

Patient Attitudes Toward Self- or Partner-, Friend-, or Family-Administered Long-acting Injectable Antiretroviral Therapy: A Mixed-Methods Study Across 3 Urban Human Immunodeficiency Virus Clinics

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Background. Long-acting injectable (LAI) cabotegravir/rilpivirine (CAB/RPV) offers a novel drug delivery option for persons with human immunodeficiency virus (PWH) but requires administration every 4 or 8 weeks by a medical professional.

Methods. To facilitate LAI antiretroviral therapy (ART) scale-up, we evaluated patient interest in alternative administration approaches via a mixed-methods, serial cross-sectional study across 3 US HIV clinics. We surveyed PWH (December 2021 to May 2022) on appeal of self- or partner/friend/family-administered LAI-CAB/RPV; multivariable ordinal logistic regression explored associated characteristics. To contextualize survey results, we thematically analyzed semi-structured interview data collected from PWH (August 2020 to July 2021) on attitudes toward out-of-clinic LAI-ART administration.

Results. Among 370 surveyed PWH (median age, 46 years; 26% cisgender female, 59% Black, 56% sexual minority, 34% housing instability), self-administering LAI-CAB/RPV appealed to 67%. PWH who were White (adjusted odds ratio [aOR], 3.30 [95% confidence interval [CI], 1.42–7.64]), stably housed (aOR, 2.16 [95% CI, 1.30–3.59]), or gay/bisexual (aOR, 1.81 [1.14–2.89]) were more likely to endorse self-administration. Fewer PWH (60%) reported partner/friend/family administration as appealing; adjusted models revealed similar sociodemographic preferences for this outcome. In 72 interviews, PWH noted that acceptability of out-of-clinic LAI-ART administration was qualified by convenience, prior injection experience, and potential fear of self-inflicted pain, dependence on others, and/or HIV disclosure.

Conclusions. In a multisite sample of PWH, self- and, to a lesser extent, partner/friend/family-administration of LAI-CAB/RPV appealed to most; however, was less appealing among populations more impacted by health disparities. Innovative LAI-ART delivery options could free up in-clinic resources to focus scale-up among marginalized populations.

Keywords. cabotegravir/rilpivirine; implementation science; long-acting injectable antiretroviral therapy; persons with HIV; self-administered injection.

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Long-acting injectable (LAI) antiretroviral therapy (ART) is a novel human immunodeficiency virus (HIV) treatment approach that has the potential to transform the care landscape for persons with HIV (PWH) and be leveraged as a tool to help end the HIV epidemic in the United States (US) and beyond [1, 2]. The mainstay of HIV treatment—oral ART—has evolved from toxic, large-sized multipill regimens dosed every few hours to well-tolerated, smaller, once-daily single-tablet regimens [3, 4]. Despite these remarkable scientific advances, in 2021, only 66% of US PWH were virologically suppressed, with significant disparities across the care continuum by race/ethnicity, sex/gender, and geography [5].

Co-formulated intramuscular (IM) cabotegravir/rilpivirine (CAB/RPV) administered as 2 intragluteal injections every 4 or 8 weeks was approved in 2021 [6, 7] and 2022 [8], respectively, for use in nonpregnant/breastfeeding PWH with sustained virologic suppression [9]. Use of LAI-ART may help overcome some of the challenges of access or adherence to daily oral ART, such as pill tolerability or fatigue, daily reminder of HIV status, and/or privacy concerns from possessing pill bottles for HIV treatment [10, 11]. However, LAI-ART is not yet widely available for all PWH—either due to limited clinical data in key populations, including those with viral nonsuppression, or due to real-world implementation challenges [12–14].

Use of LAI-CAB/RPV requires that PWH present to clinic every 4 or 8 weeks for administration by a healthcare professional; thereby creating new demands on clinic organization, personnel, and space (often already constrained), as well as on the patient who, if virologically suppressed, is likely accustomed to semiannual clinic visits [15]. There is an urgent need to innovate and test alternative modalities and strategies for LAI-ART delivery that could be employed outside of the clinic, such as self-administered injections; however, patient interest in these approaches is largely unknown [16].

We assessed attitudes toward administration of LAI-CAB/RPV by oneself or someone in one's personal life across 3 urban HIV clinics in the US, and explored whether specific groups in a sociodemographically diverse sample of PWH might be receptive to out-of-clinic LAI-ART delivery. The overall goal was to inform the development of implementation strategies that would safeguard resources for those who require most in-clinic support, while offering flexibility to those who prefer alternative HIV treatment access options.

METHODS

Study Design and Setting

In this mixed-methods, serial cross-sectional study, we evaluated patient interest in LAI-CAB/RPV administration by oneself or someone in their personal life as part of a larger multisite study assessing LAI-ART implementation across 3 urban HIV clinics (Ward 86, San Francisco, California; University of Chicago, Chicago, Illinois; and Grady Ponce de Leon Center, Atlanta, Georgia). We utilized 2 data sources: a survey on preferences for LAI-CAB/RPV care delivery and qualitative interviews assessing attitudes toward LAI-ART. Survey and interview data were collected at each of the sites among temporally distinct groups of PWH as follows: Formative qualitative work (collected 2020–2021) was used to inform survey design (administered 2021–2022), and subsequent interview data helped contextualize survey results.

