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ORIGINAL PAPER

Barriers and Facilitators of PrEP Adherence for Young Men and Transgender Women of Color

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Abstract

We aimed to discover barriers and facilitators of HIV pre-exposure prophylaxis (PrEP) adherence in young men and transgender women of color who have sex with men (YMSM/TW). Short-term and sustained adherence were measured by urine tenofovir concentration and pharmacy refills, respectively. Optimal adherence was defined as having both urine tenofovir concentration consistent with dose ingestion within 48 h and pharmacy refills consistent with ≥ 4 doses per week use. Participants completed semi-structured interviews exploring adherence barriers and facilitators. Participants (n = 31) were primarily African-American (68%), mean age 22 years (SD: 1.8), and 48% had optimal adherence. Adherence barriers included stigma, health systems inaccessibility, side effects, competing stressors, and low HIV risk perception. Facilitators included social support, health system accessibility, reminders/routines, high HIV risk perception, and personal agency. Our findings identify targets for intervention to improve PrEP adherence in these populations, including augmenting health activation and improving accuracy of HIV risk perception.

Keywords HIV prevention · Pre-exposure prophylaxis · Social support · Adherence

Resumen

Nuestro objetivo fue descubrir los obstáculos y facilitadores de la adherencia al profilaxis de pre-exposición al VIH (PrEP) en hombres jóvenes y mujeres transgénero que tienen sexo con hombres (YMSM/TW) y quienes son minorías étnicas. La adherencia, a corto plazo y sostenida, se midió mediante la concentración de tenofovir en la orina y las prescripciones completadas en la farmacia. La adherencia óptima se definió basado en una concentración de tenofovir en la orina consistente con el uso de PrEP en las ultimas 48 horas y prescripciones completadas en la farmacia consistentes con ≥ 4 dosis por semana. Los participantes completaron entrevistas semiestructuradas que exploraron los obstáculos y facilitadores de la adherencia. Los participantes (n = 31) fueron principalmente afroamericanos (68%), con una edad media de 22 años (SD: 1.8) y 48% obtuvieron adherencia óptima. Participantes discutieron varios obstáculos, incluyendo el estigma, acceso limitado a los sistemas de salud, los efectos secundarios asociados a PrEP, competencia con otras prioridades, y la baja percepción del riesgo de VIH. Los facilitadores incluyeron apoyo social, acceso al sistema de salud, recordatorios/rutinas, alta percepción

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de riesgo de VIH y agencia personal. Nuestros hallazgos identifican oportunidades para mejorar la adherencia al PrEP en estas poblaciones a través de intervenciones, incluyendo la activación de salud y cambios en la percepción del riesgo al VIH en estas comunidades.

Introduction

Oral daily tenofovir disoproxil fumarate-emtricitabine (TDF–FTC) as HIV pre-exposure prophylaxis (PrEP) has the potential to prevent HIV acquisition by over 90% [1–3]. Across PrEP trials, this level of protection is dependent on high levels of adherence [1, 3–8]. Unfortunately, among racial and ethnic minority adolescent/young adult men and transgender women who have sex with men (YMSM/TW) reported adherence rates have been suboptimal in United States-based clinical trials and demonstration projects, despite disproportionally high rates of HIV acquisition [9]. In the Adolescent Trials Network (ATN) open label trial of TDF–FTC-based oral PrEP in 18–22 year-olds, only 34% of participants had protective levels of tenofovir at trial's end, and African-American participants had mean serum tenofovir concentrations below the protective threshold at all measurement points during the trial [10]. Rates of PrEP discontinuation have also been higher in MSM and TW of color, compared to white MSM and TW, in several U.S. based observational studies [11, 12]. For PrEP to turn the tide of HIV incidence in YMSM/TW, it is critical to identify factors associated with adherence in these key populations.

