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Challenges to PrEP use and perceptions of urine tenofovir adherence monitoring reported by individuals on PrEP

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ABSTRACT

Maximizing the impact of HIV pre-exposure prophylaxis (PrEP) requires optimizing access and adherence for those at risk of contracting HIV. This study examined challenges to the processes of accessing and adhering to PrEP encountered by participants from a large, U.S. urban clinical center and assessed the utility of objectively monitoring PrEP adherence via urine. Most participants (65%) reported starting PrEP within 1–3 months of hearing about it, although 35% of participants encountered a provider unwilling to prescribe PrEP. Self-reported adherence was high among this population, with remembering to take the medication reported as the major barrier to adherence (44%) rather than cost or stigma. Urine tenofovir (TFV) monitoring was highly acceptable to this population, and participants indicated greater willingness to undergo urine monitoring every 3 months compared to finger prick (dried blood spot), phlebotomy, or hair follicle testing. These findings highlight the importance of focusing efforts toward reducing obstacles to PrEP use and support the use of urine TFV adherence monitoring as a marker of PrEP adherence.

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PrEP; access; adherence; urine tenofovir monitoring

Introduction

Following the uptake of HIV pre-exposure prophylaxis (PrEP) in the form of Tenofovir/emtricitabine (TDF/FTC) (Riddell, Amico, & Mayer, 2018), it is critical to reduce barriers to PrEP access and adherence, especially as experienced by Black and Hispanic populations who constitute disproportionately fewer prescriptions despite facing disproportionately higher HIV risk (Centers for Disease Control and Prevention, 2018; HIV.gov, 2018). Previously cited barriers to accessing PrEP include stigma associated with HIV, lack of PrEP awareness, structural barriers such as insurance coverage, and lack of prescriber knowledge (Calabrese & Underhill, 2015; Haire, 2015; Horberg & Raymond, 2013; Lelutiu-Weinberger & Golub, 2016).

Many barriers to adherence to PrEP have been documented as well, including stigma associated with HIV, side effect concerns, concern that PrEP does not fully protect against HIV, and PrEP's potential impact on drug resistance (Golub, Gamarel, Rendina, Surace, & Lelutiu-Weinberger, 2013; Van der Elst et al., 2013). These may be compounded by common challenges of taking daily medication such as remembering and understanding how to take medication correctly (American Medical Association, 2016). Thus, it is important that we invest in initiatives specific to adherence, especially following a recent report documenting an increase in HIV acquisition among patients prescribed PrEP (Eaton et al., 2018).

For supporting adherence to PrEP, therapeutic drug monitoring (TDM) has shown promise, particularly via urine tenofovir (TFV) monitoring (Koenig et al., 2017) and plasma monitoring (Landovitz et al., 2017). Advantages of urine-based TDM include high concentrations of TFV in urine, noninvasiveness, and the 14-day stability of TFV in urine (Koenig et al., 2017). However, to fully reap the benefits of urine TDM for PrEP, concerns regarding acceptability need to be considered.

This study characterized challenges to access and adherence faced by patients of a large, urban, youth PrEP program in Philadelphia, as well as the theoretical acceptability of using urine TDM to monitor adherence to PrEP.

Methods

Young adults age 18–34 from the youth PrEP program of an urban community health center in Philadelphia were asked to complete a 54-item anonymous survey assessing their experiences accessing and adhering to PrEP. The

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agency's IRB approved this study. All participants were required to be currently prescribed PrEP, with a target population of approximately 250 PrEP users. Therefore, this study focuses on challenges faced by individuals who ultimately started PrEP rather than the experiences of individuals who failed to initiate. Participants completed the survey either on paper in-clinic or online via Qualtrics using flyers including survey links and QR codes. Participants completed check-box consents to maintain anonymity. This study was not incentivized.

Responses, in the form of 5-point Likert scales, numeric write-ins, and nominal responses assessed the following: (1) Demographics (2) Prior experiences accessing PrEP (i.e., acquiring a prescription) and current experiences adhering to PrEP (i.e., challenges to taking the medication) and (3) PrEP adherence monitoring preferences, including attitudes toward urine TFV monitoring. Primary outcomes included time-to-initiation from first hearing about PrEP, major challenges to accessing and adhering to PrEP, and urine test acceptability, with outcomes compared between demographic categories. Of the 54 items, a subset of questions concerning Internet and app usage is not included in this manuscript.