Patient Consent

The University of California, San Francisco served as the single institutional review board for this multisite study. Written informed consent was obtained from all participants.

Quantitative Survey

As part of a broader survey examining preferences for LAI-ART program delivery features (described elsewhere [17]), we assessed patient interest in accessing HIV treatment as LAI-CAB/RPV administered by oneself or someone in their personal life. An a priori sampling plan ensured ≥ 100 participants per site and that ≥ 100 participants across sites were less well-engaged in care, defined as most recent HIV-1 RNA ≥ 200 copies/mL or no HIV-1 RNA available from the medical record and < 2 primary care visits attended in the past 12 months. Providers and staff referred patients to study coordinators, and surveys were interviewer-administered in person. Patients were reimbursed \$40.

For this analysis, the outcome was appeal of LAI-CAB/RPV administered by oneself (primary) or someone in their personal life (secondary), assessed by asking: “How appealing would it be to give yourself the long-acting injections?” and “How appealing would it be for someone from your personal life (like a partner, friend, or family member) to give you the long-acting injections?” Both questions utilized a 5-level Likert response (extremely, very, moderately, slightly, or not at all appealing), or participants could decline to answer.

Quantitative Data Analysis

Frequencies and measures of central tendency were conducted to describe participant characteristics. To identify key subgroups of PWH that may be interested in novel approaches to LAI-CAB/RPV administration, unadjusted and adjusted ordinal logistic regressions for the primary and secondary outcomes were conducted, controlling for clinically relevant covariates. Covariates included age, race/ethnicity, sex assigned at birth, gender identity, sexual orientation, housing status (stable defined as owning/renting), recreational drug use (self-reported use of opiates or stimulants in the past 30 days), health literacy assessed by the validated 4-item Brief Health Literacy Screening Tool (BRIEF) (considered “adequate” if score ≥ 17) [18], and study site. Covariate categories and referents are provided in Tables 1 and 2, respectively.

In ordinal logistic regression, resulting odds ratios indicate the odds of being in a higher versus lower category on the ordered outcome. For variables that violated the proportional odds assumption, partial proportional odds were fitted, resulting in a separate odds ratio for each category of the outcome; the lowest (“not at all appealing”) category was the referent. Missing data were minimal ($< 5\%$) and ignored.

All analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, North Carolina).

Semi-structured Interviews

We conducted 1-time, semi-structured interviews with patients recruited via maximal variation sampling across the 3 sites who were aged ≥ 18 years, receiving HIV primary care at the clinic

Table 1. Characteristics of Patients at 3 Urban Human Immunodeficiency Virus Clinics Who Were Surveyed on Appeal of Self- or Partner/Friend/Family-Administered Long-acting Injectable Cabotegravir/Rilpivirine, December 2021–May 2022

Characteristic	Total Patients (N = 370)
Site	
San Francisco, California (Ward 86)	143 (38.7)
Chicago, Illinois (University of Chicago)	107 (28.9)
Atlanta, Georgia (Grady Ponce de Leon Center)	120 (32.4)
Administered in Spanish	16 (4.3)
Age, y, median (range)	45.5 (19.0–77.0)
Age group, y	
18–29	57 (15.4)
30–49	158 (42.7)
≥50	155 (41.9)
Race/ethnicity	
Non-Latinx Black	220 (59.5)
Non-Latinx White	61 (16.5)
Latinx	47 (12.7)
Non-Latinx Other	42 (11.4)
Gender	
Cisgender female	97 (26.3)
Cisgender male	245 (66.4)
Transgender female	19 (5.2)
Gender minority (nonbinary, genderqueer)	9 (2.4)
Sexual orientation	
Gay	137 (37.3)
Bisexual	50 (13.6)
Heterosexual	163 (44.4)
Other	17 (4.6)
Housing	
Stably housed	244 (66.0)
Unstably housed	114 (30.8)
Homeless	12 (3.2)
Education	
Bachelor's degree/Any postgraduate	51 (13.8)
Some college/associate's or technical degree	132 (35.7)
High school/General Education Development	112 (30.3)
Less than high school	75 (20.2)
Description of financial situation	
Comfortable, can purchase extras	66 (18.1)
Have the necessities/money to cover needs	125 (34.3)
Barely paying the bills	82 (22.5)
Struggling to survive	92 (25.2)
Opiate or stimulant use past 30 d	71 (19.3)
Health literacy^a	
Extremely low	52 (14.6)
Moderately low	91 (25.5)
Adequate	214 (59.9)
Currently on oral antiretroviral therapy	353 (98.3)
Well-engaged in care ^b	269 (72.7)
Most recent viral load ≥200 copies/mL ^c	75 (22.0)
Primary care visits in past 12 mo	
<2 visits scheduled	41 (11.1)
<2 visits scheduled and attended	43 (11.6)
≥2 visits attended	286 (77.3)

Data are presented as No. (%) unless otherwise indicated.

