

# 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

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## Abstract

To better understand acceptability of long-acting injectable antiretroviral treatment (LAI-ART) regimens for HIV management, we conducted seven semi-structured focus group discussions with experienced HIV care providers and persons living with HIV (PLWH) and five individual interviews with parents of children living with HIV in the western United States. Although providers were wary about a potential negative impact on consistent engagement in care, they predicted that patients, especially those with adherence challenges, would be enthusiastic about LAI options. Many PLWH, especially young adults, welcomed the option of an LAI-ART regimen; however, others feared injections and expressed concerns about possible side effects, dosing more frequent than every 2 weeks, additional costs, and lower efficacy. Parents' interest varied according to their child's age and sensitivity to injections. In summary, potential users considered LAI-ART generally acceptable yet voiced possible concerns as well, especially if their current pill-based regimen was effective in achieving viral suppression.

**Keywords:** long-acting injectable ART, acceptability, HIV/AIDS, qualitative

## Introduction

THE DEVELOPMENT OF oral combination antiretroviral therapy (ART) regimens has been transformative for HIV treatment, delaying disease progression and enhancing longevity.<sup>1,2</sup> However, limitations of current regimens include the need for lifelong adherence to daily pill dosing, which may be a considerable challenge for important subsets of persons living with HIV (PLWHA), including adolescents and those with depression or substance use disorders.<sup>3,4</sup> Moreover, oral regimens have the potential for interactions that can decrease absorption in the gastrointestinal tract. Specifically, drugs such as proton pump inhibitors and topical antacids that modify gastric acidity or can bind other agents due to ion interactions can negatively affect absorption of several antiretroviral agents.<sup>5</sup> In addition, persons who cannot take medications by mouth, including those who are critically ill or undergoing surgery, have limited or no ef-

fective antiretroviral options. Long-acting injectable ART (LAI-ART) formulations could overcome these challenges. Moreover, LAI-ART that achieves high levels in tissue reservoirs could potentially have increased efficacy compared with oral regimens.

Multiple LAI-ART strategies are under investigation.<sup>6</sup> The most advanced LAI regimen in development is a two-drug combination of an integrase inhibitor [cabotegravir (CAB)] and a non-nucleoside reverse transcriptase inhibitor [rilpivirine (RILP)], administered as separate injections. A phase II study documented the regimen's effectiveness and tolerability,<sup>7</sup> and phase III studies are underway.

Patient acceptance of LAI-ART for treatment is critical to its success, yet scant research has addressed this important area.<sup>8-10</sup> Most empirical reports of LAI-ART focus on the pharmacology of drugs in development,<sup>11-13</sup> rather than patient perspectives. Other publications are opinion based but lack any supporting data from patients.<sup>10,14</sup> Patient

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preferences will likely affect future interest in and success with long-acting combination formulations and may be useful in guiding their development.

The objective of the current study was to assess potential acceptability and elicit preferences among potential end users for characteristics of a proposed LAI-ART treatment regimen as part of a planned conjoint analysis.

## Methods

### Setting

Research was conducted between June 2016 and June 2017. HIV care providers and adult PLWH were recruited at an HIV clinic at Harborview Medical Center in Seattle; parents of children with HIV were recruited from Seattle Children's Hospital in Seattle; and young adults with HIV were recruited from a primary care clinic in rural Southern California (Riverside Neighborhood Health Clinic). The study received approval from the University of Washington, Seattle Children's Hospital, and University of California, Los Angeles Institutional Review Boards. All participants provided written informed consent.

### Recruitment and data collection

Clinic personnel recruited participants, briefly described the study, and referred interested individuals to study staff for screening and scheduling. Participants were selected purposefully to achieve a diverse population of potential end users of LAI-ART. Eligibility criteria included being  $\geq 18$  years of age and English speaking. Participants completed a brief demographic questionnaire and received a gift card (\$35) and transportation reimbursement for participating. A facilitator conducted one focus group discussion (FGD) with HIV care providers ( $n=7$ ) and one FGD with each of the following populations of PLWH: heterosexual men ( $n=8$ ), men who have sex with men (MSM,  $n=8$ ), women ( $n=9$ ), and individuals who had struggled with adherence ( $n=4$ ). The facilitator led two FGDs with young adults ( $n=2$ ,  $n=4$ ). Scheduling conflicts and geographic dispersion from the clinic precluded the originally planned FGD for parents of children with HIV. Instead, parents ( $n=5$ ) participated in in-depth interviews (IDIs) via telephone.

