



# Identifying Strategies for Improving Pre-exposure Prophylaxis Adherence: Perspectives from a Sample of Highly Adherent Young Men Who have Sex with Men

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## Abstract

Most research on pre-exposure prophylaxis (PrEP) adherence and persistence uses a deficit-based approach to identify negative influences on PrEP adherence; however, an alternative set of approaches (such as resilience, asset-based, and positive variation) may identify equally important positive influences on PrEP adherence. Thus, the current study presents qualitative perspectives of PrEP adherence strategies from a sample of adherent YMSM. PrEP-using YMSM living in the Chicago area from a larger cohort study were recruited into a 90-day diary study that measured sexual health behaviors including PrEP use. A subset ( $n=28$ ) were then recruited for in-depth interviews between April and September 2020 covering topics of PrEP use and adherence. Thematic analysis was used to interpret patterns within the data. The analytic sample ( $n=19$ ) consistently reported high levels of adherence. Adherence strategies were organized into three broader categories: psychological (e.g. mindfulness, pill auditing), technical/instrumental (e.g. automated reminders, pill organizers), and social strategies (e.g. checking in with friends, or getting suggestions from friends). The majority of participants described using multiple strategies and changing strategies to respond to barriers to adherence. Other themes that were related to adherence included having a daily medication history and a generally positive outlook toward the PrEP regimen. Those who had medication histories were able to draw from experience to develop strategies for PrEP adherence. Findings suggest the need for pre-emptive counseling for PrEP-initiators on the use of multiple strategies, how to prepare for PrEP adherence, to adapt to challenges, and to adopt a range of potential strategies for adherence.

**Keywords** HIV · PrEP · Resilience · MSM · Positive deviance · Assets

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## Resumen

La mayoría de las investigaciones sobre el cumplimiento y la persistencia de la profilaxis pre-exposición (PrEP) utiliza un enfoque basado en el déficit para identificar las influencias negativas en el cumplimiento de la PrEP; sin embargo, un conjunto alternativo de enfoques (como resiliencia, basado en las capacidades o recursos, y variación positiva) puede identificar influencias positivas igualmente importantes en la adherencia a la PrEP. Por lo tanto, el estudio actual presenta perspectivas cualitativas de las estrategias de adherencia a la PrEP de una muestra de los hombres jóvenes que tienen sexo con hombres (YMSM) adherentes. Los YMSM que usaban PrEP que vivían en la región de Chicago de un estudio de cohorte más grande fueron reclutados en un estudio diario de 90 días que midió los comportamientos de salud sexual, incluido el uso de PrEP. Luego se reclutó un subconjunto ( $n = 28$ ) para entrevistas en profundidad entre abril y septiembre de 2020 que cubrieron temas de uso y adherencia a la PrEP. El análisis temático se utilizó para interpretar patrones dentro de los datos. La muestra analítica ( $n = 19$ ) reportó consistentemente altos niveles de adherencia. Las estrategias de adherencia se organizaron en tres categorías más amplias: psicológicas (p. ej., atención plena, auditoría de píldoras), técnicas/instrumentales (p. ej., recordatorios automáticos, organizadores de píldoras) y estrategias sociales (p. ej., ponerse en contacto con amigos o recibir sugerencias de amigos). La mayoría de los participantes describieron el uso de múltiples estrategias y el cambio de estrategias para responder a las barreras a la adherencia. Otros temas relacionados con la adherencia incluyeron tener un historial de medicación diario y una perspectiva generalmente positiva hacia el régimen de PrEP. Aquellos que tenían antecedentes de medicación pudieron aprovechar la experiencia para desarrollar estrategias para la adherencia a la PrEP. Los hallazgos sugieren la necesidad de asesoramiento preventivo para los iniciadores de la PrEP sobre el uso de múltiples estrategias, cómo prepararse para la adherencia a la PrEP, cómo adaptarse a los desafíos y adoptar una variedad de posibles estrategias para la adherencia.

## Introduction

Daily oral pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention strategy [1] and has reshaped HIV prevention for young men who have sex with men (YMSM) who are at elevated risk for HIV acquisition [2]. However, since the initial public release of PrEP, there have been continued concerns about adherence [3] and discontinuation, particularly among YMSM [4–6]. Addressing these shortcomings is crucial to maximizing the individual and population protective benefits of PrEP.

Though results are mixed about the association between age and current PrEP use, existing evidence suggests that PrEP use is highest among MSM between the ages of 20 and 40 [7]. Estimates of PrEP adherence among MSM vary widely (22–90%) [8] and studies that focus exclusively on YMSM tend to report lower PrEP adherence on average (e.g. 20–55% among YMSM ages 18–22), while studies with samples of adult MSM with greater age variability (e.g. samples of 18 and older) report high adherence (80% or higher) [5]. Studies using objective measures found adequate blood concentration of PrEP in 34% of participants among YMSM in an early demonstration project [9] and 38.8% in broader samples of adult MSM in a measurement study nested within a large clinical trial [10]. These findings highlight the importance of better understanding the factors that impede or promote adherence among MSM, and among YMSM in particular.