^aBased on the 4-item Brief Health Literacy Screening Tool.

^bDefined as virally suppressed (HIV-1 RNA <200 copies/mL) or ≥2 primary care visits attended in prior 12 months.

^cTwenty-nine (7.8%) did not have a viral load result in their medical record in the past 12 months.

for the past year, and spoke English or Spanish. A comprehensive description of the qualitative methodology employed in this mixed-methods study has been previously published [19]. In brief, interview domains included attitudes about LAI-ART, including benefits and disadvantages of out-of-clinic injections and administration by oneself or someone in their personal life (ie, partner, friend, or family member). Interviews occurred in person in a private space within the clinic or via video-conferencing, lasted 60–90 minutes, and were audio-recorded. Audio-recordings were professionally transcribed (and translated if Spanish speaking), and uploaded into Dedoose software (version 9.0.90). Participants were reimbursed \$50.

Qualitative Data Analysis

Using a codebook of 78 inductive and deductive codes, each interview was assigned a primary coder and a secondary reviewer, resolving disagreements via consensus. This analysis is based on data from a code report on “LAI-ART administration preferences.” Author L. F. C. conducted the initial analysis by reviewing and summarizing the data to identify patterns and themes. K. A. K. served as a secondary analyst, reviewing the code report to verify the themes as well as to ensure all dimensions of the themes were thoroughly explored. The broader team reviewed the final analysis and provided additional input to refine study implications.

RESULTS

Quantitative Survey

From December 2021 through May 2022, 370 PWH completed the survey. Median age was 46 (range, 19–77) years, 26% were cisgender female, and 8% identified as a gender minority, 59% Black, 13% Latinx, and 56% sexual minority. Approximately 73% were well-engaged in care (defined above), despite 34% experiencing unstable housing or homelessness and 19% reporting opiate or stimulant use in the past 30 days. Table 1 provides additional characteristics, including site distribution.

Surveyed Appeal of Self-administering Injection

Self-administration of LAI-CAB/RPV was endorsed as appealing by 247 (67%) patients overall; among whom 115 (47%), 52 (21%), 48 (19%), and 32 (13%) rated this option as extremely, very, moderately, or slightly appealing, respectively; the remaining 123 (33%) reported this option as not appealing (Figure 1).

In models assessing appeal of self-administering LAI-CAB/RPV, the proportional odds assumption was not violated. In the unadjusted model, the odds of increasing appeal of self-administration were significantly greater for PWH who were non-Latinx White, stably housed, had adequate health literacy, and identified as gay, bisexual, or other identity (Table 2).

Table 2. Patient Characteristics Associated With Appeal of Self- or Partner/Friend/Family Member-Administered Long-acting Injectable Cabotegravir/Rilpivirine Among 3 Urban Human Immunodeficiency Virus Clinics in the United States (N = 370 Patients)^a

Characteristic	Appeal of Self-administered Injection		Appeal of Partner/Friend/Family Member-Administered Injection	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age, χ^2 (df)	4.27 (2)	7.41 (2)*	0.53 (2)	2.25 (2)
18–29	1.03 (.59–1.78)	1.28 (.69–2.38)	1.20 (.69–2.07)	1.60 (.86–3.01)
30–49	1.49 (1.00–2.23)*	1.86 (1.19–2.91)**	1.12 (.75–1.67)	1.22 (.77–1.92)
≥50	Ref.	Ref.	Ref.	Ref.
Race/ethnicity				
Non-Latinx White	2.55 (1.53–4.25)***	2.09 (1.19–3.67)***	^b	1.92 (1.11–3.32)*
Black/Latinx/Other	Ref.	Ref.	Ref.	Ref.
Gender				
Cisgender male	1.02 (.69–1.51)	.96 (.60–1.55)	.87 (.59–1.29)	.77 (.47–1.26)
Cisgender female/gender minority	Ref.	Ref.	Ref.	Ref.
Sexual orientation				
Gay/bisexual/other	1.71 (1.17–2.48)**	1.81 (1.14–2.89)**	1.35 (.93–1.97)	1.37 (.88–2.22)
Heterosexual	Ref.	Ref.	Ref.	Ref.
Housing				
Stably housed ^c	2.00 (1.35–2.96)***	2.17 (1.41–3.34)***	1.54 (1.04–2.28)*	1.63 (1.05–2.54)*
Unstably housed or homeless	Ref.	Ref.	Ref.	Ref.
Opiate/stimulant use				
Past 30-d opiate/stimulant use	0.93 (.58–1.48)	0.77 (.49–1.20)	1.13 (.71–1.80)	0.92 (.53–1.62)
None	Ref.	Ref.	Ref.	Ref.
Engagement in care				
Well-engaged ^c	1.34 (.89–2.03)	1.31 (.83–2.05)	1.26 (.83–1.91)	1.20 (.76–1.89)
Less well-engaged	Ref.	Ref.	Ref.	Ref.
Health literacy				
Adequate	1.55 (1.06–2.27)*	1.31 (.87–1.97)	1.24 (.85–1.83)	1.10 (.72–1.67)
Inadequate	Ref.	Ref.	Ref.	Ref.
Site χ^2 (df)	2.43 (2)	3.87 (2)	5.45 (2)	2.44 (2)
San Francisco	1.43 (.91–2.25)	1.67 (.95–2.05)	1.70 (1.08–2.69)*	1.76 (.99–3.10)
Atlanta	1.18 (.74–1.90)	1.54 (.92–2.56)	1.24 (.77–2.00)	1.32 (.79–2.21)
Chicago	Ref.	Ref.	Ref.	Ref.

