

# PrEP Use and HIV Incidence Among Youth At-Risk for HIV Infection in Los Angeles and New Orleans: Findings From ATN 149

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**Introduction:** Expanding HIV pre-exposure prophylaxis (PrEP) use is key to goals for lowering new HIV infections in the U.S. by 90% between 2022 and 2030. Unfortunately, youth aged 16–24 have the lowest PrEP use of any age group and the highest HIV incidence rates.

**Methods:** To examine the relationship between HIV seroconversion and PrEP uptake, adherence, and continuity, we used survival analysis and multivariable logistic regression on data of 895 youth at-risk for HIV infection enrolled in Adolescent Trials Network for HIV Medicine protocol 149 in Los Angeles and New Orleans, assessed at 4-month intervals over 24 months.

**Results:** The sample was diverse in race/ethnicity (40% Black, 28% Latine, 20% White). Most participants (79%) were cis-gender gay/bisexual male but also included 7% transgender female and 14% trans masculine and nonbinary youth. Self-reported weekly PrEP

adherence was high (98%). Twenty-seven participants acquired HIV during the study. HIV incidence among PrEP users (3.12 per 100 person year [PY]) was higher than those who never used PrEP (2.53/100 PY). The seroconversion incidence was highest among PrEP users with discontinuous use (3.36/100 PY). If oral PrEP users were adherent using 2-monthly long-acting injectables, our estimate suggests 2.06 infections per 100 PY could be averted.

**Conclusions:** Discontinuous use of PrEP may increase risk of HIV acquisition among youth at higher risk for HIV infection and indications for PrEP. Thus, to realize the promise of PrEP in reducing new HIV infections, reducing clinical burdens for PrEP continuation are warranted.

**Key Words:** HIV prevention, PrEP adherence, adolescents, men who have sex with men, cohort studies

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## INTRODUCTION

The U.S. National HIV/AIDS Strategy aims to reduce new HIV infections by 75% between 2022 and 2025 and by 90% by 2030.<sup>1,2</sup> Pre-exposure prophylaxis (PrEP) is a key prevention strategy for achieving these targets and ending the U.S. HIV epidemic. A goal of the “Ending the HIV Epidemic in the U.S.” (EHE) initiative<sup>3</sup> is to have 50% of people who could benefit from PrEP using it by 2030.<sup>4</sup> The Centers for Disease Control and Prevention estimates that nationally in 2020, just over 300,000 individuals had received PrEP among the 1.2 million individuals with indications for PrEP.<sup>5</sup> The PrEP coverage ratio, the ratio of the number of PrEP users to the numbers with indications for PrEP across all age groups, was 24.7% in 2020.<sup>4</sup> The coverage ratio for youth aged 16–24 was only 15.6, the lowest across all age groups,<sup>4</sup> despite behaviors that increase their exposure to the HIV virus. The Centers for Disease Control and Prevention reports that about half of sexually active adolescents used a condom the last time they had sex.<sup>6</sup> Consistent with those data, HIV incidence (per 100,000 population) in 2019 among youth is high (27.5 among 20–22 years; exceeded only by 25–29-year-olds’ rate of 31.4, and falls off for 30 years and older).<sup>7</sup>

In addition, among youths who start PrEP, adherence is often low. Previous studies document that adherence to PrEP can be particularly challenging for adolescents and youth

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because of unstable housing, food insecurity, and other factors associated with poverty, including not having a schedule for taking medication or having a place to store medication.<sup>8</sup> Low-risk perception has also been noted.<sup>9</sup> Equally important is the need to be a continuous user of PrEP. Although taking more than 5 PrEP doses<sup>10</sup> a week seems to protect against acquiring HIV, continuity in PrEP use over time has not been as thoroughly examined. The current study focuses on the relationship between different patterns of PrEP use and the incidence of HIV in a population of youth at high risk for acquiring HIV in Los Angeles and New Orleans.

