Published in final edited form as:

J Acquir Immune Defic Syndr. 2017 December 15; 76(5): 501–511. doi:10.1097/QAI.0000000000001538.

Plasma Tenofovir-levels to Support Adherence to TDF/FTC Pre-exposure Prophylaxis for HIV Prevention in MSM in Los Angeles, California

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Conflicts of Interest:

No other potential conflict of interest relevant to this article was reported.

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Abstract

BACKGROUND—TDF/FTC PrEP is effective against rectal HIV acquisition when taken as prescribed. Strategies that identify and intervene with those challenged by adherence to daily medication are needed.

SETTING—PATH-PrEP was an open-label single arm interventional cohort study conducted at 2 community-based clinical sites in Los Angeles, California.

METHODS—We enrolled self-identified MSM and TGW 18 years of age at elevated risk of HIV acquisition. Participants received a PEP or PrEP-based HIV prevention package for at least 48 weeks. Plasma TFV levels from each PrEP visit assessed as below the limit of quantitation (<10 ng/mL) triggered increased adherence support.

RESULTS—301 participants enrolled. Forty-eight-week retention in the PrEP cohort was 75.1%. Biomarker evidence of PrEP adherence consistent with 4 doses per week at weeks 4, 12, 24, 36, and 48 were found in 83.1%, 83.4%, 75.7%, 71.6%, and 65.5% of participants; younger and African-American participants were less likely to have protective drug levels. Most of those with suboptimal adherence had adherence improvement after brief intervention. One seroconversion occurred in a participant who discontinued PrEP. Nearly half (46.4%) of participants were diagnosed with at least one incident STI during 48 weeks of study follow-up.

CONCLUSIONS AND RELEVANCE—PrEP was acceptable and well tolerated in a diverse population of MSM in Los Angeles. A brief intervention triggered from biomarkers of poor adherence was associated with improved adherence. Drug level monitoring has the potential to allow targeting of additional adherence support to those struggling with daily tablet adherence.

Background

Tenofovir-based oral Pre-exposure Prophylaxis (PrEP) is highly effective for HIV protection against rectal exposures when taken consistently. iPrEx, the first randomized placebo controlled study of PrEP estimated the efficacy of tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)-based PrEP to be 44%, with protection above 90% in those who had detectable drug levels in plasma samples.¹ More recent data suggest 86% reduction in HIV-acquisition among men who have sex with men (MSM) in the United Kingdom randomized

to immediate open-label daily TDF/FTC PrEP compared to those randomized to delayed PrEP.² A study of coitally-dependent TDF/FTC PrEP in Quebec and France showed 86% reduction in HIV acquisition in a placebo-controlled comparison.³ The mean number of tablets taken per week in the coitally-dependent strategy was approximately four.

Open-label PrEP cohorts have demonstrated extremely high levels of protection for MSM who had pharmacologic biomarkers consistent with sustained use of four or more tablets per week.^{4,5} These studies identified key populations that may have challenges adhering to PrEP at the requisite level for protection, including those disproportionately affected by HIV in the United States – young individuals and Black MSM.⁶ An open-label PrEP study of youth age 18–22 highlighted a residual 3.3% (95% CI, 0.1–6.5%) annual HIV incidence largely attributable to non-adherence,⁷ and a demonstration study for Black MSM (BMSM) that co-packaged PrEP with a client centered care coordination model (C4) found a residual 2.9% (95% CI 0.9–6.8%) annual incidence among BMSM who ever took PrEP, and a 7.7% (1.6%–22.5%) annual incidence among BMSM who never took PrEP.⁸

Although generally safe and well tolerated, TDF/FTC PrEP is often characterized as having three main categories of side effects: an initial gastrointestinal “start-up” syndrome lasting 2–4 weeks and experienced by approximately 20% of users; elevations in serum creatinine occurring in approximately 0.2% of users and reversible upon discontinuation; and loss of 1–1.5% of bone mineral density over the first year of use, with return to baseline levels upon discontinuation.⁹

While PrEP is gaining attention and acceptance as a potent HIV prevention strategy by consumers and providers alike, the cost- effectiveness of PrEP for MSM is most compelling among those who are young and most consistently at-risk.^{10,11} For MSM who are not recurrently at risk, post-exposure prophylaxis (PEP), a limited course of 28 days of antiretroviral treatment initiated as quickly as possible after exposure, may be lower burden, is of shorter duration, and may have less toxicity.