FGDs were conducted in private conference rooms by a trained behavioral scientist with content area expertise (J.M.S.), who was not involved in providing clinical care to participants. A research assistant (Z.H.M.) took detailed notes during the FGDs. IDIs with parents were conducted by telephone by J.M.S. or Z.H.M. Interviews lasted  $\sim 30$  min, while FGDs lasted  $\sim 90$  min. Both FGDs and IDIs were digitally recorded with permission and transcribed verbatim.

Semistructured FGDs and IDI guides were developed based on literature reviews and interviews with experts in HIV care provision and related research. After sharing their experiences of current pill-based regimens, participants were asked to provide their initial reactions to the idea of a "new HIV regimen or treatment that does not have to be taken daily and will be given by injection." Initially, no further description was provided. Next, participants were asked to discuss specific attributes of such a regimen, such as where it had to be administered (clinic vs. home), how painful the injection was (mild vs. moderate), the site of injection

(abdomen vs. thigh), severity of site reactions (mild vs. moderate), number and volume of injections per dose, dosing frequency (such as every week or every other week), effectiveness (same vs. better than current regimens), and side effects (same vs. fewer than current regimens). Beyond these queries, no details about specific products in development were provided. Interviewers facilitated discussions of these product attributes, including barriers to use. They also probed for other influential attributes. Finally, facilitators elicited "deal breakers" or attributes that would render LAI-ART regimens completely unacceptable.

### Participants

A description of the participants is provided in Table 1. The seven providers comprised a physician, physician assistant, nurse, social worker, case manager, and two medical assistants, who, on average, had been providing HIV care for 16 years (range, 4–30). Among the 36 PLWH, all of whom were ART experienced, 1 was diagnosed within the last year, 8 within 2–5 years, 5 within 6–10 years, and 22 more than 10 years ago. Six lived in someone else's house or apartment and another eight reported an unstable living situation. Monthly income was less than \$1000 for 69%, and 77% were not working. The six young adults ranged in age from 20 to 26. The children with HIV to whom parents referred averaged 10 years of age (range, 8–12).

### Data analysis

We performed a directed content analysis to identify factors most strongly influencing LAI-ART regimen preferences and overall acceptability.<sup>15</sup> Dedoose v.7.5.10 software was used to support coding, analysis, and data management. A codebook was created deductively based on the domains probed in the discussion guide and inductively based on open-ended responses about general acceptability of injectable medication scenarios and personal experiences with ART and HIV. Each transcript was coded independently by J.M.S., Z.H.M., or K.B.-S., using an agreed-upon final version of the codebook. To increase reliability, investigators swapped transcripts and reviewed already coded transcripts to ensure code application consistency and accuracy. Following coding and coding review, emergent themes and key concepts were identified and compared within and between the providers, subgroups of PLWH, and parents.

## Results

The findings are reported below in terms of the main themes that emerged, with reference to any difference by demographic subgroup (i.e., PLWH, young adults with HIV, providers, and parents). Themes included participants' first reactions to the prospect of an injectable HIV treatment, which varied considerably and were subject to some qualifications. The key attributes consistently mentioned were the importance of the injectable option being at least as effective in suppressing viral load as pill-based regimens and having minimal side effects. Fear of needles and dislike of injections were other important themes, but the ensuing discussions revealed these could be mitigated by other considerations—such as preferred bodily site of injection, needle size, quantity of medication, and number of injections per dose, as well as

TABLE 1. DESCRIPTION OF PARTICIPANTS

Characteristics	Providers (n=7)	PLWH (n=36)	Parents of HIV+ children (n=5)
	Median (range) or n (%)		
Female	5 (71)	11 (31)	3 (60)
Age in years	56 (28–65)	52 (20–64)	35 (33–58)
Self-reported race			
Black/African American	0 (0)	18 (50)	0 (0)
White	6 (86)	9 (25)	5 (100)
Other/mixed/none of the above	1 (14)	9 (25)	0 (0)
Hispanic/Latino/Chicano	1 (14)	4 (11)	0 (0)
US born	6 (86)	34 (94)	5 (100)
Highest level of education			
Primary (1–8 years)	0 (0)	1 (3)	0 (0)
Secondary (9–11 years)	0 (0)	9 (25)	0 (0)
High school graduate/GED	0 (0)	18 (50)	0 (0)
Associates/technical school	2 (29)	6 (17)	2 (40)
College (BA/BS)	1 (14)	2 (6)	2 (40)
Advanced degree	4 (57)	0 (0)	1 (20)

GED, general education diploma; PLWH, persons living with HIV.

the location of the injection—either at home or in the clinic. Certain subgroups seemed more receptive to LAI-ART, including young people and those experiencing adherence challenges. Finally, the “deal breakers” discussed at the closing of each FGD confirmed expressed barriers, including number of injections per dose, any associated cost, and frequency of required injections.

