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A Qualitative Exploration of Women's Interest in Long-Acting Injectable Antiretroviral Therapy Across Six Cities in the Women's Interagency HIV Study: Intersections with Current and Past Injectable Medication and Substance Use

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Abstract

Medications for antiretroviral therapy (ART) and preexposure prophylaxis (PrEP) are currently daily pill regimens, which pose barriers to long-term adherence. Long-acting injectable (LAI) modalities have been developed for ART and PrEP, but minimal LAI-focused research has occurred among women. Thus, little is known about how women's history of injection for medical or nonmedical purposes may influence their interest in LAI. We conducted 89 in-depth interviews at 6 sites (New York, NY; Chicago, IL; San Francisco, CA; Atlanta, GA; Chapel Hill, NC; Washington, DC) of the Women's Interagency HIV study. Interviews occurred with women living with HIV ($n = 59$) and HIV-negative women ($n = 30$) from November 2017 to October 2018. Interviews were recorded, transcribed, and analyzed using thematic content analysis. Women's prior experiences with injections occurred primarily through substance use, physical comorbidities, birth control, or flu vaccines. Four primary categories of women emerged; those who (1) received episodic injections and had few LAI-related concerns; (2) required frequent injections and would refuse additional injections; (3) had a history of injection drug use, of whom some feared LAI might trigger a recurrence, while others had few LAI-related concerns; and (4) were currently injecting drugs and had few LAI-related concerns. Most women with a history of injectable medication would prefer LAI, but those with other frequent injections and history of injection drug use might not. Future research needs to address injection-related concerns, and develop patient-centered approaches to help providers best identify which women could benefit from LAI use.

Keywords: HIV, women, antiretroviral therapy, long-acting injectable

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Introduction

For people at risk of HIV and people living with HIV (PLWH), preexposure prophylaxis (PrEP) prevention and antiretroviral therapy (ART) for treatment require daily pill intake. Oral PrEP decreases risk of HIV acquisition[1,2] and oral ART facilitates viral suppression and lowers transmission.[3] However, daily pill-taking is limited by adherence, whose barriers include individual-level factors (e.g., side effects,[4] substance use,[5] and pill fatigue[6]), clinic-level factors (e.g., medical mistrust,[7] provider communication), and sociostructural factors (e.g., care access, transportation, and stigma).[6,8] Certain barriers are particularly salient for women, including social and economic gender inequalities,[9] self-efficacy, caregiving responsibilities,[10] intimate partner violence,[11] and pregnancy-related interactions.[12]

Women constitute only 5% of PrEP users in the United States and discontinue use more quickly than men.[13] Women living with HIV (WLWH) need an alternative to daily pill taking:[14] only 60% of WLWH on ART are virally suppressed at 12 months,[15] less than their male counterparts.[16] The only group of women for whom HIV diagnoses have not decreased is women aged 55 and older,[16] who are also more likely to have comorbid conditions that also require injectable medications.[17] Women who inject drugs face intersecting adherence barriers,[18] are at higher risk of HIV acquisition than men,[19] and have worse HIV outcomes.[18,20] Also, recent studies of long-acting injectable (LAI) acceptability have raised concerns that LAI HIV therapy may trigger recurrence for people who previously injected drugs.[21,22]

LAI ART has the potential to transform HIV prevention and treatment by eliminating the need for daily adherence. LAI formulations of ART[23,24] were noninferior, and LAI formulations of PrEP[25,26] were superior, to daily pills in Phase III trials for maintaining viral suppression and preventing HIV, respectively. Once approved, LAI PrEP would be administered as bimonthly intramuscular injections; LAI PrEP was well-tolerated and highly acceptable.[27] Monthly LAI ART for PLWH is under review by the Food and Drug Administration,[28] and bimonthly administration is currently in clinical trials (ATLAS 2M).[29] Over 90% of trial participants reported a preference for LAI over oral ART.[30,31]