Optimal maintenance of a daily PrEP regimen requires a high level of weekly adherence (> 4 pills per week) [11], and persistence (consistent long-term use without

discontinuation) [6]. Studies have identified various factors that are associated with low adherence, including structural (e.g., access to affordable healthcare, access to health insurance), logistical (e.g., schedules), psycho-social (e.g., low risk perception, low decision making power, substance use), trait-based (forgetfulness), and biological factors (e.g. side effects) [3, 7]. Even with studies addressing these varied influences, few have focused on identifying factors that help maintain high PrEP adherence. Some existing literature has identified positive factors associated with adherence, such as having an established daily routine, being experienced with medication use, and using automated reminders and pillboxes [7]. Importantly, these existing studies about adherence strategies focus primarily on adult MSM [7], which may limit their relevance for adolescent and young adult MSM.

In addition to issues maintaining optimal adherence, evidence suggests that YMSM are more likely to discontinue PrEP than adult MSM [6, 12–14]. YMSM also have unique profiles relative to older adult MSM including reduced financial capability, higher levels of familial oversight, and higher likelihood for housing instability [7, 15, 16]. It stands to reason that YMSM may have unique needs regarding adherence strategies to support a PrEP regimen. This highlights a critical need for understanding discontinuation and persistence among YMSM. Other significant factors contributing to PrEP discontinuation that have been identified in the literature include substance use, difficulties getting to a doctor, lack of insurance coverage, having fewer sexual partners, and perception of low risk for HIV [6, 12, 13]. Discontinuation is also more common among Black compared to White

PrEP-users [12], which is of particular concern given that 1 in 2 gay Black MSM will be diagnosed with HIV in their lifetime [17]. While many factors overlap between adherence and discontinuation, some factors like disruptions in insurance may be conceptualized as more closely linked to longer term disruptions (e.g. missing refills) rather than fluctuations week to week or day to day. While this literature has identified factors contributing to low adherence and high PrEP discontinuation, public health has made modest gains in reducing racial differences in patterns of PrEP use, making research addressing PrEP in samples of racially diverse YMSM critical.

A considerable limitation of the aforementioned literature on PrEP use, adherence, and discontinuation is that the vast majority of research utilizes a deficit-based approach. This means that these projects sought to identify factors that contribute to low adherence or discontinuation of PrEP regimens, rather than factors that enhance and support PrEP adherence or maintenance [18]. To this point, out of a 2019 systematic review of 52 published articles only 6 examined factors that facilitate PrEP adherence and none of these studies focused on YMSM [7]. Researchers have critiqued applying exclusively deficit-based approaches to health research and suggest that integrating factors that have a positive influence on health outcomes may yield more effective interventions [19]. More specifically, deficit-based approaches help public health researchers diagnose factors that may be contributing to health disparities and negative outcomes such as PrEP discontinuation (e.g. lack of insurance), but these approaches do not necessarily provide clear insights into what is already working well among adherent PrEP users, or possible solutions that may improve PrEP outcomes [19]. Multiple alternative approaches and frameworks have been proposed to address this issue.

### Resilience, Positive Variation, and Asset-Based Approaches

In a commentary about applications of resilience theory in research addressing gay and bisexual men's health, Herrick et al. [19] summarized two key components of resilience as defined in the literature (1) "positive adaptation in the face of adversity and risk", and (2) "resilience is a process" as opposed to a static or innate trait (p. 2). Fergus and Zimmerman [20] provide examples of risk factors that may need to be overcome such as the chronic stress of taking a daily pill for individuals living with HIV; however, the use of resilience frameworks in regard to PrEP use among YMSM has been limited. In a study of Black YMSM and transgender women that utilized a resilience framework, researchers identified some social network-level resources that increased the likelihood of PrEP use such as having parents or other members in one's close network [21]. Despite existing

literature on resilience and PrEP being limited, resilience models have potential applications for PrEP use. Applications of these perspectives have the potential to identify the ways in which YMSM face and overcome challenges to maintaining high PrEP adherence.

Another relevant framework is what we refer to as the *positive variation* approach (also referred to as *positive deviance* in some research) which strives to identify individuals who exhibit behaviors that lead to better health outcomes than their peers in order to identify uncommon strategies for success [22, 23]. This framework suggests that some adaptive behaviors may *vary* from what is normative or more common in a population, and be *positive* in the sense that they encourage success in achieving desired outcomes. Positive variation strategies identify individuals who have better health indicators than their peers in order to find and understand uncommon supportive behaviors that may be responsible for the relatively better health profiles. In contrast to resilience, positive variation focuses on uncommon behaviors and does not exclusively examine response to adversity. Ober et al. [23] applied a positive variation framing when eliciting HIV prevention behaviors among substance-using Black MSM who maintained an HIV-negative status despite using substances. They identified fifteen different behaviors that participants attributed to their HIV negative status such as screening potential casual sexual partners online and restricting drug use to certain environments and social groups that may present a lower risk (such as using substances only among trusted friends).