Recently, the HPTN 083 study found that long-acting injected PrEP was effective in preventing HIV infection among gay, bisexual and other men who have sex with men (GBMSM), and transgender women.<sup>11</sup> The relative risk for incident HIV infection in the group assigned to receive LAI cabotegravir compared with daily oral PrEP was 0.34 (95% CI: 0.18 to 0.62). A similar hazard rate existed among the group aged 30 or under (0.33; 95% CI: 0.17 to 0.65).<sup>11</sup> The authors hypothesize that the greater HIV incidence among those in the oral PrEP group could be attributable to “inadequate adherence” among participants, because daily oral PrEP has been shown to be 99% effective in preventing HIV infection when taken as directed.<sup>11</sup> LAIs can ensure the delivery of PrEP for a month or more at a time (currently 2-month duration); thus, they have the potential to address the barriers in adhering to a daily medication schedule. However, an analysis of whether the reduced transmissions from LAI PrEP relative to oral medication was cost-effective, calculated an incremental cost-effectiveness ratio of \$1,582,000 per quality-adjusted life years among GBMSM/transgender women at high risk of acquiring HIV.<sup>12</sup> This value is well above the usual willingness-to-pay threshold of \$50,000–\$300,000.

This paper seeks to elucidate the relationship between patterns of PrEP use adherence and continuity over time, HIV seroconversion, and implication for LAI PrEP among youth at risk for HIV infection in Los Angeles and New Orleans.

## METHODS

### Study Participants

This analysis builds on a sample of at-risk youth enrolled in a randomized controlled trial within the Adolescent Trials Network (ATN) for HIV/AIDS Interventions (ATN 149; # NCT03134833).<sup>13</sup> The randomized controlled trial included interventions targeting improvement of the HIV Prevention Continuum; engagement in health care, HIV/STI testing, and promoting youth choice of prevention methods, including condom use, reducing numbers of sex partners, postexposure prophylaxis, and PrEP use.<sup>7</sup> Interventions included daily automated text messaging and monitoring (AMMI) for all participants on prevention, wellness and resources, plus daily medication adherence reminders (if taking medications) as enhanced control. Participants were randomized to be offered online peer-support discussion forums, or strength-based telehealth coaching delivered by near-peer paraprofessionals, the combination of 2 plus text messaging, or to receive AMMI only.

In 2 regional sites—Los Angeles, CA, and New Orleans, LA, 1482 seronegative young people between 14 and 24 years were initially recruited from 13 community-based organizations and clinics serving sexual and gender minorities, people experiencing homelessness, and postincarcerated youth, and through dating apps and peer referrals. After initial recruitment, 1268 participants attended their first follow-up visit and were scheduled to be followed every 4 months for up to 24 months. Data were collected from May 2017 to October 2021. By design, some lower-risk participants (ie, cis-gender females and heterosexual males) were followed for only 12 months ( $n = 373$ ), and none subsequently seroconverted. This left a final cohort of 895 (546 from Los Angeles and 349 from New Orleans) GBMSM, and transgender or gender-diverse youth, including trans women and men who were followed for up to 2 years and included in this analysis.

### Ethical Considerations

The research was approved by the institutional review board of the University of California, Los Angeles, which served as the institutional review board of record for the collaborating institutions. Participants provided written informed consent in-person with research assistants. Each participant were provided with a unique ID and data were stored in secured drives. The research analysts only had access to de-identified data for analysis.

### Measures

#### PrEP Use

We derived the PrEP use dependent variable from a “currently on PrEP” variable collected at baseline and every four-month follow-up visit. We distinguished people who had ever used PrEP during the study from those who had not, and used multivariable logistic regression to identify factors most highly associated with PrEP use.

#### PrEP Adherence

We examined two measures of adherence. The first measure was a self-report provided by PrEP users at each 4-month visit about how regularly they took PrEP in the past 30 days. We grouped answers of “every day” with “almost every day” to form a group labeled “adherent.” This choice is supported by published literature on PrEP adherence.<sup>14,15</sup> The second measure included a 5-item Likert-scale such as responses ranging from none of the time to all of the time. The “all of the time” and “most of the time,” responses from the sample had a high level of concordance with responses to the “every day/almost every day” question. Thus, we only used the first measure of adherence to define “adherent” group. One-month recall of self-adherence on HIV medication has been established to be a reliable and accurate method.<sup>16</sup> Additional support for the validity of self-report data comes from a study of people living with HIV on ARVs—those who reported more than 80% adherence on a single-item adherence measure were more likely to be virally suppressed than those reporting less than 80% adherence.<sup>17</sup>

Although PrEP users reported high levels of adherence to daily dosing schedules there is also data that PrEP users

discontinue or cycle on and off PrEP use over longer periods.<sup>18</sup> To capture the variation in an individual's PrEP use over time, we created a unique measure for each participant's "consistent use" that documented whether "current PrEP use" was reported continuously for at least 5 times of 7 data points (0, 4, 8, 12, 16, 20, and 24 months) over the 2 years. In summary, measures "current PrEP use" and "adherence" were time-variant and could vary at each visit (see A-2 A1 Appendices A-1 and A-2, Supplemental Digital Content, <http://links.lww.com/QAI/C107>), whereas "consistent use" was defined for the entire study period.

