BMC Infectious Diseases

RESEARCH

Open Access

Long-acting injectable antiretroviral treatment: experiences of people with HIV and their healthcare providers in Uganda

Henry Zakumumpa[1*], Adolf Alinaitwe[2,4], Marjorie Kyomuhendo[3] and Brenda Nakazibwe[1,5]

Abstract

Introduction Long-acting injectable antiretroviral treatment (LAI-ART) has emerged as a novel alternative to the burden of daily oral pills. The bi-monthly intramuscular injectable containing cabotegravir and rilpivirine holds the promise of improving adherence to ART. The perspectives of potential users of LAI-ART, the majority of whom reside in Eastern and Southern Africa, are still largely unexplored. We set out to understand the experiences of people with HIV (PWH) who received LAI-ART at Fort Portal Regional Referral Hospital in mid-Western Uganda for at least 12 months.

Methods This qualitative study, conducted between July and August 2023, was nested within a larger study. We conducted four focus groups with 32 (out of 69) PWH who received intramuscular injections of cabotegravir and rilpivirine. In-depth interviews were held with six health workers who delivered LAI-ART to PWH. Data were analyzed by thematic approach broadly modeled on the five domains of the Consolidated Framework for Implementation Research (CFIR).

Results There was high acceptability of LAI-ART (30 /32 or 94%) participants requested to remain on LAI-ART even after the end of the 12-month trial. Adherence to ART was reportedly improved when compared to daily oral treatment. Participants credited LAI-ART with; superior viral load suppression, redemption from the daily psychological reminder of living with HIV, enhanced privacy in HIV care and treatment, reduced HIV-related stigma associated with taking oral pills and that it absolved them from carrying bulky medication packages. Conversely, nine participants reported pain around the injection site and a transient fever soon after administering the injection as side effects of LAI-ART. Missed appointments for receiving the bi-monthly injection were common. Providers identified health system barriers to the prospective scale-up of LAI-ART which include the perceived high cost of LAI-ART, stringent cold chain requirements, physical space limitations, and workforce skills gaps in LAI-ART delivery as potential drawbacks.

Conclusion Overall, PWH strongly preferred LAI-ART and expressed a comparatively higher satisfaction with this treatment alternative. Health system barriers to potential scale-up are essential to consider if a broader population of PWH will benefit from this novel HIV treatment option in Uganda and other resource-limited settings.

*Correspondence:
Henry Zakumumpa
zakumumpa.henry09@gmail.com; henry.zakumumpa@mak.ac.ug

Full list of author information is available at the end of the article

Trial registration Trial Registry Number PACTR ID PACTR202104874490818 (registered on 16/04/2021).
Keywords HIV treatment, ART, PWH, Uganda, Antiretroviral therapy, Global health delivery

Background

Long-acting injectable antiretroviral treatment (LAI-ART) has emerged as a novel alternative to the burden of daily oral HIV treatment [1]. The bi-monthly intramuscular injectable containing cabotegravir and rilpivirine holds the promise of improving adherence to ART and viral load suppression in low-income countries where the 95-95-95 targets have not yet been fully achieved [2]. This is particularly so among sub-groups of people with HIV (PWH) with adherence constraints. Some of the common barriers to adherence to ART include individualized stigma, forgetfulness, being away from home, depression and alcohol misuse [2]. Sub-groups with adherence challenges include older adolescents, children/caregivers and sex workers who experience constraints in observing the daily oral pills routine [3]. LAI-ART is said to reduce HIV-related stigma among those taking daily oral pills such as in discordant couples [1]. Clinical trials conducted in high-income countries demonstrate that LAI-ART is non-inferior to daily oral ART [2]. The World Health Organization approved LAI-ART in 2022. In July 2023, ViiV Healthcare, a pharmaceutical company committed to sharing the intellectual property underpinning LAI-ART making generic production a possibility for millions of PWH in low and middle-income countries (LMICs) [4].

Most of the evidence on therapeutic efficacy and the notion of high acceptability of LAI-ART has emerged out of clinical trials and controlled environments in high-income settings [5–7].

There is little research around 'real world' implementation experiences in high-burden, LMICs such as Uganda [5]. The perspectives of potential users of LAI-ART, the majority of whom reside in Eastern and Southern Africa are still largely unexplored [3]. The medication safety of LAI-ART in African populations is largely unknown. Little is known on the operational context and health system capacity for the implementation of LAI-ART in Eastern and Southern Africa, even though over 55% of the global population of people living with HIV reside in this region [5]. Implementation research on patient experiences of LAI-ART in LMICs can inform decision making by policy makers and funders such as the President's Emergency Plan for AIDS Relief (PEPFAR).

HIV epidemiological context in Uganda

Uganda has a generalized HIV epidemic with one of the largest populations of PWH in Eastern and Southern Africa, the region with largest HIV burden in the world [8]. Over 1.4 million Ugandans are accessing ART. Since 2004, ART has been widely available at public facilities country-wide with funding from external donors particularly PEPFAR which accounts for almost two thirds of HIV spending [8].

Uganda has registered remarkable strides in its national HIV response from a high of almost 30% HIV prevalence at ante natal sites in the 1990s to about 6% in 2023. Viral load suppression rates in some parts of Uganda do not meet UNAIDS 95-95-95 targets [8]. Viral load suppression rates in Uganda vary widely in some sub-populations and communities. In some studies, conducted in Uganda, viral load suppression rates have been reported to be as low as 8% and at 24% among children, at 48% at military hospitals and at 74% at some sites in Eastern Uganda [3].

In Uganda, select sub-groups of PWH have sub-optimal rates of adherence to ART and these include adolescents, children and younger men compared to older age groups [3]. Multi-level interventions are therefore needed in these sub-groups to accelerate progress towards attaining targets for viral load suppression [3].

To this end, in December 2022, Uganda approved long-acting injectable ART joining Zimbabwe in providing regulatory approval [9].

Little is known about the experiences and preferences of PWH regarding LAI-ART as an alternative option to oral HIV treatment [10–12]. A notable exception is a study conducted in Uganda by Kennedy and colleagues [13], however this study explored the perceptions of potential users of LAI-ART in Uganda.

To the best of our knowledge this is the first study in Uganda to report qualitative findings of PWH in Uganda who actually received LAI-ART for 12 months and their attending clinicians. The objective of this paper is to document the experiences of 32 (out of 69) PWH who received LAI-ART and the health workers who offered this treatment option for at least 12 months in mid-Western Uganda.

Methods

Research design

We adopted a qualitative exploratory research design [14–16], to understand the experiences of PWH under long-acting injectable antiretroviral treatment (LAI-ART) as compared to oral HIV treatment (containing tenofovir, lamivudine, dolutegravir) which they had been on in the past 12 months prior to initiation on LAI-ART. In so doing, we undertook a post-hoc evaluation of the intervention which was rolled out in April 2021 [17–19]. The first patient enrollment date was on 15th September 2021. Trial participants were started on an oral

Table 1 The updated five CFIR domains as described by Damschroder et al. 2022 [21]

Innovation domain
Innovation: The "thing" being implemented, e.g., a new clinical treatment

Outer Setting domain
Outer Setting: The setting in which the Inner Setting exists, e.g., hospital system, school district, state. There may be multiple Outer Settings and/or multiple levels within the Outer Setting, e.g., community, system, state

Inner Setting domain
Inner Setting: The setting in which the innovation is implemented, e.g., hospital, school, city. There may be multiple Inner Settings and/or multiple levels within the Inner Setting, e.g., unit, classroom, team

Individuals domain
Individuals: The roles and characteristics of individuals

Implementation Process domain
Implementation Process: The activities and strategies used to implement the innovation
Project Implementation Process: Document the implementation process activities and strategies used to implement the innovation.

