AIDS and Behavior (2023) 27:1478–1485
https://doi.org/10.1007/s10461-022-03883-3

ORIGINAL PAPER

The Relationship Between HIV Pre-exposure Prophylaxis Stigma and Treatment Adherence Among Current HIV Pre-exposure Prophylaxis Users in the Southeastern U.S.

Olivia T. Van Gerwen[1] · Ibrahim Yigit[2] · Kaylee B. Crockett[3] · Bulent Turan[4,5]

Accepted: 27 September 2022 / Published online: 8 October 2022

Abstract

Despite efficacy in HIV prevention, Pre-exposure Prophylaxis (PrEP) is underutilized in the US, especially among populations at highest risk. PrEP-related stigma may play a role. We developed measures of PrEP-related stigma dimensions and PrEP adherence. We administered them to current PrEP users. We hypothesized that PrEP-related stigma would negatively impact PrEP adherence. Questionnaire measures were developed using data from previous qualitative work and existing validated HIV-related stigma measures. The resultant survey was administered to current PrEP users from two Birmingham, Alabama PrEP clinics. Plasma tenofovir disoproxil fumarate levels were collected to measure PrEP adherence. Exploratory factor analyses were performed to determine the factor structure of each PrEP-related stigma dimension (internalized, perceived, experienced, anticipated, disclosure concerns). Separate binary logistic (or linear) regressions were performed to assess associations between PrEP-related stigma dimensions and adherence (treatment adherence self-efficacy, self-reported adherence, and plasma tenofovir levels), adjusting for education, race, and time on PrEP. In 2018, 100 participants completed the survey, with 91 identifying as male and 66 as white. Only internalized stigma was associated with lower self-reported PrEP adherence. Exploratory mediation analyses suggested that the association between all stigma dimensions and self-reported PrEP adherence is mediated by PrEP adherence self-efficacy. No associations were found between any PrEP-related stigma measures and plasma tenofovir levels. Internalized PrEP stigma may reduce PrEP adherence, possibly by reducing PrEP adherence self-efficacy among experienced PrEP users. Further investigation of how stigma dimensions affect PrEP adherence in populations at risk for HIV may shed light on drivers of PrEP underutilization.

Keywords HIV pre-exposure prophylaxis · Adherence · Stigma · PrEP

Introduction

Several clinical trials have demonstrated daily oral HIV pre-exposure prophylaxis (PrEP) with the antiretroviral combination of either tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) or tenofovir alafenamide and emtricitabine (TAF/FTC) to be well tolerated and effective in decreasing the risk of HIV acquisition in high-risk populations, such as men who have sex with men (MSM) and transgender women (TGW) [1–5]. The 2021 guidelines from the Centers for Disease Control and Prevention (CDC) now include intermittent dosing strategies (i.e., 2-1-1 oral PrEP) and long-acting injectable options such as cabotegravir in addition to the mainstay of consistent, daily dosing of either TDF/FTC or TAF/FTC. Even with these new additions, PrEP adherence remains paramount to successful HIV prevention [6].

✉ Olivia T. Van Gerwen
oliviavangerwen@uabmc.edu

1 Division of Infectious Diseases, University of Alabama at Birmingham, 703 19th Street South, ZRB 218A, Birmingham, AL 35233, USA

2 Department of Psychology, Faculty of Arts and Sciences, TED University, Ankara, Turkey

3 Department of Family and Community Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

4 Department of Psychology, College of Social Sciences and Humanities, Koc University, Istanbul, Turkey

5 Department of Psychology, University of Alabama at Birmingham, Birmingham, AL, USA

The Southeastern United States experiences the highest rates of new HIV diagnoses nationwide. In 2018, of 37,968 new HIV diagnoses in the U.S., 51% were in the Southeastern U.S. [7]. Despite the large burden of disease faced by this region and PrEP's efficacy and safety, the Southeastern U.S. has the lowest levels of PrEP use of any region in the nation, especially relative to its HIV burden [8]. Research on the psychosocial predictors of non-adherence among individuals taking PrEP is limited. Studies on perceived barriers to PrEP by potential PrEP users suggest that social stigma may be an important barrier to adherence [9].

Stigma is defined as a personal characteristic or attribute that confers a negative value or judgment onto an individual, thereby socially discrediting the individual [10]. Several factors associated with PrEP make it stigmatizing for those who take it, including the fact that it is an HIV medication and, thus, puts users at risk of being perceived by partners as HIV-positive [11, 12]. Another factor is the perception that being on PrEP insinuates participation in promiscuous sexual behavior that may put one at risk of HIV [13, 14]. PrEP-related stigma is further magnified when it intersects with stigmatized identities such as being part of a racial, sexual, or gender minority [15]. Understanding the nuances and drivers of stigma experienced by potential and current PrEP users could provide insights into how providers can optimize PrEP uptake and adherence. There has been great interest in developing instruments to measure PrEP stigma in recent years [16–18], but fully validated instruments for U.S. populations are few [19]. These existing instruments also do not measure for multiple dimensions of stigma.