## Statistical Analysis

We report descriptive statistics in proportion, and used  $\chi^2$  test for unadjusted analysis for differences in PrEP use by participant characteristics. We ran a multiple logit regression model for adjusted analysis.

We estimated the time at risk for a new HIV diagnosis by calculating the days between each respondent's enrollment in the study and the date when an HIV diagnosis was made or when they had their final study visit. Then, we divided the numbers of new infections overall and in each subsample by the cumulative time at risk to obtain an incidence rate per 100 person-years. The analysis was performed using STATA v17 (StataCorp LLC, College Station, TX). Because only a small number of participants on PrEP seroconverted, we did not run regression models because of sample size, but reported the effect of any PrEP use and consistent PrEP use on seroconversion outcome using incidence rate ratios from the survival analysis.

To understand the impact of LAI on this sample, we did a hypothetical scenario analysis for HIV incidence if all PrEP users in our sample were given LAI. To do this, we multiplied the observed incidence rate for sample members taking oral PrEP by 0.34; the relative risk for LAI users derived from HTPN 083.<sup>11</sup> In the 083 trial, the number of seroconversions fell from 1.22 per 100 person-years in the oral PrEP group to 0.41 per 100 person-years in the cabotegravir group, for a relative risk of 0.336. The rate of infections averted is estimated to be 66% (1–0.34) of the observed amount experienced by oral PrEP users if all had been on long-acting PrEP.

## RESULTS

### PrEP Use

Overall, 11.3% of participants reported being on PrEP at baseline. The study had 80% cis-gender GBMSM participants. Table 1 contrasts the characteristics of the youth in the sample who ever used PrEP during their study participation (27%) with those who never used PrEP (73%). Thirty-nine percent of trans females and 27.6% of GBMSM had used PrEP. In contrast, only 19% of other gender groups, including trans males and nonbinary youth with male or female assigned at birth, had tried PrEP. Education level was also significantly related to PrEP use ( $P < 0.001$ ). PrEP use rose linearly with education level, from 16.5 percent of those not completing high school to 45% of college graduates. There were no statistically significant relationships between ever using PrEP and race/ethnicity ( $P = 0.48$ ), employment

( $P = 0.67$ ), or city ( $P = 0.24$ ). Logit regressions in Table 2 confirm that these relationships hold even after controlling for several factors simultaneously in a multivariable analysis, including location and assigned study arms.

### PrEP Adherence and Continuation

PrEP use initially increased from 11% of respondents at baseline to about 16% at subsequent follow-ups (see Appendix A-1, Supplemental Digital Content, <http://links.lww.com/QAI/C107>). At baseline, 98% reported high adherence as taking PrEP "every day or almost every day" with rates ranging between 89.9% and 97.1% at follow-up visits (see Appendix A-2, Supplemental Digital Content, <http://links.lww.com/QAI/C107>). Only 18.5% of the ever-PrEP users reported continuously taking PrEP once they had begun using it in the first 8 months of the study. The remaining 81.5% reported discontinuous use of PrEP, that is, not reporting PrEP use continuously for 5 or more visits once started. As a sensitivity analysis, a second, less-stringent measure of consistency allowed for at least 4 uninterrupted current PrEP use responses, with 25.5% of PrEP users meeting this definition.

### Seroconversion

There were 27 seroconversions during the study period. Table 3 shows the numbers of seroconversion and rates by PrEP use. Two-year HIV incidence rate was 2.68/100 person-years (PY) (95% CI: 1.84 to 3.91). The incidence was much higher in New Orleans, 4.93 (95% CI: 3.18 to 7.64), compared with that in Los Angeles, 1.16 (95% CI: 0.55 to 2.44). Contrary to the expectation, people who had ever used PrEP had a higher incidence rate of 3.12 (96% CI: 1.56 to 6.25) per 100 PY than PrEP nonusers 2.53 (95% CI: 1.61 to 3.96) with an incidence rate ratio of 1.24 (95% CI: 0.47 to 2.96,  $P$  value 0.61) (Table 2). However, only 1 youth who reported using PrEP continuously (ie, over 5 or more 4-month assessment periods) had seroconverted by the end of their study follow-up (incidence 2.09, 95% CI: 0.29 to 14.86).