The PATH (PrEP and Testing/linkage to care for HIV Prevention)-PrEP study was a demonstration project at two community-based clinical sites in Los Angeles that aimed to evaluate uptake, adherence, persistence to PrEP, and to assess the acceptability and impact of using drug levels to implement an escalating adherence intervention. Plasma drug levels were resulted on average three weeks after visits and then reported to participants within 48 hours. PATH-PrEP triaged participants to a combination HIV prevention strategy that included either PrEP or as-needed PEP. We supported adherence to daily oral PrEP using tiered adherence support guided by plasma drug concentrations over one year of follow-up. A vitamin D and calcium supplementation sub-study will provide insight into the ability to mitigate bone mineral density loss among PrEP users. The primary outcome was the level of adherence to daily oral TDF/FTC as categorized using intra-erythrocytic tenofovir-diphosphate (TFV-DP) levels in dried blood spots (DBS).^{12–14}

Methods

Study Participants

The PATH-PrEP study included self-identified MSM, MSM/W, and transgender women age 18 years or older, HIV-uninfected at study entry by rapid enzyme-linked immunosorbent assay (EIA) and viral load, with adequate screening laboratory parameters, and without symptoms suggestive of primary HIV infection. The study was approved by the institutional review boards at the University of California Los Angeles and Charles R. Drew University of Medicine and Science, and all participants provided written informed consent before screening. The Los Angeles LGBT Center (LA LGBT Center) formally relied on the UCLA IRB for regulatory oversight. The protocol was registered at clinicaltrials.gov as NCT01781806.

Study Design

Our study was a two-arm, open-label study. Participants were triaged at study entry into either a PEP-based or a PrEP-based cohort based on self-reported risk behavior. Criteria for entering the PrEP cohort included condomless anal intercourse (cAI) with 3 or more male sex partners (HIV-infected or of unknown HIV serostatus) in the past 3 months, a sexually transmitted infection (STI, gonorrhea, chlamydia, or syphilis) diagnosis or PEP use in the past 12 months, or being in a sexual partnership with someone known to be HIV-infected for at least 4 weeks. All other participants not meeting the above-mentioned risk criteria were offered as-needed PEP services. Participants initially triaged to the PEP-based cohort were reassessed at each follow-up visit for changes in self-reported risk behavior and were offered “escalation” to the PrEP-based cohort if above criteria were met. Eligible PrEP-cohort participants who opted not to initiate TDF/FTC, or discontinued TDF/FTC for safety or change in perceived risk status were followed on-study, but off study medication.

PrEP-cohort participants received daily oral TDF/FTC (Truvada, Gilead Sciences, Foster City, California, USA). PEP-cohort participants received 2- or 3-drug PEP medication within 72 hours of a high-risk sexual exposure to an HIV-infected or HIV-status unknown partner as per Los Angeles County Division of HIV and STD Programs (DHSP) programmatic protocols.

All participants received a comprehensive HIV prevention package that included regular HIV and STI testing (with on-site treatment of STIs), risk reduction and standardized adherence counseling, and provision of condoms.

Participants were followed for 48 weeks after enrollment; participants who escalated from the PEP-based to the PrEP-based cohort were followed for 48 weeks after initiation of PrEP-cohort participation, regardless of previous duration of follow-up in the PEP-based cohort. HIV antibody tests (OraQuick, OraSure Technologies, Inc., Bethlehem, Pennsylvania, USA) on phlebotomized blood, and safety laboratory testing were performed at screening, entry, and all follow-up visits. HIV RNA testing was also performed at screening. At one of the clinical sites (LA LGBT Center), pooled RNA testing was performed on all HIV-non-reactive samples throughout the study; at the other site (OASIS Clinic) RNA testing was only performed after screening with clinical suspicion of primary HIV infection.

Adherence to TDF/FTC was assessed by self-report measures, plasma TFV levels and dried blood spots to determine TFV-DP and FTV-TP concentrations (both by liquid chromatography tandem mass spectrometry (LC-MS/MS)) at all time points.^{1,4} TFV plasma levels were measured in at each visit and results were available within 7–21 days, and levels below the limit of quantitation (BLQ, lower limit of quantitation 10 ng/mL) triggered outreach and implementation of an escalated adherence support approach. A random sample of one-third of selected participants received MEMS caps (AARDEX Ltd., Sion, Switzerland) to measure pill-bottle opening events as a surrogate of adherence.

At each visit participants received Integrated Next Step Counseling (iNSC, Support Level 1¹⁵), a strengths-based discussion focused on the identification of sexual health protection and PrEP adherence needs. Developed for and used in iPrEx OLE, iNSC is based on a situated application of the Information, Motivation, Behavioral Skills model of health behavior adoption¹⁶, which posits that adopting a given behavior is a function of behavior-specific information, motivation, and behavioral skills. It is a basic guided approach for eliciting interactions intended to promote high levels of information, motivation, and skill relevant to sexual health and PrEP uptake utilizing motivational interviewing and other counseling and communication strategies.