This work is informed by stigma frameworks in the HIV stigma literature, which define stigma as societal beliefs that affect individuals with perceived stigmatized traits (i.e., living with HIV) via multiple dimensions including community stigma, internalized stigma, anticipated stigma, and experienced stigma [20–22]. These stigma mechanisms have downstream effects on health behavior and outcomes such that people living with HIV (PLWH) who experience higher levels of HIV-related stigma have lower adherence to antiretroviral therapy (ART) and less engagement in HIV care [23–26]. One potential pathway for these effects of stigma on adherence is self-efficacy—the confidence in oneself to adhere to a treatment plan [27, 28]. Previous research suggests that the association between internalized HIV stigma and health outcomes may be mediated by adherence self-efficacy [26, 29]. There are emerging data as well related to the impact of PrEP stigma on PrEP adherence. Multiple studies suggest that PrEP adherence may be negatively influenced by PrEP stigma in some populations, specifically MSM [12, 30]. It is also likely that PrEP stigma impacts other points on the PrEP care continuum, such as initiation and retention in care, leading to low numbers of patients receiving and remaining on PrEP [31].

In this study, we developed measures of dimensions of stigma related to PrEP and evaluated associations with PrEP adherence, using both self-reported adherence measures and plasma TDF levels. To date, most studies investigating the role of PrEP-related stigma on PrEP adherence have only utilized self-reported adherence measures, so the addition of biological measures in this study is novel. We also sought to explore self-efficacy as a potential mediator in PrEP adherence. Informed by qualitative work with people currently using or eligible for PrEP in the community of Birmingham, Alabama [32], we developed a multi-part survey instrument and administered it to patients currently on PrEP in either of the only two clinics providing PrEP services in Birmingham, Alabama at the time of the study.

Methods

Measure Development

Measures for the study were developed in two phases. In the first phase, 44 current and potential PrEP users participated in qualitative in-depth interviews (emerging themes were reported elsewhere [32]). Recruitment flyers were posted in community-based health clinics providing sexual health services in Birmingham. Participants met with experienced interviewers and were asked to share their perspectives on attitudes about PrEP in their community. The research team then developed measures relevant to understanding PrEP-related stigma as well as PrEP adherence. Questionnaire items were adapted from in-depth interview content as well as validated HIV stigma measures such as the HIV Stigma Scale [21, 33]. The item inventory was then tested using cognitive interviews with 17 current PrEP users. Based on the feedback obtained in the cognitive interviews, the research team met again and narrowed down the items by scales (internalized, perceived, experienced, anticipated PrEP-related stigma and PrEP-related disclosure concerns). We also developed measures of PrEP stigma in healthcare settings and community HIV stigma, which were not included in the current study. The study measures are detailed in Table S1.

Participants, Settings, and Procedure

Participants in this study were current PrEP users recruited from two clinical sites between May 2018 and November 2018. Individuals were eligible for the study if they were over 18 years old, English-literate, and they attended a return visit for PrEP services. Potential participants were approached by research staff during their visit and asked if they were willing to participate in a research survey on attitudes about PrEP. Participants who expressed interest were

invited to a private room for a verbal and written explanation of the study procedures by the research staff. They were informed that their participation in the study would have no effect on their healthcare and their providers would not have access to study-related data. All participants underwent an informed consent process.

The adapted questionnaire and socio-demographic questions were given to 100 participants who agreed to participate in the study. The surveys were administered electronically via Qualtrics (Provo, UT, USA) on an in-room computer, laptop, or iPad in the exam room prior to their provider visit. Participants were compensated $30 for completing the survey and received an additional $10 for a blood draw to measure their plasma tenofovir level. This study protocol was approved by the Institutional Review Board of the University of Alabama at Birmingham (Protocol # IRB=170414005).

Measures

PrEP-Related Stigma Dimensions

All PrEP-related stigma items were adapted from existing, validated HIV stigma measures [20, 21, 33, 34] and the qualitative interview data collected in our study [32]. Unless otherwise specified, participants responded to items using a 4-point Likert scale. For each scale, composite scores were calculated using the mean of the items.

Internalized PrEP Stigma Participants responded to 8 items, including: "I feel ashamed of being on PrEP," and "Being on PrEP makes me think I'm a slut."

Perceived PrEP Stigma in the Community Participants responded to 14 items (e.g., "Most people look down on people who are on PrEP" and "Most people think PrEP is a green light to have as much sex as you want.").

Experienced PrEP Stigma Participants responded to 19 items assessing their experiences of being treated differently because they were taking PrEP for HIV prevention. Example items included, "Some family members have looked down on me because I am on PrEP," and "Someone who learned I was on PrEP assumed I was sleeping around."

Anticipated PrEP Stigma Seventeen items assessed participants' perceived likeliness they would be treated differently if others found out they were taking PrEP. Example items included, "Sexual or romantic partners will look down on me if they learn I am taking PrEP," and "Some people will assume I am sleeping around if they find out I am on PrEP." Participants responded using a 5-point scale from 1 = Very unlikely to 5 = Very likely.

PrEP-related Disclosure Concerns Participants responded to 16 items regarding concerns about others' learning they were taking PrEP for HIV prevention. Items included, "I would not tell others I am taking PrEP because they would make assumptions about my sex life," and "I regret having told someone I am taking PrEP."