Discontinuous PrEP users had an incidence rate of 3.36/100 PY (95% CI: 1.60 to 7.05), which was higher than that of PrEP nonusers. The incidence rate ratio was 0.62 (95 CI: 0.01 to 4.85) with nonsignificant  $P$  value (0.74). The large confidence intervals reflect a small sample size for seroconversions among PrEP users ( $n = 8$ ). The sensitivity analysis using the less stringent measure of continuous PrEP use (see Appendix A-4, Supplemental Digital Content, <http://links.lww.com/QAI/C107>) found 3 seroconversions among the continuous use group, for an incidence rate of 4.31/100 PY (95% CI: 1.39 to 13.36) compared with an incidence rate of 2.68 (95% CI: 1.12 to 6.44) among discontinuous users. This suggests that a lax consistency measure is not a useful indicator and that our primary definition is a better measure of longer-term continuous PrEP use.

### Implications of LAI PrEP

The fact that consistent PrEP users experienced fewer seroconversions supports the idea that the dependability of

**TABLE 1.** Participants' Characteristics by PrEP Use During Study

Characteristics	Full Cohort	Never Used PrEP	Ever Used PrEP	P
	N (Column %)	N (Row %)	N (Row %)	
N	895	652 (72.8)	243 (27.2)	
Gender identity and sexual orientation				0.01
Cis gay, Bi, and other MSM	710 (79.3)	514 (72.4)	196 (27.6)	
Trans female	59 (6.6)	36 (61.0)	23 (39.0)	
Other gender groups	126 (14.1)	102 (81.0)	24 (19.0)	
Race/ethnicity				0.51
African American/Black	361 (40.3)	271 (75.1)	90 (24.9)	
Latino/Hispanic	254 (28.4)	179 (70.5)	75 (29.5)	
White	181 (20.2)	128 (70.7)	53 (29.3)	
Asian/HPI/NA/AN/Others	99 (11.1)	74 (74.7)	25 (25.3)	
Education				<0.001
Less than high school	137 (15.6)	114 (83.2)	23 (16.8)	
High school	206 (23.3)	163 (79.1)	43 (20.9)	
Some higher education	419 (47.6)	300 (71.6)	119 (28.4)	
Completed higher education	119 (13.5)	65 (54.6)	54 (45.4)	
Employment				0.64
Employed	442 (50.3)	316 (71.5)	126 (28.5)	
Not employed	185 (21.1)	138 (74.6)	47 (25.4)	
Student	251 (28.6)	186 (74.1)	65 (25.9)	
Place of residence				0.24
Los Angeles	546 (61.0)	397 (72.7)	149 (27.3)	
New Orleans	349 (39.0)	255 (73.1)	94 (26.9)	
Laboratory confirmed STI at baseline	145 (17.1)	86 (59.3)	59 (40.7)	<0.001
Always used condom with all partners (reported at baseline)				0.10
Yes	436 (48.9)	328 (75.2)	108 (24.8)	
No	455 (51.1)	320 (70.3)	135 (29.7)	
Intervention arms				0.38
AMMI	313(35.0)	237 (75.7)	76 (24.3)	
AMMI + peer support	205 (22.9)	149 (72.7)	56 (27.3)	
AMMI + coaching	196 (21.9)	142 (72.4)	54 (27.6)	
AMMI + coaching + peer support	181 (20.2)	124 (68.5)	57 (31.5)	

having PrEP in one's system for a month or more at a time may reduce the rate of HIV infection. One way to ensure that PrEP dosage is delivered consistently is to provide LAI PrEP, which currently covers PrEP for 2 months without daily adherence burdens. We estimated that if PrEP were delivered as a long-acting injection, to individuals in this study who used PrEP, where the incidence rate was 3.1/100 PY, the incidence rates would fall to 1.04/100 PY ( $3.1 \times 0.336$ ) at 24 months. This represents 2.06 infections/100 PY averted using LAI. When applied to the subgroup of discontinuous PrEP users who experienced an incidence rate of 3.36/100 PY, LAI PrEP would reduce their incidence rate to 1.16/100 PY ( $0.336 \times 3.36$ ). This represents 2.23 infections averted per 100 PY.

**DISCUSSION**

Our results suggest the need for caution in rolling out PrEP, because we found that those who had any exposure to PrEP experienced a higher rate of HIV incidence than those who never tried PrEP. However, this inference should be taken with caution, given that individuals more likely to be

offered, seek, and use PrEP could be at a high risk of HIV infection. Further indication that those at higher risk of HIV were more likely to use PrEP comes from the logit regression (Table 2) that found any PrEP use was significantly higher among persons with laboratory-confirmed STI at baseline.

