying DO YOU REMEMBER? And I could reply saying 'yes I remember'. 23-year old female

One client mentioned that the sound of the message alerting them to the reminder SMS during working hours was becoming a concern to his colleagues,

> They did not see the SMS but were hearing the message delivery tone which came at 08.30 and 09.00 am and then asked me why so often messages every day on the same time. I told them they were the lottery messages, then they never asked me again. 38-year old male

Ethicality

During the exit interviews, participants In both intervention arms, indicated that the intervention was consistent with their values and preserved their privacy, particularly regarding disclosure of their HIV status. However, the living arrangements of a few participants increased their risk of someone seeing the SMS content. This was reflected in the exit interviews where 8% reported that the content of the message was "not good" or "not good at all" and recommended the word "medication" should be removed from the reminder SMS "don't forget to take medication".

During the in-depth interview, patients did not report ethical issues; those who lived with family members, mentioned that they could comfortably accommodate the intervention within their life. Some reported that family members who had seen the devices, provided moral support for medication adherence. Furthermore, respondents who shared phones with their spouses mentioned that the intervention did not bring any domestic dispute when receiving the reminder SMS, but rather, motivated them to take their medication. No participants raised any ethical issues related to religion, tribe or culture.

> My children know about my situation and were happy that I got that device to help me because they knew it would help me to not forget when it was time for me to take my medication or to lose any tablets. That is what made them very happy about the device. 45-year old female

> For my daughter to be aware of my situation, receiving the SMS was a great opportunity for me and helped me to not feel having HIV was my punishment for misbehaving. So, my daughter knows well that if I will leave the study I die. 38-year old male

> I share my phone with my husband, so when the message comes in, he just tells me the KCMC doctors have asked you to take your medications. 47 years old female

Self-Efficacy

In the exit interviews, participants did not mention being unable to use the intervention. Participants described a certain level of determination to overcome any obstacles that would interfere with their engagement with the intervention. Participants also described how the interventions influenced them to set better health goals for themselves. Therefore, no subtheme emerged that was related to self-efficacy. However, the in-depth interview participants described how the intervention influenced their behaviour and promoted positive changes to ensure they adhere well with treatment.

> Before the project I was drinking alcohol extensively. So, when I came home at night it was difficult for me to take medications at that time while my wife adhered to the medications. I had to pretend in front of her I took medication while I did not. Now since I know I am being monitored, I have stopped drinking alcohol and decided to stick on my medications as usual. 45-year-old of male

Intervention Coherence

The majority of participants claimed to understand how the interventions worked. In the exit interviews 91% of respondents indicated that they were able to reply to the SMS, 85% mentioned they had no difficulty charging the

device, 97% indicated it was easy to refill medication, and 95% reported to understand how the graph works.

The in-depth interviews participants were able to explain how the device worked and were familiar with how the device communicated about their adherence, how the SMS reminders were being sent, how the report shows adherence data on the tablets and how to open and refill the device.

> When the message comes 'Did you take your medications on time,' I knew it was the time for my medications. Sometimes it was written 'Do you take your medication as per the doctor's prescription?' After that I knew it was almost my time for medication, so even though I was busy, I prepared myself for taking my medication. 54-year old male

For many, this intervention was the first exposure to the use of digital tools in the generation of real-time reports, however this was well understood and appreciated.

> When she was asking me about my health status and the improvement of my medication intakes, she opened her big telephone and read the progress of how I replied the messages. She showed me the messages that I did not reply to and those I had replied to. 45-year old female

Opportunity Costs

Very few participants mentioned that they had to incur personal costs in order to take part in the study. Out of all those who participated in the exit interviews; 91% reported to have incurred no additional costs for the sake of the study. However, one participant in the in-depth interviews described how she gave up her house in the village and had to move closer to town in order for the device to work. Another reported having to pay to charge the device so that she did not miss any messages or prevent reports being sent.

> The reason I moved from the village to town was because my device was not communicating and the report was showing I was not opening the device even though I had. 42-year old female

> I stayed with the device for six months before it lost charge, and because at home we did not have electricity, I had to take it to a young man who was educated, I told him not to open it but just to charge it and he charged me 1USD. 45-year-old female

Discussion

This mixed-methods study describes the findings of a post-intervention evaluation conducted to measure the acceptability of RTMM and SMS interventions aimed to improve adherence to ART among PLHIV. We found a high level of intervention satisfaction, with 98% of participants expressing that they would like to continue using the interventions. Moreover, 99.5% of participants who received the RTMM intervention found that it was easy to manage, including opening of the device, refilling the pills, and recharging the box. This finding was comparable to that in the SMS arm, where only 6% of participants reported to have experienced difficulties in responding to the SMS-reminders. Both of these DATs were found to be acceptable among PLHIV in this ART adherence trial in Tanzania.

