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PrEParing for Long-acting Injectable PrEP in the South: Perspectives from Healthcare Providers in Georgia

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Abstract

New modalities of Pre-exposure Prophylaxis (PrEP) such as long-acting injectable PrEP (LAI-PrEP) promise increased prevention of HIV transmission; however, similar biomedical interventions have not been met with universal adoption by healthcare providers or populations most affected by HIV. This qualitative study explores healthcare provider considerations for the rollout of LAI-PrEP. Eleven key-informant in-depth interviews were conducted with clinicians who prescribe daily oral PrEP. Participants reviewed a currently proposed LAI regimen and were asked to reflect on its implications for their clinical practice. Interviews were transcribed verbatim and thematically coded, with results organized using the Consolidated Framework for Implementation Research (CFIR). All participants expressed interest in prescribing LAI-PrEP and anticipated that at least some patients would be interested. Participants identified characteristics of the intervention, inner intervention setting, and outer intervention setting that will be influential in bringing LAI-PrEP to scale. Clinicians in the South have unique insights into the challenges and opportunities for successful rollout of future PrEP regimens. Bringing these insights into a CFIR framework highlights the nuances surrounding LAI-PrEP, including structural concerns such as cost barriers and access to in-person healthcare services. It is critical to address these challenges to ensure successful implementation of new PrEP formulations.

Keywords

PrEP; Healthcare Provider; South

Introduction

In the United States (US), 1.1 million people are currently living with HIV, with over 38,000 persons newly diagnosed in 2017 (UNAIDS, 2018). Southeastern states account for more than half of new diagnoses (Centers for Disease Control and Prevention). In Atlanta, Georgia in 2016, 35,402 individuals were living with HIV (Sanchez et al., 2014). The South has unique prevention challenges due to geographically dispersed populations and fewer resources for safety net healthcare program (Sullivan et al., 2019).

Since its approval in 2012, daily oral pre-exposure prophylaxis (DO-PrEP) has moved to the forefront of HIV prevention strategies with evidence of high levels of efficacy (Grulich et al., 2018). Despite guidelines recommending the widespread use of PrEP, only 26 per 100,000 persons in the US who had indications for PrEP were prescribed it in 2017 (Siegler et al., 2018; WHO, 2015).

Long-acting injectable PrEP (LAI-PrEP), formulations of antiretroviral medication administered periodically by injection, may be an attractive alternative and overcome some barriers to DO-PrEP (Murray et al., 2018). The safety and tolerability of one LAI-PrEP regimen, long-acting cabotegravir (CAB LA, GSK1265744), in HIV-uninfected men has been demonstrated in two Phase IIa trials supporting 8 week intervals for injection (Landovitz R, 2017; Markowitz et al., 2017). CAB LA is currently being studied at ten sites in eight countries ([NCT02720094](#)) (Landovitz R, 2017). Early results suggest that LAI prep is superior to DO-PrEP (Landovitz et al., 2020).

Given the potential benefits of LAI-PrEP and the lagging dissemination of DO-PrEP in the South, the primary objective of this study was to understand existing facilitators of and barriers to prescribing PrEP in Georgia and identify provider attitudes and concerns that may need to be considered before the introduction of LAI-PrEP. We organized the findings using the Consolidated Framework for Implementation Research (CFIR) (Damschroder et al., 2009).

Methods

We conducted 11 key-informant in-depth interviews (IDIs) with PrEP-prescribing healthcare providers in Metro-Atlanta, GA between February and October 2018. The semi-structured IDI guide explored provider perspectives on LAI-PrEP provision, with a focus on provider willingness to provide LAI-PrEP, concerns, and sources of information. The study was approved by the Emory University Institutional Review Board.

Procedures

Eligible participants had prescribed daily, DO-PrEP to one or more patients in the last year, and provided care in the state of Georgia. IDIs were conducted in person or over the phone by three authors (CX, JS, RD). Participants completed a questionnaire characterizing their clinical practice. Participants were shown a pictorial diagram (via e-mail) featuring DO-PrEP and CAB LA prescribing and testing regimens (Figure 1). Participants were asked to draw on their experiences prescribing DO-PrEP in order to reflect on potential benefits and

challenges of a LAI-PrEP regimen. Interviews were recorded digitally and transcribed verbatim. Participants received a \$50 gift card.

Thematic Analysis

Verbatim transcripts were imported into MAXQDA (Software, 2016). The codebook was developed iteratively beginning with deductive themes and refining through reading transcripts and discussing new (inductive) codes which were then applied by two coders. The codebook was finalized and re-applied by a third coder after addressing any discrepancies. We examined codes and compared across cases to summarize findings using 5 major CFIR framework domains to organize results (see Table 2) (Damschroder et al., 2009). The authors met regularly to discuss the progress, emergent themes, and to assess saturation.