The development of LAI ART for HIV prevention and treatment is occurring in the context of a noticeable shift toward injectable forms of prophylactic and therapeutic medicine. LAIs have also been developed as alternatives to oral contraception[32] and medications to treat schizophrenia and bipolar disorders, opioid use disorder,[33] and diabetes management; in most instances these have increased patient satisfaction.[34,35]

The increasing use of LAIs means that patients are more likely to have a medical history of periodic or even frequent injections and thus preexisting preferences. Some patients may undergo simultaneous courses of LAI medications, which may create barriers around injection site pain or traveling to clinics. However, concurrent research has hypothesized that the structured setting for clinical administration of LAI ART could instead improve HIV medication adherence for such populations.[36] Given promising Phase III trial results, and to better understand how LAI ART for HIV therapy can be used by women with a history of injectable medications and substance use, we interviewed women enrolled in the Women's Interagency HIV study (WIHS), the largest prospective cohort study of WLWH and women at risk for HIV infection in the United States.

Methods

Study participants included WLWH and women at risk for HIV at six WIHS sites (Atlanta, GA; San Francisco, CA; Washington, DC; Chapel Hill, NC; Bronx, NY; Chicago, IL). Additional details about the study sample, including drug use and HIV-related risk behaviors are reported elsewhere.[37] We conducted 89 in-depth interviews, of which 59 were with WLWH (10 per site, with the exception of 9 interviews at Washington, DC) and 30 were with HIV-negative women (5 per site). The parent study explored women's interest in, and willingness to use, LAI HIV therapy.[38,39] We therefore recruited women with a history of both daily oral pill taking (e.g., birth control) and injection (e.g., vaccines, substance use, birth control) to examine how a range of experiences with injections may influence women's interest in HIV therapy.

Data collection occurred from November 2017 to October 2018. Participants provided informed consent before each 60 min interview. Interviews were conducted in person by a trained qualitative interviewer, digitally recorded and professionally transcribed. Each participant was compensated $50 for her participation, plus travel compensation as necessary. The Institutional Review Boards at all participating sites provided approval before interview initiation.

Interviews focused on women's attitudes and willingness to use LAI ART for HIV treatment and prevention, with a particular focus on injection history and its relationship to LAI interest. Interview questions were open-ended and explored women's experiences with injectable medication, related knowledge and attitudes, and perceived barriers and facilitators toward LAI ART for treatment and prevention.

Data were analyzed using thematic content analysis.[40,41] Two members of the study team conducted line-by-line open coding on the first five interviews of each group (WLWH and HIV-negative women) to develop a provisional coding scheme focused on identifying women's attitudes about LAI ART for treatment and prevention, as well as the perceived barriers and facilitators toward their use; thematic codes based on existing literature were subsequently added to ensure that theory-based and emergent concepts were included. Team members then cross-coded a random sample of 10 additional transcripts to refine the code dictionary and develop a codebook. This codebook was reviewed and amended by other team members.[42] Two coders then independently applied this final coding scheme to all interview transcripts, with analyses exploring potential axes of difference such as age, region, and race/ethnicity. Ongoing discussions were scheduled within the team to resolve any discrepancies.

Results

Participants' median age was 51 years (range, 32–72) and the majority of particlpants were women of color (96%). Most women were unemployed (66%) and earned <$12,000/year (59%) (Table 1). The majority of women would prefer LAI PrEP (50%) or LAI ART (56%) over daily pills. Over two-thirds had used an injectable medication (Table 2).

Table 1. Demographic Characteristics

Characteristic	*Total (N=89)*	*Median*	*Percentage*
Age (32–72) years		51	
32–39	14		16
40–49	22		25
50–59	38		43
60+	15		17
Race			
Black/African American	68		76
Caucasian	4		5
Hispanic	4		5
Biracial	10		1
Other (Native American)	5		6
Education			
Less than high school	22		25
Completed high school/GED	27		30
Some college	26		29
College or graduate school	14		16
Household income[a]		$10,800	
$0–$11,999	40		47
$12,000+	46		53
Relationship status			
Single	37		42
Dating >6 months	21		24
Married/long-term partnership	31		34
Children			
Has children	69		78
Does not have children	20		22
Insurance			
Uninsured	8		9
Public insurance	73		82
Private/other insurance	8		9

[a]Some values missing/unanswered.
GED, graduate equivalency degree.