PrEP Adherence Outcomes

PrEP Adherence Self-efficacy Adherence self-efficacy was assessed using 11 items assessing perceived ability to start and maintain a PrEP treatment regimen, adapted for this study from a measure of ART treatment adherence self-efficacy [28]. Participants received a stem question, "How confident are you that you can do these things related to PrEP?" Items included, "Integrate PrEP into your daily routine," and "take PrEP daily as prescribed." For these measures, participants were asked to rate the responses on a scale of 1–10, with 1 being "cannot do at all" and 10 being "completely certain can do."

Self-reported PrEP Adherence We adapted the one-item validated measure of ART adherence to assess PrEP adherence [35–37]. Participants were asked to rate how good a job they did taking PrEP as prescribed in the past 30 days using a 6-point scale from *Very poor* to *Excellent*. This single item can be used as a tool to establish thresholds for guiding patient-provider discussions about ART adherence in clinical settings [38]. Self-reported PrEP adherence was high in our sample, having a negative skew. Following the dichotomization strategy when assessing ART adherence with this measure, responses were dichotomized for analysis to reflect 0 = suboptimal adherence (any response less than "excellent" job at taking PrEP as prescribed) and 1 = optimal adherence ("excellent" job at taking PrEP as prescribed) [35].

Plasma TDF Levels Plasma TDF levels have been used to measure PrEP adherence in several previous trials [39–41]. Participants who volunteered for the optional blood draw had an additional 1 mL of blood drawn during their regular clinic lab work. Specimens were immediately centrifuged for 10 min to separate the plasma. The plasma was transferred to a polyprophylene vial with screw top cap labeled with the participant's ID number and date/time of blood draw. Cryovials were frozen at – 20 °C until transferred to a lab for measurement of plasma TDF levels. Continuous TDF levels were measured for plasma samples with quantifiable levels. For analysis, TDF concentrations were dichotomized as > 40 ng/mL suggestive of recent consistent dosing and < 10 ng/mL suggestive of recent inconsistent PrEP dosing [40]. It is important to note that measurement of TDF levels are not a perfect measure of adherence given their half-life of 17 h [42].

Data Analysis

First, descriptive statistics for the sample were calculated. Second, exploratory factor analyses were performed to

determine the factor structure of each PrEP-related stigma dimension. Next, separate regression analyses (binary logistic and linear regression) were used to examine the association of each PrEP-related stigma dimension with PrEP adherence self-efficacy, self-reported PrEP adherence, or plasma TDF levels. Lastly, mediation analyses were conducted to examine whether PrEP adherence self-efficacy mediates the association between PrEP-related stigma dimensions and self-reported PrEP adherence (or plasma TDF levels) using the PROCESS macro for SPSS. We utilized 95% percentile confidence intervals (CIs) and 2000 bootstrapping resamples in mediation analyses. In this procedure, if confidence interval does not include zero, the indirect effect is significant, suggesting mediation [43]. In all analyses, covariates included education, race, and time on PrEP.

Results

Descriptive statistics regarding demographics are presented in Table S2. The average age of the sample was 35.8 ± 11.4 years. The average duration on PrEP was 15.7 ± 13.1 months. Ninety-one participants identified as cisgender men (91%), with the remainder identifying either as cisgender women, transgender women, or another gender identity (n = 9). Sixty-six participants identified as white, 23 as black, 6 as Hispanic or Latinx, 1 as Asian, and 4 as multirace. Regarding relationship status, 47 participants reported being sexually active, but not being in a dedicated relationship, 27 were in an exclusive sexual relationship with one partner, 13 were in a relationship and having sex with people outside of that relationship, and 8 were not sexually active. Seventeen participants reported having a sexual partner living with HIV. Regarding adherence, self-reported adherence was available for 99 participants and plasma TDF levels for 84 participants.

Factor Structure and Reliability of PrEP-Related Stigma Dimensions

A series of factor analyses were conducted to identify the factor structure of PrEP-related stigma dimensions (i.e., internalized, anticipated, experienced, perceived community stigma, and disclosure concerns). First, data for each stigma dimension were checked for suitability for factor analysis. Bartlett's test of sphericity was significant ($p < 0.001$) for internalized [$\chi^2(28) = 888.64$], anticipated [$\chi^2(136) = 1341.25$], experienced [$\chi^2(171) = 1470.13$], perceived community stigma [$\chi^2(91) = 831.54$], and disclosure concerns [$\chi^2(120) = 1119.02$]. Additionally, Kaiser–Myer–Olkin (KMO) value was 0.86 for internalized stigma, 0.88 for anticipated stigma, 0.88 for experienced stigma, 0.89 for perceived community stigma, and 0.91 for disclosure concerns, suggesting suitability for factor analysis [44]. Next, we ran separate factor analyses to determine the number of factors to retain. The method of scree plots suggested single-factor solutions for all stigma dimensions. Results yielded single factors for all stigma scales that explained 73.90% of the variance for internalized stigma, 53.92% for anticipated stigma, 51.06% for experienced stigma, 51.15% for community stigma, and 55.54% for disclosure concerns. Factor loadings for items ranged between 0.77 and 0.96 for internalized stigma, 0.64 and 0.80 for anticipated stigma, 0.55 and 0.81 for experienced stigma, 0.50 and 0.80 for perceived community stigma, and 0.54 and 0.88 for disclosure concerns.