Abbreviations: CI, confidence interval; df, degrees of freedom; OR, odds ratio.

^aN = 367 for all unadjusted analyses except for heterosexual (n = 364), substance use (n = 365), and health literacy (n = 356); n = 353 for adjusted analyses.

^bPartial proportional odds results for this covariate are reported in this footnote given the violation of the proportional odds assumption: For extremely/not at all: OR, 1.76 (95% CI, .94–3.32); very/not at all: OR, 1.70 (95% CI, .87–2.99); moderately/not at all: OR, 3.50 (95% CI, 1.91–6.23)***; slightly/not at all: OR, 4.08 (95% CI, 2.00–8.34)***.

^cStably housed: owning or renting; well-engaged in care: virally suppressed (HIV-1 RNA <200 copies/mL) or ≥2 primary care visits attended in prior 12 months.

*P ≤ .05.

**P ≤ .01.

***P ≤ .001.

In the covariate-adjusted model, the appeal of self-administering LAI-CAB/RPV was significantly greater for PWH aged 30–49 versus ≥50 years (adjusted odds ratio [aOR], 1.86 [95% confidence interval [CI], 1.19–2.91]), non-Latinx White participants versus people of color or those identifying as Latinx (aOR, 2.09 [95% CI, 1.19–3.67]), and PWH stably housed versus those reporting unstable housing or homelessness (aOR, 2.17 [95% CI, 1.41–3.34]). For PWH who reported gay, bisexual, or other identity, the odds of reporting self-administration as appealing were almost twice that of heterosexual PWH (aOR, 1.81 [95% CI, 1.14–2.89]). Other factors, including cisgender male identity, recent substance use, care engagement, health literacy, and study site, were not significantly associated with this outcome (Table 2).

Surveyed Appeal of Receiving Partner/Friend/Family-Administered Injection

Administration of LAI-CAB/RPV by someone in their personal life was endorsed as appealing by fewer patients overall, but still a majority (n = 221 [60%]), among whom 72 (49%), 47 (32%), 49 (34%), and 53 (36%) rated this option as extremely, very, moderately, or slightly appealing, respectively; the remaining 146 (40%) reported this option as not appealing (3 were missing data) (Figure 1).

In models assessing appeal of partner/friend/family-administered LAI-CAB/RPV, the proportional odds were not violated, except for the unadjusted model evaluating race/ethnicity, for which partial proportional odds were reported

Appeal of out-of-clinic administration of long-acting injectable cabotegravir/rilpivirine by self or partner/friend/family member