Table 2 Emergent themes aligned under CFIR's five 'domains'

Implementation Process domain	Innovation domain	Individuals domain	Inner setting domain	Outer setting domain
• Patient selection criteria	• Bi-monthly interval of treatment	• Reduced HIV-related stigma	• Cold chain requirements	• High demand for LAI-ART from community
• LAI-ART delivery	• Perceived improved adherence to ART	• Diminished daily psychological burden of living with HIV	• Workforce skills requirements	• Patient centred HIV care context • Quest for better HIV therapies
• Monitoring	• Perceived superior viral load suppression	• Better satisfaction with HIV treatment	• Perceived high cost of LAI-ART	
		• Perceived fewer side effects		

formulation of LAI-ART for the first four weeks after the enrollment date. We interviewed PWH who received LAI-ART for at least 12 months and their attending HIV clinicians and nurses. PWH had been on the oral standard of care before switching to LAI-ART (containing tenofovir, lamivudine, dolutegravir). The clinical trial in which our study participants engaged was part of an open label, multi-centre clinical trial implemented in Uganda, Kenya and South Africa with funding from Janssen pharmaceuticals [17]. The clinical trial in Uganda received local ethical approval [17–19] from the Uganda National Council of Science and Technology (HS1117ES) and the clinical trial is registered with the National Drug Authority of Uganda (CTC0161/2021) [20]. The underpinning clinical trial is registered with the Pan African Clinical Trials registry (PACTR ID: PACTR202104874490818).

Theoretical orientation

This qualitative study of post-implementation experiences of LAI-ART by PWH and their providers was underpinned by the updated Consolidated Framework for Implementation Research (CFIR) [21]. The CFIR is a widely used framework that is informed by a robust literature review of facilitators and barriers to implementation of health care interventions from a multi-level lens of 'five domains' namely; (i) Innovation domain (ii) outer setting domain (iii) Inner setting domain ii) outer setting, (iv) Individuals domain (v) Implementation process domain. A detailed description of the five CFIR domains and 'sub-domains' used in this study is shown in Table 1.

The CFIR was used as an overarching deductive framework in developing our qualitative interview guides as well as in the analysis and presentation of data shown in Table 2.

Study site

Fort Portal Regional Referral Hospital (FPRRH) is at the highest level of tertiary care in mid-Western Uganda [22]. The hospital caters to patients from Fort Portal as well as other neighboring districts.

The HIV clinic at FPRRH has over 17,000 active PWH on ART and operates on a five-day-a-week basis, on an outpatient basis. The clinic runs as an autonomous service unit under the hospital [23] with its own dedicated workforce (HIV clinicians, nurses, counsellors), separate physical space within a large hospital complex, triage systems and a dedicated HIV-specific laboratory.

Fort Portal Regional Referral hospital was one of three sites in Uganda [17, 18] implementing a clinical trial of LAI-ART with funding from Janssen pharmaceuticals [17–19]. FPRRH was selected because it was the first site to enroll participants in the LAI-ART clinical and because it had the longest implementation experience of LAI-ART in Uganda.

Selection of study participants

For this qualitative post-hoc evaluation, we enrolled 32 (out of 69) adult PWH who took part in a clinical trial of LAI-ART for at least 12 months. The detailed inclusion and exclusion criteria for those who participated in the clinical trial underpinning this study are described in the results. In terms of study procedure, we approached the study coordinator of the clinical trial at FPRRH and described our study objective of understanding the experiences of PWH under the novel option of LAI-ART. The study coordinator then informed PWH who participated in the clinical trial of our study objective. PWH who offered to participate in this study on a purely voluntary basis and could offer written informed consent were enrolled in this post-hoc qualitative evaluation.

We enrolled three HIV clinicians (including the site Principal Investigator) and three nurses who implemented the 12-month clinical trial.

Data collection

Focus group discussions

We explored the experiences of PWH under the novel long-acting injectable alternative as compared to their previous experience on oral HIV treatment. We conducted four gender-disaggregated focus group discussions (FGDs) involving thirty-two participants. Each of the FGDs comprised eight participants. A pre-tested focus group guide informed by the CFIR framework was used entailing 17 open-ended questions. We conducted face-to-face FGDs in a quiet room at the study site. We conducted two focus groups involving females and two FGDs involving male participants. The focus groups were conducted between July and September 2023. The FGDs were audio-recorded with the consent of participants. Each of the two lead investigators was assisted by a research assistant who took notes and operated the recorder. The focus groups were conducted in *Rutooro* the local language spoken in mid-Western Uganda. On average, each of the focus groups lasted one and a half hours. A sample focus group guide is attached (supplementary file).

In-depth interviews

In addition, we conducted in-depth interviews (IDIs) with six health workers who offered LAI-ART as part of the clinic trial. These included three HIV clinicians and three nurses. The face-to-face IDIs were conducted at FPRRH in the offices of the health workers. The IDIs were conducted in the English language and were led by the first and last author. The interviews were audio-recorded. The interview guide used in the IDIs is attached (supplementary file). The objective of the IDIs was to understand the facilitators and barriers to implementation of LAI-ART from a provider perspective of health system context [21].

Data analysis

We followed the procedures recommended for qualitative data analysis proposed by Miles and Huberman [24]. Broadly, we followed four steps in analysis although it was a largely iterative process. Our audio files were translated into text transcripts. In the case of our focus groups, the transcripts were translated from *Rutooro*, a local Ugandan dialect spoken in Mid-Western Uganda, to English by a professional language translator proficient in both languages. Our first step entailed transcript review. The verbatim transcripts were read multiple times for data familiarization by two authors. We applied the framework approach to qualitative data analysis [25], hence our five deductive thematic categories informed by the CFIR framework guided data analysis (e.g. i) Innovation domain ii) outer setting domain iii) inner setting domain iv) individual's domain v) implementation process domain). In the second stage, three authors inductively generated codes from multiple readings of the FGD and IDI transcripts. In the third stage, the inductively generated 'sub-themes' were then grouped under the five CFIR 'domains' or deductive thematic matrices (e.g. i) Innovation domain ii) outer setting domain iii) inner setting domain iv) individual's domain v) implementation process domain). Hence we utilized a hybrid approach of both inductive and deductive theme development [26]. The fourth stage involved overall interpretation and synthesis [27] involving all co-authors. Disagreements in the assignment of themes and sub-themes were resolved by consensus in a team-based process.

