

RESEARCH ARTICLE

Assessing acceptability of pre-exposure prophylaxis (PrEP) among participants in an HIV vaccine preparedness study in southwestern Uganda

Sarah Nakamanya^{1*}, Rachel Kawuma¹, Denis Kibuuka¹, Sylvia Kusemererwa¹, Sheena McCormack², Eugene Ruzagira^{1,3}, Janet Seeley^{1,3}, on behalf of the PrEPVacc Study Group¹

1 Medical Research Council/Uganda Virus Research Institute (MRC/UVRI) and London School of Hygiene and Tropical Medicine (LSHTM) Uganda Research Unit, Entebbe, Uganda, **2** MRC Clinical Trials Unit at UCL, London, United Kingdom, **3** London School of Hygiene and Tropical Medicine, London, United Kingdom

¶ The PrEPVacc Study Group list can be found in Acknowledgments.

* Sarah.Nakamanya@mrcuganda.org



OPEN ACCESS

Citation: Nakamanya S, Kawuma R, Kibuuka D, Kusemererwa S, McCormack S, Ruzagira E, et al. (2022) Assessing acceptability of pre-exposure prophylaxis (PrEP) among participants in an HIV vaccine preparedness study in southwestern Uganda. *PLoS ONE* 17(7): e0271104. <https://doi.org/10.1371/journal.pone.0271104>

Editor: Hamid Sharifi, HIV/STI Surveillance Research Center and WHO Collaborating Center for HIV Surveillance, Institute for Future Studies in Health, Kerman University of Medical Sciences, ISLAMIC REPUBLIC OF IRAN

Received: February 4, 2022

Accepted: June 24, 2022

Published: July 29, 2022

Copyright: © 2022 Nakamanya et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its [Supporting Information](#) files.

Funding: The PrEPVacc trial is funded by the Second European & Developing Countries Clinical Trials Partnership (EDCTP2); (Grant reference: RIA2016 - 1644) in collaboration with support

Abstract

Background

Daily oral pre-exposure prophylaxis (PrEP) use is highly effective against HIV infection. However, the uptake of PrEP among individuals at high-risk of HIV acquisition in sub-Saharan Africa varies because of availability and acceptability. We assessed the acceptability of PrEP among participants in a prospective HIV vaccine preparedness study in Masaka, southwestern Uganda.

Methods

From November 2018 to August 2019, 20 participants (10 female) were purposively selected for in-depth interviews (IDIs) at 3 and 9 months' post-enrolment in the vaccine preparedness study. Four focus group discussions (FGD) (two among men) were conducted with 29 individuals categorized as: younger (18–24 years) men, younger (18–24 years) women, older (≥ 30 years) men, and older (≥ 30 years) women. Apart from IDI specific questions on recent life history including work experience, relationship history and places lived, topics for IDIs and FGDs included knowledge of HIV, perceptions of HIV risk (including own risk), knowledge of and use of PrEP. The Theoretical Framework of Acceptability was used to structure a thematic framework approach for data analysis.

Results

Participants understood that PrEP was an oral pill taken daily by HIV negative individuals to prevent acquisition of HIV. Overall, interest in and acceptability of PrEP was high, more than half expressed positivity towards PrEP but were not ready to initiate taking it citing the burden of daily oral pill taking, related side effects, stigma and distrust of PrEP. Fourteen

from industry partners and sponsored by Imperial College London, UK. Sheena McCormack was supported by Medical Research Council (Grant MC_UU_00004/03). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. This study is also made possible by the support of the American People through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through United States Agency for International Development (USAID). The contents of this publication are the sole responsibility of the PrEPVacc Team and do not necessarily reflect the views of PEPFAR, USAID, or the United States Government.

Competing interests: The authors have declared that no competing interests exist.

participants (from IDI and FGD) initiated PrEP, although some (one FGD and two IDI participants) stopped taking it due to side effects or perceived reduced risk.

Conclusion

We observed a keen interest in PrEP initiation among our study participants. However, a limited understanding of PrEP and associated concerns impeded uptake and sustained use. Hence, interventions are needed to address end-user challenges to increase uptake and support adherence.

Introduction

The HIV-epidemic continues to be a major global public health problem with around 1.5 million new infections in 2020, of which over two-thirds were in sub-Saharan Africa (SSA) [1]. Almost one-half of new global HIV infections occur among key populations, such as men who have sex with men (MSM), people who inject drugs, sex workers, transgender people and their sexual partners, migrants, truck drivers, fisher-folk, adolescent girls and young women, prisoners, plantation workers, miners, 'boda-boda' (motorcycle taxi) riders and uniformed services personnel [2, 3]. In SSA, 39% of new HIV infections in 2020 were among key populations [1]. Data reported to UNAIDS in 2019 on uptake of combination HIV prevention services revealed that among key populations, less than 10% had access to multiple prevention services in parts of Africa, including Uganda [4].

Oral HIV pre-exposure prophylaxis (PrEP), the use of antiretroviral drugs (ARVs) by HIV-negative people to reduce the risk of HIV acquisition, is a highly effective HIV prevention tool and has the potential to substantially reduce HIV incidence among members of key populations [5]. PrEP is recommended by WHO and implemented in an increasing number of countries in SSA [6, 7]. Although willingness to use PrEP appears to be high among certain populations in SSA, uptake rates are low [8, 9].

The acceptability and interest in an intervention such as PrEP is key to its success as individuals are more likely to take it up and/or adhere to it if they consider it acceptable and beneficial to them [10, 11]. Factors that influence individuals' acceptability of an intervention have been shown to include its appropriateness in addressing the problem, and suitability for an individual's lifestyle, convenience, social acceptability and effectiveness [12]. These factors could also determine adherence to that intervention.