Results

Overall, clinicians had positive responses to LAI-PrEP regimens and held diverse opinions regarding key areas for CFIR constructs. DO-PrEP clinicians described potential barriers for the dissemination of LAI-PrEP, but anticipated interest in LAI-PrEP from both clinicians and their patients. A visual summary is provided in Figure 1. Tables 2 show themes by category and representative quotes. For characteristics of clinicians and their practices see Table 1.

Characteristics of the Intervention

Clinicians described benefits (e.g. less frequent dosing) and drawbacks (e.g. more frequent office visits) to LAI-PrEP. An injection would lessen the daily cognitive burden on users; however, the regimen included elements seen as increasing complexity and reducing trialability.

Clinicians emphasized keeping LAI-PrEP as simple as possible while maintaining safety. About half suggested a need for accessible locations such as pharmacies for testing and injections. All providers suggested that the dosing schedule and frequency of visits could be barriers. Clinicians were concerned with how the difference in frequency of PrEP-related visits for each type of regimen (DO-PrEP and LAI-PrEP) may result in confusion when scheduling at clinics. A smaller subset of providers favored seeing patients more frequently to monitor progress. Currently, DO-PrEP is used both prior to initiating the injectable to monitor side-effects (using an oral form of the drug contained in LAI-PrEP), and when discontinuing LAI-PrEP (using tenofovir-based oral PrEP) to avoid the development of drug resistance (“covering the tail”). Providers suggested that the oral lead-in and tail coverage might confuse patients. In the experience of several providers, discontinuation of DO-PrEP often involves patients ceasing their visits without discussion which raised concerns about the feasibility of providing tail coverage as the LAI-PrEP formulation washes out of the body over months. Clinicians emphasized effectiveness and safety as paramount (see Table 2).

Inner Setting

Providers discussed the inner setting primarily in terms of logistical clinical concerns (see table 2). For example, providers discussed the varying testing schedules between forms of PrEP and how these differences may cause confusion for clinic staff. While salient, these concerns were also noted as being easily addressed with training and standard operating procedures.

Outer Setting

Clinicians described the outer setting in terms of patient needs, the characteristics of their service populations, and structural concerns, and described it as the most formidable challenge to effective implementation of LAI-PrEP. No clinician described anticipating an immediate high demand for LAI-PrEP among current patients; however, nearly all suspected that at least some patients would be interested. Many providers commented that patient requests would heavily influence how much they prescribe LAI-PrEP, indicating that demand-generating interventions would be important.

Most clinicians cited working with populations vulnerable to HIV (e.g. gay and bisexual men, transgender people, or sex workers) and the high prevalence of HIV in the South as primary influences on their decision to provide DO-PrEP and possibly LAI-PrEP in the future.

Structural concerns were often mentioned, including the cost of the medication, insurance coverage, housing instability, and patients' access to clinics. These concerns then raised questions about the role of publicly-funded clinics and whether medication assistance programs would be expanded to cover LAI-PrEP.

Individuals Involved

Clinicians noted a desire for clearly communicated evidence about the intervention to all involved. Nearly universally, clinicians anticipated that their peers would have interest in providing LAI-PrEP; however, they had some important caveats. Clinicians suspected that general practitioners and other providers who do not perceive HIV prevention as relevant to their practice may be less likely to provide LAI-PrEP. Nearly all clinicians described the effectiveness of DO-PrEP as a primary reason why they originally began prescribing.

Implementation Process

Clinicians provided suggestions for ensuring smooth implementation. Several cited injectable contraceptives as a model from which to learn. Others emphasized the importance of marketing, reference materials, and complementary interventions such as mobile apps, suggesting that it is important to market LAI-PrEP to providers as well as to patients.

Discussion

Our analysis found high interest for LAI-PrEP. As the clinical trials evaluating the efficacy of LAI-PrEP come closer to completion, preparing the public health system for LAI-PrEP

may help to bolster uptake, particularly among populations disproportionately impacted by HIV including youth and racial/ethnic minority populations (Kuhns et al., 2017).

Clinicians were enthusiastic about having another option to add to their HIV prevention portfolio. Additional interventions to promote LAI-PrEP, enable informed choices between different PrEP regimens, and connect patients to support should be designed, including maximizing the use of mobile/online resources (Muessig et al., 2015; Sanchez et al., 2014).

Our findings complement previous research that found a more rapid roll-out of LAI-PrEP would be facilitated by preemptive public health communication emphasizing safety and efficacy and promoting success stories from a range of types of providers (Berwick, 2003). By anticipating clinical needs and implementing complementary interventions to enhance diffusion, a wider array of clinicians may adopt LAI-PrEP more rapidly.