Currently, little is known about the specific barriers and facilitators to PrEP adherence in sexual and gender minority youth of color. In adult PrEP studies, stigma and side effects have been identified as adherence barriers [13, 14]. In a qualitative study of YMSM/TW using PrEP, Stroholm et al. identified substance abuse and disruptions in routine as barriers to adherence [15]. However, data on obstacles to adherence in YMSM/TW of color are limited, particularly in community based samples [16, 17]. While data on the determinants of antiretroviral (ART) adherence in youth living with HIV demonstrate the key roles played by stigma, social support, substance abuse, and health systems factors, such as insurance, caution must be exercised in extrapolating these data to HIV negative youth on PrEP [18–22]. The determinants of PrEP adherence behavior in youth are likely distinct. For example, for PrEP adherence, compared to ART adherence, there is no protective benefit to adherence during periods devoid of risk, and adherence is not driven by the goal of life-sustaining treatment [23].

The objective of our research was to elucidate perceived adherence barriers and facilitators among both optimally adherent and non-adherent YMSM/TW of color in order to identify potential targets for future adherence interventions. As little is known about the drivers of adherence behavior, there is a critical need to draw on existing behavioral theory to identify pathways toward adherence behavior among youth at risk for HIV infection. We have previously used Fishbein's Integrated Behavioral Model to develop a theoretical model of PrEP uptake in young transgender women [22, 24]. Here, we draw on Fishbein's constructs of attitudes, perceived norms and personal agency to determine how these factors may impact PrEP adherence, as well as how environmental constraints may impede adherence success.

Methods

Study Design, Participants, and Setting

This mixed methods study was nested within a prospective observational cohort study aiming to elucidate the social determinants of adherence to daily oral PrEP among YMSM/TW of color. Eligible participants were between the ages of 15–24 years; self-identified as African-American, Latino/a, mixed race, and/or a person of color; were assigned male sex at birth; had self-reported HIV-negative status; had a history of sex with cisgender men and/or transgender women; were prescribed TDF–FTC-based PrEP for ≥ 3 months; and were able to understand written and spoken English. We included only participants who had three months of verified PrEP prescription in order to capture those who had sufficient time to develop a pattern of adherence, and per ATN data demonstrating substantial drop offs in adherence when study visits changed from one to three-month intervals [10]. Prescription of PrEP was verified by clinical and pharmacy records. The primary recruitment site was the Youth Health Empowerment Project (YHEP), a community-based federally qualified health center in Philadelphia providing comprehensive primary care to youth living with and at risk for HIV infection [25]. Participants were also recruited from additional clinical sites, social media, social venues, and geosocial mobile dating applications (see Table 1). Approval was received from the Institutional Review Boards of the Children's Hospital of Philadelphia, Philadelphia FIGHT Community Health Centers, and the City of Philadelphia Department of Public Health. Interview participants received $35 for the baseline study visit and $25 for the 6-month study visit.

Procedures

All participants in the main study completed computer assisted survey instruments (CASI) and urine measurement of tenofovir at baseline and six-month follow-up visits. A

Table 1 Demographic and clinical characteristics of the sample (n = 31)

Characteristic	Mean (SD)/number (%)
Age (years)	22.0 (1.8)
Race	
African-American	21 (68%)
Asian	2 (6%)
Mixed Race	8 (26%)
Other	5 (16%)
Latino/a	2 (6%)
Gender	
Cisgender male	28 (90%)
Transgender female	3 (10%)
Unstable housing in past year	13 (42%)
> Four sexual partners in last 6 months	14 (45%)
Experienced stigma (more than a few times a year)	
Race-based	17 (55%)
Sexual orientation-based	19 (61%)
Gender-based	7 (23%)
Age-based	7 (23%)
Time on PrEP (months, Median [IQR])	10 (IQR 6–24)
Site of recruitment	
Youth Health Empowerment Project Clinic	22 (71%)
Geosocial mobile applications	5 (16%)
Other community and clinical venues	4 (13%)
Adherence	
Immediate (Urine TFV ≥ 1000 ng/ml)	20 (67%)
Sustained (PDC ≥ 0.57)	17 (59%)
Optimal adherence (immediate & sustained)	15 (48%)

Race total > 100% because participants were able to report multiple races. Discrimination total > 100% because participants were able to report multiple types