Once identified, these adaptive behaviors can inform interventions that encourage dissemination and adoption. By retrospectively examining the strategies of a mostly-adherent sample of PrEP-users, not only is it possible to gain an understanding of how they became adherent, but it may also identify adaptive behaviors that can be packaged and pre-emptively imparted on PrEP-initiators as they begin the daily oral regimen. Positive variation approaches have been used before to identify adaptive HIV prevention techniques, but have not been used systematically in research addressing PrEP adherence. However, applications of this perspective have the potential for identifying less common strategies for adherence with the aim of disseminating such strategies to a broader population.

By contrast to both resilience and positive variation approaches, an asset-based approach focuses primarily on community-level resources (e.g., MSM organizations, informal social groups, influential community leaders, etc.) that may be identified, interconnected and enabled to promote desired health outcomes in a community [24]. While there have been calls to employ an asset-based approach to HIV prevention among MSM in the U.S., explicit applications of this model remain limited. However, public health educators have proposed asset-based models to inform prevention and

care of HIV [25, 26]. For example, Mayer et al. proposed the integration of asset-based models into HIV care suggesting that health educators should consider integrating existing social support networks and community organizations into models of care [25]. Similarly, Von Hippel proposed a model for identifying, evaluating, and integrating existing community assets and innovations into public health intervention development in order to disseminate interventions that amplify the impact of these positive factors [26], however, this approach is not yet widely used.

Researchers have also discussed these three models as being complementary and overlapping [25, 26]. For instance, public health researchers have conceptualized the combination of positive variation and asset-based intervention development as a process through which public health researchers identify existing positive variation behaviors or community assets that promote desired health outcomes, evaluating and refining these behaviors and assets, and then developing interventions that are designed to enhance health promotion through diffusion of identified behaviors and improved connection to identified assets [26]. Moreover, researchers have also called for the integration of asset-based and resilience models in order to study existing strategies and assets in the lives of MSM with the aim of diffusing and scaling interventions that leverage these strategies and assets to promote comprehensive HIV care for MSM [25]. By employing tenets of these three models in tandem researchers can move beyond deficit-based thinking and identify innovations and assets on multiple levels of the social ecology that influence resilience among PrEP users in order to inform intervention.

## The Current Study

Given the limited literature addressing positive influences on PrEP adherence among YMSM this study uses a positive approach informed by existing positive frameworks from the broader public health literature (resilience, positive variation, and assets). Our study uses thematic analysis to examine perspectives from a racially-diverse, mostly adherent sample of PrEP-using YMSM to better understand how they overcame challenges and barriers to adherence when starting a PrEP regimen and what adaptive strategies these YMSM used to achieve consistently high adherence. We present an inductive framework for understanding positive influences on high adherence among YMSM. The discussion considers implications for positive frameworks (resilience, positive variation, and asset-based approaches) by examining the lived experiences of a sample of highly-PrEP-adherent YMSM and organizing our results to align with constructs from these frameworks.

## Methods

### Procedures and Recruitment

This analysis utilizes in-depth interview data collected as part of a mixed methods study, called Day2Day (D2D), examining patterns of PrEP use and adherence among YMSM. Participants for D2D were recruited from a large on-going cohort study based in the Chicago metropolitan area called RADAR ( $n = 1129$ ). The methods for the RADAR cohort study are described in more detail elsewhere [27]. Participants were recruited for D2D during their regular RADAR cohort study visits, which occur every 6 months. At the time of their RADAR study visit, participants were eligible for D2D if they were: age 18–29, cisgender MSM or non-binary assigned male at birth, and had reported being a current PrEP user. Enrolled participants then participated in a 90-day diary study that involved daily surveys assessing PrEP use and related factors (enrollment ongoing, current  $n = 79$ ). Upon completion of the daily diary study, a subset of participants was invited to participate in individual in-depth qualitative interviews (IDI) (currently  $n = 28$ ). Recruitment and data collection for D2D are ongoing, and we are purposefully recruiting participants for IDIs who exhibit varied patterns of PrEP use and who are diverse in race/ethnicity, based on daily diary entries. This analysis only included participants who had both self-report and dried bloodspot indicators for high adherence (see section “[Characterizing PrEP Adherence](#)”). Note that we paused enrollment into the diary study due to the onset of the COVID-19 pandemic, meaning that we subsequently paused IDI several months later after all previously enrolled participants completed their remaining diary surveys. This left us with a subset of participants who had completed IDI, most of whom exhibited relatively high levels of adherence during the daily diary study. Thus, these analyses reported on IDI data from an analytic sample of 19 PrEP-adherent YMSM. The IDI instrument addressed aspects of identity (e.g. race, ethnicity, sexuality), experiences with health-care, and sexual health behaviors including PrEP use. The IDIs included in this analytic sample were conducted over a secure video conferencing software after participants provided verbal consent (waiver of signed consent approved by IRB) and audio recorded between April and September 2020.