Results

Demographic profile of focus group participants

As illustrated in Table 3 below, there was equal representation of male and female participants in the focus groups comprising PWH. Most of the participants were aged 35–44 years (43.75%) followed by those aged 55–64 years (25.00%) and 25–34 years (18.75%) respectively. The least represented age group was those between 45 and 54 (12.50%). Regarding the participants' marital status, most were married (75.00%) compared to the unmarried (25.00%). Additionally, most participants had attained basic primary education (75.00%) compared to those who achieved secondary education (25.00%). Because the majority of participants had attained a basic primary education, our focus groups were conducted in *Rutooro* the local language spoken in mid-Western Uganda to enable effective participation of all PWH in the proceedings of our FGDs. Regarding the participants' duration on ART, the majority had received treatment for 11 to 15 years (56.25%), followed by those on treatment for 6–10 years

Table 3 Demographic characteristics of participants in the focus groups

FOCUS GROUP PARTICIPANT CHARACTERISTIC	Frequency ($n=32$)	Percent (100%)
Gender		
Male	16	50.00%
Female	16	50.00%
Age range		
25–34	6	18.75
35–44	14	43.75
45–54	4	12.50
55–64	8	25.00
Marital status		
Married	24	75.00%
Single	8	25.00%
Level of formal education		
Primary school	24	75.00%
Secondary school	8	25.00%
Length of time on ART		
5 years or less	2	6.25
6–10 years	10	31.25
11–15 years	18	56.25
16–20 years	2	6.25

(31.25%). Hence, most participants had been on ART for multiple years with only a few participants reporting a treatment duration of less than five years (6.52%).

Implementation process domain

Selection of participants for the trial

Health workers comprising three HIV clinicians and three nurses described the selection criteria for participants in the LAI-ART clinical trial arm of the study. They observed that although the demand from RoC for LAI-ART was overwhelming, those selected to participate in the clinical trial had to meet stringent eligibility criteria. The only virological criteria set for participants in the trial was having achieved a viral suppression which was defined as having less than 200 copies of HIV per milliliter of blood. Secondly, as described by a health worker, the other criteria demanded that one had no active tuberculosis disease before enrollment in the trial:

> *'To be enrolled for the injectable, we had a certain criterion we follow to put them on because currently, the first group we considered patients who were suppressed, who were stable, their viral load has been suppressed all through ever since they started ART. So, we wanted to see if the injectable ART can maintain the viral load suppression like the oral alternative' [IDI, HCP_03].*

The third criteria was that patients with liver or hepatitis disease and those using herbs concomitantly with ART were excluded. Likewise, pregnant or breastfeeding females were not eligible to participate in the trial. Tests were done to include only PWH, whose vital organs such as the liver, kidney, and heart had no indication of disease. As one of the health workers observed:

> *'We did extensive screening to rule out those patients who have like liver disease, we could do ALT (elevation of alanine aminotransferase) to assess. Also, you know our patients take drugs and take alcohol at times and herbs. So you may find when the liver is already damaged so when you are putting some body on the new product they say it's the product now not the other social life style, so we had to rule out that' [IDI, HCP_01].*

In the same vein, a PWH corroborated the health worker's aforementioned submission noting that *'this is how the injection started. They took us for a test that day, checking the heart, the kidney, the liver, blood pressure, blood sugars so that's how I started like that and I moved to the injection'* [Male 41, PWH, _08].

Having followed the selection criteria, 69 eligible PWH were enrolled on the LAI-ART clinical trial for 12 months effective 15th September 2021.

Although there was extreme demand for enrollment in the clinical trial by PWH, the health workers observed that some participants initially selected to participate in the trial became ambivalent. This ambivalence was attributed to 'conspiracy theories' and misinformation about the new HIV therapies as propagated by peers in the community.

'Some patients told us that they were scared by false rumors from their peers regarding injectable ARVs. They were told false tales that the injection was harmful and that it was meant to eliminate those with HIV with a lethal injection. Of course this was untrue and we had to counsel those had received this misinformation' [IDI, HCP_03].

Consequently, during the enrollment of PWH on the clinical trial, health workers routinely informed the participants about the objectives of the clinical trials to wade off misinformation.

Intervention delivery

Prior to the administration of the bi-monthly injection, participants were initially started on an oral formulation of the trial medication, comprising cabotegravir and rilpivirine, for four weeks to ensure that there were no adverse drug reactions and that the medication was well tolerated.

'We first give them oral medicine of the injectable, so when they take this particular medication entailing Cabotegravir and Rilpivirine, the body gets used and if there is any reaction, we can see easily from the oral treatment and if there's any reaction we can stop. But if there is no reaction to the oral treatment it's obvious that on the injection somebody will do well' [IDI, HCP_02].

Thereafter, two separate injections containing cabotegravir and rilpivirine respectively, were administered intramuscularly on the buttocks, to each participant every two months. A trained health worker administered the injections in a private room at the trial site set up to administer the bi-monthly injections. Describing the injection administration process, a PWH stated thus:

'When you come from home and you arrive at the hospital, the doctor reviews you while checking in your patient file. The other health worker then goes into the store for the injectable drug and retrieves it from the fridge and places it aside. Now the time comes the doctor gives you the paper to do some investigation may be for urine or blood. So as you come back they tell you to go up were we have a private room which is very special having all the things; like beddings - so that's where you go and you lie. The injections are always there. The nurse comes with the doctor and they inject you on the buttocks, after they put a plaster (on the injection site) to stop any possible bleeding. And they ask you to either lie for a moment or rest for a while. If you wish you can rest and if you don't want, you can go away. There is also some water to take, you can either take hot or cold water as you wish. That's how it is.' [Female 38, PWH, _06].

Furthermore, the health workers reported that since a number of participants frequently missed their appointments for administering the bi-monthly injections, reminders by phone call were necessary.

In instances where a PWH missed an injection appointment, the standard operating procedure was such that a PWH was immediately started on an oral formulation of LAI-ART for two weeks and then the missed injection was administered two weeks after the oral formulation.

Monitoring of trial participants

Telephone reminders were made to participants to attend their appointment for injection administration a day prior to the event. To ensure treatment adherence, a transport subsidy was provided to participants to enable them travel to the facility. Upon administering the injection, the health workers made a weekly call-in to the participants to ensure that they were not experiencing difficulties associated with the medication such as adverse drug reactions (ADRs).

Other monitoring measures conducted on each of the participants included viral load suppression laboratory tests once every six months, and medication safety tests such as assessing the functioning of the participants' vital organs such as the liver, kidneys and heart. In this regard, a health worker recounted:

'We assess them for safety. So, when we do safety tests, we test the liver, the kidney, the blood, we do viral load monitoring, CD4 count. We ensure that the patients are still safe on the product the laboratories are busy providing us with test results. We have to probe and see if they have any (adverse drug) reactions or presenting complaints and any other opportunistic infections so we can treat them' [IDI, HCP_01].

Innovation domain

Bi-monthly interval of treatment

Participants indicated that bi-monthly injections were a much more preferable option to oral HIV treatment involving oral daily pill taking. They expressed relief at the reduced burden of HIV treatment that requires a daily routine of swallowing a pill. According to them, they were able to spend more time at work unlike with the previous treatment options that required multiple visits to the health facilities. Likewise, both PWH and health workers mentioned how the bi-monthly treatment was advantageous regarding savings in transport costs

and reduction of time spent at the health facilities. For instance, a health worker opined thus:

> *'Sometimes they are caught up in jobs that are far away from their providers and they end up not taking the drugs. But now all those are covered with the injection, because when you see now the calendar, somebody has to take three hundred and sixty something (365) tabs in a year but for injection you only take six dozes in a year that is a very great improvement'. [IDI, HCP_04].*

Relatedly, a female participant's views applauding the benefits of LAI-ART treatment were that:

> *'What a relief! I have been saved from the daily burden of having to swallow pills. For me, injectable ART is a God-send. The daily burden of having to swallow these tablets has been taken away. I am so relieved. For me, injectables are the way to go' [Female 37, PWH, _09].*

Perceived improved adherence to ART

A recurring narrative among the participants was that LAI-ART improved their adherence to ART when compared to the oral treatment. There was unanimity among several participants indicating that they often forget to take their daily oral pills. However, with LAI-ART, most of the participants reported not having missed their bi-monthly injections since the health workers reminded of their upcoming treatment appointments.