#### Mixed initial reactions

Many initial reactions of participants were supportive of an LAI-ART regimen, especially if it met certain perimeters. For example, one woman with HIV responded, “It would be a great idea if I only had to do it once a week or once a month.” The young adults were particularly receptive. One young man expressed relief, assuming the injectable option would be superior:

“My first reaction is like [a] big sigh, like it’s a relief because for a fact they are saying that there is an injection. That’s better than a pill and we’re being told as all HIV patients, ‘hey, this pill is gonna be what is going to help you to a normal life, like outlive me.’ So, for them to say this pill is the next phenomenal thing, if the injection is that much more better I mean of course hey I’m all game for it. [It’s] gonna save my life.”  
—Young Adult MSM PLWH

One young man talked about not having to fear others’ questioning his daily pill taking. Another alluded to the freedom and normalcy the lack of a daily pill-based regimen might incur:

“Well, I think the main question is what they told you with the pill, if I am going to be able to live a normal life and be able to do things that I do on a daily basis without repercussions toward it. If I am going to be able to go out and not have to worry about collapsing or being able to enjoy my life and if that questions is answered with a yes then I’m all on board for it.”  
—Young Adult MSW PLWH

Providers felt that most PLWH would be enthusiastic and noted how LAI-ART could improve adherence by removing the constant daily reminder of being HIV positive:

“[U]niversally, patients are enthusiastic about this. ... from 1997, patients have said the same thing, ‘I don’t want to take a pill every day because it reminds me every day.’ This would really be welcomed.”—Provider

Some parents initially reacted very positively to the prospect of an injectable option, especially if their children were already regularly receiving injections.

“That sounds great to me. [My son], like I said, is on some arthritis meds and one of those is methotrexate which he gets sub-q once a week, and so he’s already used to that. That’s kind of built into our weekly routine. That seems to have worked well for him and he hasn’t responded negatively.”  
Parent

However, initial reactions varied by group and grew more nuanced as specific attributes were considered. Some PLWH were generally less enthusiastic, especially those whose pill taking had long become integrated into their daily routine. Some adult PLWH acknowledged that they might have been more open to an LAI-ART regimen when they had initiated therapy. Since most participants had a well-established and effective daily routine associated with pill taking that in some instances had taken years to achieve, they were resistant to the idea of switching to something new and wondered whether a longer dosing interval might render adherence more challenging. In addition, some PLWH mentioned that switching to LAI-ART would not do much to relieve their daily pill burden, since they also took medications for other chronic conditions, limiting the potential benefit of switching to an LAI-ART regimen.

“It wouldn’t bother me but I have so many other pills to take that I still end up taking pills everyday so I can take it or leave it.”—Female PLWH

For some parents, the developmental stage of the child was paramount in shaping their initial reactions to an injectable treatment. For example, one father initially responded, “That would be really hard for us. We would opt to stay with the pills,” largely due to the young age of his son and his difficulty with blood draws. However, after reflecting on how his

son will 1 day need to take responsibility for his own treatment, he changed his mind:

“My greatest fears for him is when he finally does tell us no or has to take responsibility for taking his pills by himself. I have great fear that that is going to be a hugely difficult for him and so, as he gets older, I would and I think my wife would agree we would certainly consider, not forcing him, but highly encouraging him to do anything he could to make sure he got what he needs to stay healthy. Even though it’s a little bit uncomfortable, it makes us a little nervous, it might be that might be the best option for him. For that reason, I’d say we would be very interested in an injectable.”—Parent

Another father was even more enthusiastic in terms of his son:

“I would be all for it, especially as he grows older and it can be delivered by the clinic. I say absolutely, you know, as he matures and becomes his own man, I would highly highly, encourage him to take the injection.”—Parent

#### *Key factors: efficacy and side effects*

Two of the most consistently and forcefully voiced factors influencing LAI acceptability were efficacy and side effects. PLWH, especially those with long-term viral suppression, raised concerns about efficacy and were adamant that an injectable medication would have to be at least as effective as their current oral regimen for them to accept it as an alternative.

