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Are HIV seroconversions among young men who have sex with men associated with social network proximity to recently or long-term HIV-infected individuals?

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Abstract

Debate remains as to the relative HIV transmission contributions from individuals who are recently HIV infected and individuals who have long-term infections. In this study, we examine the relationship between new HIV seroconversions occurring among young Black men who have sex with men (YBMSM) and network proximity to recently or long-term HIV infected individuals.

A cohort of YBMSM (N = 618) was generated through respondent driven sampling across three waves. A recent HIV infection was defined as either: 1) a confirmed seroconversion 9 months prior to interview date or 2) a laboratory confirmed acute infection; long-term HIV infected individuals were defined as a diagnosis date 9 months prior to interview date. RDS-weighted logistic regression was utilized to examine network proximity of HIV transmission events to HIV infected individuals in the network.

Within the cohort, 343 (55.5%) participants were identified as HIV seronegative at baseline. Of these, 33 (9.6%) seroconverted during the study period. The odds of seroconversion increased significantly with each additional recent HIV infected individual in one's network (AOR = 12.96; 95% CI: 5.69–29.50), but were not significantly altered by the number of long-term infected individuals in one's network. Additionally, for each member of one's network who used PrEP, the odds of seroconversion decreased significantly (AOR = 0.44; 95% CI: 0.20-0.96).

Early diagnosis and treatment is a critical first step in the HIV care continuum and together with PrEP awareness and use are critical targets for disrupting the transmission of HIV through most at risk networks.

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Introduction

High viremia during acute or recent HIV infection may translate into an increased probability of disease transmission ¹ and has been shown to have a disproportionate effect on HIV transmission among heterosexual networks.² There is still debate, however, as to whether new HIV infections are more likely to be a result of closer network proximity to those who are recently infected or those with long-term HIV infection, but are unsuppressed. Previous research demonstrates that one-third of HIV-infected adults have not reached sustained viral suppression³ and that there is continued, albeit limited, risk of transmission even among those who are on antiretrovirals for >6 months.⁴ Long-term infected individuals may also be contributing to ongoing transmission risk by increasing the number of people already infected in a stable epidemic. To appropriately identify HIV transmission risk and accurately target interventions within defined networks, it is necessary to determine how transmission events are positioned within these networks with proximity to recently and long-term HIV infected individuals.

Risk of HIV acquisition is not limited to behaviors exhibited solely by the individual but rather are influenced by both individual- and network-level behaviors.^{5–7} Previous research has demonstrated that individual-level intervention among people who inject drugs (PWID) can reduce HIV risk among the overall network.⁸ A review of networks of men who have sex with men (MSM) has found that the risk of HIV acquisition among black MSM (BMSM) increases among networks with high density and high racial homogeneity.⁹ In addition larger social support networks are associated with reduced engagement in risk-related sexual behaviors such as condomless sex and exchange sex.^{10,11} Further, past work has demonstrated that network-level behaviors within YBMSM networks are associated with individual-level behaviors⁶ and that network-level HIV prevention approaches are feasible when attempting to engage BMSM, who are at increased risk of HIV acquisition.¹²

In this analysis, we focus on Black MSM, a group at disproportionate risk for HIV infection. The majority (2 in 3) of new HIV diagnoses occur among MSM¹³ and some have estimated an overall lifetime risk of HIV infection of 1 in 2.¹⁴ Because network phenomena are more likely to concentrate HIV and other STIs within racially homogeneous groups¹⁵, examination of transmission processes within large cohorts of Black MSM is critical to limiting ongoing infection in this community. We use data from the uConnect Cohort (2013–2016) to explore the relative extent to which new HIV infections among young Black MSM are associated with proximity to recently infected persons or those with long-term infections.

Methods

Setting, sampling and visit procedures have been described previously.¹⁶ In brief, uConnect is a longitudinal population-based cohort study designed to determine factors associated with HIV risk and transmission within a sample of YBMSM primarily residing on the South Side of Chicago including adjacent southern suburbs, one of the largest contiguous Black community areas in the United States.¹⁷ Participants were enrolled at wave one and followed-up at waves two and three, no new participants were enrolled after wave one.