A first TFV measurement BLQ triggered escalation to Support Level 2, “Targeted” Integrated Next Step Counseling (tiNSC), in which the adherence support discussion included the non-detectable drug level information and problem-solving on improved dosing. Conversations were guided by an algorithm based on a participant’s response to two 10-point Likert scales, one assessing the importance of PrEP and the other assessing a participant’s confidence of taking PrEP medications daily.

A second (sequential or non-sequential) BLQ result triggered further escalation to Support Level 3, PrEP-STEPS. PrEP Steps is a six-session intervention that is based on Lifesteps^{17,18}, an antiretroviral therapy adherence intervention. PrEP Steps utilizes elements of cognitive behavioral therapy (i.e., motivational interviewing and problem-solving) to identify and address individual barriers to PrEP adherence, as well as implementation of safer sexual behaviors. The first four sessions were held weekly, while the final two booster sessions were held monthly. Sessions were approximately 45 minutes in length. All sessions involved an assessment of adherence; discussions around motivation to use PrEP and the pros and cons of use versus non-use were conducted. If barriers to adherence were identified, comprehensive problem solving that included weighing the pros and cons of all possible solutions to the barriers was performed in a collaborative fashion. Optional models were built into the intervention for participants who experienced mental health or substance abuse related concerns as barriers to adherence. After completion of escalated approach, participants returned to the basic support package (iNSC) and remained in Level 1 support unless or until another BLQ occurred. Per protocol, additional BLQ results after Level 3 were considered on a case-by-case basis.

Sexual behaviors were assessed at each study visit and were aggregated as number of partners for non-condom protected receptive anal intercourse (ncRAI) and proportion of receptive anal intercourse (RAI) events that were ncRAI.

Statistical Methods

Logistic regression was used to determine the association between each of the baseline demographic and behavioral predictors and study retention at 48 weeks, without and without adjusting for site. Logistic models were used to determine the associations between demographics and risk behaviors and intra-erythrocytic TFV-DP levels dichotomized as “protective” (>700 fmol/punch), except at week 4, where the cut-off value for protective/not protective was adjusted for number of days on TDF/FTC pre-steady state. Predictors significant with $p < 0.1$ in the bivariate models were added to the composite multivariable model, which was built in one step. Repeated measures logistic regression models were used to determine the accuracy of various self-report measures against protective TFV-DP levels.

Results

Between April 2014 and July 2016, 823 individuals expressed interest in study participation. Of these 328 were screened, and 300 MSM and 1 Transgender woman (TGW) were enrolled through two community-based clinics in Los Angeles (Figure 1, Table 1). Eligible participants met inclusion criteria as noted above; Individuals reporting PEP or PrEP use in the 60 days prior to study entry were not enrolled.

At study entry, 273 (92.4%) were assigned to the PrEP-based cohort and 23 (7.6%) were assigned to the PEP-based cohort. Six individuals originally assigned to the PEP-based cohort declined study participation (see Text, Supplemental Digital Content 1, which describes the participants assigned to the PEP-based cohort), and were considered as screen failures. During follow-up, 19 (82.6%) initially assigned to the PEP cohort “escalated” to the PrEP-based cohort based on self-reported risk behavior. Of those 19, 7 (36.8%) escalated after an episode of PEP use. For the primary analysis, we excluded the one TGW enrolled in the protocol, providing an analysis population of MSM exposed to PrEP of 296. Main findings were similar with this participant included. Of the 296, 13 participants had no visits after baseline resulting in an adherence subset of 283.

Among enrolled participants, the median age was 34 (range 20–69 years). Half (50%) identified as non-Hispanic white, 33 (11%) identified as Black/African-American, 83 (28%) identified as Hispanic or Latino, and 33 (11%) identified as another race/ethnicity. Ninety-three (31%) were uninsured, 138 (46%) had private insurance and 64 (21%) had some form of public (Medicare or state Medicaid) insurance; 2% did not report insurance coverage. Forty-six percent completed their education in high school or prior, and 30% reported an annual household income of \$20,000 or less. With respect to risk behaviors, 84% reported condomless anal intercourse in the 30-days prior to study enrollment, and 13% self-reported a prior STI diagnosis. Participants came from areas of Los Angeles County most affected by HIV (see Figure, Supplemental Digital Content 2, a comparison of enrolled participants with new HIV diagnoses from 2010 to 2012 by zip code in Los Angeles County). Fifty (16.6%) participants experienced 62 prevalent STIs that were diagnosed and treated at cohort entry.