In the current study, we assessed the acceptability of PrEP among participants in a prospective HIV vaccine preparedness study in Masaka, southwestern Uganda. All participants received information and counselling about risk reduction strategies and services, including PrEP, and referral to services if desired.

Theoretical framework

We adopted the Theoretical Framework of Acceptability (TFA) [13] to assess PrEP acceptability. Data were analysed in relation to the seven components of the TFA. For example, we looked at individual's feelings about taking up PrEP (affective attitude), their perceived/experienced amount of effort required to take PrEP (burden), the extent to which PrEP suited their lifestyles (ethicality), extent to which participants understood PrEP and how it works (intervention coherence), the extent to which benefits/profits/values were/must be given up to take

PrEP (opportunity costs), the extent to which PrEP was perceived as likely to achieve its purpose (perceived effectiveness) and participants' confidence to take and persist in the taking of PrEP (self-efficacy).

Materials and methods

Study design and setting

This was a qualitative methods study nested in an HIV vaccine preparedness study in Masaka district, southwestern Uganda. Between July 2018 and November 2019, 200 HIV negative men and women (18–45 years) determined to be at high risk of HIV acquisition were enrolled into the HIV vaccine preparedness study. Volunteers were recruited from places with known key populations and high HIV burden including trading towns along the trans-African highway [14–16] and fishing communities on the shores of Lake Victoria [17–21]. HIV risk was measured using an interviewer-administered risk assessment questionnaire. Individuals were considered to be at risk if they reported suspected/confirmed sexually transmitted infection (STI) or unprotected sex with two or more partners or unprotected sex with a new partner in the past three months or unprotected sex in exchange for money/goods in the past month. Participants were followed up every 3 months. At all visits, study participants were given information on oral PrEP including its benefits and possible side effects. A written referral to a PrEP provider was given to individuals who were willing to start PrEP and adherence counselling to those that initiated it.

Study participants, sampling, and data collection

Ten percent [20] of the HIV vaccine preparedness study participants were purposively selected to participate in in-depth interviews (IDIs). Those selected included people of different ages, sex, occupational backgrounds, and residence. Willingness to take-up PrEP was not an inclusion criterion. Interviews were conducted using a topic guide at three and nine months after enrolment. Topics covered included individuals' recent life history including work experience, relationship history and places lived, perceptions of HIV risk (including own risk), knowledge of and use of PrEP. The first interview was intended to establish rapport, to engage in a more personal and potentially sensitive conversation and to capture initial information. In addition to strengthening trust, the second (follow-up) interview filled gaps from the first interview as well as capturing new developments in the participant's life including changes in work, relationships, residence, and HIV risk perceptions. It also sought more detail on issues around PrEP including any new information, such as change in attitudes, desire to take PrEP, and reasons for not taking up PrEP.

In addition, four focus group discussions (FGDs) were conducted among 29 participants who did not participate in the IDIs. The groups were defined as follows: younger (18–24 years) men, younger (18–24 years) women, older (30+ years) men and older (30+ years) women. Information on PrEP uptake was not considered in selecting individuals for FGDs. Each group comprised six to 10 participants. Issues discussed in each FGD included HIV risk, knowledge and uptake of PrEP, and reasons for non-uptake.

All IDIs and FGDs were conducted in locations that were convenient and safe for the participants and the researchers, and that ensured privacy. No audio recorders were used as these often obstruct discussion especially on sensitive topics [22]. A male and female interviewer conducted interviews, matched by sex with participants, and took short notes during each interview, which they expanded within 24 hours after the interview. Debriefing meetings with the interviewers and the lead social scientist were held after each interview to ensure completeness of the data. Any gaps identified were filled during subsequent interviews. All interviews

were conducted in Luganda, the local language in the study area. On average, IDIs lasted for about one hour while FGDs lasted between one and a half to two hours.

Data management and analysis

The research team conducted preliminary analysis of data collected in real time as scripts were prepared grouping information in topics and informed subsequent interviews [22]. Anonymized scripts from expanded notes were saved on password-protected computers. Data analysis was conducted by the interviewers, with support from another social scientist, and used a thematic framework approach guided by the TFA. Interview scripts were initially read independently by the two interviewers, to identify recurring significant themes relevant to the constructs of the TFA. We identified five themes that correlated with the constructs of the TFA, with some of the themes cutting across the constructs. The themes included: knowledge (or lack of) about PrEP for **intervention coherence**, attitudes to PrEP for **Affective attitude**, **Opportunity cost** and **Perceived effectiveness**, barriers for **Burden**, motivation to take PrEP for **Ethicality**, and persistence on PrEP for **Self efficacy**.

The identified themes were shared and discussed with the supporting social scientist and based on the seven components of the TFA, a coding framework was developed. Codes with similar or close meanings were grouped together to generate broader themes. Data were charted on a matrix under relevant/matching themes to provide an overview and enable quick and easy navigation.

Ethical considerations

Ethical approval was obtained from the Uganda Virus Research Institute Research Ethics Committee (UVRI REC # GC/127/18/03/637) and from the Uganda National Council for Science and Technology (UNCST # HS 2392). Written informed consent to participate in all study procedures, including IDIs and FGDs was obtained at enrolment into the HIV vaccine preparedness study. Before each IDI and FGD, study staff verbally checked to confirm that participants were still interested in participating in this component of the study. Participants' privacy and confidentiality were ensured at all stages of the study by conducting interviews in a safe and private place plus anonymizing and securely storing all collected data.