Next, internal consistencies of each dimension were calculated. Cronbach's alpha coefficients were 0.94 for internalized stigma, 0.94 for anticipated stigma, 0.94 for experienced stigma, 0.92 for perceived community stigma, and 0.94 for disclosure concerns. Correlations between PrEP-related stigma dimensions and other study variables as well as descriptive statistics are shown in Table S3.

Associations of PrEP Stigma Dimensions with PrEP Adherence

To examine the association between PrEP-related stigma and variables related to adherence to PrEP (i.e., self-reported PrEP adherence, plasma TDF levels, and PrEP adherence self-efficacy), separate regression analyses (logistic or linear, controlling for covariates) were conducted for each stigma dimension. In the logistic regression analyses, only internalized PrEP stigma was significantly associated with self-reported PrEP adherence ($B = -1.10$, $AOR = 0.33$, $p = 0.045$, CI [0.11, 0.97]). There may be other psychological mechanisms that help explain the relationships between other dimensions of stigma and PrEP adherence, in addition to PrEP adherence self-efficacy. Results of all regression analyses are presented in Table S4.

Exploratory Mediation Analyses: Indirect Associations Between PrEP Stigma Dimensions and PrEP Adherence Through Self-efficacy

We conducted a series of simple mediation models where the association between PrEP stigma dimensions (i.e., internalized, perceived, experienced, anticipated PrEP stigma, and disclosure concerns) and self-reported PrEP adherence is mediated by PrEP adherence self-efficacy. The indirect effect of internalized PrEP stigma on PrEP adherence through PrEP adherence self-efficacy was significant ($B = -0.48$, $SE = 0.41$, CI [−1.55, −0.02]; see Fig. 1A). Next, we tested the mediating effect of PrEP adherence self-efficacy in the association between perceived PrEP stigma and PrEP adherence. This analysis yielded a significant indirect effect on

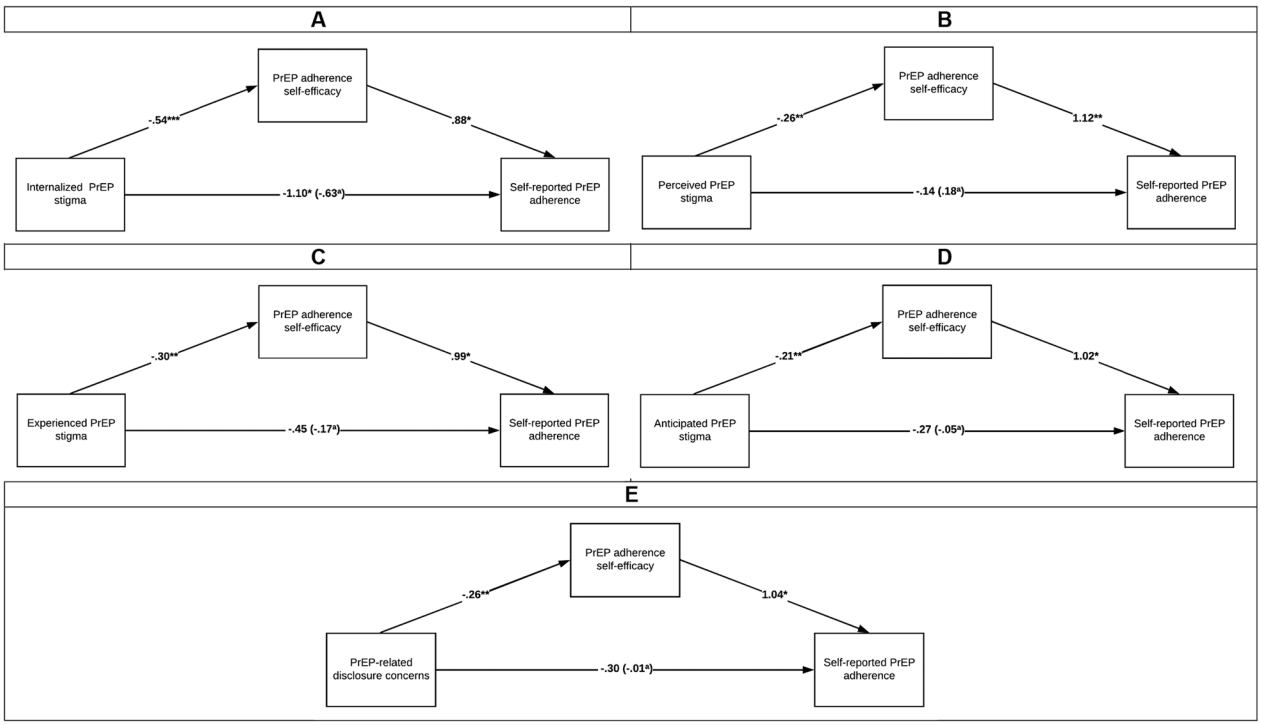

Fig. 1 **A**–**E** The indirect effects of PrEP stigma dimensions on self-reported PrEP adherence through PrEP adherence self-efficacy. *Note* Associations are presented as path coefficients (unstandardized). [a]It indicates the coefficient (direct effect) when the mediator is entered in the model. *p < 0.05, **p < 0.01, ***p < 0.001

PrEP adherence (B = − 0.30, SE = 0.27, CI [− 1.04, − 0.03]; see Fig. 1B). The indirect effect of experienced stigma on PrEP adherence through PrEP adherence self-efficacy was also significant (B = − 0.30, SE = 0.27, CI [− 1.04, − 0.03]; see Fig. 1C).