Retention rates across the cohorts are shown in Figure 1. Two participants met protocol-mandated stopping rules for TDF/FTC (elevated creatinine phosphokinase and grade 4 psychosis); 11 participants self-assessed their risk as having declined and stopped PrEP

treatment, but remained in study follow-up off TDF/FTC. Younger participants, Black/African-American participants, those with less education, and participants not privately insured were less likely to be retained in the cohort at Week 48 (Table 1). Including all participants assigned to the PrEP-based cohort, DBS-measured TFV-DP levels commensurate with 4 or more doses per week were found in 83.1%, 83.4%, 75.7%, 71.6%, and 65.5% of participants at weeks 4, 12, 24, 36, and 48 respectively (Figure 2), with lower rates of Black/African-American participants reaching this metric. Discounting participants known to have permanently discontinued PrEP for any reason, 4 or more doses per week were found in 84.5%, 84.9%, 77.5%, 73.6%, and 67.8% at these same time-points. Adherence estimated by Week 4 DBS TFV-DP level stratum and plasma TFV level stratum (from which adherence intervention escalations were triggered) are shown in Figure 3A and 3B, respectively. In a multivariable model, older and non-Hispanic White participants had greater odds of having TFV-DP levels commensurate with high levels of rectal protection against HIV acquisition; substance use, insurance status, education, and numbers of partners were not independently associated with increased odds of having protective TFV-DP levels (Table 2).

Plasma drug level results were available a mean of 21.4 days after follow-up (SD = 8.9) and tiNSC was deployed by phone within 48 hours of receipt of results at the site. Thirty-four (12%) participants experienced a BLQ plasma TFV result during study follow-up and 32 received the tiNSC intervention. Black and Hispanic/Latino participants accounted for over 70% of BLQ plasma levels, accounting for 29.4% and 41.2% respectively ($p < 0.001$). Of the 32 who received tiNSC, 16 (50%) had sustained improvements and 4 (12.5%) had short-term improvements (at least one detectable plasma level) in biomarkers of adherence after the intervention (Figure 3C). Four participants went on to trigger the PrEP-STEPs intervention for a second BLQ result: One participant received PrEP-STEPs, without effect on subsequent levels, two were lost to follow-up, and one withdrew from study participation to enter substance use rehabilitation prior to intervention delivery.

Overall, there was a modest positive relationship between TFV plasma levels and TFV-DP levels ($\rho = 0.4$, $p < 0.001$), and over the 48 weeks of follow-up a cut-off of 70 ng/mL on the TFV plasma assay had the best operating characteristics (see Figure, Supplemental Digital Content 3, a Receiver Operating Characteristic (ROC) Curve for TFV plasma levels and Protective TFV-DP levels in DBS) for association with protective TFV-DP levels at the same time point. Associations between TFV plasma levels, self-report measures, and MEMS openings were also analyzed (see Table, Supplemental Digital Content 4, Bivariate Generalized Linear Models for Objective and Self-Report Adherence Predictors of Rectally Protective TFV-DP Levels in DBS).

Percentages of participants reporting any ncRAI decreased over the first 12 weeks of study participation but then reverted to baseline levels thereafter; Numbers of episodes of ncRAI per participant decreased over the first 24 weeks of study, and then were stable thereafter (see Figure, Supplemental Digital Content 5 and 6, Percentage of participants reporting ncRAI and mean number of ncRAI episodes over time). One hundred and twenty-seven (46.4%) participants were diagnosed with 175 incident STIs over the 48 weeks of follow-up, with a parabolic distribution over the follow-up period (see Figure, Supplemental Digital

Content 7, Prevalent and incident STIs over time) 48-week incidence rate of any STI was 53.7 per 100 person-years; individual STI incidence rates are provided in (see Table, Supplemental Digital Content 8, STI incidence rates by study visit and specific STI).

One seroconversion occurred in a participant who attended study visits per protocol through week 24 and then was lost to follow-up. Despite initially good adherence (weeks 4 and 12), his week 24 DBS specimen suggested adherence on average of fewer than 2 doses per week over the prior 4–8 weeks. He had recurrent urethral and rectal STIs 7, 9 and 10 months after study enrollment, diagnosed outside of the study; he was diagnosed with HIV infection 10 months post-enrollment. Pre-ART genotyping revealed the M184V mutation. The HIV incidence rate among study participants was 0.4 per 100py. For comparison, the background incidence rate among MSM in Los Angeles County (uncontrolled for risk) is estimated to be 7.63 per 100py (Sonali Kulkarni, MD, email communication, February 2, 2017).

Rates of adverse events were consistent with current product labeling. No discontinuations occurred for renal or bone/fracture adverse events, and there were no deaths among study participants (see Table, Supplemental Digital Content 9, AEs by MedDRA preferred term and severity).