PrEP pre-exposure prophylaxis, *IQR* interquartile range, *TFV* Tenofovir, *PDC* proportion days covered by pharmacy refills

subsample of participants completed an audio-recorded, semi-structured, individual interview delineating perceived barriers and facilitators of PrEP adherence. Participants were approached at informed consent for participation in the interview sample on a rolling basis. In order to increase generalizability to other clinical site, after 20 interviews were completed from the YHEP sample, only participants from non-YHEP sites (e.g. dating apps and social media) were approached for the interview portion of the study. Once recruitment was saturated from social media and dating apps (n = 5 participants), meaning that no new potential participants were identified for one month, interview recruitment resumed at YHEP.

The present analysis consists of data from the baseline visit among participants in the interview subsample. The interview guide was developed in an iterative process with review by PrEP content experts, and piloted in a sample of n = 5 YMSM/TW prior to use in the study. The guide focused on identifying barriers and facilitators of PrEP uptake and adherence. The first section of the interview focused on participants' reasons for starting PrEP and social influences on PrEP uptake. The second focused on barriers and facilitators to adherence. Additional question prompts explored mechanisms by which each barrier and facilitator operated with respect to adherence. The third section focused on characteristics of support figures identified in the quantitative data, and is not included in the present analysis. Our initial target sample size was n = 25, driven by the goal of achieving saturation of content themes [26–28]. We initially achieved saturation by consensus of the coding team at n = 25 interviews, and then conducted an addition n = 6 interviews to verify saturation for a final sample size of n = 31.

Measures

Race, age, gender, housing and education status, and length of time on PrEP were obtained via CASI. A modified version

of the Every Day Discrimination Scale [29, 30] was used to measure experiencing stigma by race, age, appearance, gender, and sexual orientation. Short-term adherence to PrEP was measured via urine tenofovir concentration. The urine tenofovir semi-quantitative liquid chromatography–tandem mass spectrometry urine assay has been validated as an adherence monitoring strategy for TDF–FTC based PrEP [31]. Protective short-term adherence was defined as urine tenofovir concentration ≥ 1000 ng/ml at baseline, consistent with ingestion of a dose in the prior 48 h [31]. Sustained PrEP adherence was measured by the proportion of days covered (PDC) by pharmacy refills over the three months prior to baseline, calculated as the total number of pills dispensed in the three months prior to baseline, divided by number of days between first and last fills [32–34]. Pharmacy data was obtained by querying participants' electronic health records and/or pharmacies. The threshold for sustained adherence, (PDC ≥ 0.57), was selected based on the iPrEX open label extension trial, which demonstrated four doses per seven days was the protective threshold for adherence [35]. Optimal adherence was defined as having both urine tenofovir ≥ 1000 ng/ml and ≥ PDC 0.57.

Data Analysis

Interview recordings were transcribed by an independent agency, reviewed for accuracy, and imported into NVivo 11 (QSR International Pty Ltd. Version 10, 2012). We used an inductive, open-coding approach to identify content themes that emerged from the data. An inductive approach was selected given the little currently known about theoretical determinants of PrEP adherence behavior. The study team developed codes by independently reading each transcript line-by-line for the first ten transcripts, and reaching consensus on a code list that was applied to each transcript with iterative revision as needed. We used a constant comparison approach of comparing text segments to those that had been previously assigned the same code, and to segments coded separately by each analyst, to decide whether they reflected the same concept. The derived codes were subsequently applied to all transcripts. All transcripts were double-coded until each of three two-person coding teams reached satisfactory inter-rater reliability (kappa statistic ≥ 0.9) across ten transcripts. Coding discrepancies were resolved by team consensus. After completion of the coding process, the total content of each code was independently reviewed by three members of the study team (SW, JF, DP) to identify emerging content themes, with blinding to adherence results. Adherence results were then added to the data, and a coding comparison approach was used to compare and contrast content themes between participants with optimal versus suboptimal adherence.

The overall weighted kappa for inter-rater agreement for the interviews was 0.9 (98.3% agreement). To protect participant privacy, exemplar quotes have been anonymized, and are accompanied by randomly-generated initials.