“I would have to make sure these medications would be better for me than the ones I’m already taking, because the ones I’m already taking are working perfectly ... I’ll just say, ‘If it ain’t broken, don’t try to fix it.’”—Heterosexual Male PLWH  
P1: “I think the most important thing would be the effectiveness.” P2: “If it works, I’ll come in.” P3: “I’ll do it if it works”—Heterosexual Male PLWH FGD

Providers also were concerned about efficacy, noting the need to compare LAI regimens to currently available oral regimens before prescribing them. Parents concurred.

“The pills work well and (my daughter’s) viral load is undetectable and has been, so if that would change with the injections I wouldn’t switch.”—Parent

Although they mentioned side effects less frequently than efficacy, PLWH were consistent and vociferous in their rejection of any injectable alternative that might cause side effects. This was true for those who had struggled with side effects such as dizziness, nausea, diarrhea, fatigue, headaches, joint aches, and nightmares, as well as for those who had never experienced side effects.

P1: “I used to when I first started taking it and now I don’t have any side effects.” P2: “I take more pills than the HIV meds just because of all the side effects I got from the meds for the HIV.” P3: “You’d have to give me something that don’t have no side effects.”—Female PLWH FGD

Parents were concerned about side effects as well, noting that side effects would make initiating a new treatment difficult.

“It just depends on how tolerable. You know, whenever you start anything new, if it’s really bad then you’re not real motivated to do it again if the side effects are horrible.”—Parent

“We would have to judge. ... is it going to further reduce his appetite? That might be a deal breaker for us because it is so hard to get him to eat and it’s so hard to get him to keep weight up.”—Parent

Importantly, participants described implicit trust in their providers when deciding which medication scenario would be most effective for them. This trust was validated by providers’ insistence that they would not prescribe an injectable not deemed optimal treatment for a given patient.

“If the injectable is not the best therapeutic, least side effect drug. ... if it’s something that’s two years behind because it has been in development, that’s a huge deal breaker.”—Provider

#### *Fear of needles and mitigating factors*

Some PLWH, especially those who had learned to give or take injections for other medical conditions or related to recreational drug use, were not wary of injections and valued the idea of a periodic injection over daily medication. However, this was rare. A significant fear of needles, and specifically fear of injections, was common and decreased the acceptability of injectable treatment options for some. For many parents, their child’s fear of needles and the disruption of family or work routine associated with clinic visits to receive the injection weighed heavily in their negative evaluations of LAI-ART. Parents spoke of negative experiences with injections that predisposed them against an injectable treatment option.

“She does get an injection that is. ... a large needle, and it’s a large amount of medicine so it stays in for several seconds and it’s slow and it takes a long time. ... We do that every three months and she dreads it. ... So if it was adding one like that, I don’t think she would be willing to. I don’t think that the benefit would outweigh the not having to take pills every day at that point.”—Parent

“He’s from Africa and his monthly or quarterly blood draws were traumatic enough. Because he was an orphan, he went to a hospital that served the underserved, called the police hospital, and a lot of force was used. We are just now getting to the point where he will allow us to draw blood without fighting. But shots, blood draws, anything with a needle for him is extremely traumatic. It causes him to just absolutely freak out, so I would say with utmost certainty we would choose to stick with an oral medication, whether it was liquid or pill doesn’t matter, but we would not choose an injectable.”—Parent

For many adult PLWH, just mentioning that the regimen would involve injections resulted in strong, immediate negative reactions.

P1: “No, I don’t like needles.”; P2: “I’m scared of needles.”; P3: “I hate shots.”; P4: “Anything with needles, I don’t want to do it.”—Female PLWH FGD

Although former injection drug users were less afraid of pain from needles, some feared that the injectable medication might serve as a trigger to relapse or would otherwise be unwelcome:

“If you have a friend who has had a drug problem or is recovering from it and if they did have HIV themselves, I think that would really bother them and kind of scare them into wanting to do that because it might remind them of what they

did in the past and make them want to do that again.”—Young Male PLWH  
 “... because they are used to getting some benefit from having a needle in their arm and if they are not getting a benefit and it’s just pain, they hate it.”—Heterosexual Male PLWH

Some participants discussed ways they might mitigate the dislike and fear of injections. For example, among those who were uncomfortable with injections and wary of pain, a lower dose volume and smaller gauge needle were seen as ways to lessen their aversion. Also, for many participants, the bodily site for the injection modulated their acceptance. Generally, PLWH preferred injections in the arm or thigh over the abdomen or buttocks.