Results

Demographic characteristics of study participants

Half (10) of the IDI participants were women. The average age of the participants was 26 years and 29 years for men and women respectively. Six of the 10 men were married/cohabiting or in a relationship, compared to four out of the 10 women. Most participants had only primary school education (10) or no education (5). Half (5) of the men were involved in fishing while seven women either earned solely (3 women) or supplemented (4 women) their incomes with sex work. Among the FGD participants, 15 (52 percent) were men. Eleven (8 men and 6 women) participants were aged 18–24 years while the rest (7 men and 8 women) were ≥ 30 years (see [Table 1](#)).

Intervention coherence

In the TFA, this construct is defined as the extent to which participants understand the intervention and how it works. Participants described their 'knowledge about PrEP' including: meaning and uses of PrEP, who should take PrEP and PrEP dosing. Nevertheless, participants also had misconceptions regarding the use of PrEP.

Table 1. Characteristics of study participants.

Characteristic	IDI			FGD				
	Men	Women	All	Men (18–24 years)	Men (≥30 years)	Women (18–24 years)	Women (≥30 years)	All
All	10	10	20	8	7	6	8	29
Mean age (years)	26	29	27.5	23	36	23	34	23 (18–24 years) 35 (≥30 years)
Education								
Primary	5	5	10	6	4	2	4	16
Secondary	3	2	5	2	1	3	3	9
No formal education	2	3	5	0	2	1	1	4
Marital Status								
Married	5	2	7	4	5	2	2	13
Single	4	3	7	1	2	2	4	9
Separated	0	3	3	1	0	0	1	2
In a relationship	1	2	3	2	0	2	1	5
Occupation								
Sex worker	0	3	3	0	0	0	2	2
Shopkeeper	0	2	2	0	0	0	0	0
Launderer	0	1	1	0	0	0	0	0
Food vendor	0	1	1	0	0	1	0	1
Fishing-related work	5	0	5	0	3	3	0	6
Mason	2	0	2	1	0	0	0	1
Mechanic	1	0	1	2	0	0	0	2
Electrician	1	0	1	0	0	0	0	0
Farmer	1	0	1	0	3	0	2	5
Salon/Bar/lodge worker	0	1	1	0	0	1	3	4
Motorcycle taxi rider	0	0	0	2	0	0	0	2
Disc jockey	0	0	0	1	0	0	0	1
Other	0	0	0	1	1	0	0	2
None	0	2	2	1	0	1	1	3

<https://doi.org/10.1371/journal.pone.0271104.t001>

At three months of participation in the cohort study, participants had some information regarding PrEP, although it was limited. Most participants knew that PrEP was a pill (in the same form as ARVs), taken daily by HIV uninfected individuals to prevent acquisition of HIV.

“We were taught that PrEP prevents one from contracting HIV if taken like ARVs, that is, taken every day until one feels that he/she is no longer at risk of contracting HIV” (man, 31 years).

Participants also knew that PrEP was meant for individuals with elevated risk of HIV such as those in HIV discordant relationships or with multiple sexual partners or that engage sex work, and that one could stop PrEP if they felt that their HIV risk was low. Indeed, a young man narrated how he stopped PrEP after his risk reduced:

“. . . It happened that I was in a school holiday and had nowhere to access condoms yet I could land into temptations (of having sex). When school resumed, the risk ended so I stopped PrEP” (FGD, younger men).

Others explained how PrEP worked:

“It (PrEP) is one of the HIV prevention measures. It could be used if you feel at risk of HIV or if you regularly get exposed to HIV; you can take PrEP to prevent you from catching HIV” (FGD, younger men).

Participants however lacked full information regarding its effectiveness, proper dosage or where it could be accessed. Indeed, given that PrEP was still new to many, some had misconceptions that it was still undergoing clinical trials and could harm them. Others doubted whether it could really prevent one from acquiring HIV, *“I have tried to tell different people about PrEP but they strongly disagree that any drug can prevent HIV”* (man 24 years). While some, despite the fact that they had initiated taking it, did not believe in it either: *“I am just swallowing but I am not sure if it works, that is why I use other protective measures like condoms”* (woman, 30 years). Some individuals who were planning to initiate taking PrEP were also not convinced that it worked as expressed below:

“I cannot rely on the fact that I am swallowing PrEP, I will continue with using condoms. I sleep with many different people (men) and I see the kind of fluids that they release; I cannot risk” (woman, 30 years).

Information regarding PrEP was discussed with friends or family after learning about it at the research centre. However, in some cases, they would get negative or conflicting feedback, and this would distort their understanding of PrEP and thus discourage them from initiating or persisting in taking it. A woman who stopped using PrEP after experiencing side effects observed:

“My friends advised me to drop the drug (PrEP) after taking for 15 days. They (friends) asked, ‘what will you do when you catch HIV?’ Implying that I was taking ARVs when I was HIV negative yet it was meant for the HIV-infected and [it was not yet the] time for that” (woman, 37 years).

Affective attitude

This TFA construct describes how an individual feels about the intervention. In relation to the construct, we captured participants’ ‘attitudes to PrEP’, which included both perceived benefits and experiences of PrEP as well as their concerns.

Half of the participants acknowledged that PrEP was good especially for those in discordant or multiple sexual relationships. As one 23 year old man observed, this would allow the person on PrEP: *“to remain with the positive partner for the sake of raising the children together”*. Some who were practicing sex work were aware that PrEP would benefit them as expressed below:

“Since I am exposed to many ways (partners) of contracting HIV, I was attracted because (PrEP) could protect me from contracting it (HIV). For instance, if my sexual client is infected and I am not, I could remain protected from getting it” (woman, 30 years)

The theme ‘attitudes to PrEP’ cut across different constructs of the TFA, including **perceived effectiveness**, which examines the extent to which an intervention is perceived as likely to achieve its purpose. A sub theme on usefulness of PrEP was identified related to this construct.