We also tested the mediating effect of PrEP adherence self-efficacy in the association between anticipated PrEP stigma and PrEP adherence. This analysis also yielded a significant indirect effect on PrEP adherence (B = − 0.22, SE = 0.21, CI [− 0.79, − 0.02]; see Fig. 1D). Lastly, in a simple mediation model depicted in Fig. 1E, the indirect effect of disclosure concerns on PrEP adherence through PrEP adherence self-efficacy was also significant (B = − 0.27, SE = 0.25, CI [− 0.95, − 0.03]). These results provide evidence for the mediating effect of adherence self-efficacy in the association between all PrEP stigma dimensions and self-reported PrEP adherence.

Discussion

In this study, we developed and administered measures of PrEP stigma dimensions to a cohort of 100 current PrEP users in Birmingham, Alabama. Factor analyses confirmed the unidimensional structure of each stigma dimension and reliability analyses suggested good internal consistency for each. We also aimed to understand the association between PrEP-related stigma and adherence to PrEP using these newly developed measures and found only internalized PrEP stigma to be associated with low self-reported PrEP adherence. No measures of PrEP stigma were associated with low PrEP adherence measured with TDF levels. We used exploratory mediation analyses to assess whether the relationships between each measure of PrEP stigma and self-reported PrEP adherence could be explained by PrEP adherence self-efficacy and found significant indirect effects between each PrEP stigma measure (internalized, perceived, experienced, anticipated, and disclosure concerns) and self-reported PrEP adherence.

Our data aligns with findings in the HIV stigma literature that internalized stigma has the greatest impact on adherence outcomes [20, 23]. Applying negative societal beliefs to oneself about a health prevention tool like PrEP may undermine daily decisions to take one's medication as prescribed. However, there may be psychological mechanisms that help explain the relationships between other dimensions of stigma and PrEP adherence, like PrEP adherence self-efficacy. There are limited instruments available to measure the nuanced dynamics of PrEP stigma as it is experienced by current users. Further validation in larger and more diverse samples with this instrument could

provide a key tool for investigating the impact of PrEP stigma on PrEP uptake and adherence.

PrEP adherence self-efficacy as a potentially important mechanism in the association between each dimension of PrEP stigma and self-reported PrEP adherence is crucial to consider. Self-efficacy is also known to be a strong predictor of antiretroviral adherence in PLHW [26]. Two of the currently FDA-approved PrEP drugs that are available are daily oral pills [4, 5]. However, many people have difficulty taking medications daily [45]. Broader psychosocial and structural factors such as poverty, substance use, and unstable housing may also be involved in this relationship and were not investigated in this study. Innovations in intermittent PrEP dosing and long-acting injectable PrEP options will be important tools for some patients as less frequent dosing intervals may empower patients to feel that they can adhere to these medications.

Our data emphasize the importance of not only considering PrEP stigma in HIV prevention efforts but finding methodologically sound ways to measure PrEP-related stigma. Existing literature suggests that PrEP stigma is a major driver of disparities in PrEP access [12], thus preventing optimal implementation of PrEP in many settings [46]. A growing body of qualitative work in this area points to a need to develop interventions to reduce PrEP stigma, but in order to execute such interventions, we must be able to accurately measure PrEP stigma [47]. Existing studies suggest that PrEP stigma is a problematic experience for people accessing PrEP, but few examine different mechanisms of PrEP stigma on adherence among people using PrEP. Our data suggest that PrEP users in Birmingham do experience stigma, but it is internalized PrEP stigma that potentially has the greatest impact on adherence to PrEP. This is in keeping with the fact that internalized stigma has also been identified in the HIV literature to be a major predictor of poor adherence among PLWH compared to other stigma dimensions [20, 48].

One limitation of our study was the lack of racial and gender diversity represented. Most of our sample were white cisgender men who had been using PrEP for a year or more. In the Southeastern U.S., HIV most dramatically impacts racial and ethnic minorities; 74% of diagnoses occurred in Black/African-American or Hispanic/Latinx individuals in 2018 [49]. Nationwide, sexual and gender minorities (SGM) are also disproportionately impacted by HIV, with MSM and TGW experiencing higher rates than their counterparts [50–52]. Future studies are needed administering this instrument to a larger and more representative cohort of eligible PrEP users, including Black and transgender individuals. Of note, our sample seems to be quite representative of current PrEP users, emphasizing the fact that PrEP is underutilized among these marginalized populations. Measuring adherence was another challenge in our study. Self-reported adherence by participants can be subject to reporting bias [53]. Measurement of plasma TDF levels is more objective, but is limited as a measure of adherence by the fact that it has a half-life of 17 h and, therefore, may not be reliably detected even if someone is adherent if the sample is not collected in a timely manner [42]. In addition, measurement of plasma TDF levels do not capture the true dynamics of adherence among patients. For example, many may take their PrEP right before a clinic visit (which coincided with our research visit that included blood samples to assess TDF levels) because of a desire to present themselves to clinicians as adherent and actually demonstrate less adherence between visits, leading to other ways the accuracy of plasma levels could be diminished. All analyses reported are cross-sectional and should not be interpreted to imply causality. Additional research is needed to validate these measures as potential predictors of retention in PrEP care and longitudinal adherence in the context of HIV risk.