Results

The demographic and adherence characteristics of participants (n = 31) are listed in Table 1. Nearly half the sample (48%) had optimal adherence. The proportions meeting the optimal short-term and sustained adherence thresholds are displayed in Table 1. The dominant themes which emerged from the qualitative interviews, stratified by adherence category, are displayed in Table 2, with additional exemplar quotes in Table 3.

Barriers to Adherence

At least one barrier to PrEP adherence was reported by 81% of the sample (n = 25). The dominant thematic barriers were stigma, health systems inaccessibility, adverse medication effects, competing life stressors, and low HIV risk perception. The barriers discussed by the optimal and suboptimal adherence groups were qualitatively similar with the exception of HIV risk perception which was identified as an adherence barrier only in the suboptimal group.

Stigma

Stigma was the most commonly cited barrier to PrEP adherence. Stigma took multiple forms including HIV-related stigma and homophobia, and was experienced from family members, health care professionals, peers, and partners. In the quantitative data (Table 1), most participants had experienced race- and/or sexual orientation-based stigma. However, participants did not overtly connect stigma related to race and PrEP adherence in the qualitative data. Participants instead discussed judgment or scrutiny for using PrEP, fear

Table 2 Content themes by adherence category

	Optimal Adherence	Suboptimal Adherence
Barriers	Stigma	Stigma
	Health systems	Health systems
	Perceived adverse effects	Perceived adverse effects
	Competing stressors	Competing stressors
		HIV risk perception
Facilitators	Social support	Social support
	Health systems	Health systems
	Reminders/routines	Reminders/routines
	HIV risk perception	
	Personal agency	

Bolded themes indicate differences between adherence subgroups

Table 3 Exemplar quotes of barriers and facilitators

Barriers	
Stigma	"I used to be like, oh, why am I taking a pill every day? People would look at me like, that guy have HIV, if I take this pill." (Suboptimal adherence)
Health systems	"I think the biggest thing that made me stop taking it for a period of time was my pharmacy wasn't having it." (Suboptimal adherence)
Perceived adverse effects	"I was just scared about the side effects of, okay, I don't need this pill. I'm taking it to prevent something. What is this doing to my body long term?" (Suboptimal adherence)
Competing stressor	"Thinking about paying the next bill or the next event happening in my life … This wasn't necessarily in my top ten priorities when it should have been." (Suboptimal adherence)
Risk perception	"If I'm not having sex at that time, I'm like…it's okay you missed it, whatever." (Suboptimal adherence)
Facilitators	
Social support	"We got this system where … we all take it around the same time… So it's like, well, I know I took mine, you take yours." (Suboptimal adherence)
Health systems	"[The adherence counselor] has been very instrumental in making sure that I stay on PrEP." (Suboptimal adherence)
Reminders	"I use an app…It notifies me at the same time every …It's really, really helpful for me." (Optimal adherence)
Risk perception	"At first when I was taking my PrEP… before [my partner] was diagnosed with HIV, I wasn't taking it every single day... But now that he is, I do try to stay on a constant basis with it." (Optimal adherence)
Personal agency	"One thing that's kept me motivated was that I like the feeling that I'm in control of my HIV status. And I would just like to keep it that way." (Optimal adherence)

of having their sexuality inadvertently disclosed to their family or community, and stigma related to misperception of being HIV-positive.

> Oh, the biggest challenge, when people see that I'm on PrEP, they automatically try to say I have HIV or AIDS. (TH, Suboptimal adherence).

Participants also discussed stigma as a barrier to disclosing PrEP use to their support networks, which limited their ability to receive adherence support.

> The other thing I didn't mention is stigma about HIV I guess because that's the scary thing to bring up in the context of me being gay I guess, which I haven't dealt with my family. So if that stigma wasn't there then I'd love to … be able to be open about [PrEP] with my family. (YI, Optimal adherence).