“Some of us have like three women and you do not use condoms with them because you know they are your women. In case one of these women is cheating on you with another man, you

are safe if you are using PrEP. Others are 'safari' (long distance) drivers and may travel away from home and wives, they may have sex with casual partners during their travel and in this case if you are taking PrEP, you have protection" (FGD-men)

At the follow-up interview, over half of the interview participants (seven women and six men) expressed a desire to take PrEP, and four had initiated it, although one had discontinued:

"... They gave me a bottle of pills (PrEP) for one month, but I swallowed for only two weeks and stopped due to side effects. I was experiencing dizziness, headache, general body weakness, hunger (increased appetite) and vomiting. I had thought it was just one pill to take me for three months and did not know that I was to take it daily. It causes a lot of thirst and if you do not take lots of fluids (drinks), you are in trouble... I can never swallow it again. The truth is, if you do not have money, you should not swallow that drug (PrEP)" (woman, 22 years).

However, while many felt PrEP would serve a good purpose in preventing HIV, participants had some concerns such as accessing PrEP from the same facilities as those which provide HIV treatment: *"I feel I cannot go to the other place (PrEP/ART facility), I do not like the place"* (woman, 36 years) and also the reaction of persons that are close to them if they found out that they were taking PrEP as illustrated here:

"A friend of mine who is HIV positive told me it (PrEP) was like the drugs she was getting. I even felt ashamed because I had told her that the health care providers had tested me for HIV, and they gave me a negative test result. But then here I was, taking similar drugs. It would appear like I was bragging that I was HIV negative, yet the friend is HIV-infected and this claiming that I was HIV negative would make her feel bad". (woman, 35 years).

With these mixed feelings of liking the idea of PrEP and also fearing for PrEP, many decided to wait or postpone initiating it as they observed what happened to those who were taking it. Others just felt it did not make sense to take drugs when one is healthy as expressed by a 30-year-old woman responding to questions about her non-uptake of PrEP:

"People fear it (PrEP). For example, a friend of mine feared to take it and said she could not start drugs before she gets infected. 'What if it causes me problems?' This friend asked".

Burden

According to the TFA, burden is the perceived amount of effort required to participate in the intervention. We identified barriers to uptake of/and persistence on PrEP as themes under this construct.

The barriers were both perceived and experienced, which included both monetary and non-monetary costs. These ranged from the long distances to PrEP facilities, burden of daily pill taking, drug side effects, and also fear of stigma. For instance, the long distances to PrEP facilities resulting in high transport costs were an impediment to uptake or adherence to and persistence on PrEP in the case of some who failed to go for re-fills. One participant described how she had to share PrEP with a friend because she could not afford transport to go and pick up her own.

"Personally, I did not have money to go to xxxx where they had referred me, so I first shared PrEP with a friend who had it in plenty. She gave me pills for like three months and after

taking it and it worked for me (gave me good health) because I even stopped getting infections like flu or cough, I decided to go and get my own drugs” (FGD-women).

Besides the general dislike for pills, the perceived burden of taking a daily pill with the similar packaging to ARVs, caused individuals to shy away from PrEP for fear of being labelled as HIV-infected.

“If PrEP could be packed like this (pulls out a pill sachet), people would not suspect it to be HIV drugs and they would carry it comfortably. Unlike as it is now whereby they are in these plastic containers and make a lot of noise as you move. If it were sealed in a sachet, I would not have had any problem carrying it or pulling it out and swallow the drug in the presence of other people as that packaging looks like any normal drugs” (woman, 23 years).

Some participants reported discontinuing PrEP due to side effects like nausea, headaches, hallucinations, dizziness and general body weakness among other side effects, for others it was the fear of these expected problems which barred them from initiating PrEP.

“. . . people may not take PrEP thinking that it might have many side effects. For example, causing headache and general body weakness given the nature of our work (fishing), which needs much energy. Weakening the body and making it prone to diseases like HIV” (man, 31 years)

Ethicality

This TFA construct is about the extent to which the intervention fits well with an individual's value system. We identified the theme of Motivation to take PrEP as being related to this construct, whereby perceived HIV risk motivated participants to take a positive step to protect their health by taking PrEP.

Many participants, especially the younger ones, felt that PrEP was the ideal HIV prevention choice for them, given that almost all of them did not like or rarely used condoms. Even the women, especially those involved in sex work acknowledged their HIV-risk and felt PrEP would greatly help them as their sexual clients sometimes forced them into unprotected sex, intentionally broke condoms or even offered and paid higher prices for unprotected sex. Even the non sex workers did not trust their regular partners and felt PrEP would give them protection in case the partners contracted HIV from elsewhere.

“I am still at the sexually active age, so, that method (PrEP) will be very beneficial to me. A man may refuse to use a condom or may use it but then remove it during the process and for that, I cannot rely on condoms alone” (woman, 40 years).

Opportunity cost

Defined in the TFA as the extent to which benefits, profits or values must be given up in order to engage in an intervention we found this was linked to the cross cutting theme of attitudes to PrEP. Our analysis revealed participants' concerns around unintended disclosure that came with taking PrEP.

Some participants felt that taking PrEP meant losing one's privacy, trust and also respectability. They noted that it was hard to take PrEP without others noticing and as much as one may hide, others would eventually get to know. This woman (30 years) said, sadly, that:

“I disclosed to my sister about my taking PrEP after she saw me taking the pills, but the sister instead told our mother that I am HIV positive and on treatment. My sister’s child also supplemented that she saw me taking the pills from the toilet, which was not true”.

Men expressed similar fears, a 24 year old man said:

“Some other people fear to be known that they are taking PrEP by their friends and relatives/ family because they will judge them and sometimes suspect them to have HIV”.