Eligibility Criteria—Study respondents were eligible to participate if they 1) selfidentified as African American or Black, 2) were assigned male at birth, 3) were between 16 and 29 years of age (inclusive), 4) reported oral or anal sex with a male within the past 24 months, 5) spent the majority of their time on the Southside of Chicago, and 6) were willing and able to provide informed consent at the time of the study visit.

RDS Sampling—Our goal was to purposively recruit a diverse group of YBMSM to serve as seeds who would be interested and willing to participate in the study and who would be able to recruit others like themselves. While ten seeds were recruited via connections to the House/Ball community, the majority of the seeds were recruited via avenues that were less specific (e.g., via web sites, Facebook postings, community events, college campuses etc.) There was a total of 62 seeds with no additional seeds having been recruited past baseline. Each participant was invited and given instructions about recruiting other eligible MSM they knew using six coupons with unique ID numbers. The distribution of successful referrals were 0 (6.4%), 1 (44.3%), 2 (24.4%), 3 (15.1%), 4 (5.9%), 5 (2.5%) and 6 (1.4%). This was repeated for each new participant whether they were a seed or a sprout. Each respondent, seed and recruit, were offered \$60 for their participation in the interview and were told they would receive an additional \$20 for each recruit who participated.

Interview—Between August 2013 and January of 2016, YBMSM were recruited in Chicago using respondent-driven sampling (RDS) across three waves, each separated by nine months. All interviews were conducted using Computer Aided Personal Interviewing (CAPI) with some portions of the interview self-administered. The interview itself involved different types of questions and activities: background and socio-demographic questions, self-administered scales of substance use, HIV care continuum measures, and collection of dried blood spots for HIV related testing.

As part of data collection at each wave, participants were asked detailed information regarding sexual partners and confidants, including names, if known. Entity resolution¹⁸ was conducted across all participants and waves for network members reported in order to identify unobserved ties which may exist. The algorithm used to complete entity resolution was verified by two separate analysts and any new matches were confirmed manually; this process has been described in detail elsewhere ¹⁹, and is described in Supplementary Materials 1.0.

Measures

Our main outcome indicated whether an HIV seronegative individual at baseline seroconverted during the study period and was treated as a binary variable. HIV infection status (including acute infection) was determined by 4th generation HIV immunoassay (Abbott ARCHITECT HIV Ag/Ab Combo assay), HIV-1/-2 Ab differentiation (Bio-Rad Multispot HIV-1/-2 Rapid Test) and HIV RNA testing (Abbott ReaLTime HIV-1 assay) applied to samples eluted from dry blood spots (DBS)²⁰. Chicago Department of Public Health (CDPH) HIV surveillance data were utilized to determine date of HIV diagnosis. Acute infections were defined as individuals who had 4th gen antigen positivity in the absence of antibody confirmed via HIV RNA. These individuals and those found to have

HIV antibody or HIV RNA in the absence of antibody at prior waves of the study were categorized as seroconverted participants. Separately, individuals identified as HIV-positive at baseline were stratified to either recently infected or long-term infected. A recent HIV infection was defined as either: 1) a confirmed seroconversion 9 months prior to interview date; or 2) a laboratory confirmed acute infection. Long-term HIV infected individuals at baseline were defined as those who were HIV-positive with a diagnosis date 9 months prior to interview date. Analyses included only those individuals who had completed all three waves of the study.

Separate network typologies were examined in order to remove the effects of individual network size from any observed association between infection type and seroconversion. These included each individual's total network size defined as the summation of non-repetitive ties to non-sexual confidant network and sexual network parnters (referred to herein as "total network"). Participants were able to self-report up to six sexual partners in the past six months and five confidants. Only named partners who were also study participants were included in this analysis as these were the only individuals on who we had laboratory confirmed HIV status. The confidant and sexual networks are not mutually exclusive; however, duplicate ties were removed when analyzing the total network. The network typology included entity resolution¹⁸ across waves and were operationalized as a continuous variable, network degree. Network degree is defined as the number of connections each individual has to all other individuals in the network. Similar to total network degree, we also separately assessed, and included, the number of ties to HIV-negative individuals in one's network.