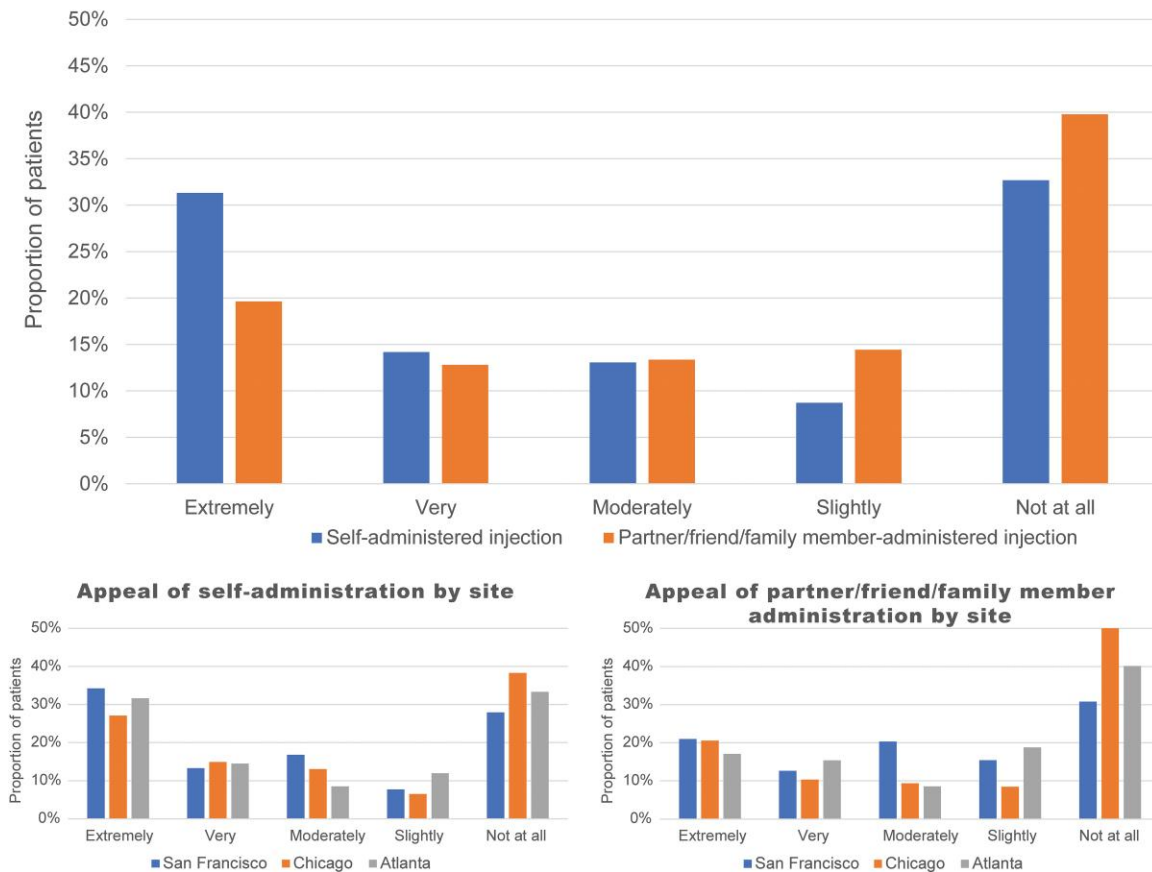


Figure 1. Appeal of long-acting injectable cabotegravir/rilpivirine administered out-of-clinic by oneself or a partner/friend/family member among US persons with human immunodeficiency virus (N = 370) across 3 urban clinics overall (top panel; stratified by self-administration or partner/friend/family administration). Separately, appeal of receiving injections administered by oneself (bottom left panel) or a partner/friend/family member (bottom right panel) by individual site (San Francisco, Chicago, or Atlanta).

(Table 2). In the unadjusted model, odds of increasing appeal to receive LAI-CAB/RPV administered by a partner/friend/family member were significantly greater for PWH stably housed and for PWH from San Francisco (but not Atlanta) versus Chicago (Table 2).

In adjusted models, the appeal of having a partner/friend/family member administer LAI-CAB/RPV was greater for non-Latinx White participants compared with other racial/ethnic groups (aOR, 1.92 [95% CI, 1.11–3.32]) and for PWH stably housed compared with those who reported unstable housing or homelessness (aOR, 1.63 [95% CI, 1.05–2.54]). Other covariates were not significantly associated with this outcome (Table 2).

Qualitative Interview

From August 2020 to July 2021, 72 PWH participated in semi-structured interviews. Demographic characteristics of those interviewed were similar to those surveyed (median age, 46 years;

35% cisgender female/gender minority; 46% Black, 33% Latinx; 35% reported unstable housing/homelessness).

Interview Data Contextualize Survey Findings

The majority of interviewees provided perspectives that suggested more avoidance and apprehension of potential self-administering LAI-ART. However, as participants reflected on the logistics of clinic-based injections, some became more open to the idea, particularly individuals who could envision LAI-ART integrated into their life outside the clinic. Most interview participants did not endorse partner/friend/family-administered injections, especially if they could not identify a trusted person to perform this task: “I live alone. I wouldn’t have anybody to really do it for me” (Black gay male, aged 27 years, Chicago). This shared opinion remained firm throughout the interviews.

We identified 2 primary thematic domains: (1) key factors driving the acceptability of, and (2) implementation considerations for, self- or partner/friend/family-administered LAI-ART.

Table 3. Emergent Themes With Associated Descriptions and Exemplar Quotes From Patients Interviewed on Acceptability of Out-of-Clinic Administration of Long-acting Injectable Antiretroviral Therapy Across 3 Urban Human Immunodeficiency Virus Clinics, August 2020–July 2021