Table 2. Descriptions of Women's History of Injection

Characteristic	*Total (N=89)*	*Percentage*
Ever used any injectable medication	60	68
Ever used Depo	22	27
Ever other injectable medication[a]	53	62
Was this injectable medication routine?	10	19
Ever drug use	49	55
Ever injection drug use	13	15
Current injection drug use	1	1
Regular flu shot	57	72

[a]The other injectable medication women listed included the following: Hepatitis medication; STI antibiotic B-12 Shot; Diabetes medication; pain medication; Iron; IV fluids; epidural; dialysis; Epi pen; Steroid injection; Cortisone shots; and Chemotherapy infusion.

Women's previous experiences with injections occurred primarily through substance use, physical comorbidities (e.g., diabetes, hepatitis C), birth control (Depo-Provera), or vaccines. Four primary categories emerged based on women's own histories of injection and their perception of others' experiences: (1) women who received episodic injections (e.g., for birth control or physical comorbidities) and had few LAI-related concerns; (2) women who required frequent injections (e.g., diabetes) and would refuse additional injections; (3) women with a history of injection drug use, some of whom feared LAI might trigger a recurrence, while others had few LAI-related concerns; and (4) women who were currently injecting drugs and had few concerns about LAI. Themes did not differ based on women's HIV status. Additional quotes are provided in Table 3.

Women who received episodic injections and had few concerns

Women believed that people with a history of injection medication, ''already had the experience with shots so they'll be less afraid of it'' (Caucasian, 30, Atlanta, HIV negative). Another woman seconded this based on her previous experiences with medical injections for comorbidities: ''It doesn't bother me getting shots whatsoever, because like I said, the hep C treatment, there were a lot of shots I had to give myself'' (Black, 62, Bronx, WLWH). Numerous women compared HIV therapy to birth control options (i.e., daily oral pills vs. Depo-Provera), and thought that injections would take away the feeling of:

> ''Oh, my God. I got to take these pills…People will take shots for birth control, like Depo and things like that. It would feel like more like that. That would be easier'' (Black, 43, UNC, WLHW).

These individuals focused primarily on how an experience with injections would allow people to feel comfortable with future injections and did not feel that taking multiple injections at once would be a barrier.

Women who required frequent injections and did not want additional injections

In contrast, women with a history of frequent medication-related injection expressed reticence to add LAIs to their regimen: ''Even though I take needles because I've got an insulin pump…I'm already doing enough with needles so I just stick with the pills'' (Black, 45, UNC, WLWH). One woman shared how having to take shots to prepare for a kidney transplant made her: ''More tolerant to them but it doesn't mean I like them…So I'm not going to subject myself to taking a shot that I don't have to take'' (Black, 58, UNC, WLWH).

A number of women reported being terrified of needles and explained that they would not use LAI formulations no matter how much they disliked pills. Similarly, some participants described other women who have aversions to injections and therefore would need help administering them:

> ''I go and give [my friend] her insulin shot every morning because she just can't stick herself and she fusses about the shot. You're going to have pros and cons definitely. I think that older people aren't going to want to take that shot, they're going to want their pill'' (Black, 62, Atlanta, WLWH).