P1: “Well, I tell you right now you ain’t shooting my stomach. No!” P2: “As far as my stomach concerned we know that’s a no no.” P3: “Not gonna be my stomach.”—Female PLWH FGD

For adolescents, the preferred injection site depended on potential site reactions and their impact on physical appearance. Rashes or bruising at or around easily visible injection sites were not acceptable.

“I’m kinda sort of big on my appearance. ... (so) you don’t (want to) have to worry about a big red rash or if someone is looking at you like, ‘Oohh, what is that about?’”—Young Adult MSM PLWH  
 “My legs are my best feature so I wouldn’t want like bruising or anything on them.”—Young Adult MSM PLWH

Preferences for injection site often depended on self-administration versus clinic administration as well as the frequency and number of injections. Participants with some experience self-injecting were more confident they could administer the injections where necessary. If a monthly injection or just one injection per dose were required, PLWH would accept less desirable bodily injection sites. Providers pointed out that thigh and abdomen injections are easier for someone to self-administer, and that autoinjectors might be solutions that would make self-injection an easier and more acceptable option.

“[A]n auto-injector would take away the stress of it. The dosing? Just push the button and it is done. And also you don’t have to worry about needle sticks afterwards because it retracts.”—Provider

While some participants, especially those with busy schedules, preferred the convenience of home-based injections, the majority preferred administration at the clinic to avoid self-administration. PLWH in the women’s group preferred the clinic because they were often there for other medical reasons anyway, it was not inconvenient to come in, and they preferred not to have syringes in the home. The young adults noted the advantages of a clinic administration because of the professional care involved and privacy entailed. Parents, who generally lived much farther from the clinic, were concerned about the time that would be involved with clinic-administered injections.

“I would say we would feel comfortable giving it to him at home. We live in a small town about 2.5 hours from the hospital and that would be kind of a burden for us, but obviously we would do it if that was the only option but I think we

would prefer to be able to do it. At home would be the best way.”—Parent

PLWH were also open to the idea of going to a local pharmacy for injections (except for those in very small communities) or having a home visit (many currently get their medications delivered to their home). For some PLWH, dispensing location preferences depended on the dosing frequency.

“If it was a weekly thing, I would much prefer to do it at home, but if it was a monthly thing, I wouldn’t mind going to the clinic.”—Heterosexual Male PLWH

Providers were concerned that some PLWH with unstable living conditions could not properly store the medication or would not reliably adhere, making self-injection unfeasible.

#### *Potentially receptive subgroups*

Despite concerns from many PLWH, young adult PLWH and adult PLWH struggling to maintain adequate adherence felt that within the appropriate set of parameters, LAI-ART could be beneficial and an acceptable alternative to oral regimens. This was true for some even if it involved frequent injections:

“So it’s like taking that pill everyday versus taking a shot once a week? That once a week is definitely gonna win,”  
 —Young Adult Male PLWH

In addition, some parents viewed LAI-ART favorably because of the difficulty of administering daily doses to their children and the greater privacy and normalcy injections might confer over pills.

“I think it would be fabulous not to have to do medicine every day. ... we choose not to disclose so it really is hard when he wants to go like have a sleep over at a friend’s house and I have to send him with a baggy of medicine.”—Parent

Providers and PLWH identified specific populations, such as homeless persons or injection drug users, who might benefit from an injectable alternative to pills.

“If you was homeless and they said oh we can give it to you in a shot, I don’t have to worry about my pill bottles or going to pick up my meds then I would be okay let’s do it”  
 —Heterosexual Male PLWH

#### *Deal breakers*

With respect to “deal breakers” identified toward the end of discussions, multiple injections per dose, increased cost, and shorter intervals between injections were raised as significant barriers to acceptability. Surprisingly, the most frequently mentioned deal breaker was the need to receive more than a single injection per visit. Injections were viewed by many as unpleasant, and the idea of having an unpleasant procedure repeated more than once during a single visit was unacceptable. Many participants who identified fear of needles as a huge barrier were also afraid of pain. However, even those generally comfortable with injections were adamant about getting only one injection per visit. Participants in the women’s and MSM FGD were emphatically against multiple injections.