Participants felt that such disclosure of PrEP use, whether intentional or not could be misinterpreted and expose one’s infidelity or promiscuity and could result in suspicion, distrust or loss of partner, as well as domestic violence in some extreme cases. Indeed, in the FGDs conducted with men, they preferred not to disclose their use of PrEP to their more stable partners because they felt it would jeopardize those relationships

“No, it would be better if my wife did not know about my taking PrEP because she will think I am womanising since we always test negative together” (FGD-men).

Self-efficacy

Defined using the TFA as participants’ confidence to take and adhere to PrEP. The construct was linked to the theme on persistence on PrEP.

As we have noted above, the awareness that PrEP would protect them from acquiring HIV motivated some of the participants to start using it despite the perceived/experienced challenges associated with taking PrEP, *“Everyone loves his/her life and people will surely take and adhere to PrEP if they are sure that they are protected from HIV”* (man 44 years). They reported devising ways to facilitate their PrEP taking and adherence, so they could persist with regular PrEP use. For example, one of the women initially had problems swallowing the pills due to the big size, she recalled how she finally, comfortably, took her PrEP:

“Even if I do not have money for transport to go for refills, I can walk to the PrEP facility because is it near [. . .] however when I had just started PrEP, I found the pill big to swallow but I would break it into two pieces and still swallow. I am now used to the pill and no longer have issues with the size. I disclosed to household members including my partner that I am on PrEP and given the fact that I disclosed, I freely take my PrEP without hiding the pills nor taking them stealthily. Not even the girls (partner’s granddaughters) hide their pills (PrEP). We keep our PrEP in the open and if you visit our home and see it, it is all up to you” (woman, 40 years).

Generally, many participants expressed a liking for PrEP and acknowledged that it would benefit them particularly because of their risk of HIV infection. However, this did not always translate into uptake, as we outline above, as many had concerns about the nature and dosing of pills as well as the structures through which those pills are being delivered.

Discussion

Our study findings show that individuals at high risk of HIV infection who were enrolled in an HIV vaccine preparedness study in Uganda were interested in taking oral PrEP because they understood that it would protect them against acquisition of HIV, a finding corroborated by other recent work in Uganda [11, 23, 24]. However, among those who had chosen to start PrEP many did not initiate and/or persist with the drug. This was attributed to the burden of daily oral pill taking, concerns regarding side effects, and stigma. To some extent, the negative

influence from other people as well as the lingering doubts regarding the drug's efficacy negatively influenced uptake. In addition, the limited understanding of PrEP as well as the fears/concerns exhibited by our study participants prevented some of them from taking up the intervention much as they considered it beneficial, as documented in other studies [25]. Research has shown how anticipation of negative effects can influence intervention acceptance, uptake, and adherence [23, 26, 27].

To build individuals' confidence in their ability to take PrEP [self-efficacy], it is necessary that they get detailed information on how PrEP works, what to expect in terms of side effects, and how to deal with these issues [28–30]. The common reports of stigma hindering uptake of PrEP among our study participants were similar to the findings from other studies [11, 31]. For example, research on uptake of PrEP has reported that stigma associated with being labelled as HIV-infected and being suspected of infidelity or promiscuity, was a barrier to uptake of PrEP [11, 32, 33].

Similarly, the stigma related to the PrEP facility which was the same place where people on ARVs picked their refills was noted. As a result, participants in this study expressed their dislike for the PrEP/ARV facility and said they could not go there to pick PrEP. This was in agreement with earlier research [34], which found that the integration of PrEP with HIV care services hindered PrEP uptake, thus emphasising the need for alternative PrEP delivery approaches. PrEP needs to be integrated into broader health promotion and divested of its association with HIV-treatment structures using differentiated service delivery through community-based structures. Such changes to delivery would be influential in terms of improving access and acceptability.

We found that some participants who initiated PrEP stopped taking it after experiencing side effects. This reflects that acceptance of an intervention may change as people gain experience with using it as well as more information and understanding about the side effects themselves. This change may sometimes be related to the burden that is associated with taking on the intervention [26, 35]. Whereas previous conceptualization of acceptability emphasizes that individual perceptions of an intervention greatly influences its acceptability [12], our findings concur with Sekhon's argument that acceptability is dynamic and may change after experiencing the intervention [13].

Bandura [36] suggests that the amount of effort that people invest in taking up an intervention will translate to uptake and the level of resilience when faced with challenges: 'The stronger the perceived self-efficacy, the more active the efforts' (p. 194) and 'The stronger the efficacy expectation, the higher was the likelihood that a particular task would be successfully completed' (p. 207). Indeed, participants in our study who initiated PrEP but seemed not to believe in its efficacy, were likely not to persist with it. Research has shown that an individual may reinforce their self-efficacy if they believe the intervention will benefit them [37] and they receive support from research/health care staff. For example, providing individuals with risk information and reminders of their risk behaviour can change their assessments of risk [38, 39]. Therefore, interventions to address such concerns may improve acceptability.

The belief held by a few of our participants that they did not need to take PrEP because they were not at risk or had other HIV prevention methods, corroborates the findings of other studies which show that individuals exhibiting optimal beliefs in susceptibility are not likely to accept any recommended health action [25, 40]. Therefore, HIV prevention interventions need to be explicit as to what might cause HIV risk if these interventions are to benefit the targeted groups of key or high risk populations [41]. Again, some individuals are reluctant to disrupt or abandon other HIV prevention methods like condoms or couple HIV counselling and testing which they believe to have worked well for them and which they highly value [26].

A limitation of our study was that our participants were selected from a vaccine preparedness study cohort where they regularly received health education and HIV prevention services including information on PrEP. However, the latter could have been affected by staff perceptions and attitudes towards oral PrEP. Hence, our findings may not be generalizable to other at-risk populations who do not get such services. Further still, the association of PrEP with stigmatised populations, experiences and attitudes on PrEP may differ in a general population where there is less 'branding' or targeting of certain groups [34]. Nevertheless, our study provides useful insights into the challenges of PrEP use among individuals at high risk of HIV infection in the study area and similar settings. The combination of repeat IDIs and FGD data allowed for a deeper understanding of participants' knowledge and acceptability of PrEP.