Table 3. Interest in Long-Acting Injectable HIV Therapy Among Women with a History of Injection—Additional Quotes

Theme	*Quote*
Episodic injections few concerns	‘‘But people that take insulin, it’s another shot to help you live. I mean, how hard could it be’’ (Black, 45, San Francisco, WLWH). ‘‘It really doesn’t bother me, you know? I’ve taken shots for my MS, as well as with the diabetes’’ (Black, 57, Chapel Hill, HIV negative) ‘‘They already had the experience with shots they’ll be less afraid of it’’ (Caucasian, 30, Atlanta, HIV negative). ‘‘No, I think they would choose it because they have experience with injecting themselves. That would be easier for them.’’ (Black, 46, Atlanta, HIV negative)
Frequent injections and did not want more	‘‘That’s why I would do the pill, because sometimes bruising—you know, I’ve done enough blood draws to have bruising and it’s not a cute look’’ (Black, 54, San Francisco, HIV negative). ‘‘I know with my mom…it’s kind of a drag for her sometimes’’ (Black, 40 Atlanta, WLWH).
Women with a history of illegal drug use who did not want additional injections	‘‘I had an aunt who was a heroin addict, and when she became diabetic, she said the needles used to trigger something in her, seeing the needles’’ (Caucasian, 56, Washington DC, WLWH). ‘‘I think they need a pill’’ (Black, 54, Atlanta, HIV negative). ‘‘‘Oh my God I’m going to get this shot’ and it will provide temptation or whatnot and see how it affects them. Or they might be a really addictive personality and say I can’t even get that shot because that will send me right off and trigger’’ (White, 54, San Francisco, HIV negative). ‘‘I have a friend that’s in recovery and that was one of his things, was injection. And I think that if he—he’s not HIV positive, thank God, but if he was, it might be a trigger for him’’ (Mixed Race, 39, San Francisco, WLWH).
Women with a history of illegal drug use who were open to injections	‘‘They’re so used to getting popped, especially when you used to be an ex-addict…It’s just like, ‘Okay, another shot, whatever’’’ (Black, 60, Washington DC, WLWH). ‘‘People that shoot up drugs, they’ll be quick to do it, too, because they already know how to use the needle’’ (Black, 45, Atlanta, WLWH). ‘‘I’ll tell you who it’ll really benefit. Somebody that’s an I.V. drug user. They’ll really benefit from that, because, if they’re out there shooting up and stuff, taking their medicine every day—you might be homeless, anything. Even that, homelessness. If you have those kind of variables going on in your life, not having to keep up with pills and only having to turn up somewhere one time a month to get a shot is going to be a whole lot easier for you than the other’’ (Black, 52, Chapel Hill, WLWH). ‘‘Because it’s giving a different message. It’s not, you know, drugs like that. But, you know, if they don’t have no kind of effect in that kind of way then they should be all right. It’s not like weed or alcohol, <laughs> you know?’’ (Black, 44, San Francisco, HIV negative).
Women who currently inject drugs	‘‘People that shoot up drugs, they’ll be quick to do it, too, because they already know how to use the needle’’ (Black, 45, Atlanta, WLWH). ‘‘They’re already shooting up so why not the shot?’’ (Black, 53, Atlanta, HIV negative). ‘‘I think that the intravenous drug users would love to have that’’ (Caucasian, 54, San Francisco, HIV negative).

WLWH, women living with HIV.

Women with a history of illegal injection drug use

Participants were divided on how women who used to inject drugs might react to LAIs. Among women who had a history of injecting drugs, some stressed that they would avoid LAIs because even the sight of a needle, ‘‘can be a trigger’’ (Caucasian, 57, Atlanta, WLWH).

Additional women predicted that monthly or bimonthly injections could lead to recurrence of substance use. One shared that she ‘‘tried to shy away from needles, because it brings back the flashbacks of getting high’’ (Black, 62, Bronx, WLWH). Another added that ‘‘I think it would make them leery. Because they finally stopped using a needle and now, you want me to shoot myself again with something else? So no’’ (Black, 52, Chicago, WLWH). Participants stressed how even something that *looks* like a needle could be triggering: ‘‘I was at a NA meeting and the secretary of the meeting was jotting down notes and he had a mechanical pencil...And she, the lady that was there with me, she tapped me and, ‘Would you ask him would he change to an ink pen or something?’ Because the tip of that mechanical pencil reminded her of a needle and she was an intravenous user, you know. And just in that meeting that had an effect on her (Black, 61, Chicago, HIV-negative).’’