Theme	Thematic Summary	Exemplar Quote(s)
Thematic domain 1: drivers of acceptability		
Subtheme 1 (ST1)	Convenience and ease of use motivated appeal of out-of-clinic injections	ST1: "Some people don't have transportation places. So, you know, even better they can do it they self at home ... So, not just like the convenience of it, but literally if you're having trouble getting there, then that's a good option for you." (30 y, Black gay male, Atlanta)
Subtheme 2 (ST2)	Prior experience with injectables impacts acceptability	ST2: "The idea of self-administering it is a bit of a turnoff. And it's probably memories of my brother dealing with his [diabetes] ... I'm assuming there'd be a lot of ancillary things ... You've got your two vials. You've got your syringe, your needle, your alcohol prep pads ... There's a lot of prep and a lot of [steps] to get it done." (58 y, White gay male, San Francisco)
Subtheme 3 (ST3)	Fear of self-inflicted pain hinders self-injection acceptability	ST3: "If you're going to have a painful shot like that, you should be laying down ... because when you say it could be less than a penicillin, more than a flu, that to me says to me it's going to be more like the penicillin and you're just not saying it yet ... If I stick myself in the butt with a needle and then hurting myself, that's kind of like along the lines of suicide." (65 y, multiracial gay male, San Francisco)
Subtheme 4 (ST4)	Fear of dependence on others and HIV disclosure hinders injection by a partner, friend, or family member	ST4: "If I had [a partner], I would want to train them—I would teach them how to do it, and since I don't, that would not be an option. I can't train my dog to do it for me, and he's the only one that lives with me. It's kind of like—as far as a neighbor, I used to think the whole world needs to know [about my HIV status], and now I'm finding out it's not." (62 y, White heterosexual male, San Francisco)
Thematic domain 2: implementation considerations		
Cross-cutting theme 1 (CCT1)	Balancing convenience and confidentiality concerns, implication for product packaging	CCT1-1: "Now, I do live in a safe environment where people know that I'm HIV-positive so it wouldn't bother me. If it's something you had to store in like a refrigerator, I wouldn't mind that either. But if I wasn't in such a secure environment—if the medication had to be stored in something cool—I wouldn't be comfortable with it because I wouldn't want people to know." (46 y, Black gay male, Atlanta) CCT1-2: "When it comes to the disposing of the needles, I think they should be mailed out with some sort of biohazardous box ... some way to get rid of the needles [safely] that's not like you just throw them away in the trash can and then somebody finds them. And you don't have to explain to them that you're not, like, shooting up with drugs, that you're, like—that you're actually taking medicine. Like, I don't want to have to explain that empty needle in the trashcan to my grandmother, you know?" (27 y, Black gay male, Chicago) CCT1-3: "Just so you know, simple [text message] reminder ... Hey, you're due for your shot within this period, please confirm when you took it, or please confirm that you got this message and you're aware of it." (52 y, White gay male, San Francisco)
Cross-cutting theme 2 (CCT2)	Balancing professionalism and self-efficacy concerns, implication for product attributes	CCT2-1: "But I'm not up for poking myself ... It's a risk because you don't know if you're going to do it right or if you're going to hit a bone. I mean, you could injure yourself." (57 y, Latino bisexual male, San Francisco) CCT2-2: "Like the way they did with Humira was like the first time or the first couple of times, you came into the office and then the individual, the nurse watched you do it so they could say, that is how you do it or here's how better to do it." (61 y, White gay male, San Francisco) CCT2-3: "If they made it like an EpiPen that was already loaded with the dose, and all you had to do was jam it into your butt. But if it's a process where you've got a vial like you have insulin, and you've got to draw and fill up the syringe and knock out the air bubbles and all of that kind of crap ... I think it gets a little bit more challenging and it makes me a little bit more nervous that I might screw something up." (58 y, White gay male, San Francisco)

Abbreviation: HIV, human immunodeficiency virus.

Regarding determinants of acceptability, 4 subthemes emerged that unveiled a deeper understanding of the survey results by providing insights into what would make self- or partner/friend/family-administered injections more versus less acceptable. Furthermore, viewpoints were expanded among PWH in the surveyed minority who appeared to find self- or partner/

friend/family-administered injections as less or not appealing. Two cross-cutting themes around implementation were also revealed, with implications for training opportunities and product design. Exemplar quotes for subthemes (thematic domain 1) and cross-cutting themes (thematic domain 2) are included in [Table 3](#).

Thematic Domain 1: Drivers of Acceptability

Subtheme 1: Convenience and Ease of Use Motivated Appeal of Out-of-Clinic Injections. In general, participants noted the potential for improved convenience in not being tethered to the clinic for frequent injection visits, acknowledging other obligations (eg, employment, caregiving) or external factors (eg, weather, transportation) that could impact their adherence to in-clinic injections (Table 3).

Subtheme 2: Prior Experience With Injectables Impacts Acceptability. Informants frequently referenced their prior experience with injections (including medications or substances, eg, insulin, hormone therapy, heroin), either firsthand or witnessed. Past experience in some cases led to appeal of self-administering LAI-ART for reasons of being in control of medication adherence or improved convenience. However, for others it led to aversion considering the process and supplies needed, unless it would be life-saving (Table 3).

Subtheme 3: Fear of Self-inflicted Pain Hinders Self-injection Acceptability. The intramuscular/buttock location of the injection made it difficult to conceptualize self-administration in terms of the actual technique (awkward positioning) as well as the potential for self-inflicted pain, which informants nearly uniformly wanted to avoid at all costs (Table 3). However, those with past experience self-administering injections explained it can potentially be less painful with time given one's bodily awareness and improved injection technique. As a transgender woman who self-administers hormones stated: "You know where it hurts and where it doesn't hurt. And you can inject yourself much more caringly" (Latinx transwoman heterosexual, aged 38 years, San Francisco).