While these interviews occurred during the COVID-19 pandemic, all participants began their 90-day diary entries prior to the week of March 20, 2020 and 82% of participants completed their final survey entry prior to March 20, 2020, which is when the state of Illinois announced a stay-at-home order [28]. Themes included in this analysis

**Table 1** Demographics of young MSM PrEP users (n = 19)

Variable	N	%
<b>Race/Ethnicity</b>		
Asian or Pacific Islander	2	10.53
Black or African American	3	15.79
Hispanic/Latino(a)	5	26.32
White	7	36.84
Multi-racial	2	10.53
<b>Sexual orientation</b>		
Gay	17	89.47
Bisexual	2	10.53
<b>Age</b>		
Mean	25.57	
Std Dev	1.93	
Minimum	23	
Maximum	30	
<b>Adherence patterns</b>		
Self-report adherence (daily diary data over 90 days)		
Adherent (> 4 pills per week)	19	100
<b>DBS test</b>		
Adherent (> 700 TFV-DP fmol/punches at all available time points for active PrEP prescription)*	18	94.73

\*One participant switched to a Emtricitabine/Tenofovir formulation within 6 months of the study, so DBS test was not possible

were based on retrospective reflections on initiating and adjusting to a daily PrEP regimen, which occurred prior to the COVID-19 pandemic for all included participants.

## Sample Characteristics

Demographics were collected at baseline as part of the parent cohort study visit procedures. These characteristics are summarized in Table 1. The average length of the interview was 53 min. The sample was racially diverse (26.3% Hispanic/Latinx, 36.8% white, 26.3% Black or African American, 10.5% multiracial, and 10.5% Asian or Pacific Islander). The average age was 25 years. Most participants identified as gay and one participant identified as bisexual. All participants identified as cisgender men and were on a daily oral PrEP regimen at the beginning of the study.

## Characterizing PrEP Adherence

Participant PrEP adherence was characterized in three ways. First, their adherence was quantitatively evaluated based on 90-day diary data, which defined adherence as taking four or more doses per week consistently throughout the study. This threshold was determined based on previous literature which suggests that efficacy reduces when weekly doses dip below four pills per week [11]. Second, dry blood spot

**Table 2** Strategies for adherence in order of most frequent to least frequent strategy (n = 19)

Strategy	N	%
Integrating into daily routine	16	84.2
Automated reminders	10	52.6
Multiple storage locations or mobile storage for easy access	9	47.4
Taking PrEP with other meds	6	31.6
Daily pill organizer/days of the week storage container	5	26.3
Storage in visible location	4	21.1
Social strategy	3	15.8
Research participant	2	10.5
Self-audit	1	5.3
Physical reminders	1	5.3

(DBS) samples were collected up to three times per participant during the 90-day diary study (i.e., at 30, 60, and 90 days). These DBS samples were used to conduct assays of intracellular TFV-DP and FTC-TP using a validated liquid chromatography-tandem mass spectrometry method, as reported previously where 700 + fmol/punch(es) of tenofovir-diphosphate (TFV-DP) indicated 4–7 doses of Truvada per week for the preceding 4–8 weeks [29]. These first two methods were then compared to understand the adherence profile of each participant during the diary study. Lastly, during the qualitative interviews participants then discussed current and past adherence including adherence previous to the 90-day diary study. Aspects of these qualitative descriptions are included in the thematic analysis. As the aim of the current analysis is to examine high adherence, we narrowed the sample to those who were confirmed adherent (n = 19) meaning we dropped 9 individuals from the analysis, because they had conflicting self-report and DBS results.

## Analysis

Interviews were audio recorded and transcribed. A team of three coders developed a thematic codebook including both inductive and deductive themes. In an initial assessment of coding in the first quarter of transcripts, the coders reached an average of 0.87 (lowest 0.86, highest 0.87) indicating excellent agreement [30]. The final codebook was applied to all transcripts. A final assessment of Kappa was applied after coding, which yielded Kappa scores > 0.70 indicating good intercoder reliability [30]. Thematic analysis was used to interpret patterns within the data. Final codes included in this analysis pertained to specific strategies to support adherence, pill storage, previous medication history, and feelings about PrEP adherence. Findings are summarized with representative quotes.

## Results

While all participants were adherent during the time of the daily diary study, most participants described having some lapses in adherence at some time point previous to entering the D2D study. Participants described a range of strategies to develop and maintain PrEP adherence, which are presented in Table 2 in order of most frequently to least frequently endorsed. When analyzing the data with resilience, positive variation, and assets as guiding frameworks we found that existing positive approaches did not have compelling fit with the current data. We therefore inductively categorized these strategies into three broader categories: (1) psychological, (2) technical/instrumental, and (3) social strategies (see Table 3). In addition to these strategies, participants described relying on prior experience with medications and a generally positive view of PrEP use. Each of these themes are discussed below.

### Psychological Strategies

Participants described several psychological strategies, which involved attempts to reframe pill taking or develop cognitive strategies to improve pill taking. These examples included integrating PrEP into their routine, taking periodic pill audits, pairing their pill taking with other medication, and non-specific mindfulness techniques. For example, participants described generally integrating their PrEP regime into their daily life. While integrating PrEP into a daily routine was the most commonly endorsed strategy (84.2%, 16/19, having reported this strategy), it was also one of the least specific strategies. Participants described either making a commitment to taking PrEP at the same general time of day (e.g., morning, or evening) or taking PrEP with a specific marker in the day, such as a specific daily activity (e.g., lunch, waking up, going to bed, brushing teeth, etc.). Roughly a quarter of participants described pairing PrEP with other medications or vitamins and taking them at the same time.