> *'I would forget that I have to swallow the medicine by the time I remember four hours have already gone past the time of taking it. And it would stress me. Even when you go to the clinician for review and they do pill counting, the numbers aren't balancing and the clinician says now you have brought less or, you have brought many, how has it come to this?' [Female, 37, PWH, FPRH].*

Nonetheless, the health workers observed that although they consistently reminded the participants to come for their bi-monthly injections as scheduled, some of them missed their treatment due date and had to be prompted with numerous reminders.

Perceived superior viral load suppression by LAI-ART Innovation

Superior viral load suppression was another element of the LAI-ART innovation. Participants in the clinical trial reported that they had registered better viral load suppression rates while under LAI-ART compared to the time they took daily oral pills. When probed on how they were able to ascertain this improvement viral load suppression, they indicated that viral load monitoring was conducted every six-months during the clinical trial. Consequently, the results of these tests confirmed a viral load suppression. As a female participant put it:

> *'I have taken about three viral load tests since I started the injection and it is clear from the numbers after the tests that my viral load is improving compared to when I was on the tablets' [Female, 32, PWH, FPRH].*

On their part, the health workers concurred with the participants that their viral load suppression rates had improved under LAI-ART in comparison with oral treatment. Moreover, they noted that no cases of relapse were reported once a PWH had attained viral load suppression. To elucidate this view, a health worker explained that:

> *'The injectable is doing good because with it you are unlikely to suffer a viral load rebound compared to our experience with patients on oral treatment where viral load was undetected for prolonged periods but then viral load becomes high again. That one is not easy to get on with the injectable.' [IDI, HCP_03].*

Individuals domain

Perceived reduced HIV-related stigma

Regarding Individuals domain, PWH indicated that being on LAI-ART reduced the HIV-related stigma associated with taking daily oral pills. Such stigma was reportedly rampant in their own households, the community and workplaces. They observed that the bi-monthly injection enhanced privacy since it was administered by a health worker in a private room within the health facility. As a respondent articulated:

> *'But nowadays I can go a whole month without anyone at home seeing me swallowing tablets. So for me that fear stopped because I now feel free. Before I would say 'oh' if I visit home, they see me starting look to for water with which to swallow the tablets. And how to pull them (tablets) out of the bag, even getting space to swallow them was a headache and then even when I put the tablet packaging back in the bag it makes noise. But now all that trouble ended even me now I am like other people without HIV'[Female, 28, PWH, FPRH].*

Similar ideas were expressed by the health workers who noted that LAI-ART lessened HIV-related stigma associated with taking oral treatment in the presence of family and work colleagues. For example, a health worker narrated:

> *'You find that that if a patient has to swallow his medicine and there is a colleague in the house or even their own child, that day they will miss and if the colleague stays for a week the patient will miss for a week. But the injectable you just take your injection and go home.' [IDI, HCP_02].*

The other indication of perceived reduced stigma manifested in the participants' expression of relief at being freed from the burden of carrying bulky six-monthly oral medication refills packaging from facilities to their homes. The bulky medication often invited curiosity from community members, which was a manifestation of external pressure as stipulated in the outer setting domain. Therefore, according to the participants', LAI-ART saved them from inadvertent disclosure of their HIV treatment, since the injection was administered discreetly.

Reduced psychological burden of living with HIV

A recurring theme in our focus groups with PWH was the view that being on LAI-ART liberated them from the daily psychological reminder of living with HIV. PWH emotively described how taking oral pills daily reminded them that they lived with HIV infection. As a male participant put it:

> *'The injection (LAI-ART) has somehow made be forget that they I have HIV. When I used to take oral tablets, I was reminded every day that I have HIV. You know as you are there enjoying yourself and having fun then you suddenly remember you have to go home and take the medicine. It always interrupted my life' [Male, 35, PWH, FPRH].*

Better satisfaction with HIV treatment

PWH described experiencing a better satisfaction with their HIV treatment under LAI-ART in comparison to the oral standard of care. Several participants mentioned they had developed fatigue with the daily routine of taking oral tablets.

> *'For me I feel the injection has worked much better than the other medicines (oral tablets), the other medicines (oral pills) were also working for me but I feel the injection has superseded them. I had grown tired of taking tablets. Tablets had even taken away my peace.' [Female, 28, PWH, FPRH].*

Additionally, the participants perceived LAI-ART to be a more convenient treatment option since it allowed them more time to work due to the reduced health facility visits. Similarly, they reported reduced transport costs associated with less visits to the health facilities for medication refills.

Given the reported benefits of LAI-ART, PWH expressed their interest to remain on the treatment even after the end of the 12-month clinical trial phase.

Indeed, the health workers attested that that all the majority of participants requested to remain on LAI-ART after the end of the clinical trial since they experienced improved quality of life. Accordingly, the health workers confirmed that the manufacturer had granted the participants' request.

> *'They have reported good quality of life because they are adhering well. They aren't falling sick frequently, they are not getting opportunistic infections because they are taking their injection well and they are doing really well. Actually, the majority requested to remain on the injectable even beyond the trial period of 12 months. Fortunately, the manufacturer agreed to provide the injectable beyond the clinical trial' [IDI, HCP_06].*

Furthermore, PWH called for longer intervals between their appointments for injection administration from the current eight weekly intervals. PWH were unanimous in expressing preference for six-monthly long –acting injectables.

> *'For me I am requesting for a longer interval between the injections from the two months to six months. If there is a way of increasing the months of the injection we would very grateful about it because two months, you know for us who are employed we seem like we are escaping from work. If you request for permission to be off-work every two months they complain at work that she is always asking for off-duty permission every two months' . [Male, 35, PWH, FPRH].*

Perceived fewer side effects

During our focus groups with PWH, they frequently compared injectable ART with oral dolutegravir (DTG)-based ART. As such, there was consensus among PWH that they had experienced significantly less side effects over the 12-month LAI-ART trial compared to the time

they transitioned to dolutegravir (DTG)-based ART over a similar period [28]. In the words of a female participant:

> *'For me the injection has no harm it has ever done to me for the time I have been on it.*
> *However, when I was taking the oral tablets, they are the ones that would do me bad. Whenever I would take the tablets, they would give me headaches and also weaken me physically but when I moved to the injection, and I have never been put down (physically). I immediately exist the facility after I am injected and right away I head go straight to the garden.' [Female, 28, PWH, FPRH].*

Another dominant narrative among the participants was that the side effects, of hyperglycemia, reduced libido and insomnia previously experienced on oral treatment, has ceased upon transition to LAI-ART. For instance, a male PWH described how his uptake of LAI-ART had improved his libido:

> *'When I was on dolutegravir (DTG) oral tablets my mood for sex was very low. However, ever since I started getting this injection, my interest in having sex has improved. I now have frequent sex every week with my partner than I used not to have' [Male, 34, PWH, FPRH].*

Nonetheless, some participants reported experiencing side effects while on LAI-ART. The most common side effects reported by participants was pain around the injection site which lasted between two and three days after administration of the injection.

> *'I feel pain around at the spot on the buttocks where the injection was administered. Where they inject you is the very place you feel the pain. When I bend there is pain, when I walk I feel the pain. Walking after the injection has been administered you feel as if your legs are very heavy to lift. The pain usually lasts about four days ' [Female, 32, PWH, FPRH].*

In light of this, the health workers concurred that LAI-ART has some side effects particularly around the injection site.