Our study supports several other studies in finding that patients are happy and satisfied with DAT-based interventions.[30,31] In our study some participants mentioned various psychological barriers that could have impacted on uptake and satisfaction, including: stigma and worry of exposure [17]. A study in Kenya reported that high levels of satisfaction with the digital health intervention was associated with high levels of social support and quality of life [19]. Similar findings were noted in another study in which those who disclosed their HIV status appeared to find the SMS interventions worthwhile as they felt to be cared for and supported by others [28].

Our study was embedded within a larger trial to assess the effectiveness of DATs to improve adherence. Despite other studies finding RTMM and SMS being effective in improving adherence, we were not able to show such an effect.[23] The interventions were only effective in participants who had a viral load <1000 copies/mL at study entry. So, despite the interventions being acceptable, they did not lead to the desired effect. Our mixed method study findings suggest that the intervention could be improved by overcoming certain barriers. For example, it was suggested by some of the participants to tailor interventions, taking user preferences into account, including personalized SMS contents (eg, not to use the word take "medication"), receiving SMS more frequently for some participants (eg, everyday SMS reminder) or less often for others (eg, weekly SMS). Using tailored interventions with personalized SMS was also reported to be preferred by participants of studies conducted in Kenya and Uganda[14,32] and may be considered in future research.

There are several limitations of our study. First, we could not conduct a pre-intervention evaluation to assess previous experiences and expectations. Studies have recommended that a pre-evaluation may examine the appropriateness of the intervention and suitability before being implemented.[33] Second, the implementation of the intervention by the study nurses may have been suboptimal, hampering the acceptability of the intervention. During conversations with the study nurses, we found they had struggled with the intervention due to high workloads, high social desirability rates despite extensive training and participants not showing up for clinic visits. Unfortunately, we do not have details about the exact conduct of the intervention by study nurses. Studies have shown that better understanding of implementation of the interventions by health care staff would result in more positive patient experiences.[34–36] Observations during instruction of the interventions and during feedback sessions could have given better insight on whether the interventions were conducted by study nurses as intended,[33] and thus more acceptable to participants. Finally, we were not able to interview those participants who were lost-to-follow-up during the study. Those participants may report more negative ideas and opinions on the acceptability such as experienced stigma, less perceived effectiveness, and limited ethicality. Fortunately, the number of lost-to-follow-up was low with 13.9%.

The major strength of the study is the mixed-method design which provided both a quantification of acceptability and more detailed information about the different aspects of acceptability. With that information, we will be able to design future studies investigating the implementation and effectiveness of tailored SMS, using a pragmatic cluster trial. Another strength is the application of the TFA framework which offered comprehensive insight in the study participants' perceptions of acceptability that can be considered for future research.

Conclusion

This mixed-methods study provided insights into participants' experiences in relation to the acceptability of the DAT interventions used in a trial aimed to improve ART medication adherence. In our exploration of each of the constructs of the TFA, we found that the interventions were generally acceptable as patients felt highly motivated to adhere to ART medication and were satisfied with the intervention. However, patients also reported challenges with respect to the content and number of SMS, carrying of the devices and network availability. Future studies on DATs and their implementation should address these barriers.

Data Sharing Statement

Data are available and we intend to share after signing the Data Transfer Agreement. This is according to our National Health Research Ethic Regulatory Board. Contact person is Dr. Marion Sumari-de Boer, email: m.sumari@kcri.ac.tz.

Acknowledgment

We thank the participants for their involvement in our study and for allowing us to study potentially sensitive data. Furthermore, we thank the administration of the Kilimanjaro Christian Medical Centre and Majengo Dispensary for allowing us to conduct this study in the hospital and the nurse counselors for recruiting the participants. Also, we thank Janet Prvu Bettger, ScD, FAHA is an Associate Professor - health services researcher at Duke University and Jenny Renju Lecturer at London School of Hygiene & Tropical Medicine for providing technical expertise for writing scientific qualitative manuscript. Last, we thank the European and Developing Countries Clinical Trials Partnership (EDCTP) for the financial support to conduct the study.

Disclosure

Prof. Dr. Peter Reiss report grants from Gilead Sciences, ViiV Healthcare, Merck & Co, Scientific Advisory Board participation, honorarium paid to institution from Gilead Sciences, ViiV Healthcare, Merck & Co, and Teva Pharmaceutical Industries, outside the submitted work. The authors report no other conflicts of interest in this work.

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