Two participants also described doing an audit of their pills relative to the date they received their prescription. This strategy was used to calculate the number of days that they missed and how soon they need to get their next prescription.

I look at the day it was filled and then I count backwards, and I'm like, okay, if I took it today, I would have this many pills. And if I didn't take it today, I would have this many pills. That's how, if I ever can't remember if I took it, that's how I figure it out. -Participant 40, Asian/Pacific-Islander, age 29

Another strategy mentioned by a couple participants was non-specific mindfulness after missing a dose. For example, Participant 60 (*Black/Latino, age 24*) described an unstructured mindfulness approach centered on slowing down his morning routine.

If I forgot this morning, for example, tomorrow I'd wake up and just remember to be a little bit more patient with my routine and be a little bit more mindful of making sure everything is done for myself before leaving the house.

### Technical/Instrumental Strategies

Technical or instrumental strategies involved the use of virtual technology or physical strategies for improving adherence. The second most common strategy was the use of automated reminders such as using the calendar or alarm app on a smart phone, with about half of participants reporting this strategy. The third most common tactic (47.4%, 9/19) was having multiple PrEP storage locations or a mobile storage location. Mobile storage locations included easily portable containers, such as a backpack, to ensure access to PrEP at all times. For example, Participant 7 (*Latino, age 25*) described taking a small number of pills with several extra whenever traveling, while leaving the bulk of pills at home to avoid losing them.

I guess I would bring the bottle with me, usually, and sometimes I would honestly just empty the bottle out

**Table 3** Inductive framework for PrEP adherence strategies

Strategy type	Definition	Relevant examples
Psychological	Psychological strategies involve attempts to reframe pill taking or adherence internally through cognitive processes, or intentional mental shifts to enhance adherence	Integrating into daily routine, self-audit of pills, mindfulness
Technical/instrumental	Technical/instrumental strategies involve a technical or material tool to enhance adherence	Physical reminders, automated reminders, pill organizers, multiple storage containers at multiple locations, mobile storage, visible storage, reminders through participation in research studies
Social	Social strategies pertain to leveraging social contacts and support to enhance adherence	Check-ins with existing family/friend support networks

and leave some in my place. If I was going for a weekend or something, I would just put four pills in the bottle and be like, ‘Okay. I’m ready... I don’t like bringing the whole pill bottle with me because if something happens, like if I lose it’—but I’ll make sure to always bring maybe two extra pills just in case if I do end up staying longer or doing something else.

Participants also mentioned keeping multiple containers in multiple locations (e.g., at home, in a backpack, in a car, and at work). For some, such as individuals with variable work schedules, this meant that they always had access to a pill when it was time to take it. For others, this was meant to address the potential for forgetting when at home and then remembering later in the day when in a different location.

Roughly a quarter of participants described using a daily pill organizer. While using a pill organizer may seem like an obvious strategy, many participants described getting a pill organizer as a reaction to struggling with adjustment to the daily regimen. Some participants discussed getting a pill organizer from their doctor when they began the regimen.

Only one participant described using a physical reminder in their living space which included having a written message on the bathroom mirror as a physical reminder.

### Social Strategies

Nearly a quarter of participants described the positive influence of their existing social networks, such as friends and family, on their PrEP adherence; however, the ways in which this operated varied. Generally, description of social influences included getting adherence strategy advice, and direct or indirect reminders from friends or family. For example, participant 38 described consulting a friend about strategies for adherence after initially struggling.

I kept telling my friend because he has to take pills every day. I was like, ‘I don’t know how you do this. I can’t.’ He was like, ‘You need to go to Walgreens and buy the pill thing for every day.’ I was like, ‘Oh, okay.’ Now, when I did that, I took over the world. I was consistent. I was good. So, that helped. –Participant 38, Black, age 27

It should be noted that this friend was not necessarily on PrEP, but was on a daily medication, which highlights the transferability of adherence skills across individuals and across daily medication regimens.

Other social interactions were direct or indirect reminders when participants missed a dose. For example, participant 9 described being reminded of missing a dose when his friends who were also taking PrEP would talk about missing a dose: “I pretty much know to take [PrEP], and I have other friends who take it, so when they say, ‘Oh, I forgot to take

mine,’ sometimes it reminds me.” Implicit in stories like that of participant 38 (Black, age 27) and participant 9 (Black, age 25) is that the individual and their sources of social support need to be open about being on the PrEP regimen.

Another way social support served as a motivator was through ongoing conversations about persistence in the PrEP regimen. One such example was Participant 41 who described having a conversation with his mother as a teenager about needing to be persistent with his depression medications and PrEP medications. He described having another similar conversation later on with a sponsor in an addiction recovery program. The memories of these conversations still motivate him to take his pills.