> *'Patients do get some reactions though not so much. The most common one is pain around the injection site. This is an injection, where the injection goes pain is a given. But what I have seen in the first few months when they have just started injection, those people get that pain at the injection site off like three days on average. But its mild. I have received some complaints from patients that the get some kind of pain but usually after those four days the pain is gone.' [IDI, HCP_02].*

PWH perceived the technique of injection administration to be influential on whether they experienced pain at the injection site pain. PWH reported that they experienced less effects of injection site pain if the injection was administered by particular health workers. Interestingly, two health workers appeared to agree with PWH view that injection administration technique determined the presence or absence of pain.

> *'For the pain around the injection site, it may be due to the technic of administration rather than the drug itself. So, if you administer the injection properly there will be no problem. The other thing with administering the injection is focusing much on the proximity because we need this drug to go in the muscle. For patients with a body mass index above 30, those people who are chubby they have advised us to use a 2.5-inch needle so that the drug can reach the muscle. The needles we use are usually 1.5 inches.' [IDI, HCP_01].*

The other most frequently cited side effect of LAI-ART by PWH was the onset of a fever after the injection was administered. The pain was reported to disappear within less than a week after administering the injection. As corroborated by one of the participants:

> *'When they injected me the first time, I got some coldness like a fever, it took about two days only and it ceased. Then I settled. [Female, 37, PWH, FPRH].*

Likewise, a male participant reaffirmed his experience noting that:

> *'I only got a little fever after the injection when I returned home. I kind of feel chilly but I spend only two days feeling like and I after which I am well again.' [Male, 28, FPRH]*

Indeed, the health workers indicated that they knew before the trial that LAI-ART may have drug-drug interactions with medications for treating active tuberculosis. As such they opted to exclude some potential participants who were on medication for active tuberculosis (TB).

> *'We ruled out patients with TB because this drug also interacts with anti-tuberculosis medication. So, patients on anti-tuberculosis medication had to be withdrawn from the injection.' [IDI, HCP_06].*

Inner setting

Over the 12- month clinical trial phase, health workers reported that they had gained proficiency and competencies in being able to delivery ART.

> *'' We have learnt how to give injectable ART because we were the first people to give it in the whole of Africa, so that was a good milestone. It's quite exciting to be part of the trial because we didn't know the technics of how to deliver it. Now we can comfortably know what to expect.' [IDI, HCP_01].*

Even when there was enthusiasm around the skills gained in LAI-ART delivery, several implementation barriers to potential roll-out were identified.

Cold chain requirements

Health workers reported that delivering LAI-ART requires stringent cold chain standards to preserve the efficacy of the medication at set temperatures. It was reported that LAI-ART medication particularly rilpivirine needs to be stored in deep freezers at set cold conditions (−2° to 8 °C). This implies that storage of rilpivirine demands constant electricity supply and a standby generator in event of power black outs which are not uncommon in Uganda.

> *'You have to have a deep freezer in which to store the rilpivirine at very cold temperatures which means your monthly bill for electricity will be high. We are fortunate that the funder is covering all these costs but what happens when the funding stops?' [IDI, HCP_01].*

Workforce skills in LAI-ART delivery

The trial personnel interviewed for the study indicated that health workers training was imperative for LAI-ART delivery. The workforce skills trainings needed for LAI-ART delivery were wide ranging and include technique of injection administration, identifying eligible PWH for LAI-ART and laboratory monitoring such as tracking viral load and timely identification of adverse drug reactions.

Perceived high cost of LAI-ART

Because of the novelty of the injectable treatment option, health workers perceived LAI-ART to be an expensive treatment option compared to oral HIV treatment. The costs of LAI-ART which were cited include the cost of the brand drug (cabotegravir and rilviprine) for which there are no generic options yet, the associated consumables such as needles, the procurement of appropriate bio-waste bins, the need for physical space such as private rooms for administering the injections.

> *'We have been able to provide LAI-ART due to generous support from the funder. We had funding for needles, freezers, the medication itself (LAI-ART), we have funds to send reminders to patients, we designated a special room for them for administering the injection. We were able to delivery this treatment option due to substantial funding from our sponsor under a clinical trial arrangement but in our normal operational context I am not sure how it would be to meet all the demand that is out there'[IDI, HCP_02].*

Outer setting

High demand for LAI-ART

Health workers recounted experiences of overwhelming demand from participants at the study site during the process of selection of participants to enroll in the LAI-ART clinical trial.

> *'That was the trickiest part of the study because everybody who would come, would really wish to be part of it. Some people would fast and pray so that the computer gives them the injection, so that was the trickiest part of it.' [IDI, HCP_01].*

Overall, PWH perceived being on LAI-ART as a privilege they cherished. They used descriptors such as 'precious', 'divine providence' and 'treasured' to describe how they considered themselves fortunate to have been selected to undergo the clinical trial. As a female participant intimated:

> *'For me I think it's the grace of God. You know it's God that chooses. For me to be selected among the hundreds at this hospital to receive the injectable, it is a blessing from up above', . [Female, 28, PWH, FPRH].*

Given the reported benefits of LAI-ART, PWH expressed their interest to remain on the treatment even after the end of the 12-month clinical trial phase.

Indeed, the health workers attested that that the majority of participants in the clinical trial requested to remain on LAI-ART even after the end of the 12-month trial since they experienced improved quality of life. Accordingly, the health workers confirmed that the manufacturer had granted the participants' request.

> *'They have reported good quality of life because they are adhering well. They aren't falling sick frequently,*

they are not getting opportunistic infections because they are taking their injection well and they are doing really well. Actually, the majority requested to remain on the injectable even beyond the trial period of 12 months. Fortunately, the manufacturer agreed to provide the injectable beyond the clinical trial' [IDI, HCP_06].

Discussion

This study was conducted to gain insight into the experiences of 32 individuals (out of a total of 69 participants) from the HIV care cohort which participated in a clinical trial involving long-acting antiretroviral therapy (LAI-ART) for 12 months at Fort Portal Regional Referral Hospital in mid-Western Uganda. There was high acceptability of LAI-ART and participants requested to remain on LAI-ART and were retained on this treatment even after the end of the 12-month trial. PWH perceived their adherence to ART to have improved when compared to their experiences under the oral treatment option. Participants reported that they had registered superior viral load suppression under LAI-ART. PWH credited LAI-ART with liberating them from the daily reminder of living with HIV, it enhanced privacy in HIV care and reduced HIV-related stigma associated with taking oral pills in the presence of family or co-workers as well as in carrying bulky medication refill packages.

On the other hand, pain around the injection site, a transient fever soon after administration of the injection were frequently cited as side effects. Previous studies have identified pain around the injection site as one of the side effects of LAI-ART [29–31]. A potentially new finding from our study is that PWH perceived the technic employed by the health worker in administering the injection as influential on whether they experienced pain around the injection site. It was reported that the pain is not experienced when the injection is delivered by particular health workers due to a perceived technique used. This warrants further research and may point to the need for training health workers in administering LAI-ART injections. The side effects reported in our study should be understood in the context of the extensive exclusion criteria for participants selected for the clinical trial (such as excluding those without disease in their kidney, liver, heart). It is plausible that with a broader patient population a wider range of side effects may be experienced hence further research is warranted [32].