Discussion

Pre-exposure prophylaxis using coformulated TDF/FTC is arguably the most potent HIV prevention tool in the arsenal of effective HIV prevention interventions. Issues with differential drug pharmacokinetics in rectal tissue versus female genital tissue compartments and confounding of efficacy estimates by poor adherence has hamstrung consensus on its effectiveness across populations.¹⁹ Anecdotal epidemiologic observations of declining new HIV infections have buoyed PrEP supporters²⁰ and the ecological observation of increasing rates of bacterial STIs have galvanized PrEP detractors.²¹ The optimal way to support PrEP adherence, and in fact the extent to which such support is required for effectiveness remain areas of great interest and importance to the field.¹⁵

We conducted the first trial to demonstrate the acceptability, challenges, and utility of using plasma TFV drug level monitoring with feedback to help support adherence to daily oral PrEP in a population of MSM at two community-based sites in Los Angeles, California. There are concerns that efforts to support adherence to PrEP agents are likely to be resource and skill intensive, and may be a prohibitive barrier to scale-up. The central tenet of the approach was that those who could be determined to be adhering at some pre-defined level should require little additional adherence support, and resources could be targeted to those who despite ongoing interest in using PrEP struggle with adherence. We observed clinically that there appear to be subsets of PrEP users that have minimal to no challenges with adherence, and therefore deployment of adherence support efforts beyond a basic, in-clinic adherence and sexual health check-in, would be most cost-effective if targeted.

Our study overlaid measurement of adherence using objective biomarkers (plasma TFV, DBS TFV-DP), with electronic drug monitoring (MEMSCaps) and self-report. We used the plasma TFV levels to apply escalating adherence support. Our results suggest that the

majority of those challenged by adherence initially were favorably impacted by a brief intervention centered around a discussion of biomarker results; however, for a minority these benefits were not sustained over time. These results support the ongoing development of alternate prevention modalities, including injectable or slow-release implantable options that could increase the options for choice to those who find daily pill-taking to be prohibitive.

Consistent with previous demonstration projects, we found that younger PrEP-users and African-Americans were less likely to achieve rectally-protective levels of adherence as measured by both DBS TFV-DP and plasma TFV levels, even when controlling for education, income, and other comorbidities.⁵ Other work (HPTN 073) documents the social-political barriers to PrEP uptake and use among Black MSM in the US and the promise for intervention approaches that are navigational, peer or near-peer delivered, and focused on comprehensive wrap-around services.⁸ Identifying and intervening on barriers to uptake, retention, adherence, and persistence to PrEP among those most affected by the epidemic will be critical to PrEP use translating into public health and epidemic impact.

Also consistent with other work, HIV seroconversions were rare, and associated with PrEP non-use.^{4,5} The seroconversion with M184V (3TC and FTC resistance associated) virus again reminds the clinician of the possibility of transmitted viral resistance and the hazards of restarting TDF/FTC PrEP after hiatus during which occult seroconversion might have occurred; the participant who seroconverted during this study was able to be suppressed on a well-tolerated first-line ART regimen without complication.

Interestingly, stimulant substance use was not associated with study retention or adherence. Previous data have identified clear associations between stimulant drug use and subsequent HIV seroconversion; and that a substantial proportion of HIV infections among MSM are attributable to stimulants (methamphetamine in particular)^{22–24}. Our results where drug levels were independent of alcohol or drug use are promising in that TDF/FTC PrEP may be highly impactful on HIV incidence at the population level if targeted to those using stimulants; in fact, a recent analysis even suggested improved adherence among some stimulant users.²⁵

Although we saw high rates of bacterial STIs in study participants, despite declines in proportions of self-reported ncRAI, we are cautious in both interpretation and attribution of these findings. STI rates have been increasing among MSM long prior to the advent of PrEP,^{26,27} and never before have highly sexually active otherwise healthy MSM been engaged in longitudinal symptomatic STI screening as frequently as every 3 months. We interpret the high rates of STIs in this study as a unique opportunity to interrupt the transmission cycle at an early time point after acquisition, thereby reducing numbers of exposed partners and secondary infections.

Although the protocol was open to transgender women and marketing materials were developed with transgender community consultation to improve trans-competency of staff and instruments, we only enrolled one transgender woman. Data from designated PrEP studies designed for, and with comprehensive input from transgender individuals are critically needed, and are underway.

Should point-of-care drug level assays become a clinical reality (such as under investigation), these could be used as an important triage criterion for identifying those who might be challenged by daily oral adherence either for additional adherence interventions or alternative prevention strategies that do not require daily oral dosing.

These data expand the current understanding of the need for adherence support in PrEP clinical programs, and advance the understanding of which consumers may struggle with daily oral adherence, and support further study of biomarker-based adherence support.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was funded by the California HIV Research Program via Award E111-LA-002. Gilead Sciences provided drug supply and additional support for some drug-assay testing.