Conclusion

We observed considerable interest in taking PrEP among our study participants. However, limited understanding of and concerns about PrEP could impede its uptake and sustained use. Provision of comprehensive information about PrEP, instituting measures to destigmatize PrEP use by integrating into broader health promotion and providing in non-health facility settings, plus the introduction of more user-friendly PrEP formulations, such as injectable PrEP, could improve uptake and adherence.

Supporting information

S1 File. Registration cohort–baseline data.
(XLSX)

S2 File. Registration cohort–followup data.
(XLSX)

Acknowledgments

We are grateful to all the participants for agreeing to participate in the study and giving us their time, and the PrEPVacc study staff at the MRC/UVRI and LSHTM Uganda Research Unit at Masaka for implementing the study. We thank the Community Advisory Board (CAB) members who worked as a link and supported this research within the communities. We thank Professor Pontiano Kaleebu for his support and leadership role in conducting the study. We thank the entire PrEPVacc team (listed below) for their support:

PrEPVacc Team List

South Africa:

South African Medical Research Council: Glenda Gray Nishanta Singh, Zakir Gaffoor, Neetha Morar, Thandiwe Sithole, Kubashni Woeber, Samantha Siva, Eldinah Hwengwere;

Africa Health Research Institute: Rujeko Samantha Chidawanyika, Nteboheleng Mahapa, Phindile Khanyile, Janet Seeley

Tanzania:

Mbeya Medical Research Centre: Lucas Maganga, Wiston William, Emmanuel Kapesa, Elizabeth Danstan, Doreen Pamba, Marco Missanga Amani Kway, Abisai Kisinda, Lilian Njovu, Lwitiho Sudi, Revocatus Kunambi;

Muhimbili University of Health and Allied Sciences: Said About, Patricia Munseri, Eligius Lyamuya, Frank Msafiri, Agricola Joachim, Edith Tarimo, Diana Faini Tumaini Nagu, Deus Buma, Muhammad Bakari,

Uganda:

MRC/UVRI and LSHTM Uganda Research Unit: Pontiano Kaleebu, Freddie Mukasa Kibengo, Ayoub Kakande, Jennifer Serwanga, Janet Seeley, Rachael Kawuma, Christian Hansen Holmes, Sheila Kansime, Eugene Ruzagira, Sylvia Kusemererwa, Sylvia Masawi, Vincent Basajja, Tobias Vudriko, Peter Hughes, Shamim Nabukenya, Gertrude Mutonyi, Rita Nakiboneka, Susan Mugaba, Sarah Nakamanya, Denis Kibuuka.

Mozambique:

National Health Institute, Maputo: Ilesh Jani, Edna Viegas, Isabel Remane, Odete Bule, Edna Nhacule, Patricia Ramgi, Raquel Chisumba, Eduardo Namalango, Yolanda Manganhe, Carmelia Massingue, Igor Capitine, Jorge Ribeiro

Trial oversight and management support

Jonathan Weber, Cherry Kingsley, Tom Miller, Sheena McCormack, Angela Crook, David Dunn, Henry Bern, Aminata Sy, Simona Salomone, Liz Brodnicki, Sarah Joseph, Claire Wenden, Giuseppe Pantaleo, Song Ding, Charlotta Nilsson, Arne Kroidl, Julie Fox, Gustavo Doncel, Allison Matthews, Jim Rooney, Carter Lee, Merlin Robb

Monitoring:

IAVI: Kundai Chinyenze, Jacqueline Musau, Mabela Matsoso, Mary Amondi, Ansuya Naidoo, Paramesh Chetty, Anne Gumbe

Disclaimer: The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official views of the MRC/UVRI & LSHTM Uganda Research Unit, neither those of the sponsor or funders.

Author Contributions

Conceptualization: Sarah Nakamanya, Rachel Kawuma, Sheena McCormack, Janet Seeley.

Data curation: Sarah Nakamanya, Rachel Kawuma, Denis Kibuuka.

Formal analysis: Sarah Nakamanya, Denis Kibuuka.

Investigation: Eugene Ruzagira.

Methodology: Janet Seeley.

Project administration: Sylvia Kusemererwa, Eugene Ruzagira, Janet Seeley.

Supervision: Janet Seeley.

Writing – original draft: Sarah Nakamanya, Rachel Kawuma, Sylvia Kusemererwa, Eugene Ruzagira, Janet Seeley.

Writing – review & editing: Sarah Nakamanya, Rachel Kawuma, Denis Kibuuka, Sylvia Kusemererwa, Sheena McCormack, Eugene Ruzagira, Janet Seeley.

References

1. Joint United Nations Programme on HIV/AIDS. Factsheet: global AIDS update. Geneva: UNAIDS; 2021 [Available from: <https://www.unaids.org/en/resources/fact-sheet>]
2. World Health Organization. Focus on key populations in national HIV strategic plans in the WHO African Region. Geneva: WHO. Regional Office for Africa; 2018.
3. World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: WHO; 2016. Report No.: 9241511125.
4. Joint United Nations Programme on HIV/AIDS. Communities at the centre. Global AIDS update 2019. Geneva: UNAIDS; 2019.
5. Ministry of Health. Consolidated guidelines for the prevention and treatment of HIV and AIDS in Uganda. Kampala: Ministry of Health, Government of the Republic of Uganda; 2020.