Despite the compelling evidence that PrEP is highly effective in averting new infections and that PrEP users reported high levels of daily adherence, the fact that discontinuous PrEP users had a higher incidence of HIV than any PrEP users suggests that discontinuation of PrEP use is a more significant risk factor than lack of daily adherence. Similarly, Spinelli and Buchbinder<sup>19</sup> found that seroconversions were 7.5 times higher after stopping PrEP than while on PrEP.

Furthermore, consultation with our study youth advisory board in reviewing study results on PrEP use suggested that the more significant barriers to PrEP use are the hassles of refilling prescriptions monthly or repeating clinical visits every 3 months. Furthermore, because we observed that most seroconversion among PrEP users happened toward the end

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**TABLE 2.** Association of Any PrEP Use With Demographic Characteristics and Risk Behaviors at Baseline (Multivariable Logistic Regression)

Variables	Odds Ratio	95% CI	<i>P</i> > <i>z</i>
Gender identity and sexual orientation			
Cis gay, Bi, and other MSM	Ref		
Trans female	2.032	1.105 3.738	0.023
Other gender groups	0.737	0.446 1.220	0.235
Laboratory confirmed STI at baseline	2.151	1.448 3.196	<0.001
Race/ethnicity			
African American/Black	Ref		
Latino/Hispanic	1.167	0.752 1.811	0.490
White	1.157	0.744 1.800	0.518
Asian/HPI/NA/AN/Others	0.989	0.548 1.778	0.965
Place of residence			
Los Angeles	Ref		
New Orleans	1.096	0.752 1.597	0.633
Education			
Less than high school	Ref		
High school diploma/equivalent	1.543	0.819 2.907	0.180
Some higher education	2.379	1.343 4.214	0.003
Completed higher education	5.191	2.647 10.180	<0.001
Always used condom during sex (reported at baseline)	0.832	0.599 1.155	0.272
Employment			
Employed	Ref		
Unemployed	1.217	0.872 1.700	0.248
Intervention arms			
AMMI	Ref		
AMMI + peer support	1.168	0.757 1.804	0.483
AMMI + coaching	1.265	0.818 1.956	0.291
AMMI + coaching + peer support	1.321	0.845 2.065	0.222
Intercept	0.109	0.054 0.222	

of the study period (visits 5 and 6; see Appendix A-3, Supplemental Digital Content, <http://links.lww.com/QAI/C107>), which is generally considered with the COVID-19 pandemic, barriers related to access to medical care might have played a part as well. LAI PrEP can reduce daily adherence barriers, but unfortunately, the current formulation requires clinical visits every 2 months, increasing the clinical

burden and risk of discontinuation over the long-term. An ongoing clinical trial (NCT04925752)<sup>20</sup> will examine the effectiveness of a longer-acting injectable PrEP for 26 weeks and may offer a solution, but it still does not address quarterly STI screening recommendations for PrEP users. Cis-gender men, and youth in particular, have the lowest levels of consistent health care engagement in the U.S., which is exacerbated by medical mistrust, stigma, and insurance barriers for gay and bisexual men of color who are at the highest risk of acquiring HIV in the U.S.<sup>21</sup> Other interventions may require more targeted outreach,<sup>22</sup> particularly to patients who have missed visits, since analyses indicate that people who miss visits while in care are more likely to discontinue treatment.<sup>23</sup>

In coming years, with the increased use of generic Truvada and possible reductions in the price of LAI PrEP agents, such as cabotegravir, the lack of cost-effectiveness of LAI PrEP<sup>12</sup> may change. Furthermore, longer-lasting injectable PrEP could significantly reduce the risks of discontinuation. Nevertheless, our results suggest that only starting someone on PrEP without mechanisms in place for continuous use is not sufficient for averting new HIV infections. Previous research has documented that taking 4 or more oral doses of PrEP in a week provides good protection against acquiring HIV.<sup>16,17</sup> Only a small share of the youth in this study was able to continue using PrEP between each 4-month visit, despite reporting high levels of daily adherence when they were taking it. Thus, the measures of adherence commonly used may not address the most relevant margin. Therefore, this paper introduced a novel measure of adherence—consistent use of PrEP over time. Inconsistent users had a greater incidence rate than consistent users.