The authors would like to thank and acknowledge Laura Packel, George Lemp, Glenn Gaylord, Ralph Meneghetti, Corinne Beniassians, Kayla McLaughlin, Tymeshia Randolph, Sarah Livingston, Henry Meraz Jr., Kevin Marx, Felipe Findley, Thuymien Nguyen, Jessica Kuo, Kiesha McCurtis, Irma Franco-Gonzalez, Brenda Ng and Rebecca Guzman.

Sources of Funding:

RJL has received honoraria and travel support from Gilead Sciences. KRA has received grants from Gilead Sciences through the University of Michigan during the conduct of this study. LB has received grants from Gilead Sciences during the conduct of this study. PLA has received grants from Gilead Sciences. JFR is employed by Gilead Sciences.

This work was also supported by the Center for HIV Identification, Prevention, and Treatment (CHIPTS) NIMH grant MH58107; the UCLA Center for AIDS Research (CFAR) grant 5P30AI028697; and the National Center for Advancing Translational Sciences through UCLA CSTI Grant UL1TR000124. The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH.

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Figure 1.

Figure 2.

Figure 3.

Bivariate Logistic Regression Tests of Baseline Demographics on Study Retention at Week 48, January 2013 - May 2016 (n = 300).^a

Table 1

	Total (n = 300)	Retained (n = 224)	Not Retained (n = 76)	Unadjusted p-value	Adjusted p-value ^b	Adjusted OR (95% CI)
Baseline Characteristics	n (%)	N (%)	n			
Site						
Los Angeles LGBT Center	250 (83.3)	191 (85.3)	59 (77.6)	0.13	N/A	N/A
Oasis	50 (16.7)	33 (14.7)	17 (22.4)			
Age at First Visit						
18–25	38 (12.7)	23 (10.3)	15 (19.7)	0.02	0.01	0.24 (0.09–0.67)
26–35	137 (45.7)	97 (43.3)	40 (52.6)			0.40 (0.17–0.92)
36–45	72 (24)	59 (26.3)	13 (17.1)			0.80 (0.30–2.11)
46 or Older	53 (17.7)	45 (20.1)	8 (10.5)			1 [Reference]
Race/Ethnicity						
White	151 (50.3)	119 (53.1)	32 (42.1)	0.05	0.08	1 [Reference]
Hispanic	83 (27.7)	58 (25.9)	25 (32.9)			0.64 (0.35–1.17)
Black or African American	33 (11)	19 (8.5)	14 (18.4)			0.40 (0.18–0.89)
Asian/PI	19 (6.3)	15 (6.7)	4 (5.3)			1.05 (0.32–3.40)
Other	14 (4.7)	13 (5.8)	1 (1.3)			3.66 (0.46–29.2)
Educational Level						
High School or Less	32 (10.7)	21 (9.4)	11 (14.5)	0.006	0.005	0.49 (0.19–1.31)
Some College	106 (35.3)	69 (30.8)	37 (48.7)			0.49 (0.23–1.05)
Bachelors Degree	106 (35.3)	90 (40.2)	16 (21.1)			1.52 (0.66–3.51)
Post-graduate study/degree	56 (18.7)	44 (19.6)	12 (15.8)			1 [Reference]
Family Income						
\$20,000 or Less	91 (30.3)	64 (28.6)	27 (35.5)	0.21	0.17	0.53 (0.27–1.06)
Between \$20,001 and \$50,000	114 (38)	83 (37.1)	31 (40.8)			0.60 (0.31–1.16)
More than \$50,000	95 (31.7)	77 (34.4)	18 (23.7)			1 [Reference]
Insurance Status						
Private Insurance	138 (46)	114 (50.9)	24 (31.6)	0.03	0.03	1 [Reference]