Analyses were performed in Microsoft Excel using StatPlus, with demographics analyzed with descriptive statistics. We examined access and adherence outcomes to report averages from Likert scale data, which were rated 1–5, with 1 indicating least and 5 indicating greatest difficulty/concern/willingness. We additionally reported our averages, sums of independent random variables, with standard deviations and/or confidence intervals to contextualize them with respect to a normal distribution of averages around the true mean. Binary outcomes received the same treatment. We compared these data along demographic lines, using t-tests for Likert averages and X^2 tests for binary data. Lastly, we compared PrEP adherence monitoring preferences using ANOVA.

Results

From March 2017 through December 2017, 40 subjects completed the survey, with 36 completing paper surveys in-clinic and 4 completing the Qualtrics survey, out of approximately 250 approached (Table 1).

From access and adherence data, key findings included 65% reporting a time-to-initiation of less than 3 months after first hearing about PrEP (Table 2). Participants reported little difficulty obtaining a PrEP prescription at a Likert score of 1.5 (SD = .78). For participants who reported a previous experience in which a provider refused to prescribe PrEP ($n = 14$ or 35%), 9 did not know the provider's reason for refusing,

Table 1. Study Demographics.

Demographics	Mean	Range
Age	22 years	18–32 years
Sexual partners in last year	5.9 (median 4, SD 5.8)	0–30
	Number of participants	%
Race[a]		
Black	26	65%
White	13	32.5%
Native American	2	5%
Other	2	5%
Non-Black (calculated)[b]	14	35%
Ethnicity		
Not Hispanic/Latinx	30	75%
Hispanic/Latinx	10	25%
Sex assigned at birth[c]		
Male	35	87.5%
Female	5	12.5%
Current gender identity descriptors[a]		
Male	32	80%
Female	5	12.5%
Genderqueer/Non-binary/Genderfluid or Transgender	3	7.5%
Other	1	2.5%
Sexual behavior[c]		
MSM	35	87.5%
Not MSM	5	12.5%
Condom use		
Sometimes, rarely, or never	22	55%
Always or often	18	45%
Length of time on PrEP		
>1 year	16	40%
6–12 months	10	25%
3–6 months	2	5%
1–3 months	4	10%
<1 month	8	20%

[a]Participants selected all that apply, with a total of 40 respondents.
[b]This is the calculated demographic of individuals who did not identify as "Black", used for the statistical comparison between participants who identify as Black and participants who do not identify as Black.
[c]All transgender/non-binary participants selected MSM as a descriptor, with all reporting male sex assigned at birth.

Table 2. Access Experiences.

Access—time to initiation How long was it between the first time you heard about PrEP and when you got your first dose of PrEP?	*n*	%
<1 month	16	40%
1–3 months	10	25%
3–6 months	5	12.5%
6 months to 1 year	5	12.5%
>1 year	4	10%
Access – yes-no questions	**Yes (of 1.000)[a]**	**95% CI**
Did you experience any stigma or judgment from your provider in trying to get a PrEP prescription?	.051	0 to .120
Did you feel comfortable telling your friends you were starting PrEP?	.80	.674 to .926
Did you feel comfortable telling your family that you were starting PrEP?	.65	.50 to .80
Did you feel that you had enough information and the right resources to figure out how to get a PrEP prescription?	.925	.842 to 1.00

[a]1.000 = 100%.

3 reported the provider was concerned using PrEP would decrease risk reduction behaviors such as condom use, 1 participant reported the provider was not sure the patient was eligible, and 1 participant reported the provider did not want to prescribe that type of medication. Despite this, when asked to identify "the biggest barrier to getting on PrEP", there was no consensus among the 33 write-in responses. Only 4 participants cited finding a provider as the main barrier, ranking third behind 11 citations for "no barrier" and 5 citations for cost. Participants reported they were moderately concerned about cost prior to accessing PrEP at a Likert score of 2.46 (SD = 1.67).

Concerning adherence, participants reported missing less than one dose of PrEP per week on average (0.87 with 95% CI: 0.61–1.13), with Black participants reporting more missed doses than other races (1.15 compared to 0.31, $p < .001$). Participants who were not comfortable telling their friends they used PrEP missed more doses of PrEP weekly than those who were comfortable disclosing PrEP use (1.44 compared to 0.73, $p = .0064$). Qualitatively, participants reported that the biggest barrier to PrEP adherence was remembering to take their medication (44% of 34 write-in responses). This study did not identify any differences comparing Hispanic/Latinx and non-Hispanic/Latinx populations.