Subtheme 4: Fear of Dependence on Others and HIV Disclosure Hinders Injection by a Partner, Friend, or Family Member. Envisioning someone from their personal life able and consistently available to administer injections was challenging for most informants, as they couldn't imagine someone they could entrust with this degree of responsibility. One informant jokingly remarked, "Here's the problem about having a partner that knows you're sick or whatever, they get tired and end up overdosing you and you're dead" (Black heterosexual male, aged 57 years, Chicago). Interpersonally, major challenges included a desire to avoid invoking the role of caregiver onto others and the potential fear of HIV disclosure. If an entrusted person was easily identifiable, informants reported openness to this option, if proper training were secured (Table 3).

Thematic Domain 2: Implementation Considerations

Informants identified potential challenges to self- or partner/friend/family-administered LAI-ART relevant to the out-of-clinic setting for injection provision, in addition to the

personnel involved, that have implications for product design and training opportunities.

Cross-cutting Theme 1: Balancing Convenience and Confidentiality Concerns, Implication for Product Packaging. Some informants expressed interest in out-of-clinic LAI-ART administration options, while also articulating key components that would need to be in place to ensure success, including delivery of medication, refrigeration needs, and securing and disposal of supplies. Safe and reliable housing as well as being able to maintain privacy regarding HIV status and needle use were identified as key requisites of whether this option would be feasible and/or desirable (Table 3, cross-cutting theme [CCT] 1-1). Similarly, some PWH recognized anticipated judgment from others in their life discovering the medication or injection supplies as a major drawback (Table 3, CCT1-2). Interviewees who voiced readiness to engage in out-of-clinic LAI-ART administration highlighted the need for injection reminders and closed-loop communication with the clinic upon administration (Table 3, CCT1-3).

Cross-cutting Theme 2: Balancing Professionalism and Self-efficacy Concerns, Implication for Product Attributes. Participants with limited experience with injectable treatment were initially resistant to self-administration options: "I don't have no problems with the needle if it's in somebody else's hands" (Black heterosexual cisgender female, aged 46 years, Atlanta). Administering injections was viewed as a professional skill that most informants, at least initially, did not believe themselves to be capable of due to the complexity, degree of work, and/or perceived risk of self-injury if not done properly (Table 3, CCT2-1). Those with previous experience with injectable treatments could more easily imagine receiving injection training by a professional if offered and adopting a graduated approach from clinic to out-of-clinic administration (Table 3, CCT2-2). A minority reported only feeling comfortable with out-of-clinic administration by oneself and/or someone in their personal life if training/skill were removed, such as predosed auto-injector pens, which involve correct placement and pressing a button (Table 3, CCT2-3).

DISCUSSION

Among a sociodemographically diverse sample of PWH with a median age in the fifth decade of life (thus broadly representing the population affected by the US HIV epidemic), self-administration of LAI-CAB/RPV appealed to about two-thirds of individuals, whereas slightly fewer found it appealing for someone in their personal life to give them injections. These attitudinal findings were supported by a mixed-methods design leveraging a multisite implementation science research infrastructure studying the implementation of LAI-ART across 3 urban HIV clinics. Furthermore, we identified key subgroups of PWH who may

be interested in self- or partner/friend/family-administered LAI-CAB/RPV in a nonclinical intimate setting. Greater appeal of self-administering LAI-CAB/RPV was reported by PWH who were younger, non-Latinx White, stably housed, and gay/bisexual, whereas partner/friend/family administration was appealing to PWH who were non-Latinx White and stably housed.

A separately sampled group of PWH recruited across the 3 sites for semi-structured interviews provided key insights into attitudes shaping acceptability of and implementation considerations for novel approaches to LAI-CAB/RPV administration. Emergent themes were congruent with findings from the quantitative survey overall: namely, that appeal of self-administered injections was not universally shared among participants, and partner/friend/family administered injections even less so. Despite recognizing many positive attributes of receiving LAI-ART outside of the clinic, including improved convenience, and eliminating the need to secure transportation, the feasibility of this option seemed inaccessible to many. Primary reasons cited were the lack of training and technical challenges to effective administration of deep gluteal injections; potential for self-inflicted pain or harm; lack of environmental or psychosocial safety needed to facilitate injectable medication and supplies storage; and not feeling comfortable asking someone for help administering LAI-ART, either because they had no one trusted to ask, would not want to risk HIV disclosure, or feared the vulnerability associated with depending on someone in their personal life to help care for them. While significant psychosocial barriers to accessing LAI-ART remain critical to overcome, optimizing product design and packaging may have a significant impact on seeing this option as viable and personally relevant.

Taken together, these findings contribute valuable data to the evolving landscape of LAI-ART delivery in the US by highlighting subgroups of PWH who may elect to pursue out-of-clinic injections if given the opportunity. This is critical given that early implementation of LAI-CAB/RPV has identified several challenges, centered on new burdens incurred by the clinical infrastructure and personnel required to safely shift patients from oral to LAI-ART [13]. For virally suppressed PWH, procuring oral ART simply entails a provider electronically prescribing medication to the patient's preferred pharmacy and encouraging continued adherence. However, use of LAI-CAB/RPV requires an interprofessional team dedicated to clinical eligibility verification; navigation of drug authorization, procurement, and storage; trained staff and dedicated clinic space to conduct frequent injection visits; and intensive patient tracking and monitoring of injection visit adherence and tolerability [13, 20, 21]. When using LAI-CAB/RPV in PWH who are not virally suppressed, the demands of successfully providing this treatment alternative may be even greater given the potential need for adherence and other support, including wraparound services [12, 14, 22].