6. Ahmed N, Pike C, Bekker L-G. Scaling up pre-exposure prophylaxis in sub-Saharan Africa. *Current Opinion in Infectious Diseases*. 2019; 32(1):24–30. <https://doi.org/10.1097/QCO.0000000000000511> PMID: 30461452
7. O'Malley G, Barnabee G, Mugwanya K. Scaling-up PrEP Delivery in Sub-Saharan Africa: What Can We Learn from the Scale-up of ART? *Current HIV/AIDS Reports*. 2019; 16(2):141–50. <https://doi.org/10.1007/s11904-019-00437-6> PMID: 30796608
8. Pillay D, Stankevitz K, Lanham M, Ridgeway K, Murire M, Briedenhann E, et al. Factors influencing uptake, continuation, and discontinuation of oral PrEP among clients at sex worker and MSM facilities in South Africa. *PLOS One*. 2020; 15(4):e0228620. <https://doi.org/10.1371/journal.pone.0228620> PMID: 32352969
9. Stankevitz K, Schwartz K, Hoke T, Li Y, Lanham M, Mahaka I, et al. Reaching at-risk women for PrEP delivery: What can we learn from clinical trials in sub-Saharan Africa? *PLOS One*. 2019; 14(6):e0218556. <https://doi.org/10.1371/journal.pone.0218556> PMID: 31226165
10. Hommel KA, Hente E, Herzer M, Ingerski LM, Denson LA. Telehealth behavioral treatment for medication nonadherence: a pilot and feasibility study. *European Journal of Gastroenterology and Hepatology*. 2013; 25(4):469. <https://doi.org/10.1097/MEG.0b013e32835c2a1b> PMID: 23325274
11. Sundararajan R, Wyatt MA, Muwonge TR, Pisarski EE, Mujugira A, Haberer JE, et al. Understanding PrEP Acceptability Among Priority Populations: Results from a Qualitative Study of Potential Users in Central Uganda. *AIDS and Behavior*. 2022; on line. <https://doi.org/10.1007/s10461-022-03606-8> PMID: 35133529
12. Sidani S, Miranda J, Epstein DR, Bootzin RR, Cousins J, Moritz P. Relationships between personal beliefs and treatment acceptability, and preferences for behavioral treatments. *Behaviour Research and Therapy*. 2009; 47(10):823–9. <https://doi.org/10.1016/j.brat.2009.06.009> PMID: 19604500
13. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Services Research*. 2017; 17(1):1–13.
14. Musumari PM, Techasrivichien T, Srithanaviboonchai K, Wanyenze RK, Matovu JKB, Poudyal H, et al. HIV epidemic in fishing communities in Uganda: A scoping review. *PLOS One*. 2021; 16(4):e0249465. <https://doi.org/10.1371/journal.pone.0249465> PMID: 33793652
15. Morris CN, Ferguson AG. Estimation of the sexual transmission of HIV in Kenya and Uganda on the trans-Africa highway: the continuing role for prevention in high risk groups. *Sexually Transmitted Infections*. 2006; 82(5):368–71. <https://doi.org/10.1136/sti.2006.020933> PMID: 16854995
16. Morris CN, Morris SR, Ferguson AG. Sexual behavior of female sex workers and access to condoms in Kenya and Uganda on the Trans-Africa highway. *AIDS and Behavior*. 2009; 13(5):860–5. <https://doi.org/10.1007/s10461-008-9431-z> PMID: 18665445
17. Seeley J, Nakiyingi-Miuro J, Kamali A, Mpendo J, Asiki G, Abaasa A, et al. High HIV incidence and socio-behavioral risk patterns in fishing communities on the shores of Lake Victoria, Uganda. *Sexually Transmitted Diseases*. 2012; 39(6):433–9. <https://doi.org/10.1097/OLQ.0b013e318251555d> PMID: 22592828
18. Kwena Z, Bukusi E, Ng'ayo M, Buffardi A, Nguti R, Richardson B, et al. Prevalence and risk factors for sexually transmitted infections in a high-risk occupational group: the case of fishermen along Lake Victoria in Kisumu, Kenya. *International Journal of STD & AIDS*. 2010; 21(10):708–13.
19. Asiki G, Mpendo J, Abaasa A, Agaba C, Nanvubya A, Nielsen L, et al. HIV and syphilis prevalence and associated risk factors among fishing communities of Lake Victoria, Uganda. *Sexually Transmitted Infections*. 2011; 87(6):511–5. <https://doi.org/10.1136/sti.2010.046805> PMID: 21835763
20. Kissling E, Allison EH, Seeley JA, Russell S, Bachmann M, Musgrave SD, et al. Fisherfolk are among groups most at risk of HIV: cross-country analysis of prevalence and numbers infected. *AIDS*. 2005; 19(17):1939–46. <https://doi.org/10.1097/01.aids.0000191925.54679.94> PMID: 16260899
21. Kamali A, Nsubuga R, Ruzagira E, Bahemuka U, Asiki G, Price M, et al. Heterogeneity of HIV incidence: a comparative analysis between fishing communities and in a neighbouring rural general population, Uganda, and implications for HIV control. *Sexually Transmitted Infections*. 2016; 92(6):447–54. <https://doi.org/10.1136/sextrans-2015-052179> PMID: 26933046
22. Rutakumwa R, Mugisha JO, Bernays S, Kabunga E, Tumwekwase G, Mbonye M, et al. Conducting in-depth interviews with and without voice recorders: a comparative analysis. *Qualitative Research*. 2020; 20(5):565–81. <https://doi.org/10.1177/1468794119884806> PMID: 32903872
23. Kawuma R, Nabalwany Z, Seeley J, Mayanja Y. “I prefer to take pills when I plan to have sex”: Perceptions of on-demand versus daily oral pre-exposure prophylaxis among adolescents in Kampala, Uganda. *African Journal of AIDS Research*. 2022; 21(1):8–14. <https://doi.org/10.2989/16085906.2022.2039727> PMID: 35361065