And then flash forward to PrEP, my sponsor at that time, when I told him, I felt guilty because I missed so many. And I confided in him and he yelled at me ... So as bad as that sounds, that comes to my mind. Actually, some of the times, I wouldn’t take it because I wouldn’t remember until I was in bed. It’s like, ‘oh, help me get out of bed and take it. I’ll just take it tomorrow.’ But I hear that voice. –Participant 41, White, age 27

### Multiple Strategies

Most participants (89.5%, 17/19) spoke about using multiple strategies to build or maintain adherence. This included the use of multiple strategies that complement and mutually reinforce each other, and the use of multiple strategies as “fail-safes” or additional “safety-nets” to catch missed doses later in the day. An example of multiple complementary strategies would be using bedtime as a schedule marker to prompt PrEP use, leaving the pill bottle visible on the nightstand next to the bed, and setting a reminder for bedtime. Other times multiple strategies were discussed as ways to catch a missed dose that wasn’t taken at the normal time. One such example is provided by Participant 41 (White, age 27):

There were times where I would go through a period where I would just forget to take it. And each time that happened, maybe not every time that happened, but most of the times when that happened, I would try to do something different. I would download this pill reminder app or set reminders on my iPhone. I have that little capsule from Gilead that I would keep an extra pill in case I were to go to a friend’s or to a hookup’s and not go home and I wouldn’t have my PrEP available.

### Modifying Strategies as Needed

Participants faced several reasons for modifying their adherence strategies. A substantial minority (31.6%, 6/19)

described needing to adapt to changes in their lives. Some also described simply needing to adjust their original strategies or changing to a new strategy to improve adherence. For example, Participant 40 (Asian/Pacific Islander, age 29) discussed adjusting his pill schedule to make taking PrEP easier by aligning the timing with his other medications. In this way he was able to adjust his initial strategy to make it more effective.

Now just to simplify and streamline things, my other medications, I would take PrEP in the middle of the day... And my other medications I was taking at night. So, I just slowly adjusted until they were all in the morning so I didn't have to have separate reminders every day.

### Medication History

While participants were not systematically asked about their medication history prior to taking PrEP, about half of the participants volunteered information about their medication history when asked about their experience adjusting to PrEP. About a quarter of all participants described being experienced with daily medications or supplements prior to beginning the PrEP regimen. These individuals largely linked this medication history with the ease of adapting to a PrEP regimen. For example:

So, I've already had experiences where I needed to take medication regularly or semi-regularly. So, with PrEP, it was just like, one, it was easy for me to get into it, and two, it was like, I'm doing it because it gives me a sense of security so I'm going to be sure to take it. And if it for some reason was hard for me to get into the routine, I always have that in the back of my mind that this is something I need to take if I don't want to freak out about things that I have been freaking out about. So, it was pretty easy for me to work it into my routine. –Participant 12, White, age 24

In this sense, having previous experience with medication provided participants with knowledge of how it feels to adjust to a daily medication regimen and served as a foundation for participants to build their strategies for the PrEP regimen even when facing issues with motivation or PrEP adherence.

About a quarter of participants described being inexperienced with daily medications or supplements. By contrast, these individuals largely described a steep learning curve when adjusting to PrEP. For example, participant 3 attributed the struggle with adjusting to PrEP to not being used to taking a daily pill.

It was simple, just one pill a day, but I think the one trouble that I had when taking it was the fact that I've

never had to take a medicine like that every single day. So, for me, it was getting accustomed to the routine.– Participant 3, Latino, age 25

While these participants all were able to overcome this lack of experience and become adherent to a daily PrEP regimen, they often pointed out the need to develop additional support strategies to achieve adherence due in part to their inexperience.

### Positive Feelings Regarding Adapting to PrEP

When addressing their adjustment to their PrEP regimen, about 70% (13/19) of participants described having particular feelings about adjusting to PrEP. Most participants that discussed their feelings (about three quarters) described a positive feeling such as an ease to adjusting to PrEP or excitement for taking PrEP. This general positive orientation toward PrEP may be a positive asset that helps with motivation for adherence. Several participants even described feeling excited about PrEP: “I think in the beginning, it was kind of it was fun,” said Participant 14 (White, age 24), while Participant 3 (Latino, age 25) indicated that he “was very excited about it [starting PrEP].”

Only a couple participants described negative or challenging feelings, and even in these cases participants described overcoming these challenges. (i.e., “It was definitely difficult the first couple of weeks, just the simple act of just taking a pill, but I just know the more I just actively tried to think about, the easier it became” –Participant 9, Black, age 25). While one participant described anxiety over missed doses (i.e., “I would get anxiety, like, “Oh, maybe this doesn't work.” So then I would take the two” –Participant 7, Latino, age 25), other participants described anxiety as manageable knowing that the efficacy does not drop much from a single missed dose (i.e. “No anxiety. It was kind of like, “Uh, I forgot to take it.” I feel—I've seen the protection probability tables and I know, obviously, I should take it every day. It's still pretty forgiving. So that takes some anxiety off, and it's still fine” –Participant 18, Latino, age 23). One participant described anxiety as a motivator for staying adherent: “The anxiety of my sexual health contributed to it ... that mentality really set in of like, ‘If I don't take this every single day, I literally will get HIV.’ And it's like a twisted mindset but, hey, it works” –Participant 26, multi-racial, age 23.