Patient preferences

Overall, participants described a better satisfaction with LAI-ART when compared to the oral standard of care. Our focus groups appear to suggest a better quality of life under LAI-ART relative to daily oral pills. The notion that PWH perceive the LAI-ART treatment option results in a better quality of life when compared to oral treatment concurs with findings by Koester and colleagues in the United States [12].

In this study, PWH indicated a preference for longer intervals between injection appointments beyond the eight weeks under the clinical trial. A number of our participants called for a six-monthly interval between injections. Perhaps this is because in Uganda, less- intensive HIV care models known as 'differentiated service delivery' (DSD) models provide for multi-month dispensing of up to six months for stable patients [32]. This may, in part, reflect wishes by PWH for the novel LAI-ART option to align with DSD ethos of more patient-centred HIV care entailing reduced frequency of engagement with the formal health system [33, 34].

Health workers described extreme demand by PWH for the LAI-ART option and the opportunity to participate in the trial which was perceived as a precious opportunity to receive LAI-ART and the benefits that accrue from it such as improved adherence to ART, reduced treatment burden, less HIV-related stigma and relief from having to remember to swallow oral tablets on a daily basis. Our study contributes to the emerging evidence suggesting that LAI-ART improves adherence to ART and reduces HIV-related stigma [11–13].

Taken together, our study appears to suggest that demand for LAI-ART was high but supply-side bottlenecks may hinder wider access in LMICs in a prospective public health approach [35]. It is worth noting that participants in the clinical trial requested to remain, and were retained on LAI-ART even after the end of the 12-month trial.

In this study, missed appointments for receiving the bi-monthly injection were reported by PWH and were identified by health workers as an area necessitating interventions such as phone-based reminders. Missed appointments for the injection have been identified in previous studies as requiring attention [36, 37]. This is an area worthy of attention in potential scale-up planning and program design given accumulating evidence in this regard [12].

Health system readiness and implementation climate considerations

The health workers we interviewed indicated a myriad of implementation needs before LAI-ART can be scaled-up 'in HIV clinic contexts where resources are constrained' [12].

Firstly, providers perceived LAI-ART to be of high cost relative to oral treatment due to the resource in-puts required in routine service delivery in terms of the necessary consumables such as disposable needles, cold chain facilities for storing rilviprine, modifying physical spaces

within already congested facilities as rooms for administering the injections, retooling health workers in LAI-ART delivery and instituting monitoring systems such as reminders to PWH to attend their injection appointments [12]. From their perspective, extending this novel treatment to the wider population of PWH may be hindered by operational limitations. The backdrop was that the clinical trial received substantial funding by the sponsor and that the trial was implemented in 'vertical' fashion given that it was not fully embedded in the existing HIV treatment delivery systems at the study site. Hence based on their assessment, it may be practical for select sub-groups with sub-optimal adherence to get priority in potential scale up initiatives. Considering the perspectives of the trial personnel in our study around the perceived high cost of LAI-ART, we call for studies examining cost effectiveness in Uganda and other LMICs. Such studies can inform policy decision making by governments and major donors such as PEPFAR. Kityo and colleagues [11] have enumerated the potential implementation barriers to uptake of LAI-ART in LMICs. Kennedy and colleagues [13] have alluded to the potential health system constraints in low and middle income countries such as commodity stock-outs. A recent study in the United States by Koester and colleagues alludes to the need for reconfiguring routine HIV service delivery to enable uptake of LAI-ART such as the 'difficulty integrating long-acting antipsychotics into clinic flow' [12].

Providers identified health system barriers to roll-out such as the perceived high cost of LAI-ART, stringent cold chain requirements, physical space limitations, workforce skills gaps in LAI-ART delivery as a potential draw backs. Our findings add to the emerging evidence on health system barriers to LAI-ART roll out in low-income countries [4, 6, 11, 13] including in high-income countries such as the United states [2, 12]. There has been a discourse around pushing for generic versions of LAI-ART [38, 39]. However, studies suggest that LAI-ART may not be amenable to generic production due to 'complex manufacturing platforms' [11]. Individual-level barriers such as the likelihood of missing injection appointments and the need for reminders have been identified as potential implementation constraints [11].

In our in-depth interviews, health workers mentioned that prior to roll out of the clinical trial, that they were aware of potential drug-drug interactions between LAI-ART and some anti-tuberculosis medications and as such several prospective participants were excluded from participating in the trial. This notion presents limitations to the number of PWH who are eligible to access LAI-ART given the intersection between tuberculosis and HIV [1, 40].

Our study findings align well with previous qualitative studies which have reported high acceptability of LAI-ART by PWH particularly those from high-income settings [41–44]. Mantsios and colleagues [41] in findings that mirror those of our study found that women in the United States and Spain expressed relief at the daily burden of having to remember to take oral treatment and that LAI-ART is 'emotionally freeing and empowering'. These studies highlight the potential of LAI-ART in overcoming HIV-related stigma at the individual and community-levels [44]. In this study, PWH reported that LAI-ART has fewer side effects relative to their prior experience on dolutegravir (DTG)-based oral HIV treatment. Our study findings broadly align with previous ones that suggest that LAI-ART has a favourable adverse effect profile [45, 46] which enhances its appeal for roll-out and implementation in high-burden countries.

Recommendations

Considering the perceived high costs needed to deliver LAI-ART by providers despite the extreme demand by PWH, cost-effectiveness studies in low-income settings are warranted. In a related recommendation, we call for systematic criteria for selecting sub-populations of PWH to access LAI-ART particularly in high-burden but resource-limited settings such as Uganda. Engaging leading funders of HIV programs in Eastern and Southern Africa such as PEPFAR in supporting pilot LAI-ART scale-up initiatives for priority sub-populations is worthwhile given their influence in setting HIV policy [47, 48].

In this study, we found that missed appointments for injections by PWH were not uncommon. Our study underscores the importance of innovations around sending reminders to PWH to report for their injection appointments. There is an emerging implementation science around phone-based reminders for improving adherence to treatment which may have value in LAI-ART roll-outs in settings such as Uganda and beyond [49, 50].

In this study we found that the two most frequently mentioned side effects were pain around the injection site and a transient fever soon after the injection was administered. More research is warranted around medication safety in a broader range of PWH in Eastern and Southern Africa considering that in this clinical trial only those without evidence of disease in their vital organs were enrolled [51, 52].

Study limitations

Our study had multiple limitations. Our small sample size and the extensive exclusion criteria for participating in the LAI-ART clinical trial limits the extent of generalizability of our study findings to the general population of recipients of HIV care in Uganda. One of the strengths of this study is that it reports actual experiences of recipients of HIV care who received this novel treatment

option for at least 12 months unlike many studies reporting the perspectives of potential users.

Conclusion

Overall, PWH indicated a strong preference for LAI-ART and expressed a comparatively higher satisfaction with this treatment option. Health system barriers to potential scale-up are important to consider if a wider population of PWH are to benefit from this novel treatment option in Uganda and other resource-limited settings.

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ADRs	Adverse Drug Reactions
ART	Anti-retroviral therapy
ARVs	Anti-retrovirals
DTG	Dolutegravir
LAI-ART	Long Acting Injectable Antiretroviral Treatment
MOH	Ministry of Health
PEPFAR	The Presidents' Emergency Plan for AIDS Relief
PLHIV	People Living with HIV
SSA	sub-Saharan Africa
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-09748-5.

Supplementary Material 1

Acknowledgements

We gratefully acknowledge the Joint Clinical Research Centre (JCRC) which led implementation of this clinical trial at Fort Portal Regional Referral Hospital in Mid-Western Uganda.