Health Systems Inaccessibility

Health systems barriers primarily focused on issues of accessibility to clinical or pharmacy services due to insurance, transportation, or difficulty navigating complex health systems. For some participants, accessing PrEP was their first experience of filling a prescription and navigating their own health care. However, there was also overlap between health systems and stigma, as participants discussed stigmatization arising from encounters with clinicians and pharmacies:

> I don't really want to have to go all the way to [clinic] just to go get PrEP. And I don't want it sent to my house … I'm not gonna have it dropped off in the mailboxes. I don't want to deal with my neighbors and I don't know who's gonna be there when I come down. So then you gotta get a whole new thing of it, and that's weird. And not to my grandparents' house because I don't want anybody seeing the program on it, and say okay, well looks it up, it's HIV medication… clearly he has HIV, not something else. (UZ, Suboptimal adherence).

Side Effects

Adverse medication effects were identified as an adherence barrier that was both directly experienced (i.e., having or perceiving the untoward effect) or feared (i.e., worry about future side effects). The most common experienced symptomatic adverse effects were nausea, diarrhea, headaches, and "brain fog". Most participants who experienced side effects reported a transient presentation of headaches and nausea which resolved shortly after starting PrEP:

> And I remember having the first side effect, which was the headaches. And, I mean, the throbbing headache. It felt like somebody was hitting upside the head with a pot. And I called my friend, and I said, we have to go to the doctor's because I need to find out what's going on. And, of course, he was supportive and came with me. But I found out it was one of the symptoms of the pill, and I was asked, do you want to stop taking the pill? And when I felt like – because the headache was that bad, I was like, I was ready to say yes. But my friend encouraged me to stay on it because any medicine comes with the side effects, but after – the medicine takes time getting into your system, it goes

away. And since then, which was probably almost four months now, I have not had another side effect, and I've really been doing well. (AY, Optimal adherence).

Feared effects include loss of bone mineral density and concerns that chronic use of TDF–FTC could cause unknown complications. One participant discussed difficulty justifying PrEP's prevention benefits with his fear of long-term side effects:

It'd be like, okay, I'm taking this pill. I'm just taking all this medication and I'm just doing this stuff to my body. Do I need to be doing this stuff to my body? I'm choosing to do this stuff to my body. (DO, Suboptimal adherence).

Competing Stressors

Participants reported a variety of competing life priorities that either directly interfered with PrEP adherence (e.g., work schedules that physically prevented participants from taking PrEP) or indirectly (e.g., not being able to prioritize HIV prevention). For some participants, this included stress resulting from caretaking roles for others in their families or communities:

So my grandmother's ill. So is my mother and my great grandmother. And I live with all three of them, so I'm – I picked up a job to help out with the family and help out with the financial situation and stuff. And so I'm working long hours, and those hours run into my time of me taking my PrEP. I don't like carrying my PrEP everywhere with me because I didn't have a proper container to put it into keep it contained and stuff. So I would work from 4:00 to 12:00, and PrEP time is at 9:00. And I don't get home until like 1:00. So it would be like, I'm too tired to even think about anything else, go straight to sleep. (BZ, Optimal adherence).

Another participant discussed the challenge of being a first-time medication taker, and the difficulties of identifying a time for pill taking amidst a complex work schedule:

... my schedule just wasn't normal and then I wasn't used to being on medication every day. I was never sick or anything so I never had to take a pill continuously except for antibiotics when I had the flu or something. (IL, Suboptimal adherence).

Risk Perception

Low perceived vulnerability to HIV centered on participants either using PrEP sporadically, for example, only on weekends, or around periods of sexual activity. This was a more salient theme in the suboptimal adherence group, and ultimately led to discontinuation for some participants.

Like if you asked me not too long ago, sometimes back then I used to miss some days of PrEP. But I had to stop because I'm like – it wasn't no point for me missing my days of PrEP. I guess, I stopped taking it for those days because I really wasn't being sexually active. I only was taking PrEP because like I told you when I be start off, I was very sexually active. It's not no more I'm not really – I don't think about sex that much no more – at all. (IZ, Suboptimal adherence).

Facilitators of Adherence

While all participants with optimal adherence identified facilitators, only 69% of those in the suboptimal group reported any facilitators. Emergent themes with respect to facilitators were social support, supportive health systems, reminders/routines, high HIV risk perception, and personal agency. Notably, we identified qualitative differences in the facilitators described by the two groups, with only the optimally adherent participants discussing HIV risk perception and personal agency as facilitators.