Clinicians emphasized structural concerns that may affect the rollout of LAI-PrEP such as insurance, housing instability, adequate personnel to administer the drug, and medication storage. The concerns about insurance are reflected in previous literature and may compound issues surrounding access to LAI-PrEP for specific populations such as racial/ethnic minorities. (Bauermeister et al., 2013) (Wehby & Lyu, 2018). To better address structural barriers, practitioners need to consider creative approaches to increasing access. For example, the provision of LAI-PrEP could learn from other medical interventions, such as injectable hormones for contraception, which are now provided by pharmacists in some states (Vu et al., 2019).

Conclusion

With LAI-PrEP on the horizon, biomedical HIV prevention is poised to take an important leap forward. Public health experts should utilize this time before market availability of LAI-PrEP to prepare thoughtfully for its successful rollout and implementation, particularly in the South, where HIV prevention interventions are needed most.

Acknowledgments

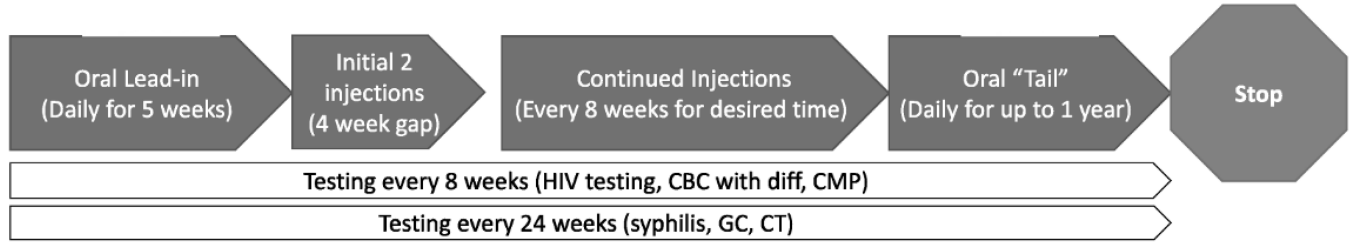
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Possible Injectable PrEP Regimen



Current Truvada Regimen

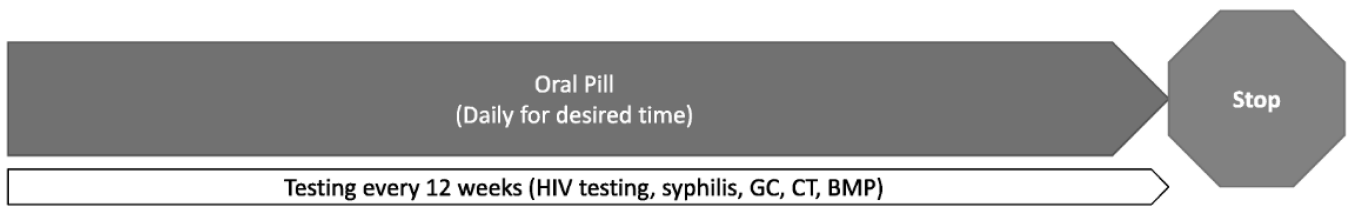


Figure 1. Example regimen for CAB LA provided to participants at the time of interview either on paper or via e-mail.

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Table 1.

Key informant characteristics and demographics (n=11)

Variable	% (n)	Mean (SD)
Length of Interview		36.2 (11.4)
Mode of Interview		
Phone	72.7% (8)	
In-person	27.3% (3)	
Gender		
Male	36.4% (4)	
Female	63.6% (7)	
Race		
Black	18.2% (2)	
White	63.6% (7)	
Asian	9.1% (1)	
Latino/Hispanic	9.1% (1)	
Age		44 (9.7)
Role		
Medical doctor	63.6% (7)	
Nurse practitioner	18.2% (2)	
Registered nurse	9.1% (1)	
Physician assistant	9.1% (1)	
Type of Practice *		
Academic	27.3% (3)	
Community/Public Health Clinic	27.3% (3)	
Clinical Care	9.1% (1)	
Correctional Health	9.1% (1)	
Single specialty Group	18.2% (2)	
Multi-specialty Group	9.1% (1)	
Primary Care	9.1% (1)	
Solo	9.1% (1)	
Ambulatory Care	9.1% (1)	
Department of Health	9.1% (1)	
Racial Make-up of Practice Population		
Majority Black	81.8% (9)	
Majority white	18.1% (2)	
Socio-economic Make-up of Practice Population		
Majority Low-income	72.7% (8)	
Majority Middle income	18.2% (2)	
Majority middle to upper-income	9.1% (1)	
Number of STI Diagnoses in Practice per Quarter		
<5	18.2% (2)	
5–10	9.1% (1)	

Variable	% (n)	Mean (SD)
>10	72.7% (8)	
Specific Populations Prescribed PrEP in last Quarter*		
Men who have sex with men	72.7% (8)	
Transgender	54.5% (6)	
Heterosexual	63.6% (7)	
Injection Drug Users	18.2% (2)	

* Participants could respond with multiple answers.