Conclusions

In conclusion, among PrEP users in the Southeastern U.S., internalized stigma is associated with lower self-reported PrEP adherence. PrEP adherence self-efficacy may play a role in this relationship such that the various dimensions of PrEP stigma may diminish self-efficacy and thereby PrEP adherence. Additional longitudinal research is needed on these relationships. No dimensions of PrEP stigma were found in this study to influence PrEP adherence as measured by plasma TDF levels. This sample lacked racial and gender identity diversity and while it represents the demographics of current PrEP users in the Southeastern U.S., more research is needed to investigate how PrEP-related stigma dimensions impact adherence among PrEP users, especially those from racial and gender minorities with less experience with PrEP.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10461-022-03883-3.

Acknowledgements We wish to acknowledge staff at the UAB 1917 Clinic and the Birmingham Magic City Wellness Center for their contributions to participant recruitment and data collection with particular thanks to Kachina Kudroff, Michael Fordham, Joshua Hicks, and Will Rainer. We thank the participants of this study for their time and effort sharing information for this study.

Disclosure OTVG has received research grant funding from Gilead Sciences, Inc. and Abbott Molecular and serves on advisory boards for Scynexis. No other authors have any financial disclosures.

Author Contributions OTVG—data curation, writing (original draft, review, and editing); IY—data analysis, data curation, writing (review and editing); KBC—conceptualization, funding acquisition, writing (review and editing); BT (conceptualization, methodology, funding acquisition, writing (review and editing).

Funding This research was supported by the University of Alabama at Birmingham Center for AIDS Research, a National Institutes of Health (NIH) funded program (P30 AI027767) that was made possible by the following institutes: NIAID, NCI, NICHD, NHLBI, NIDA, NIA, NIDDK, NIGMS, and OAR. The contents of this publication are the sole responsibility of the authors and do not represent the official views of the NIH or AHRQ.

Data Availability Not applicable.

Code Availability Not applicable.

Declarations

Conflict of interest Not applicable.

Ethical Approval This study protocol was approved by the Institutional Review Board of the University of Alabama at Birmingham (Protocol # IRB=170414005).

Consent to Participate Participants underwent informed consent prior to participating in any research activities.

Consent for Publication Not applicable.