Some women with a history of drug described how it would be an individual-level decision about whether a history of injection drug use might limit their willingness to use LAIs:

> ''It goes two ways. Some people will be like, 'Hell yeah, I can do that,' because it's easy to just shoot it with the needle. Some people will be like, 'Oh, no, that needle gives me flashbacks,' and it's a trigger'' (Black, 53, Chicago, WLWH).

In contrast, several women agreed that having injected drugs would not affect their willingness to receive injections. A woman with injection history shared that ''When they do phlebotomy on me, and they take my blood, or whatever, it just doesn't…I never thought of it like that. It don't bother me'' (Black, 61, Chicago, WLWH).

Another woman with a history of injection drug use shared that she was ''needle shy once we stop shooting ourselves,'' but that ''I don't care. I just want to get my meds in me'' (Black, 56, Chicago, WLWH). Another woman with a history of drug use seconded that sentiment and shared that a woman's experience with injecting: ''would probably make them just get the shot. They're used to sticking their self any way, why not?'' (Black, 55, Chicago, WLWH).

Another woman with a history of injection drug use felt that being comfortable with needles would certainly make someone comfortable with LAI: ''It'd be a breeze…They wouldn't even have to think about it'' (Black, 45, Chicago, HIV-negative). This highlights the importance of patient-provider communication to identify unique needs among women with injection drug use histories.

Women who currently inject drugs and had few concerns about LAI

Most women felt that people who currently inject drugs would be especially willing to try LAI ART for treatment and prevention. A woman with a history of drug use noted: ''it wouldn't matter to them, a needle's a needle, you know?'' (Black, 52, Chicago, WLWH).

One woman with a history of drug use stressed that people who currently inject drugs might have hectic and unpredictable lives that would make daily pill taking challenging. Comparatively, getting to an appointment every 1–2 months seemed manageable: ''If I'm doing drugs, I'm all over the place. I'm not thinking about that. I'm not thinking about no pill, and I think that's a part of a lot of the issues…Every two months you should be able to make it to appointment but if I got to take them pills every day and I'm out there smoking and drinking and doing what I'm doing, no ma'am, because I've been in that situation'' (Bi-racial, 54, Atlanta, HIV negative).

Rather than a matter of preference for or aversion to needles based on histories of drug use, this response considers how LAI might fit more seamlessly into the challenging realities of daily life for those who inject drugs. These categorizations focused on the fact that people who use injection drugs may benefit from the different administration schedule of LAI (monthly vs. daily pills) and noted that there may be fewer fears around needles as a result of exposure.

Discussion

This study examined how a history of injection influences women's attitudes toward LAI ART and PrEP. Overall, participants highlighted how LAIs may improve adherence by freeing women of treatment fatigue and reminders associated with daily pill-taking, eliminating potential stigma, and facilitating confidentiality.[38,39] Study findings indicate that future discussions about the women that could most benefit from LAI ART and PrEP should incorporate injection history, as the women we interviewed had existing preferences based on their experiences with injection; these themes did not differ by women's HIV status.

Most women felt that a history of periodic injectable medications would increase LAI interest. The limited existing research on previous injection and LAI acceptability suggests that it may facilitate future LAI uptake, including among patients with diabetes[6] and on antipsychotics.[43] However, a study of patient attitudes toward LAI buprenorphine for opioid-use disorder found that perceptions varied widely.[44] This is particularly salient since research has outlined how LAI antipsychotics and LAI opioid agonist therapies are often associated with coercion, involuntary hospital admittance, and court-ordered treatment.[45,46]

While women with periodic injections were open to LAI, those with consistent LAI use were more reticent, including those with negative past experiences. This included a desire to limit the number and frequency of injections. Women also wanted to avoid more frequent clinic visits. Thus, LAI ART and PrEP would ideally coincide with existing LAI treatments (e.g., birth control) to minimize such structural barriers, an approach currently used in some clinics that colocate care for HIV and substance use.[47]