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Table 2: Summary of findings categorized by key constructs of the Consolidated Framework for Implementation Science with selected supporting quotes

CFIR Construct and definition (Damschroeder, et al., 2009)	Summary of Findings	Selected quotes
<p>Intervention Characteristics: includes constructs related to the proposed intervention such as source of the intervention, strength, quality, relative advantage, adaptability to local needs, the ability to test it out (trialability), cost, etc.</p>	<ul style="list-style-type: none"> Effectiveness is the most important metric for providers Benefits of a less frequent dosing schedule LAI-PrEP is easily concealable to avoid stigma High frequency appointments may be favored by providers, but a barrier for patients Complex uptake and tail may confuse patients, reduce trialability, and pose a barrier to uptake 	<p>“There’s a lot of people that are non-adherent to taking pills or don’t find it easy to adhere to taking a pill every day. For those people, it could be an important intervention. One of the major drawbacks of this regimen is it still has to be injected every two months... We need something that is minimum six months to a year in duration, and this is not that product.” IDI-7</p>
<p>Inner Setting: Includes constructs interior to the implementation environment such as structural characteristics of clinics, existing networks, culture, implementation climate, etc.</p>	<ul style="list-style-type: none"> Concern over detail of clinical logistics Provision of necessary refrigerated storage Minimum credentials of personnel for administration and impact on clinic flow Concerns over details of insurance reimbursements Differing schedules for different forms of PrEP may be confusing Logistics may be easily addressed with examples of standard operating procedures 	<p>“It would be easier once the staff had some guidance as to how – ‘Where am I storing the medicine? Who is bringing the medicine? Is the patient bringing the medicine? Are we reconstituting it?’ Or are we basically giving the medicine to the patient in the office? Are we essentially selling the medicine to the patient? Where am I administering the shot? What body part? What blood work?’ With a little training, everything can be done.” IDI-6</p>
<p>Outer Setting: Includes constructs exterior to the implementation environment including patient needs, patient resources, policies, etc.</p>	<ul style="list-style-type: none"> Providers are acutely aware of high HIV prevalence in the South Patient requests for PrEP prior to becoming a PrEP provider Concerns over insurance coverage of novel forms of PrEP Concerns over cost as a barrier to patients Concerns about accessing providers who prescribe LAI-PrEP, such as distance and transportation 	<p>“...there were guys that would come in and when we’d start talking about sex and about protection and about safer sex one of us would bring it up in the conversation, or someone would say, “I heard—isn’t there a pill that’s out” this, that, and the other, and then it started to kind of snowball from there.” IDI-1</p>
<p>Individuals Involved: Includes constructs relating to implementers or recipients of the intervention such as knowledge, beliefs, self-efficacy, etc.</p>	<ul style="list-style-type: none"> Need for strong scientific evidence from reputable sources when introducing LAI-PrEP Some providers don’t perceive themselves as HIV prevention providers and may need targeted communication 	<p>“I think that by the time it is available for PrEP it will have been in some use for treatment... so at least from the HIV treatment side, we’ll be able to provide some clinical experience for PrEP providers for what it’s like to utilize these medications with patients. I’d like to see those data. Some are available, but I’d like to see it in clinical use on the HIV treatment settings.” IDI-3</p>
<p>Implementation Process: Includes constructs related to the process of implementing the proposed intervention such as planning, engagement, execution of the intervention, and evaluation.</p>	<ul style="list-style-type: none"> May need to target specific types of providers or populations who are more receptive during initial rollout Need to message to GPs or other providers who are not “typical” PrEP providers with specialized communication strategies May need to provide standard operating procedures for ease of implementation May need desktop/mobile applications and complementary interventions to facilitate provision, and adherence 	<p>“And I think we really haven’t identified the best way to do that. We talk about identifying key leaders in the group, specifically within African Americans, because I’m going to focus more so on that when we’re talking about access, and understanding, and information about PrEP. I think it’s peer groups that will definitely get that information, specifically for MSM, but also for heterosexual men and women in terms of just talking about this concept. And then there’s always the idea of medical mistrust. Again, the innate mistrust of the medical community from African Americans that is borne out of years of abuse that it’s very hard to find someone who really doesn’t interact with the healthcare system, but I can recognize that they’re at risk for HIV, STDs, and other healthcare issues. Yet, they don’t interact with that healthcare system then you want to ask them to take this pill or get this injection everyday for something that they do not have, and it’s kind of a change in that conversation in terms of prevention.” IDI-4</p>