References

1. Grohskopf LA, Chillag KL, Gvetadze R, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. J Acquir Immune Defic Syndr. 2013;64(1):79–86. https://doi.org/10.1097/QAI.0b013e31828ece33.
2. Murnane PM, Celum C, Mugo N, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. AIDS. 2013;27(13):2155–60. https://doi.org/10.1097/QAD.0b013e3283629037.
3. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363(27):2587–99. https://doi.org/10.1056/NEJMoa1011205.
4. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367(5):399–410. https://doi.org/10.1056/NEJMoa1108524.
5. Mayer KH, Molina JM, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. Lancet. 2020;396(10246):239–54. https://doi.org/10.1016/s0140-6736(20)31065-5.
6. Centers for Disease Control and Prevention. US public health service: preexposure prophylaxis for the prevention of HIV infection in the United States—2017 update: a clinical practice guideline. 2018. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Accessed 19 July 2021.
7. Centers for Disease Control and Prevention. HIV in the United States by region. https://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html. Accessed 9 July 2021.
8. Siegler AJ, Mouhanna F, Giler RM, et al. The prevalence of pre-exposure prophylaxis use and the pre-exposure prophylaxis-to-need ratio in the fourth quarter of 2017, United States. Ann Epidemiol. 2018;28(12):841–9. https://doi.org/10.1016/j.annepidem.2018.06.005.
9. Jaiswal J, Griffin M, Singer SN, et al. Structural barriers to pre-exposure prophylaxis use among young sexual minority men: the P18 cohort study. Curr HIV Res. 2018;16(3):237–49. https://doi.org/10.2174/1570162x16666180730144455.
10. Goffman E. Stigma; notes on the management of spoiled identity. Englewood Cliffs: Prentice-Hall; 1963.
11. Van der Elst EM, Mbogua J, Operario D, et al. High acceptability of HIV pre-exposure prophylaxis but challenges in adherence and use: qualitative insights from a phase I trial of intermittent and daily PrEP in at-risk populations in Kenya. AIDS Behav. 2013;17(6):2162–72. https://doi.org/10.1007/s10461-012-0317-8.
12. Golub SA. PrEP stigma: implicit and explicit drivers of disparity. Curr HIV/AIDS Rep. 2018;15(2):190–7. https://doi.org/10.1007/s11904-018-0385-0.
13. Haire BG. Preexposure prophylaxis-related stigma: strategies to improve uptake and adherence—a narrative review. HIV AIDS (Auckl). 2015;7:241–9. https://doi.org/10.2147/HIV.S72419.
14. Calabrese SK, Underhill K. How stigma surrounding the use of HIV preexposure prophylaxis undermines prevention and pleasure: a call to destigmatize "Truvada Whores." Am J Public Health. 2015;105(10):1960–4. https://doi.org/10.2105/ajph.2015.302816.
15. Kennedy CE, Baral SD, Fielding-Miller R, et al. "They are human beings, they are Swazi": intersecting stigmas and the positive health, dignity and prevention needs of HIV-positive men who have sex with men in Swaziland. J Int AIDS Soc. 2013;16(4S3):18749. https://doi.org/10.7448/IAS.16.4.18749.
16. Klein H, Washington TA. The Pre-Exposure Prophylaxis (PrEP) Stigma Scale: preliminary findings from a pilot study. Int Public Health J. 2019;11(2):185–95.
17. Atkins K, Kan L, Musau A, Reed J, Were D, Mohan D. Adaptation and psychometric evaluation of a scale to measure oral pre-exposure prophylaxis-related stigma among key and vulnerable populations in Kenya. J Int AIDS Soc. 2022;25(Suppl 1): e25929. https://doi.org/10.1002/jia2.25929.
18. Siegler AJ, Wiatrek S, Mouhanna F, et al. Validation of the HIV pre-exposure prophylaxis stigma scale: performance of likert and semantic differential scale versions. AIDS Behav. 2020;24(9):2637–49. https://doi.org/10.1007/s10461-020-02820-6.
19. Algarin AB, Hee Shrader C, Hackworth BT, et al. Development and validation of the community PrEP-related stigma scale (community-PSS). AIDS Educ Prev. 2021;33(2):120–8. https://doi.org/10.1521/aeap.2021.33.2.120.
20. Earnshaw VA, Smith LR, Chaudoir SR, Amico KR, Copenhaver MM. HIV stigma mechanisms and well-being among PLWH: a test of the HIV stigma framework. AIDS Behav. 2013;17(5):1785–95. https://doi.org/10.1007/s10461-013-0437-9.
21. Berger BE, Ferrans CE, Lashley FR. Measuring stigma in people with HIV: psychometric assessment of the HIV stigma scale. Res Nurs Health. 2001;24(6):518–29. https://doi.org/10.1002/nur.10011.
22. Earnshaw VA, Chaudoir SR. From conceptualizing to measuring HIV stigma: a review of HIV stigma mechanism measures. AIDS Behav. 2009;13(6):1160–77. https://doi.org/10.1007/s10461-009-9593-3.
23. Turan B, Rice WS, Crockett KB, et al. Longitudinal association between internalized HIV stigma and antiretroviral therapy adherence for women living with HIV: the mediating role of depression. AIDS. 2019;33(3):571–6. https://doi.org/10.1097/qad.0000000000002071.
24. Turan B, Crockett KB, Buyukcan-Tetik A, et al. Buffering internalization of HIV stigma: implications for treatment adherence and depression. J Acquir Immune Defic Syndr. 2019;80(3):284–91. https://doi.org/10.1097/qai.0000000000001915.