### Discussion

This analysis presents strategies for PrEP adherence as they were discussed by a mostly adherent sample of PrEP users. Understanding factors that contribute to successful PrEP adherence, allows researchers to identify modifiable



behaviors that may be promoted, and existing assets that may be accessed, to ensure PrEP adherence. While we observed some alignment in the data with existing frameworks used to examine positive influences on health, such as asset-based, positive variation, and resilience, no single framework captured the breadth of strategies used to achieve high adherence by our participants. Thus, we present an inductive framework for understanding PrEP adherence strategies, which include psychological, technical/instrumental, and social strategies.

### Psychological Strategies

Psychological strategies made up the most commonly endorsed category of strategies, but they included some of the least specific/prescribed approaches, such as integrating PrEP into a daily routine or general mindfulness. These strategies, particularly the non-specific examples, may be more prone to failure and may be more successful if supported by other more structured strategies. Nonetheless, such techniques may speak to the potential appeal of more formalized mindfulness interventions among some YMSM. Researchers have proposed such interventions for increasing medication adherence more broadly [31]. Moreover, strategies such as pill auditing (counting pills and subtracting the day since prescription) may not immediately occur to YMSM who are initiating their first daily medication. Less common strategies that have been devised by a subset of PrEP users may represent “positive variation” and warrant being incorporated into strategic communication with YMSM who are initiating PrEP. These types of strategies may not otherwise occur to first-time PrEP users.

### Technical/Instrumental

Use of technology was relatively commonplace, such as the use of automated reminders in mobile phones. The widespread use of technology to support adherence may suggest an openness to other forms of technology, such as PrEP navigation apps or e-health interventions. While use of more traditional instrumental strategies like a pill organizer may be more common in populations that have experience with pill-taking (such as older adult populations or individuals with chronic conditions) this analysis suggests that this strategy may be less common for a population that largely has a lack of previous exposure to medication regimens (such as among YMSM). It may not be reasonable to expect YMSM to identify these strategies on their own. Thus, YMSM may need targeted communication about strategies that are generally perceived as more common in older populations.

### Social Strategies

The presence of pre-existing and supportive social networks was central to the adherence of a subset of participants. We know from previous literature that MSM report PrEP stigma [32, 33], and PrEP-related stigma has been identified as a barrier to PrEP uptake and adherence [34, 35]. On the other hand, disclosing PrEP use to significant others and family is associated with higher adherence [36], and at least one other study found relationships between social assets, such as family support, and PrEP use [21]. The current findings suggest that disclosure to supportive friends or family may be leveraged to create a supportive environment where PrEP users can receive and give check-ins around adherence and experiences with PrEP. Some ways that participants described social influence improving adherence was through sharing experiences with PrEP with friends (such as receiving or sharing new strategies for adherence from friends) as well as having shared accountability through regular check-ins about pill taking and adherence (both in person and via text message). Pre-existing social support structures that contribute to these social strategies could be conceptualized as assets. These natural tendencies could be amplified through interventions that encourage disclosure to supportive friends or family and that create supportive networks (such as online support groups for PrEP users). Some interventions, such as the MPowerment [37] and Many Men Many Voices [38] programs, address HIV prevention at the community-level, however, the development and adaptation of community-level interventions may further benefit from an explicit and broader application of assets-based approaches to draw on pre-existing social resources in PrEP user’s lives.

### Medication History

While it may not always be anticipated in a young adult sample, having previous experience with daily medication or supplements was an asset that some participants accessed when adjusting to a daily PrEP regimen. This speaks to the transferability of adherence strategies across daily medications. It may be useful for healthcare providers to assess previous experience with daily medications to encourage new PrEP users to integrate their adjusting to PrEP into these previous experiences. Young people are less likely to have had prior experience with taking daily medications compared to adult and older populations, so we cannot assume that they will be able to quickly attain adherence without more structured support. However, these findings suggest that once YMSM are able to establish a routine around pill-taking, then they will need less support and these skills may further generalize to adherence to other future medication regimens. Thus, it may also be useful to identify new PrEP users who do not have experience with a daily medication

routine to provide targeted messaging about adherence strategies to jumpstart this adaptation.

### Positive Feelings Toward PrEP

We observed generally positive feelings in regard to adjusting to a PrEP regimen. Participants described having a positive orientation toward PrEP and being able to overcome any anxiety related to adherence. In this regard, PrEP may differ from other medications that treat symptoms of a chronic condition or long-term infection such as anti-retroviral therapies (ART) for HIV. While PrEP researchers may draw from adherence literature addressing ART in devising adherence strategies, there may be considerable differences in the ways that PrEP users think about their PrEP use compared to how people living with HIV think about ART. For example, previous literature suggests that a constellation of generally negative feelings such as worry, anxiety, HIV stigma, and negative self-image related to needing to take HIV medication may disrupt self-efficacy in taking ART, increase negative feelings, and decrease motivation for staying adherent among some people living with HIV [39].