Author contributions

HZ conceptualized the study, collected the data, analyzed the data and produced the initial manuscript draft. AA, MK and BN contributed to data analysis and provided comments on the draft manuscript. All authors approved the final manuscript.

Funding

This paper was written under the auspices of a post-doctoral research grant managed by the Consortium for Advanced Research Training in Africa (CARTA/2020/354.707 A).

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available due to ethical reasons but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The clinical trial underpinning this study received formal ethical approval from a local Institutional Review Board (IRB) at Joint Clinical Research Centre in Kampala, Uganda and permission to conduct the clinical trial was secured from the Uganda National Council of Science and Technology. The clinical trial reported here is registered with the National Drug Authority (NDA) of Uganda. Study participants were approached individually at the study site and informed of the present study's objectives and invited to participate voluntarily with indication that it was their prerogative to withdraw at any time. Each of the participants who agreed to participate in the study signed a written informed consent. The study was guided by the treaty of Helsinki regarding human subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]School of Public Health, Makerere University College of Health Sciences, Kampala, Uganda
[2]Joint Clinical Research Centre, Fort Portal Regional Centre of Excellence, Fort Portal, Uganda
[3]College of Humanities and Social Sciences, Makerere University, Kampala, Uganda
[4]ART Clinic, Fort Portal Regional Referral Hospital, Fort Portal, Uganda
[5]Uganda Ministry of Science, Technology and Innovation, Republic of Uganda, Kampala, Uganda

Received: 11 March 2024 / Accepted: 12 August 2024
Published online: 28 August 2024

References

1. Phillips AN, Bansi-Matharu L, Cambiano V, Ehrenkranz P, Serenata C, Venter F, Pett S, Flexner C, Jahn A, Revill P, Garnett GP. The potential role of long-acting injectable cabotegravir–rilpivirine in the treatment of HIV in sub-saharan Africa: a modelling analysis. Lancet Global Health. 2021;9(5):e620–7.
2. Kanazawa JT, Saberi P, Sauceda JA, Dubé K. The LAIs are coming! Implementation science considerations for long-acting injectable antiretroviral therapy in the United States: a scoping review. AIDS Res Hum Retroviruses. 2021;37(2):75–88.
3. Izudi J, Cattamanchi A, Castelnuovo B, King R. Barriers and facilitators to viral load suppression among people living with HIV following intensive adherence counseling in Kampala, Uganda: a qualitative study. Soc Sci Med. 2024;343:116595.
4. UNAIDS. 2022. Delays in global, affordable access to long-acting, injectable HIV medicines would cost lives, say AIDS campaigners.https://www.unaids.org/en/resources/presscentre/featurestories/2022/november/20221116_long-acting-injectable-HIV-medicines
5. Dawood H. The optimum implementation of long-acting injectable cabotegravir–rilpivirine in sub-saharan Africa. Lancet Global Health. 2021;9(5):e563–4.
6. Norcross C, Ombajo LA, Kassim S, Garrett N, Cresswell FV, Ruzagira E. Long-acting antiretrovirals: research and implementation considerations in Africa. Lancet HIV. 2023;10(7):e428–9.
7. Carillon S, Laborde-Balen G, Diop M, Diop K, Breton G, Ndiaye B, Taverne B. Implementing long-acting injectable antiretroviral treatments in Senegal: issues, challenges and conditions for introducing them. Qualitative study with healthcare providers and patients. AIDS care 2023 Sep 8:1–7.
8. Zakumumpa H, Bennett S, Ssengooba F. Alternative financing mechanisms for ART programs in health facilities in Uganda: a mixed-methods approach. BMC Health Serv Res. 2017;17:1–1.
9. VOA. Uganda approves injectable HIV drug amid increasing infections. https://www.voaafrica.com/a/uganda-approves-injectable-hiv-drug-amid-increasing-infections-/6893766.html
10. Slama L, Porcher R, Linard F, et al. Injectable long acting antiretroviral for HIV treatment and prevention: perspectives of potential users. BMC Infect Dis. 2023;23:98. https://doi.org/10.1186/s12879-023-08071-9.
11. Kityo C, Cortes CP, Phanuphak N, Grinsztejn B, Venter F. Barriers to uptake of long-acting antiretroviral products for treatment and prevention of HIV in low-and middle-income countries (LMICs). Clin Infect Dis. 2022;75(Supplement4):S549–56.
12. Koester KA, Colasanti JA, McNulty MC, Dance K, Erguera XA, Tsuzuki MD, Johnson MO, Sauceda JA, Montgomery E, Schneider J, Christopoulos KA. Assessing readiness to implement long-acting injectable HIV antiretroviral therapy: provider and staff perspectives. Implement Sci Commun. 2023;4(1):128.
13. Kennedy CE, Zhao T, Vo AV, Nakubulwa R, Nabakka P, Jackson J, Rosen JG, Chang LW, Reynolds SJ, Quinn TC, Nakigozi G. High acceptability and Perceived Feasibility of Long-Acting Injectable Antiretroviral Treatment among people living with HIV Who Are Viremic and Health Workers in Uganda. AIDS Patient Care STDs. 2023;37(6):316–22.