To examine whether seroconversions were more likely to be associated with the number of recent or long-term HIV-infected individuals in one's network, we determined the number of recent and long-term infected individuals in each individual's total network. Recent network degree was defined as the number of ties to those with a recent HIV infection. Likewise, long-term network degree was defined as the number of ties to those with a long-term HIV infection.

Demographic and Risk Characteristics

Demographic and risk characteristics are operationalized as in previous work.^{21,22} Employment was categorized as not employed, part-time employment (<30 hours/week), or full-time employment (>30 hours/week). Health coverage was defined as having any health insurance public or private plan. Student status was defined as being an active high school or post-secondary school student. Relationship status was defined as currently in a main or casual relationship or single. Sexual identity was categorized as gay, bisexual, or other. Criminal justice involvement was defined as any arrest, detention, or parole in the respondent's lifetime. Housing stability was defined as being homeless at any point during the past 12 months. Risk behaviors included condomless sex and group sex and were each defined as at least one occurrence in the past 12 months. Due to the high usage of marijuana in this population it was treated as a separate variable with use of marijuana categorized as never, intermittent (up to and including multiple times per week), and heavy (at least once per day). All other drugs were combined into a single, binary variable (including: ecstasy, E

or molly (MDMA); poppers (volatile nitrates); crack (cocaine); acid, LSD, mushrooms, G or GHB, K or special K, PCP (psychedelics); oxycodone, Vicodin, T3, etc (prescription pain killers)). Other drug use was defined as any use in the past 12 months. Alcohol use was categorized as never, one to two drinks per year, one to two drinks per month, one per week, and greater than one per week. Number of PrEP users in each participant's network was utilized as a continuous variable ("Have you ever used PrEP?"). Having a profile on the social networking site Grindr© or Jack'd© was utilized as a binary variable.

Statistical Analyses

Unadjusted and adjusted RDS-weighted logistic regression models were utilized to examine characteristics associated with odds of serconversion over the study period. Individuals who were HIV-positive did not contribute to the regression analysis. All covariates identified as statistically significant at the p .05 level, using the log-rank test, or known confounders were included in the multivariable regression model.

All analyses were performed in Stata v14.0.23

Results

Sample characteristics

The final analytic sample included 343 respondents identified as HIV seronegative at baseline. These respondents were generated through RDS chains of up to 13 waves in length and with a median of 2 recruits per participant. Sample characteristics for respondents are presented in Table 1 and are stratified by seroconversion during the study period. Our sample contained 310 (90.4%) individuals who remained HIV-negative throughout the study and 33 (9.6%) who seroconverted during the study period. Among those who were HIV-positive at baseline, and who had an available date of diagnosis (n = 131), 54 (41.2%) were recent infections and 77 (58.7%) were long-term infections. At baseline, the majority of total respondents were employed at least part-time (184, 53.6%), had health coverage (180, 52.5%), had condomless sex at least once in the past 12 months (195, 56.9%), and used marijuana at least intermittently (241, 70.3%). We found that in the past 12 months, 60 (17.5%) participants used the following substances: MDMA (ecstasy, E, or molly) 28 (8.2%), prescription pain killers (oxycodone, Vicodin, T3, etc.) 20 (5.8%), alkly nitrates (poppers) 17 (5.0%), cocaine and/or crack 7 (2.0%), psychoactive drugs (acid, LSD, mushrooms, G or GHB, K or special K, PCP) 3 (0.9%), heroin 4 (1.2%), and methamphetamines 2(0.6%), (data not shown).