In the current analysis, these negative feelings were not observed. Contrasting the current analysis with the ART literature highlights the limitations to drawing a direct parallel between feelings about ART adherence, and feelings about PrEP adherence. Feelings in relation to adherence among PrEP users are perhaps wholly different than feelings about adherence among people living with HIV and therefore require their own literature and approach; however, it may require a comparative study that includes PrEP users and ART users to establish this difference. The generally positive valence in the current analysis may be in part due to the preventive nature of the medication, which provided a sense of security for participants.

This may present an opportunity to reinforce PrEP use and adherence in ways that are not available to messaging around ART. For example, this generally positive orientation toward the PrEP regimen may be encouraged through strategic messaging. Messaging campaigns may consider capitalizing on this affect by creating messaging that promotes the positive feelings an individual may gain from taking PrEP such as a sense of ease, security, and control rather than focusing on what an individual avoids by taking PrEP (namely, fear of HIV transmission). This kind of messaging may complement existing efforts to develop sex-positive and equitable PrEP messaging [40]. Future research may also examine differences and parallels between ART, PrEP, and other forms of daily adherence such as Birth Control to draw conclusions on the ways that these medications are conceptualized particularly when comparing preventive medications to treatments.

### Using Multiple Strategies

We also found that the vast majority of participants in this highly adherent sample described using multiple strategies. Sometimes these strategies were mutually re-enforcing such as storing pills in a visible location (e.g. the sink) and pairing pill taking with a daily task (e.g. brushing teeth). Other times the use of multiple strategies was to help with forgetting. For example, one might store their pills in a visible location at home, but also in their work bag in case they forget to take their pill at home. Both approaches seem to indicate that the use of multiple complementary strategies makes for a more robust approach to PrEP adherence. Messaging about PrEP use may integrate explicit language to encourage adopting multiple adherence strategies to enhance adherence among new PrEP users.

### Adapting to Challenges

In addition, we observed that participants overcame challenges such as unpredictable schedules, major changes in schedules, insurance lapses, side effects, mental health concerns, and substance use. About a third of participants changed their PrEP strategies to overcome challenges. These participants' experiences demonstrate that it is possible to overcome these stressors through a variety of means to achieve a high degree of adherence. We did not observe explicit descriptions of macro-social stressors such as racism, PrEP stigma, or sexual identity stigma in relation to PrEP adherence in this descriptive analysis, which rendered it difficult to map resilience onto these particular data. That being said, it may be helpful to new PrEP users to communicate that some adaptation may be necessary over time.

### Implications for Intervention

Like this study, previous studies have identified strategies that PrEP users leverage to improve their adherence, which may be scalable with the help of interventions [23], however, the current results suggest that it may not be a single strategy that supports adherence, but rather a combination of strategies which may be unique to an individual PrEP user. In this analysis most strategies were developed while adapting to the realities of a daily PrEP regimen and relatively few participants spoke of strategic health communication addressing potential stressors or strategies to overcome stressors. PrEP users may benefit from being prompted to anticipate specific stressors that may impact their adherence (e.g., disruptions in schedules, insurance lapses, mental health, substances, etc.) and encouraged to adapt strategies as needed to avoid lapses in PrEP adherence due to these stressors. A resource

that describes potential strategies may allow beginning PrEP users to select tools or behaviors that best match their needs and circumstances.

## Limitations

Some limitations of this study should be noted. This sample was mostly adherent, so we are unable to comment on the perspectives of participants with ongoing struggles with adherence. Future qualitative studies may want to employ qualitative research with new PrEP initiators. This study did not systematically probe for experiences with assets at the community level beyond those which were volunteered by participants as contributing to PrEP adherence. Future studies should examine community assets that PrEP users may not currently leverage to improve PrEP adherence as they may have the potential to improve PrEP adherence. Our sample was size typical of qualitative research studies like this, which seek to understand participants perspectives and identify relationships that are currently poorly understood. Future large-scale quantitative studies can build on this work to study the prevalence of these strategies and their statistical association with PrEP adherence in different populations. Lastly, while adherence patterns were assessed prior to the COVID-19 pandemic and the experiences analyzed in this study referred retrospectively to experiences that occurred prior to the pandemic, the interviews were conducted during the pandemic which may influence responses by participants.

## Conclusion

The utilization of frameworks that address positive influences on health (e.g. resilience, and asset-based, and positive variation frameworks) have the potential for informing support interventions for PrEP adherence. In the present analysis we identified three broader categories for strategies to improve adherence: psychological, technical/instrumental, and social strategies. Through analyzing the perspectives of mostly adherent sample of YMSM, this study identified factors that may contribute to high adherence including use of multiple strategies, being adaptable, prior medication experience, and general positive feelings toward PrEP. The strategies identified in this analysis may be scalable with the assistance of interventions and targeted health messaging to PrEP initiators. Further analysis is needed to understand how adherence and specific adherence strategies relate to structural barriers or social identities such as race.

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## Declarations

**Conflict of interest** Authors don't have conflicts of interest to report.

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