Employing differentiated service delivery for the provision of LAI-ART, including offering off-site medication administration, could help decompress clinics whose resources have been strained by the additional burdens of supplying injections [23]. Furthermore, the design and evaluation of innovative LAI-ART delivery approaches that are tailored to local context and adaptable to patient preferences and needs may be particularly critical in high-burden HIV settings such as the US South [24]. In these regions, the lack of Medicaid expansion, underfunded public health infrastructure including healthcare worker shortages, transportation challenges in the setting of rurality, and pervasive systemic racism may compound to hinder access to and uptake of LAI-ART; thus, nontraditional, differentiated medication delivery models are urgently needed, with self- or partner/friend/family administration representing one of many options.

Emerging data support the safety and effectiveness of out-of-clinic LAI-CAB/RPV administration, including demonstrated success of a 12-month home delivery program in South Carolina whereby patients (virologically suppressed) received and stored medication and a visiting nurse administered the intragluteal injections [25]. In San Francisco, feasible administration of LAI-CAB/RPV out-of-clinic has also been demonstrated via partnerships with home nursing and street medicine, including among PWH with highly prevalent substance use and homelessness [12, 26]. While these approaches may offer increased accessibility of LAI-CAB/RPV, as would administration at local pharmacies (under investigation), they require healthcare personnel to give injections and may not completely alleviate privacy concerns of PWH. Of note, a pilot substudy of ATLAS-2M participants who remained virally suppressed after receiving ≥ 3 years of gluteal CAB/RPV IM demonstrated safety, tolerability, and effectiveness of rotating injections to the lateral thigh [27]. By being more anatomically accessible, this injection site increases the possibility of self-administration in the future; interestingly, however, thigh versus gluteal CAB/RPV IM administration was preferred in only 30% of participants [27].

We found that self- and/or partner/friend/family-administered injections most appealed to PWH who were non-Latinx White and stably housed. This suggests that racial/ethnic minorities and those unstably housed, groups who traditionally have had greater challenges to viral suppression, may perceive using LAI-CAB/RPV outside of a clinical setting differently [28]. Potential drivers of these key findings may include varying levels of HIV knowledge and stigma in different communities as well as differences in access to social support and/or resource availability to support out-of-clinic LAI-CAB/RPV administration (eg, refrigeration or privacy if HIV disclosure is a concern); additional investigation is needed to ensure that as LAI-ART delivery programs evolve, disparities in HIV treatment and access are not widened in the process.

Our qualitative data shed light on the complexity of rationales supporting or opposing LAI-ART administration in an intimate setting and on necessary steps to make this a reality for different subgroups of individuals who may desire using LAI-ART. These next steps may include self- or partner/friend/family-administered injection training and skills assessment, likely beginning among interested early adopters of LAI-CAB/RPV and occurring in a graduated approach: first supervised and supported in the clinic by healthcare staff to ensure capability and confidence in safe and effective injection administration before moving to out-of-clinic administration. Additional steps required would entail verifying or assisting with securing cold-chain supply and safe medication/supplies storage, as well as facilitating timely and available communication channels around injection reminders, confirmation of injection administration, and troubleshooting of any issues that may arise. The latter may necessitate provision of cell phones for patients enrolled in LAI-ART programming and provide an opportunity for development of app-based technologies to support secure, closed-loop communication between patients and program staff.

Our study had limitations, including that most participants (>95%) had not used LAI-CAB/RPV at the time of the survey or interview, so responses represent anticipatory perspectives about hypothetical use. Furthermore, the qualitative interview guide primarily focused on acceptability of in-clinic LAI-ART delivery with the line of questioning on acceptability of out-of-clinic administration being a secondary focus; as such, in some instances, time to explore this topic was limited. Additionally, participants may have equated their perceptions of LAI-CAB/RPV with subcutaneous versus intramuscular injections, which underscores the importance of exploring preferences for innovative approaches to LAI-ART administration among early adopters of LAI-CAB/RPV who can base responses on actual experience. Finally, we were not able to evaluate preferences by all key subgroups (eg, sex and gender) surveyed, given low frequencies limiting analysis of multicategory outcomes; however, the qualitative findings provided rich insights into the perspectives of minority respondents.

In this analysis leveraging a mixed-methods approach and including a sociodemographically representative sample of PWH enrolled across 3 diverse geographic sites, we found that self- or partner/friend/family-administered LAI-CAB/RPV appealed to the majority surveyed. Furthermore, qualitative data provided deeper insights into elements driving acceptability of, and tempering enthusiasm for, novel HIV treatment approaches, lending to valuable implementation considerations. Continuing to focus on patient attitudes and beliefs is critical to the success of implementing LAI-CAB/RPV with the goal of maximizing its reach and impact for individual patients, health systems, and its role in helping to end the HIV epidemic.

Notes

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