Among study respondents who seroconverted during the study period, the majority were unemployed (27, 81.8%), had never been incarcerated (21, 63.6%), had health coverage (18, 54.5%), had condomless sex during the past 12 months (19, 57.6%), and used marijuana at least intermittently (24, 72.7%). Compared to those who did not seroconvert (mean = 0.2; range: 0–2), those who seroconverted (mean = 1.7; range: 0–5) had a significantly higher number of recent HIV infected individuals in their network (p < 0.001). There was no significant difference between those who did and did not seroconvert with reference to the number of long-term HIV infected individuals in their network nor those with concurrent

partners. Nor were there any significant differences in the total, confidant, or sexual network sizes between those who seroconverted and those who did not.

Logistic regression analysis

In the adjusted RDS-weighted logistic regression models (Table 2), we found that the rate of seroconversion increased significantly with each additional recent HIV infected individual in one's network (Adjusted Odds Ratio [AOR] = 12.96; 95% CI: 5.69-29.50). Total network size significantly increased the odds of seroconversion (Adjusted Odds Ratio [AOR] = 1.22; 95% CI: 1.01-1.46). We also found that the rate of seroconversion increased significantly among those who had health coverage (AOR = 4.15; 95% CI: 1.11-15.53), compared to those who did not have health coverage. Heavy marijuana users, compared to those who never use marijuana, were significantly less likely to seroconvert (AOR = 0.12; 95% CI: 0.02-0.72). Additionally, use of at least one substance other than marijuana, compared to those who do not use any other substance, significantly increased the odds of seroconversion (AOR = 5.63; 95% CI: 1.44-22.02).

We found that the rate of seroconversion decreased significantly with each additional network member who used PrEP (AOR = 0.44; 95% CI: 0.20–0.96). We also found that the rate of seroconversion decreased for each additional HIV-negative member in one's network (AOR = 0.14; 95% CI: 0.07–0.26). We continued to find that an increase in one's overall network size significantly increased the odds of serconversion (AOR = 8.91; 95% CI: 4.53–17.52). We found that the odds of seroconversion increased significantly among those who were unemployed (AOR = 5.27; 95% CI: 1.19–23.41) and those who used at least one other substance (AOR = 4.96; 95% CI: 1.33–18.54), compared to those employed full-time and those did not use any other substances, respectively.

Discussion

To date, little research has characterized the relative contributions of network members with recent and long-term HIV infection on seroconversion. In this study, we present new findings regarding the role of both recent and long-term HIV infected network members. First, we found that 10% of our population-based sample of YBMSM who were negative at baseline seroconverted during the 18-month study period and none of the individual level behaviors or demographics were associated with this seroconversion. Second, we found that an increase in the number of recently HIV infected individuals in a participant's network significantly increased the rate of seroconversion. Finally, we found that for each additional member of a participant's network who is using PrEP there was a significant decrease in the odds of seroconverting.

Network composition plays a key role in predicting HIV risk among young black men who have sex with men. While past research has shown that members of the same network typically share HIV risk behaviors,^{6,9} our study demonstrates that the timing of HIV infection among network members itself, either recent or long-term, may also play a role in risk of HIV acquisition. These findings are similar to past research which utilized both the Duke-UNC-Emory Acute HIV Consortium data as well as data available on long-term HIV infections from previously published studies. Study findings have demonstrated that men are

hyperinfectious during acute HIV infection, and that there is a decreased odds of transmission per coital act among those with long-term HIV infection, likely due to an increased probability of antiretroviral use.² Further, past research has shown that probability of transmission of HIV among long-term HIV infected is insufficient to sustain an epidemic.²⁴ Currently, there is no research examining the probability of HIV transmission among recent or long-term HIV infected BMSM. Our findings suggest that, in this young population, recent infection seems to be playing a larger role in the risk of HIV transmission. We also observed that differences in network composition may alter an individual's risk of HIV acquisition and may be key in targeting future interventions, particularly among those who have a recent HIV infection.²⁵