P1: “Oh, no”; P2: “No, ma’am”; P3: “You losing us now”; P4: “Two? That ain’t gonna happen”; P5: “Meeting over.”  
 —Female PLWH FGD

P1: “Well, then that (two shots) is another problem”; P2: “It has to be just one shot, I can’t handle two shots”; P3: “Umm, no”; P4: “It had to be one.”—MSM PLWH FGD

Those in the adherence-challenged group were more open to two injections, especially if the injectable regimen was more effective. While providers also predicted that two injections might be an issue, they reasoned that patients generally grow accustomed to new treatments. One female provider compared it to flu vaccinations, about which people complain yet continue to receive yearly because of the health value they provide. Parents’ reactions to more than one injection per visit were mixed and depended on the child’s personality, pain threshold, and visit frequency. Young adults did not view a double injection as a major barrier, especially those with piercings and tattoos.

“All of us here have definitely done some things. We have definitely shared a fair amount of pain. We can, you know, put our big guy underwear on and (do) two shots for like a second or two.”—Young Adult PLWH

Many PLWH also noted that cost could be a deal breaker, since many receive oral ART medications for free. One man boasted that he had not paid a penny out of his pocket in 20 years of HIV treatment. When asked if they would switch to an injectable if there were a copay associated with the injections, many PLWH flatly said no. The idea of paying for injections when there was a free alternative was generally deemed unacceptable. Reluctance to pay was especially strong among those with sustained viral suppression.

“What is the point of charging if I already get my meds free? What’s the point of it? It’s working for me and everything is good and I’m on my regimen and I am taking the pills everyday like I have to. What is the point of me paying 5 dollars for a shot?”—Female PLWH

“As the cost to the patient goes up, you’re going to have people fall right off the map. Even if they can afford it, they are not going to be willing to. I wouldn’t be willing to.”—Provider

However, some adult PLWH were willing to accept copays between \$5 and \$20 per injection, comparing it with the expense of a daily coffee, and some parents were willing to pay if the efficacy of the treatment commanded it.

“We do whatever it takes to get the medicine. . . . so say it was something great, that worked really well, and was maybe once a month, didn’t involve any pills. Then really, for that option, it would be worth trying to figure out how to come up with payment.”—Parent

In addition to multiple injections per visit and cost, injection frequency was an important deal breaker, with PLWH and providers noting that anything more frequent than weekly was unacceptable. Although providers predicted that weekly dosing would be unacceptable, weekly dosing was grudgingly perceived to be the minimal acceptable frequency among adult PLWH. Young adults were most accepting of shorter dosing intervals and appreciated any treatment option that was not daily.

“I think I’d still try the injection cause I don’t have to worry about taking something every day”—Young adult PLWH

Dislike of injections generally, coupled with the logistics of appointment scheduling, made the majority of participants most interested in monthly or quarterly injections.

“I think that if you can get it to once a month, I think that is going to be the key thing. I mean once a week you’re gonna get less people excited about it. Once a month is just so little commitment that I think everybody could adhere to that.”—MSM PLWH

“I don’t know that I’d want to come in every week to get a shot, or even once a month. I work a job that requires me to be there 8 hours a day, so I could manage every three months.”—Female PLWH

Notably, providers discouraged any interval longer than the time between currently recommended visits (every 3 months for persons initiating ART), because of fears that longer dosing intervals would cause patients to forget appointments and decrease care engagement.

“If we spread the visits out much more than three months, (patients) kinda fall off the surface and we kinda lose them.”—Provider

There were also serious concerns from providers and PLWH about adherence if odd-numbered intervals were used (e.g., every third week) or even every 2 weeks instead of weekly because of the lack of a consistent routine.

## Discussion

This qualitative study on preferences regarding LAI-ART in a diverse sample of PLWH in the western United States yielded important empirical data, including the potential impact of specific attributes on acceptability. Influential factors were weighted differently by different subgroups of PLWH. Although all stressed the need for an efficacious medication if they were to switch, and one with comparable or even fewer side effects, there was varying tolerance for different dosing schedules and aspects of the LAI regimen injections, including number of injections, pain, bodily location, site reactions, and location of administration. PLWH who had struggled with adherence and young adults (who also struggled to remain undetectable) were tolerant of less than their optimal preferences if they thought they would fare better on an injectable regimen. Frequency of injections was deemed important but tolerance for even weekly dosing was expressed, suggesting that the required intervals every 1 or 2 months would be viewed very positively.