Social Support

Participants described the ways in which individuals in their support networks, including partners, family members, health care workers, and friends helped them take their PrEP. Some mentioned chosen (or 'gay') family structures that replaced or augmented their biologic families of origin. One mechanism of social support that was repeatedly referenced was the social interaction of taking medications together, which could be accompanied by social competition that reinforced adherence. For some participants, this included taking PrEP with friends or partners, or taking their PrEP alongside an HIV-positive partner or friend taking ART. One participant who functioned as a gay father to younger MSM discussed taking his PrEP together with his gay sons who were on PrEP or ART and the emergence of social competition around adherence:

We used to text each other and be like ... oh, tell my one son to take his medication. Tell my other son to take PrEP, and it would be like even seeing it, it wouldn't be like okay, well, you gotta take PrEP, whereas afterwards I'm gonna look at it and say well, tell them to do this, like take yours. So that was kind of cool. And the competition piece kind of like died down. But it's like even when my one son found out that I'm taking PrEP, he'll be like, oh, I have to get back on PrEP. It's kind of it's something – I guess, not drilled into our heads – but that we iden-

tify something that we should be doing, like healthy behavior per se... I do feel like it's kind of not a bad competition, but it's cool. It's like if I'm gonna do it, then you're gonna do it. And if you're gonna do it, then I'm gonna do it because we want to ...to do it together... (UZ, Suboptimal adherence).

Another participant talked about harnessing social competition by creating a game between himself and his HIV-positive partner to see who could be more adherent:

Because we're both goofy and childish, we both set up a chart for the days that I either have taken PrEP in the scheduled early morning time ...or if I take it in the later of the day. So the early morning, we mark as green. The later in the day it would be yellow. And either forgetting it all or taking it at night, that will be in like the reddish area. There's only been once where I've been able to mark the entire chart for one month as green... [Then] when he became HIV positive and he had to start taking his meds, ... I made it competitive with him about who can stay on their medicine more frequently. And so far he's beating me by like three days, but it's okay. (TY, Optimal adherence).

Other participants discussed taking medications together with older relatives with chronic health conditions.

I mean, my grandmother takes medication every day at 9:00, and unlike some of my other family members, who they're more to themselves and they forget stuff easily, I give her her medication. So as long as she takes her medication, I'm taking mine.... And it's like I tell her the same thing, I don't like the taste of the pill, but I mean, it's going to help us. (ER, Suboptimal adherence).

Supportive Health Systems

While health systems were cited as a barrier, they could also function as a facilitator. We identified substantial overlap between health systems and social support, with participants discussing receiving adherence-focused social support from clinic staff such as PrEP adherence counselors.

My alarm is my guardian, but [the adherence counselor] also just like reminding me, take your PrEP, take your PrEP, you know. Like every visit like have you taken it? And just that whole process of her like constantly telling me I have to train it into myself and now I just know like automatically to take the PrEP at 10:00. (AC, Optimal adherence).

Reminders and Routines

Most participants reported using reminders and routines including mobile health (mhealth) applications, phone alarms, pill boxes, text message services, regular reminders from partners and health professionals, and keeping pills in a visible location Participants who used other medications discussed building PrEP into their existing pill-taking routines. One transgender participant discussed combining PrEP-taking with her gender affirming hormones:

When I first started out, it was very hard for me to keep timing-wise basically. But now since I'm transitioning, I take it in the morning when I take my pills also for my hormones. So I've been on almost for about a year and eight months now. (DQ, Suboptimal adherence).

For other participants, using mobile technology such as cell phone alarms, text message reminders or mhealth applications helped support consistent adherence and clinic attendance:

Today – your phone is your best friend – one of your best friends. So my phone keeps me up to date with everything. (NL, Optimal adherence).