24. Kawuma R, Ssemata AS, Bernays S, Seeley J. Women at high risk of HIV-infection in Kampala, Uganda, and their candidacy for PrEP. *SSM—Population Health*. 2021; 13:100746. <https://doi.org/10.1016/j.ssmph.2021.100746> PMID: 33604448
25. Garrett WS, Wheeler N, Oliva M, Reed C, Conley J, Alvarenga A, et al. Attitudes Toward HIV Pre-Exposure Prophylaxis In A Sample of Adolescents And Young Adults Attending A US Urban Primary Care Clinic (poster presentation 186). *Journal of Adolescent Health*. 2019; 64(2):S95.
26. Sanders C, Rogers A, Bowen R, Bower P, Hirani S, Cartwright M, et al. Exploring barriers to participation and adoption of telehealth and telecare within the Whole System Demonstrator trial: a qualitative study. *BMC Health Services Research*. 2012; 12(1):1–12. <https://doi.org/10.1186/1472-6963-12-220> PMID: 22834978
27. Bukenya D, Mayanja BN, Nakamanya S, Muhumuza R, Seeley J. What causes non-adherence among some individuals on long term antiretroviral therapy? Experiences of individuals with poor viral suppression in Uganda. *AIDS Research and Therapy*. 2019; 16(1):1–9.
28. Ogunbajo A, Leblanc NM, Kushwaha S, Boakye F, Hanson S, Smith MD, et al. Knowledge and Acceptability of HIV pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) in Ghana. *AIDS Care*. 2020; 32(3):330–6. <https://doi.org/10.1080/09540121.2019.1675858> PMID: 31597455
29. Pasipanodya EC, Stockman J, Phuntsog T, Morris S, Psaros C, Landovitz R, et al. “PrEP” ing for a PrEP demonstration project: understanding PrEP knowledge and attitudes among cisgender women. *BMC Women’s Health*. 2021; 21(1):1–10.
30. Auerbach JD, Kinsky S, Brown G, Charles V. Knowledge, attitudes, and likelihood of pre-exposure prophylaxis (PrEP) use among US women at risk of acquiring HIV. *AIDS Patient Care and STDs*. 2015; 29(2):102–10. <https://doi.org/10.1089/apc.2014.0142> PMID: 25513954
31. Muhumuza R, Ssemata AS, Kakande A, Ahmed N, Atujuna M, Nomvuyo M, et al. Exploring Perceived Barriers and Facilitators of PrEP Uptake among Young People in Uganda, Zimbabwe, and South Africa. *Archives of Sexual Behavior*. 2021; 50(4):1729–42. <https://doi.org/10.1007/s10508-020-01880-y> PMID: 33954824
32. Mwatutura C, Traeger M, Lemoh C, Stooze M, Price B, Coelho A, et al. Barriers and facilitators to pre-exposure prophylaxis among African migrants in high income countries: a systematic review. *Sexual Health*. 2021; 18(2):130–9. <https://doi.org/10.1071/SH20175> PMID: 33658106
33. Irungu EM, Baeten JM. PrEP rollout in Africa: status and opportunity. *Nature Medicine*. 2020; 26(5):655–64. <https://doi.org/10.1038/s41591-020-0872-x> PMID: 32405065
34. Amico KR, Bekker L-G. Global PrEP roll-out: recommendations for programmatic success. *The Lancet HIV*. 2019; 6(2):e137–e40. [https://doi.org/10.1016/S2352-3018\(19\)30002-5](https://doi.org/10.1016/S2352-3018(19)30002-5) PMID: 30660592
35. Mutua G, Sanders E, Mugo P, Anzala O, Haberer JE, Bangsberg D, et al. Safety and Adherence to Intermittent Pre-Exposure Prophylaxis (PrEP) for HIV-1 in African Men Who Have Sex with Men and Female Sex Workers. *PLOS One*. 2012; 7(4):e33103. <https://doi.org/10.1371/journal.pone.0033103> PMID: 22511916
36. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychological Review*. 1977; 84(2):191. <https://doi.org/10.1037//0033-295x.84.2.191> PMID: 847061
37. Sewell WC, Patel RR, Blankenship S, Marcus JL, Krakower DS, Chan PA, et al. Associations among HIV risk perception, sexual health efficacy, and intent to use PrEP among women: An application of the risk perception attitude framework. *AIDS Education and Prevention*. 2020; 32(5):392–402. <https://doi.org/10.1521/aeap.2020.32.5.392> PMID: 33112674
38. Gerrard M, Gibbons FX, Reis-Bergan M. The effect of risk communication on risk perceptions: the significance of individual differences. *JNCI Monographs*. 1999; 1999(25):94–100. <https://doi.org/10.1093/oxfordjournals.jncimonographs.a024217> PMID: 10854464
39. Baeten JM, Donnell D, Mugo NR, Ndase P, Thomas KK, Campbell JD, et al. Single-agent tenofovir versus combination emtricitabine plus tenofovir for pre-exposure prophylaxis for HIV-1 acquisition: an update of data from a randomised, double-blind, phase 3 trial. *The Lancet Infectious Diseases*. 2014; 14(11):1055–64. [https://doi.org/10.1016/S1473-3099\(14\)70937-5](https://doi.org/10.1016/S1473-3099(14)70937-5) PMID: 25300863
40. Rosenstock IM. Historical origins of the health belief model. *Health Education Monographs*. 1974; 2(4):328–35.
41. Mugo NR, Ngure K, Kiragu M, Irungu E, Kilonzo N. PrEP for Africa: what we have learnt and what is needed to move to program implementation. *Current Opinion in HIV and AIDS*. 2016; 11(1):80.