Regarding urine TFV adherence monitoring, theoretical acceptability was high (Table 3), with participants indicating greater willingness to undergo urine TFV monitoring every three months compared to a blood test from a finger prick, phlebotomy, or a hair test ($p < .001$, $F = 6.76 > F_{crit} = 2.66$). A majority preferred to have the test monthly (31.4%) or every 3 months (45.7%) versus weekly (5.7%), every 6 months (14.3%), or never (2.9%). 60.5% reported being unlikely to resume taking their PrEP before their appointment to "pass the test", with participants age 22 and older reporting they would be less likely to endorse this pattern compared to subjects 18–22 (1.74 compared to 2.95, $p = .024$). 23.1% reported concern about their urine being tested for illicit drugs, with more concern among participants age 18–22 than among older participants (2.40 compared to 1.37, $p = .033$).

Table 3. Perceptions of Urine TDM.

Urine tenofovir testing utility – Likert means[a], 1 = least 5 = greatest willingness/ worry/likelihood	AVG	SD
How willing would you be to take a blood test (finger prick) every 3 months to see if you are taking PrEP correctly?[a]	4.05	1.15
How willing would you be to take a blood test (drawn from your arm vein) every 3 months to see if you are taking PrEP correctly?[a]	3.75	1.42
How willing would you be to take a hair test (submitting 50–100 pieces of hair from your head or pubic region) every 3 months to see if you are taking PrEP correctly?[a]	3.10	1.68
How willing would you be to take a urine test (urinate in a cup) every 3 months to see if you are taking PrEP correctly?[a]	4.42	0.95
How worried would you be that your urine would be drug tested when collected?	1.90	1.53
If you hadn't been taking your PrEP, how likely is it that you would start taking it within 24 h of your lab appointment just to "pass the test"?	2.34	1.68
Urine tenofovir testing utility – yes-no questions prompt: "Patients taking PrEP typically get urine testing and blood testing every 3 months to test for HIV, sexually transmitted infections, and kidney function".	**Yes (Out of 1.000)**[b]	**95% CI**
Would it be helpful for you if a urine test that can determine how well you are taking PrEP were included in standard testing?	.897	.802–.992
Would you be interested in seeing the results?	.846	.733–.959
Would you be interested in using the test at home to assess your PrEP usage?	.615	.462–.768

[a]See ANOVA included in results for testing preference significance.
[b]1.000 = 100%.

Discussion

This study assessed participants' experiences accessing and adhering to PrEP in an urban clinic setting, including perceptions of using urine monitoring for TDM. Participants reported being able to access PrEP quickly, but notable reported barriers included provider unwillingness to prescribe. Although most participants were unsure of the reason for refusal, subjects cited provider concerns about "risk compensation", lack of knowledge about the drug, and not wanting to prescribe the "type of drug". These data suggest the need for expanded educational efforts targeting providers, a need partially addressed by the proposed United States Preventive Services Task Force recommendation regarding PrEP (USPSTF, 2018).

Regarding adherence, the most frequently reported barrier was remembering to take the medication. Additionally, participants perceived urine TDM as the preferred form of adherence monitoring, and combined with the low cost and mobility of a point-of-care urine-based assay, the potential utility of this test extends beyond resourced clinical settings to include settings where result follow-up is difficult or where lab or medical supply costs may be prohibitive. To pursue this potential, further investigation into frequency of "white coat adherence" and efforts to minimize concerns about providers screening urine for illicit drugs may be important.

As a pilot, this study was limited by sample size and conducted at only one clinical site, which may affect the external validity of some findings since values could be influenced by factors unique to the agency or city studied. Notably, responses only solicited time-to-initiation from first hearing about PrEP, which would

be greater than or equal to the length of time individuals spent seeking a prescription. Additionally, although the study population is diverse and representative in the demographics included, a survey-based study is always vulnerable to sampling bias and risks not capturing data from subpopulations less visible to the study, including low literacy and non-English-speaking populations. Finally, by surveying patients in a PrEP clinic who ultimately started PrEP despite challenges they may have faced, this study may be skewed toward identifying potentially surmountable barriers versus those precluding individuals from eventually starting PrEP. Capturing this latter population is more challenging, but future studies could recruit patients in an STD clinic or patients with newly diagnosed HIV who attempted and failed to access PrEP.

Overall, these results highlight the importance of targeting efforts toward addressing remaining challenges to PrEP initiation and longitudinal adherence. Additionally, this population perceived urine TFV monitoring as highly acceptable for use as an objective measure of PrEP adherence.

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