Two of the participants in the suboptimal group indicated that while they used reminder systems, they felt they were not effective:

Well, the last time, they did give me this pill case for the days of the week. I mean, that helps when I have to travel, but just mildly. Because, if I'm gonna remember, I'm gonna remember it. But it does help, I guess, to know, oh, did I take it today? When was the last time I take it? You know, the days. In case your days get mixed up. So that helps a little bit, but at the end of the day, if you're gonna remember it, you're gonna remember, whether it's from the bottle or from there. (XG, Suboptimal adherence).

Risk Perception

While low perceived vulnerability to HIV was a barrier to adherence, some optimally adherent participants identified assessment of their HIV risk as a key factor promoting ongoing PrEP adherence. Notably, none of the participants in the suboptimal group identified risk perception as a facilitator. Participants discussed that being in an HIV serodiscordant relationship, or having multiple partners made ongoing PrEP adherence a high priority.

Yeah. Both of us [are on] on PrEP. I think that, for him, it's good because he is more of the bottom in the relationship. More versatile, but just the roles that we play and knowing that both of our status is HIV negative,

> we do not like using condoms… so I felt like should one of us – not saying that we're planning on it, but should one of us, for whatever reason, make the mistake and step out of the relationship and do anything else, that at least we have something to be of a guard of protection… (AY, Optimal adherence).

Personal Agency

While risk perception and HIV vulnerability often had a loss-avoidant framing, participants in the optimal adherence group indicated that personal agency and health investment positively contributing to adherence. No participants in the suboptimal category discussed this theme. Specifically, participants mentioned being motivated by personal responsibility, self-care, and perceived control over their health.

> You care about yourself, you'll always remember to take it because you never know what you might be doing later on that day or who you might meet or whatever might happen. So that's just the extra step. (NL, Optimal adherence).

Another discussed framing PrEP as a part of general wellness:

> So once I became more used to taking it, it became no problem and it just became something that I do. Like it's a step to protect myself, like if you're sick you go and get cold medicine. If you want to not become sick, you eat oranges. So PrEP is my oranges. (AC, Optimal adherence).

Discussion

In this sample of YMSM/TW of color, we identified suboptimal adherence to PrEP by both short-term and sustained measures. While much research has focused on improving PrEP uptake, mathematical models suggest that only improving adherence will substantially lower population HIV transmission [36]. The majority of the YMSM/TW in the study met criteria for either short-term (67%) or sustained (59%) adherence. However, just under half met the threshold for both measures—our definition for optimal adherence. These data are in keeping with a growing body of literature demonstrating high rates of PrEP nonadherence or discontinuation in YMSM/TW of color [10, 11, 37–39]. In a recent study by Morgan et al., 33% of a cohort of YMSM/TW in Chicago had discontinued PrEP, with a significantly higher rate of discontinuation in black and Hispanic youth, compared to white youth [37]. Our data similarly underscore the need for culturally-tailored interventions to support sustained PrEP adherence in YMSM/TW of color. Our data also extends the existing literature by identifying novel targets for improving adherence, including fostering personal agency and enhancing positive social interaction around medication taking. These facilitators should be explored in future research and implementation efforts.

Despite the critical role adherence plays in PrEP effectiveness, there are currently no proven evidence-based interventions to support PrEP adherence in YMSM/TW of color. Our data identify several potential areas for intervention. While we used an inductive coding process for theme generation within our qualitative data, the resultant themes map well onto the Integrated Behavior Model, demonstrating convergent validity with existing behavioral theory. With respect to individual-level behavioral beliefs, HIV risk perception operated as either a facilitator or barrier, with the accuracy of risk perception seeming to influence the direction in which the construct operated. For suboptimally adherent participants, low perception of vulnerability to HIV may have led to sporadic use or discontinuation of PrEP. Conversely, for the optimally adherent participants, high HIV risk perception was a perceived as a key driver of sustained pill-taking behavior. This finding is in keeping with a recent study by Haberer et al. which identified a significant association between sexual activity and HIV serodiscordant partnership and sustained PrEP adherence in Kenya and Uganda [40].