Although the focus of many analyses of adherence has been on adherence to a daily oral medication schedule, equally important are longer durations of maintaining use from month to month. A number of studies have documented short durations of PrEP treatment. Among young black men in Georgia who initiated PrEP, 16% discontinued PrEP before 90 days, and 46% discontinued it later. The median duration of PrEP use was 122 days.<sup>24</sup> The problem is not unique to the U.S. Early discontinuation of PrEP is also an issue in Australia<sup>10</sup> and Belgium.<sup>25</sup> Barriers to remaining on PrEP include substance use, mental health conditions, housing loss,

**TABLE 3.** Incident HIV Infections at 24 months by PrEP Status for Sample Cohort

	Time at Risk (Person-years)	Number of Sero-Conversions	Incidence (95% CI) (per 100 Person-yr)	Incidence Rate Ratio (95% CI)	<i>P</i>
Total	1007.65	27	2.68 (1.84 to 3.91)		
Any PrEP use				1.24 (0.47 to 2.96)	
Ever PrEP users	256.09	8	3.12 ( 1.56 to 6.25)		0.61
PrEP never users	751.56	19	2.53 ( 1.61 to 3.96)		
Consistent PrEP use					
Consistent PrEP users	47.78	1	2.09 (0.29 to 14.86)	0.62 (0.01–4.85)	0.74
Inconsistent PrEP users	208.31	7	3.36 (1.60 to 7.05)		

and difficulty accessing PrEP because of the time and costs of clinic visits. Low self-perceived risk, younger age, and cannabis use also predicted discontinuation.<sup>18</sup>

Similar to other recent findings, our analysis shows the modest likely impact of LAI compared with its relatively high cost.<sup>12</sup> Policies regarding drug prices are now under discussion at the federal level, so the situation may change. Furthermore, the results suggest that discontinuous PrEP use is a greater risk than daily nonadherence in this population, likely because of burdens associated with monthly pharmacy visits for refills and quarterly clinical visits for HIV and STI testing. Finally, the impact of Truvada’s generic status on costs is not yet fully known, but it seems to be modest. Generic tenofovir has an average wholesale cost of \$1455/month compared with \$1842 per month for branded Truvada.<sup>26</sup> It is also unknown how low the price of cabotegravir will fall in response to changes in the cost of oral PrEP.

### LIMITATIONS

The fact that this paper relies on data from only 2 cities raises questions about the generalizability of our findings. However, the calculated HIV incidence rates are consistent with those reported in the literature for youth. Mustanski reports a crude incidence rate of 2.91/100 PY in a longitudinal study of adolescent and young adult GBMSM and transgender women.<sup>21</sup> A New York sample of men aged 18–19 at enrollment estimated an incidence rate of 2.85/100 PY.<sup>27</sup> The study was not powered for intervention effects on HIV incidence as an outcome. The small number of seroconversions and limited sample size prevented the use of causal inferential methods to control for self-selection of PrEP initiation, continuation, and study participation after baseline assessment. As noted earlier, conclusions regarding associations between PrEP use and HIV incidence must be made cautiously.

Our study tool did not support calculating the number of continuous days of PrEP use duration as the question only asked “current” use and date of initiation in the past 4 months, if applicable, but not detailed data on start and stop dates within 4-month periods. This limited us to do an analysis using days on PrEP as a predictor.

Finally, this analysis is embedded in a randomized controlled trial of interventions targeting improving the HIV Prevention Continuum, including PrEP use. We controlled for intervention arm assignment in the logistic regression analyses comparing ever-to-never PrEP users, finding no association. However, more detailed analyses of intervention effects on PrEP uptake and continuation are currently in progress, including analysis of barriers and intervention effects, which may further inform intervention recommendations beyond the scope of this analysis. In a study where PrEP use was not randomly assigned, it is possible that individuals who recognized their greater risk were more likely to sign up for PrEP.

### CONCLUSIONS

Reducing the discontinuation of PrEP is an important strategy for lowering seroconversion. To date, much attention

has been focused on the uptake of PrEP. This paper has shown that HIV incidence rates can be higher for discontinuous PrEP users who cycle on and off PrEP over 24 months. These discontinuous users experience higher seroconversion rates than PrEP nonusers or continuous PrEP users. Providing PrEP users with prescriptions for more than 1 month at a time could reduce the “hassle” of continuing PrEP. LAI could also address treatment discontinuation because of monthly refills, but at higher cost and clinic attendance burden. More broadly, reducing clinical burdens for PrEP continuation, such as less-frequent clinic visits, telehealth visits, mail-based home HIV/STI testing, and longer-acting injectable formulations are warranted to realize the promise of PrEP in reducing new HIV infections.

### APPENDIX

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