There are few studies in the literature in which to contextualize our findings. In the first published study of LAI-ART acceptability we could locate, Williams et al. surveyed 400 adults on ART at two sites in the United States. Overall, 61–85% would “definitely or probably” try LAI-ART, depending on dosing intervals of 1, 2, or 4 weeks.<sup>16</sup> Consistent with our findings, many were concerned about possible side effects (48%) and needle use (35%), and younger persons were more willing to try the injectables. The authors concluded that those reporting missed doses of ART and injection drug use would likely benefit the most. They found comparatively more tolerance of a price increase than did we, with more than one quarter of participants in their survey saying they would try the injectable strategy even if it cost “much more” than their current regimen.

Two other reports on participant perspectives were from the LATTE-2 trial, in which individuals were randomly assigned (2:2:1) to receive two intramuscular injections of long-acting cabotegravir plus rilpivirine at 4- or 8-week

intervals or a comparable daily pill-based regimen. Across all arms, 97% of 254 participants reported 5 or 6 on a 6-point scale of treatment satisfaction; 99% would be “highly satisfied to continue” their LAI-ART, while only 78% would elect to continue with the oral regimen.<sup>7</sup> This suggests greater enthusiasm than noted in our sample. Perhaps this is because their sample was limited to those willing to enroll in the trial of injectables in the first place. In a qualitative study associated with this trial, 39 IDIs were conducted with participants and providers from the United States and Spain.<sup>17</sup> Despite the commonly experienced adverse effects, participants were generally tolerant of the regimen, citing as advantages its convenience and greater privacy and confidentiality. Providers, although also generally supportive, noted individuals on injectables would still need to attend clinic regularly, and they expressed concern about possible resistance and more complex medication management given the long half-lives of injectable formulations. Persons identified as most suitable for injectables were those who were younger, tolerant of needles, not on other medications, with active lifestyles, or unstable in terms of experiencing homelessness, substance use, or mental illness. The finding that participants would be willing to pay \$184 (\$50–\$500) per month for injectables contradicted our results.

Rusconi et al. reported data from an Italian patient advocacy’s website survey.<sup>8</sup> Of the 488 respondents, 55% knew about LAI-ART, 83% would appreciate not taking daily ART, and 85% thought it would be convenient even though they also took non-HIV-related pills on a daily basis. If a hospital-based injection was required, 30% claimed a “benefit” if it should be done monthly, but 39% would prefer every 2 months.

Our study is limited by the restriction of its sample to potential end users in the western United States. We did not interview PLWH in other areas of the United States or around the globe, nor did we talk to other stakeholders such as public health officials, policy makers, insurance companies, and pharmaceutical manufacturers. Also, we relied on self-reported hypothetical preferences (instead of actual behavioral assessments) and reference to attributes of potential products (not specific treatments). Finally, group thinking, or agreeing with what other FGD participants have said, may have occurred. This was more likely in the case of a vocal first responder, after which other participants sometimes simply added, “Like he said.” This process may have artificially inflated the uniformity among groups. However, facilitators attempted to counter potential group thinking by sometimes going around the room and getting every person’s opinion or specifically asking for anyone with a different idea or opinion to chime in. Also, the IDIs were done individually, precluding this possible effect among parents.

Further research might consider diverse end-user populations both in the United States and globally, other methods for evaluating acceptability (e.g., discrete choice experiments, conjoint analyses), and incorporating the specific attribute profiles of LAI products as they become available—as well as even more recent technologies such as antiretroviral implants.<sup>18</sup> Acceptability and specific product references might be further studied in the course of actual trials of LAI-ART regimens, using qualitative and quantitative methods as did the LATTE-2 investigators. Such work might compare anticipated versus actual preferences or vary attributes of the

regimens to monitor the impact on preferences and uptake. Such investigations could draw from the wider literature on long-acting PrEP acceptability<sup>19,20</sup> and hormonal contraceptives.<sup>21,22</sup> Results of this research are needed to guide the development of LAI-ART products that match potential users’ preferences and to anticipate differences in uptake of LAI-ART among key end-user groups, ultimately enhancing the likelihood of its successful implementation.

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### Author Disclosure Statement

The authors have no financial conflicts of interest to declare.

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