	Total (n = 300) n (%)	Retained (n = 224) N (%)	Not Retained (n = 76) n	Unadjusted p-value	Adjusted p-value ^b	Adjusted OR (95% CI)
Baseline Characteristics						
Public Insurance	64 (21.3)	43 (19.2)	21 (27.6)			0.44 (0.22–0.87)
Not Covered	93 (31)	66 (29.5)	27 (35.5)			0.52 (0.28–0.98)
Unknown/Unreported	5 (1.7)	1 (0.4)	4 (5.3)			N/A
Relationship Status						
Single / Divorced / Widowed	197 (65.7)	150 (67.0)	47 (61.8)			1.29 (0.61–2.72)
Living with Primary / Main Partner	42 (14)	30 (13.4)	12 (15.8)			0.87 (0.33–2.25)
Have Primary Partner / Not Living Together	39 (13)	27 (12.1)	12 (15.8)	0.64	0.54	1 [Reference]
Married / Civil Union / Legal Partnership	9 (3)	9 (4.0)	0 (0)			8.08 (0.37–174)
Other	12 (4)	7 (3.1)	5 (6.6)			0.50 (0.13–1.88)
Unknown/Unreported	1 (0.3)	1 (0.4)	0 (0.0)			N/A
Any Substance Use in the Past 30 Days						
Yes	232 (77.3)	171 (76.3)	61 (80.3)	0.37	0.36	0.70 (0.33–1.50)
No	62 (20.7)	49 (21.9)	13 (17.1)			1 [Reference]
Missing	6 (2)	4 (1.8)	2 (2.6)			N/A
Polysubstance Use in the Past 30 Days						
Yes	169 (56.3)	126 (56.3)	43 (56.6)	0.39	0.40	0.75 (0.38–1.47)
No	65 (21.7)	52 (23.2)	13 (17.1)			1 [Reference]
Missing	66 (22)	46 (20.5)	20 (26.3)			N/A
Methamphetamine Use in the Past 30 Days						
Yes	36 (12)	24 (10.7)	12 (15.8)	0.21	0.22	0.62 (0.29–1.33)
No	262 (87.3)	198 (88.4)	64 (84.2)			1 [Reference]
Missing	2 (0.7)	2 (0.9)	0 (0)			N/A
Injection Drug Use in Past 3 Months						
Yes	3 (3)	3 (1.3)	0 (0)	0.99	0.99	2.23 (0.07–69.2)
No	295 (98)	219 (97.8)	76 (100)			1 [Reference]
Missing	2 (1)	2 (0.9)	0 (0)			N/A
Binge Drinking in the Past 12 Months ^c						
Yes	182 (60.7)	135 (60.3)	47 (61.8)	0.52	0.54	0.83 (0.46–1.51)

	Total (n = 300)	Retained (n = 224)	Not Retained (n = 76)	Unadjusted p-value	Adjusted p-value ^b	Adjusted OR (95% CI)
Baseline Characteristics	n (%)	N (%)	n			
No	105 (35)	81 (36.2)	24 (31.6)			1 [Reference]
Missing	13 (4.3)	8 (3.6)	5 (6.6)			N/A
Used PEP in the Past 12 Months						
Yes	81 (27)	60 (26.8)	21 (27.6)	0.77	0.67	1 [Reference]
No	219 (73)	164 (73.2)	55 (72.4)			1.14 (0.63–2.09)
Missing	0	0 (0)	0 (0)			N/A
Unprotected Anal Intercourse in the Past 30 Days						
Yes	252 (84)	192 (85.7)	60 (78.9)	0.34	0.28	1.65 (0.67–4.07)
No	30 (10)	21 (4.9)	9 (11.8)			1 [Reference]
Missing	18 (6)	11 (4.9)	7 (9.2)			N/A
Sexually Transmitted Infection Diagnosis						
Yes	39 (13)	27 (12.1)	12 (15.8)	0.29	0.37	0.71 (0.34–1.50)
No	258 (86)	195 (87.1)	63 (82.9)			1 [Reference]
Missing	3 (1)	2 (0.9)	1 (1.3)			N/A
Total	300 (100)	224 (100)	76 (100)			

^a One individual who identified as Trans was removed from the analysis

^b Adjusted for site

^c Binge drinking is defined as one or more days where there was consumption of ≥ 5 alcoholic drinks in the last 12 months

PrEP Cohort Predictors of Protective Levels of TFV-DP in Dried Blood Spot Samples (n = 283)^a

Table 2

Characteristics at Baseline	No. of Participants Undergoing Testing ^b	Level Indicative of 4 Doses/wk, % of Visits ^c	OR (95% CI) ^d	p-value	AOR (95% CI) ^e	p-value
Site						
Los Angeles LGBT Center	239	81.4	1.63 (0.93–2.87)	0.09	2.24 (1.16–4.30)	0.02
Oasis	44	72.7	1 [Reference]	NA	1 [Reference]	NA
Age at First Visit						
18–25	37	67.9	1 [Reference]	NA	1 [Reference]	NA
26–35	125	78.4	1.77 (1.00–3.12)	0.05	1.38 (0.63–3.03)	0.42
36–45	70	86.2	3.36 (1.63–6.90)	0.001	4.75 (1.68–13.47)	0.003
46 or Older	51	84.3	2.80 (1.32–5.94)	0.007	2.82 (1.14–6.96)	0.02
Race/Ethnicity						
White	145	84.6	1 [Reference]	NA	1 [Reference]	NA
Hispanic	78	78.3	0.66 (0.40–1.08)	0.1	1.17 (0.59–2.34)	0.65
Black or African American	29	52.8	0.22 (0.11–0.42)	<0.0001	0.35 (0.16–0.74)	0.006
Asian/PI	17	88.2	1.39 (0.52–3.73)	0.52	2.03 (0.62–6.64)	0.24
Other	14	88.1	1.43 (0.34–6.06)	0.63	1.49 (0.42–5.26)	0.53
Educational Level						
High School or Less	32	73	1 [Reference]	NA	1 [Reference]	NA
Some College	96	72.2	0.99 (0.52–1.88)	0.97	0.73 (0.32–1.66)	0.45
Bachelors Degree	101	88.1	2.89 (1.42–5.87)	0.004	1.30 (0.52–3.29)	0.58
Post-graduate study/degree	54	83	1.92 (0.92–4.00)	0.08	0.93 (0.35–2.46)	0.88
Family Income						
\$20,000 or Less	84	74	1 [Reference]	NA	1 [Reference]	NA
Between \$20,001 and \$50,000	109	81.3	1.54 (0.92–2.57)	0.1	1.83 (0.94–3.57)	0.08
More than \$50,000	90	84.2	1.93 (1.10–3.38)	0.02	1.06 (0.46–2.45)	0.89
Insurance Status						
Private Insurance	134	84.2	1 [Reference]	NA	1 [Reference]	NA