Opinions were mixed regarding how a history of injection drug use might influence women's willingness to use LAI ART or PrEP. Women with and without a history of drug use suggested that LAIs would be triggering, while others felt that familiarity with needles would predispose people who used injection drugs toward LAI. Many also discussed the importance of the type of needle used, as well as whether someone else gave them the shot or they gave it to themselves. Research has shown that women who inject drugs face unique barriers to ART and PrEP adherence,[18] and that WLWH who inject have worse HIV outcomes than women who do not.[18,20] These findings suggest that LAIs may support adherence for a subset of women with a history of injection drug use, although barriers remain regarding knowledge of PrEP[48] and LAIs among this population. In addition, research among women who inject drugs shows low rates of Depo-Provera use with barriers that include side effects, inability to access clinic visits, and structural drivers such as unstable housing.[49,50] Several highlighted that women who *currently* inject drugs would be particularly comfortable with LAI. These divergent findings are consistent with recent research which found that some people who formerly inject drugs viewed LAI as a potential trigger, while others were less concerned because of their experience with needles.[22] Thus, providers must consider each patient's unique history and perceptions when deciding between LAI and daily pills.

LAI contraception offers insight into the challenges of implementing and sustaining LAI ART and PrEP, as it allows patients a choice between LAI and daily pills. While enthusiasm for Depo-Provera was initially high due to convenience, privacy and its 3-month dosing,[51] side effects and transportation barriers led to improper adherence and discontinued use.[52] One-year Depo-Provera continuation rates were lower than expected (40–60% in one study).[32] Continuation rates have

been improved by delivery outside of health care institutions (e.g., pharmacies) and self-administration.[32] Contraception-focused providers suggest that LAI ART and PrEP adherence could be improved by prioritizing local health clinics and community education, emphasizing side-effects, and minimizing the need for frequent clinic visits.[53] The United States could also build on client-center approaches that have improved ART adherence across sub-Saharan Africa, including the use of family planning clinics, community health centers, pharmacies, and home-based care.[54,55] These demonstrate the need for a patient-centered model of LAI implementation where injection history is incorporated into provider-patient discussions, as this approach improves patient health outcomes.[56] Providers may suggest treatments before considering patient preferences,[57] which become especially problematic when providers' and patients' perceptions differ.[58] Patient-centered care is an increasingly emphasized model in HIV care,[57] as patient involvement improves adherence, disease coping, and quality of life,[57] low patient involvement decreases HIV medication adherence, satisfaction, and health outcomes.[59,60]

Strengths and limitations

This study was conducted in a geographically diverse sample across six US cities. Clinical trials participants are often more adherent and face fewer barriers than those who do not participate; women in WIHS mirror the US HIV epidemic and can therefore provide unique insights that clinical trial samples cannot. While younger women may be at higher risk for HIV acquisition, and thus in need of direct targeting for LAI PrEP roll-out, they may also have less history of injection-based medication use or injection drug use. The median age of this sample was 53, and women may have more history of injections than the general population. While women in this sample were on average older, one-third were of reproductive age and at higher risk. In addition, HIV women older than the age of 55 constitute the only age group in the United States for which HIV incidence is not decreasing,[16] highlighting the need to address their treatment and prevention needs. This study elicited responses based on individual women's experiences and their impressions of others' experiences, limiting the reliability of these results for specific subpopulations. Finally, some women had not heard about LAI modalities and had less time to formulate an opinion after being informed by the interviewer.

Conclusions

The role of injection history will become increasingly salient as additional medications shift toward injectable form.[61] Future studies should incorporate injection history into their research questions and examine the acceptability of LAI ART for HIV treatment and prevention among women who use drugs to examine their attitudes toward injectable medications more deliberately. LAI ART and PrEP research should also examine provider attitudes toward patients with histories of injection (both medication and substance use) to determine how knowing a patient's history influences their attitudes and clinical prescribing. As LAI ART for HIV treatment and prevention is scaled-up, systems must be created for women and providers to collaborate to best identify which women might need additional support for LAI use and which might be better candidates for daily pills.

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