25. Rice WS, Turan B, Fletcher FE, et al. A mixed methods study of anticipated and experienced stigma in health care settings among women living with HIV in the United States. AIDS Patient Care STDS. 2019;33(4):184–95.
26. Yigit I, Bayramoglu Y, Weiser SD, et al. Changes in internalized stigma and HIV health outcomes in individuals new to HIV care: the mediating roles of depression and treatment self-efficacy. AIDS Patient Care STDS. 2020;34(11):491–7. https://doi.org/10.1089/apc.2020.0114.
27. Bandura A. Human agency in social cognitive theory. Am Psychol. 1989;44(9):1175–84. https://doi.org/10.1037/0003-066x.44.9.1175.
28. Johnson MO, Neilands TB, Dilworth SE, Morin SF, Remien RH, Chesney MA. The role of self-efficacy in HIV treatment adherence: validation of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). J Behav Med. 2007;30(5):359–70. https://doi.org/10.1007/s10865-007-9118-3.
29. Seghatol-Eslami VC, Dark HE, Raper JL, Mugavero MJ, Turan JM, Turan B. Brief report: interpersonal and intrapersonal factors as parallel independent mediators in the association between internalized HIV stigma and ART adherence. J Acquir Immune Defic Syndr. 2017;74(1):e18–22. https://doi.org/10.1097/qai.0000000000001177.
30. Tangmunkongvorakul A, Chariyalertsak S, Amico KR, et al. Facilitators and barriers to medication adherence in an HIV prevention study among men who have sex with men in the iPrEx study in Chiang Mai, Thailand. AIDS Care. 2013;25(8):961–7. https://doi.org/10.1080/09540121.2012.748871.
31. Moran A, Mashele N, Mvududu R, et al. Maternal PrEP use in HIV-uninfected pregnant women in South Africa: role of stigma in PrEP initiation, retention and adherence. AIDS Behav. 2022;26(1):205–17. https://doi.org/10.1007/s10461-021-03374-x.
32. Rice WS, Stringer KL, Sohail M, et al. Accessing pre-exposure prophylaxis (PrEP): perceptions of current and potential PrEP users in Birmingham, Alabama. AIDS Behav. 2019;23(11):2966–79. https://doi.org/10.1007/s10461-019-02591-9.
33. Bunn JY, Solomon SE, Miller C, Forehand R. Measurement of stigma in people with HIV: a reexamination of the HIV Stigma Scale. AIDS Educ Prev. 2007;19(3):198–208. https://doi.org/10.1521/aeap.2007.19.3.198.
34. Nyblade L, Jain A, Benkirane M, et al. A brief, standardized tool for measuring HIV-related stigma among health facility staff: results of field testing in China, Dominica, Egypt, Kenya, Puerto Rico and St. Christopher & Nevis. J Int AIDS Soc. 2013;16(3 Suppl 2):18718. https://doi.org/10.7448/ias.16.3.18718.
35. Blake Helms C, Turan JM, Atkins G, et al. Interpersonal mechanisms contributing to the association between HIV-related internalized stigma and medication adherence. AIDS Behav. 2017;21(1):238–47. https://doi.org/10.1007/s10461-016-1320-2.
36. Feldman BJ, Fredericksen RJ, Crane PK, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav. 2013;17(1):307–18. https://doi.org/10.1007/s10461-012-0326-7.
37. Lu M, Safren SA, Skolnik PR, et al. Optimal recall period and response task for self-reported HIV medication adherence. AIDS Behav. 2008;12(1):86–94. https://doi.org/10.1007/s10461-007-9261-4.
38. Amico KR, Zuniga JM, Wilson IB, Gross R, Young B. Provider guidance for linking patients to antiretroviral therapy adherence interventions: recommendations from an IAPAC advisory committee on adherence monitoring and support. J Int Assoc Provid AIDS Care. 2013;12(2):79–83. https://doi.org/10.1177/1545109712474844.
39. Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372(6):509–18. https://doi.org/10.1056/NEJMoa1402269.
40. Donnell D, Baeten JM, Bumpus NN, et al. HIV protective efficacy and correlates of tenofovir blood concentrations in a clinical trial of PrEP for HIV prevention. J Acquir Immune Defic Syndr. 2014;66(3):340–8. https://doi.org/10.1097/qai.0000000000000172.
41. Musinguzi N, Muganzi CD, Boum Y 2nd, et al. Comparison of subjective and objective adherence measures for preexposure prophylaxis against HIV infection among serodiscordant couples in East Africa. AIDS. 2016;30(7):1121–9. https://doi.org/10.1097/qad.0000000000001024.
42. Kearney BP, Flaherty JF, Shah J. Tenofovir disoproxil fumarate: clinical pharmacology and pharmacokinetics. Clin Pharmacokinet. 2004;43(9):595–612. https://doi.org/10.2165/00003088-200443090-00003.
43. Hayes AF. Introduction to mediation, moderation, and conditional process analysis: a regression-based approach. New York: Guilford Publications; 2017.
44. Tabachnick BG, Fidell LS. Cleaning up your act: screening data prior to analysis. In: Tabachnick BG, Fidell LS, editors. Using multivariate statistics. Boston: Allen and Bacon; 2001. p. 56–110.
45. Dimitrov DT, Mâsse BR, Donnell D. PrEP adherence patterns strongly affect individual HIV risk and observed efficacy in randomized clinical trials. J Acquir Immune Defic Syndr. 2016;72(4):444–51. https://doi.org/10.1097/qai.0000000000000993.
46. Calabrese SK. Understanding, contextualizing, and addressing PrEP stigma to enhance PrEP implementation. Curr HIV/AIDS Rep. 2020;17(6):579–88. https://doi.org/10.1007/s11904-020-00533-y.
47. Dubov A, Galbo P Jr, Altice FL, Fraenkel L. Stigma and shame experiences by MSM who take PrEP for HIV prevention: a qualitative study. Am J Mens Health. 2018;12(6):1843–54. https://doi.org/10.1177/1557988318797437.
48. Turan B, Hatcher AM, Weiser SD, Johnson MO, Rice WS, Turan JM. Framing mechanisms linking HIV-related stigma, adherence to treatment, and health outcomes. Am J Public Health. 2017;107(6):863–9. https://doi.org/10.2105/ajph.2017.303744.
49. Centers for Disease Control and Prevention. HIV surveillance report, 2018 (updated). Vol. 31. 2020. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html.
50. Van Gerwen OT, Jani A, Long DM, Austin EL, Musgrove K, Muzny CA. Prevalence of sexually transmitted infections and human immunodeficiency virus in transgender persons: a systematic review. Transgend Health. 2020;5(2):90–103. https://doi.org/10.1089/trgh.2019.0053.
51. Poteat T, Scheim A, Xavier J, Reisner S, Baral S. Global epidemiology of HIV infection and related syndemics affecting transgender people. J Acquir Immune Defic Syndr. 2016. https://doi.org/10.1097/qai.0000000000001087.
52. Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2015–2019. Vol. 26. 2021. HIV surveillance supplemental report. Published May 2021. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html.
53. McGauran N, Wieseler B, Kreis J, Schüler YB, Kölsch H, Kaiser T. Reporting bias in medical research—a narrative review. Trials. 2010;11:37. https://doi.org/10.1186/1745-6215-11-37.