Characteristics at Baseline	No. of Participants Undergoing Testing ^b	Level Indicative of 4 Doses/wk, % of Visits ^c	OR (95% CI) ^d	p-value	AOR (95% CI) ^e	p-value
Public Insurance	60	71.6	0.48 (0.28–0.82)	0.008	0.66 (0.30–1.42)	0.28
Not Covered	87	80.2	0.77 (0.47–1.27)	0.31	1.12 (0.51–2.45)	0.79
Unknown/Unreported	2	--	--	--	--	--
Relationship Status						
Single / Divorced / Widowed	186	81.4	1 [Reference]	NA	1 [Reference]	NA
Have Primary Partner / Not Living Together	38	77.8	0.79 (0.42–1.46)	0.45	1.16 (0.51–2.61)	0.72
Living with Primary / Main Partner	38	80	0.90 (0.47–1.69)	0.73	1.29 (0.59–2.81)	0.52
Married / Civil Union / Legal Partnership	9	75.6	0.73 (0.20–2.69)	0.63	0.26 (0.08–0.83)	0.02
Other	11	66	0.40 (0.14–1.16)	0.09	0.44 (0.13–1.42)	0.17
Unknown/Unreported	1	--	--	--	--	--
Psychological Distress						
Low Distress (0–5)	184	88.5	1.56 (0.57–4.24)	0.39	NA	
Moderate Distress (6–13)	71	88.5	1.53 (0.57–4.11)	0.39		
High Distress (14–24)	4	83.3	1 [Reference]	NA		
Missing	24	--	--	--	--	--
ncRAI in Past 3 Months						
Yes	166	90.7	1 [Reference]	NA	NA	
No	37	89.3	0.93 (0.45–1.92)	0.84		
Missing	80	--	--	--	--	--
Number of ncRAI partners in Past 3 Months						
0–1	77	89.1	1 [Reference]	NA	NA	
>=2	126	91.2	1.04 (0.64–1.71)	0.87		
Missing	80	--	--	--	--	--
Binge Drinking in the Past 12 Months						
Yes	157	89.1	1 [Reference]	NA	NA	
No	94	87.7	0.92 (0.58–1.46)	0.72		
Missing	32	--	--	--	--	--

Characteristics at Baseline	No. of Participants Undergoing Testing ^b	Level Indicative of 4 Doses/wk, % of Visits ^c	OR (95% CI) ^d	p-value	AOR (95% CI) ^e	p-value
Any Substance Use in the Past 30 Days						
Yes	206	88	1 [Reference]	NA	NA	
No	50	89.2	1.23 (0.80–1.90)	0.35		
Missing	27	--	--	--	--	--
Methamphetamine Use in the Past 30 Days						
Yes	33	88.6	1 [Reference]	NA	NA	
No	227	85.3	1.13 (0.55–2.31)	0.75		
Missing	23	--	--	--	--	--
Exchange Sex in the Past 30 Days						
Yes	20	78.1	1 [Reference]	NA	1 [Reference]	NA
No	242	88.8	1.79 (0.93–3.43)	0.08	1.30 (0.62–2.73)	0.48
Missing	21	--	--	--	--	--

^aFour individuals were part of the LM cohort and therefore were not offered drug; thirteen individuals attended the baseline visit but missed all subsequent visits and thus never had any drug readings. None of these individuals are included in the presented data. Tenofovir diphosphate (TFV-DP) concentrations in dried blood spots (DBS) measured by liquid chromatography tandem mass spectrometry (LC-MS/MS)

^bIndicates the category an individual was in at baseline for the repeated measures

^cFour individuals had mislabeled or discarded samples for the Week 4 visit. Subsequent readings were used to impute the Week 4 drug levels.

^dAdjusted for Site Only

^eMultivariable model included site, age at first visit, race/ethnicity, educational level, family income, and exchange sex in the past 30 days