In the domain of perceived norms, stigma from family, communities and health systems functioned as an obstacle to adherence by perpetuating negative subjective and injunctive norms around PrEP use. This finding should be viewed in the context of the high levels of stigma experienced by our participants related to race, gender, and sexual orientation. For YMSM/TW of color, PrEP-related stigma may thus arise at the intersection of multiple forms of enacted stigma. This experience is likely distinct from the PrEP-related stigma that may be experienced by their white peers. Our data suggest that while youth of color face similar obstacles to PrEP adherence as those previously reported in similarly aged white peers, researchers and clinicians would be remiss to not emphasize the importance of social context in PrEP adherence for youth of color [15–17]. In developing interventions for these populations, participatory processes should be used to better delineate how intersectional stigma may perpetuate the social and structural barriers to PrEP adherence, in order to generate strategies to overcome these barriers for youth of color.

For our participants, social support, including shared adherence behavior within communities of YMSM/TW of color, may have functioned to counteract stigma and decrease the negative appraisal of competing stressors such as work and caregiver responsibilities [41]. In particular, participants frequently discussed the crucial role their HIV-positive partners and friends played in a mutually supportive

relationship around adherence to PrEP and ART. Future research may focus on targeting seromixed communities of HIV-positive and negative YMSM/TW to support network-level adherence, rather than developing interventions that are tailored by serostatus.

With respect to efficacy beliefs, we found that only the optimally adherent participants discussed the role of personal agency in supporting PrEP adherence. These data suggest that approaches such as motivational interviewing and health coaching that utilize empowerment, target self-efficacy, and harness activation (the degree to which individuals understand the need to manage their health and the extent to which they feel able to do so) may be promising strategies for improving PrEP adherence in YMSM/TW of color [42]. Within populations such as YMSM/TW of color who are disproportionally affected by stigma and emotional trauma, framing PrEP adherence as a means of increasing a locus of control around health may be a particularly salient approach.

Lastly, sustained PrEP adherence depends on the capacity of health systems to effectively deliver PrEP to youth. Participants identified key aspects of health systems that served as barriers (stigma, geographic inaccessibility) and conversely as facilitators (gender and sexuality-affirming environments, presence of PrEP adherence counselors). Health systems-level intervention such as telehealth, home-delivery, pharmacist-delivered PrEP, and community PrEP navigators are potential approaches under investigation [43, 44].

Limitations

Limitations should be considered in the interpretation of our findings. Our data represent a convenience sample of YMSM/TW in Philadelphia. While these findings therefore may not be generalizable to the larger population of youth on PrEP, they represent one of the highest risk groups for HIV acquisition in the U.S. The primary objective of this qualitative study was to gain a granular understanding of PrEP adherence behavior in YMSM/TW of color, rather than to quantitatively test hypotheses about PrEP adherence behavior. Future robust quantitative studies are needed to formally test for associations between the aforementioned barriers and facilitators and PrEP adherence behavior. We did not have data on sexual activity to correlate with adherence measurement. Therefore, it is unknown whether study participants were at risk of HIV acquisition during their periods of non-adherence or rather were non-adherent due to an accurate assessment of HIV risk and resultant calculated decision to stop PrEP. However, all participants were engaged in PrEP care at the time of the visit and had active PrEP prescriptions. Our data underscore the need for strategies for adherence measurement that account for time-varying sexual behavior, i.e. "prevention-effective adherence" [40]. Our adherence estimates should be viewed in light of our inclusion criteria which required that youth had received PrEP for at least three months prior to enrollment. We, therefore, did not include youth in the study who discontinued PrEP within the first three months after prescription, who are likely the highest risk population for nonadherence and may have different barriers and facilitators than those who persistent with PrEP use. Lastly, while qualitative data analysis may be subject to bias in the interpretation of findings, we attempted to minimize bias by blinding coders to adherence results during the initial coding and thematic generation processes.

In conclusion, our findings highlight a number of themes to explore in future PrEP adherence research, including improving the accuracy of HIV risk assessment, enhancing social support, and fostering personal agency. In order to develop evidence-based interventions to improve PrEP adherence in youth, robust quantitative studies are needed to identify which of themes can be most effectively utilized to facilitate adherence behavior among YMSM/TW of color.

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