14. Hunter D, McCallum J, Howes D. Defining exploratory-descriptive qualitative (EDQ) research and considering its application to healthcare. J Nurs Health Care. 2019;4(1).
15. Ottmann G, Crosbie J. Mixed method approaches in open-ended, qualitative, exploratory research involving people with intellectual disabilities: a comparative methods study. J Intellect Disabil. 2013;17(3):182–97.
16. Ivanova O, Cordova-Pozo K, Segura ZE, Vega B, Chandra-Mouli V, Hindin MJ, Temmerman M, Decat P, De Meyer S, Michielsen K. Lessons learnt from the CERCA Project, a multicomponent intervention to promote adolescent sexual and reproductive health in three Latin America countries: a qualitative post-hoc evaluation. Eval Program Plan. 2016;58:98–105.
17. Joint Clinical Research Centre (JCRC). CARES Clinical Trial Newsletter: https://jcrc.org.ug/wp-content/uploads/2022/02/CARES-newsletter-Final.pdf
18. Joint Clinical Research Centre (JCRC). JCRC Bulletin 2021 https://jcrc.org.ug/wp-content/uploads/2022/01/JCRC-Bulletin-2021-1.pdf
19. Joint Clinical Research Centre (JCRC). CARES Clinical Trial: https://jcrccares.org.ug/
20. National Drug Authority. Clinical Trials Register: https://www.nda.or.ug/clinical-trials/
21. Damschroder LJ, Reardon CM, Widerquist MA, Lowery J. The updated Consolidated Framework for Implementation Research based on user feedback. Implement Sci. 2022;17(1):1–6.
22. Ouma J, Jeffery C, Valadez JJ, Wanyenze RK, Todd J, Levin J. Combining national survey with facility-based HIV testing data to obtain more accurate estimate of HIV prevalence in districts in Uganda. BMC Public Health. 2020;20:1–4.
23. Zakumumpa H, Rujumba J, Kwiringira J, Kiplagat J, Namulema E, Muganzi A. Understanding the persistence of vertical (stand-alone) HIV clinics in the health system in Uganda: a qualitative synthesis of patient and provider perspectives. BMC Health Serv Res. 2018;18:1–3.
24. Zakumumpa H, Kitutu FE, Ndagije HB, Diana NK, Ssanyu JN, Kiguba R. Provider perspectives on the acceptability and tolerability of dolutegravir-based anti-retroviral therapy after national roll-out in Uganda: a qualitative study. BMC Infect Dis. 2021;21:1–3.
25. Zakumumpa H, Kiguba R, Ndagije HB, Ategeka G, Ssanyu JN, Kitutu FE. Patient experiences of sexual dysfunction after transition to dolutegravir-based HIV treatment in mid-western Uganda: a qualitative study. BMC Infect Dis. 2022;22(1):1–1.
26. Miles MB, Huberman AM. Qualitative data analysis: An expanded sourcebook. sage; 1994 Jan 12.
27. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol. 2013;13(1):1–8.
28. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: a hybrid approach of inductive and deductive coding and theme development. Int J Qualitative Methods. 2006;5(1):80–92.
29. Ivankova NV, Creswell JW, Stick SL. Using mixed-methods sequential explanatory design: from theory to practice. Field Methods. 2006;18(1):3–20.
30. Philbin MM, Parish CL, Kinnard EN, Reed SE, Kerrigan D, Alcaide ML, Cohen MH, Sosanya O, Sheth AN, Adimora AA, Cocohoba J. Multisite study of women living with HIV's perceived barriers to, and interest in, long-acting injectable antiretroviral therapy. JAIDS J Acquir Immune Defic Syndr. 2020;84(3):263–70.
31. Simoni JM, Beima-Sofie K, Wanje G, Mohamed ZH, Tapia K, McClelland RS, Ho RJ, Collier AC, Graham SM. Lighten this burden of ours: acceptability and preferences regarding injectable antiretroviral treatment among adults and youth living with HIV in coastal Kenya. J Int Association Providers AIDS Care (JIAPAC). 2021;20:23259582211000517.
32. Zakumumpa H, Rujumba J, Kwiringira J, Katureebe C, Spicer N. Understanding implementation barriers in the national scale-up of differentiated ART delivery in Uganda. BMC Health Serv Res. 2020;20(1):1–6.
33. Zakumumpa H, Makobu K, Ntawiha W, Maniple E. A mixed-methods evaluation of the uptake of novel differentiated ART delivery models in a national sample of health facilities in Uganda. PLoS ONE. 2021;16(7):e0254214.
34. Zakumumpa H, Tumwine C, Milliam K, Spicer N. Dispensing antiretrovirals during Covid-19 lockdown: re-discovering community-based ART delivery models in Uganda. BMC Health Serv Res. 2021;21(1):1–1.
35. Gilks CF, Crowley S, Ekpini R, Gove S, Perriens J, Souteyrand Y, Sutherland D, Vitoria M, Guerma T, De Cock K. The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings. Lancet. 2006;368(9534):505–10.
36. Kilcrease C, Yusuf H, Park J, Powell A, Rn LJ, Rn JO, Lmsw BD, Weld ED, Dooley KE, Arrington-Sanders R, Agwu AL. Realizing the promise of long-acting antiretroviral treatment strategies for individuals with HIV and adherence challenges: an illustrative case series. AIDS Res Therapy. 2022;19(1):56.
37. Simoni JM, Beima-Sofie K, Mohamed ZH, Christodoulou J, Tapia K, Graham SM, Ho R, Collier AC. Long-acting injectable antiretroviral treatment acceptability and preferences: a qualitative study among US providers, adults living with HIV, and parents of youth living with HIV. AIDS Patient Care STDs. 2019;33(3):104–11.
38. Brown Ripin DH, Catlin K, Lewis L, Resar D, Amole C, Bollinger RC, Flexner C. Transitioning long-acting products to a generic Marketplace: what's missing? Clin Infect Dis. 2022;75(Supplement4):S557–61.
39. Jenkins SY, Resar D, Panos Z, Staple A, Watkins M, Ripin D, Amole C. Securing accelerated access to long-acting injectable cabotegravir for HIV prevention in low-and middle-income countries. J Int AIDS Soc. 2023;26:e26101.
40. Cresswell FV, Lamorde M. Implementation of long-acting antiretroviral therapy in low-income and middle-income countries. Curr Opin HIV AIDS. 2022;17(3):127–34.
41. Mantsios A, Murray M, Karver TS, Davis W, Margolis D, Kumar P, Swindells S, Bredeek UF, Deltoro MG, García RR, Antela A. I feel empowered: women's perspectives on and experiences with long-acting injectable antiretroviral therapy in the USA and Spain. Cult Health Sex. 2021;23(8):1066–78.
42. Fletcher L, Burrowes SA, Khan GK, Sabin L, Johnson S, Kimmel SD, Ruiz-Mercado G, Pierre C, Drainoni ML. Perspectives on long-acting injectable HIV antiretroviral therapy at an alternative care site: a qualitative study of people with HIV experiencing substance use and/or housing instability. Harm Reduct J. 2023;20(1):4.
43. Collins AB, Macon EC, Langdon K, Joseph R, Thomas A, Dogon C, Beckwith CG. Perceptions of long-acting injectable antiretroviral therapy among people living with HIV who use drugs and service providers: a qualitative analysis in Rhode Island. J Urb Health. 2023;100(5):1062–73.
44. Erguera XA, Koester KA, Diaz Tsuzuki M, Dance KV, Flores R, Kerman J, McNulty MC, Colasanti JA, Collins LF, Montgomery ET, Johnson MO. Acceptability of Long-Acting Injectable antiretroviral therapy among people with HIV receiving care at three Ryan White Funded clinics in the United States. AIDS Behav 2024 Apr 10:1–3.
45. Durham SH, Chahine EB. Cabotegravir-rilpivirine: the first complete long-acting injectable regimen for the treatment of HIV-1 infection. Ann Pharmacother. 2021;55(11):1397–409.
46. Kim YS. Long-acting injectable antiretroviral agents for HIV treatment and prevention. Infect Chemother. 2021;53(4):686.
47. Mehra N, Tunje A, Hallström IK, Jerene D. Effectiveness of mobile phone text message reminder interventions to improve adherence to antiretroviral therapy among adolescents living with HIV: a systematic review and meta-analysis. PLoS ONE. 2021;16(7):e0254890.
48. Demena BA, Artavia-Mora L, Ouedraogo D, Thiombiano BA, Wagner N. A systematic review of mobile phone interventions (SMS/IVR/calls) to improve adherence and retention to antiretroviral treatment in low-and middle-income countries. AIDS Patient Care STDs. 2020;34(2):59–71.
49. Zakumumpa H, Paina L, Ssegujja E, Shroff ZC, Namakula J, Ssengooba F. The impact of shifts in PEPFAR funding policy on HIV services in Eastern Uganda (2015–21). Health Policy Plann. 2024;39(Supplement1):i21–32.
50. Zakumumpa H, Paina L, Wilhelm J, Ssengooba F, Ssegujja E, Mukuru M, Bennett S. The impact of loss of PEPFAR support on HIV services at health facilities in low-burden districts in Uganda. BMC Health Serv Res. 2021;21:1–2.
51. Steulet A, Obura B, Waitt C, Laker E, Nicol MR, Cresswell FV. Clinical pharmacology considerations and drug–drug interactions with long-acting cabotegravir and rilpivirine relevant to sub-Saharan Africa. Br J Clin Pharmacol. 2024 Mar 25.
52. Rana AI, Castillo-Mancilla JR, Tashima KT, Landovitz RL. Advances in long-acting agents for the treatment of HIV infection. Drugs. 2020;80(6):535–45.

Publisher's Note