Prior work has demonstrated that many MSM spend a significant amount of time using multiple mobile apps such as Grindr[©] and Jack'd[©] and that the age at which respondents first used these apps was significantly associated with age at the first instance of either insertive or receptive anal intercourse.²⁶ The New York Community Healthcare Network reported that, among users of hook-up apps, 80.9% of users knew that HIV was transmitted through "unprotected anal sex, vaginal sex, and – less frequently – oral sex", yet almost half of the respondents (46.6%) reported condomless anal intercourse,²⁷ a finding also found among MSM in Los Angeles.²⁸ While past research has demonstrated that hook-up sites significantly increase the risk of HIV acquisition, we did not find this to be a significant predictor of seroconversion in this study. However, one recent study found that young MSM express a willingness to participate in HIV prevention programs via these platforms²⁹, particularly among non-White MSM,³⁰ making them a potential key source for HIV prevention given the high rate of use observed in this cohort. Further research is necessary to investigate whether HIV prevention programs administered via these platforms can reduce the risk of HIV infection.

Access to health care and the use of marijuana may each play a significant role in acquisition of HIV, particularly with regards to network typology. We observed that those with health coverage were significantly more likely to seroconvert during the study period. This finding is consistent with past research suggesting that health coverage increases the rate of HIV testing (and thus the rate of diagnoses³¹), particularly among high-risk populations.³² Past research has suggested that marijuana use, either recreationally or in the context of sex, is an important risk factor for the transmission of both HIV and STIs among high-risk populations.³³ Other research has also shown that those who use marijuana either recreationally or as a sex-drug are less likely to be aware of their HIV-positive status²² and more likely to participate in HIV risk behaviors, such as group sex and condomless sex. respectively.^{33,34} Our findings, however, suggest that the role of heavy marijuana use may be more complicated than previously thought. We found that heavy marijuana users were less likely to seroconvert during the study period, compared to those who never use marijuana. Considering this finding in the context of past research, it is possible that the network context in which an individual uses marijuana may play a key role risk of HIV acquisition. Further research should be conducted to assess these conflicting findings, particularly in the context of network-level behaviors.

We observed that network-level use of PrEP significantly reduced individual-level HIV acquisition risk, supporting the findings of past research. Khan et al. (2013) tested a "firewall effect" theory, suggesting that HIV infected individuals with low infectivity may prevent the spread of the virus through the network, a theory confirmed by later work.³⁵ Our findings also support this theory and suggest that one's risk environment plays an important role in individual risk of HIV acquisition; in this study, an increase in the network-level use of PrEP may establish a firewall, essentially shielding segments of the network from onwards transmission. Encouragingly, recent work utilizing data from the National HIV Behavioral Surveillance study has found overall knowledge regarding PrEP and PEP to be on the rise between 2011 to 2014.³⁶ Further, recent increases in PrEP interest and knowledge have been found among MSM using a sexual networking site, however, uptake of PrEP use among those who would benefit most was not observed.³⁷

While we found several important factors associated with HIV seroconversion, there are some important limitations to our study. First, our study utilizes baseline characteristics to predict future HIV seroconversion and thus does not allow for causal inference. We also aimed to collect as much network data as possible, however, as with many network studies we are not observing the complete network of individuals nor were we able to determine HIV serostatus of unobserved network members. We defined long-term HIV infection as those infected in the past nine months, as opposed to six months in other past research, in order to stay consistent with the same length of time between study visits; however, utilizing a definition of six months did not alter our findings. Finally, we were only able to infer potential relationships between risk of seroconversion and recent or long-term infection among network members based upon network proximity and were not able to determine whether a transmission occurred or the direction of transmission utilizing our data.

In the context of our study limitations, we have shown that an increase in the number of acute/recent HIV infected individuals in one's network is associated with an increased rate of seroconversion. We also demonstrated that the odds of seroconversion are significantly reduced by an increase in the number of network members who use PrEP and marijuana use. Early diagnosis and treatment is a critical first step in the HIV care continuum and together with PrEP awareness and use are critical targets for disrupting the transmission of HIV through high risk networks.

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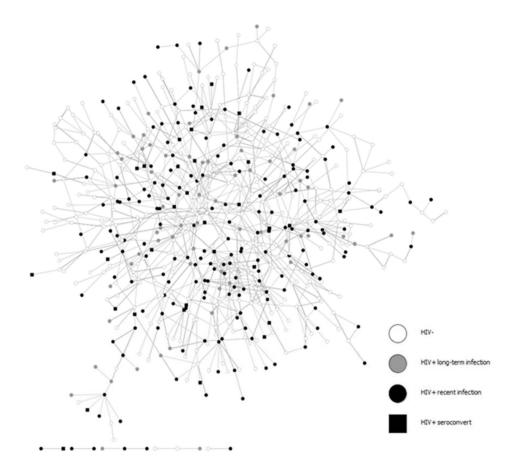


Figure 1.

Total network, including social and sexual ties, among participants who were HIV seronegative- at baseline (n = 606).

¹A recent HIV infection at baseline was defined as either: 1) a new diagnosis 9 months prior to interview date or 2) a laboratory confirmed acute infection at baseline.

²Long-term HIV infected individuals at baseline were defined as those who were HIVpositive with a diagnosis date 9 months prior to interview date

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Sample characteristics stratified by seroconversion among young Black MSM who were confirmed as seronegative at baseline via laboratory analyses in Chicago, uConnect (N = 343 persons)

	T_0	Total	Serone	Seronegative	Serocoi	Seroconverted ¹	p-value ²
Characteristic	N0.	%	N0.	%	No.	%	
Total	343	100	310	90.4	33	9.6	
Demographics , $n(\%)$							
Employment							0.250
Unemployed	159	46.4	140	45.2	19	57.6	
< 30 hours/week	93	27.1	84	27.1	6	27.3	
> 30 hours/week	91	26.5	86	27.7	5	15.1	
Housing Instability $^{\mathcal{J}}$	85	24.8	78	25.2	٢	21.2	0.611
Have health coverage	180	52.5	162	52.3	18	54.5	0.384
Current student	126	36.7	110	35.5	16	48.5	0.141
In a relationship	128	37.3	116	37.4	12	36.4	0.840
Risk behaviors, ${}^{\mathcal{3}}n(\%)$							
Condomless sex	195	56.9	176	56.7	19	57.6	0.930
Group sex	57	16.8	49	16.0	×	24.2	0.226
Drug and alcohol use, ${}^{\mathcal{F}}{}_{n(\%)}$							
Marijuana use ⁴							0.341
Never	102	29.7	91	29.4	11	33.3	
Intermittent	141	41.1	125	40.3	16	48.5	
Heavy	100	29.2	94	30.3	9	18.2	
Other Substance $Use^{3,5}$	60	17.5	52	16.8	×	24.2	0.283
Alcohol use							0.453
Never	47	13.7	41	13.2	9	18.2	
Once per day	217	63.3	195	62.9	22	66.7	
At least once per day	79	23.0	74	23.9	5	15.2	
Network degree measures, mean (range)							
Total network	10.0	1–24	9.8	1–24	11.6	7–20	0.028

	i	lotal	Seron	Seronegauve		Seroconverted ¹	p-value∽
Characteristic	No.	%	No.	%	No.	%	
Recent HIV	0.6	0-13	0.4	0-11	2.2	0–13	<0.001
Long-term HIV	1.3	1.3 0-11 1.2	1.2	0-7	2.0	0-11	0.001
HIV-negative	9.45	1–24	9.44	9.45 1–24 9.44 1–24	9.64	4-18	0.799
¹ Defined as HIV seropositive and HIV seronegative in a prior wave.	seronegative	in a prio	r wave.				
² Using chi-square analysis or T-test							
$\frac{3}{10}$ In the past 12 months							
⁴ Intermittent use is defined as less than and including weekly use; heavy use is defined as at least once per day.	and includin	g weekly	' use; he	avy use i	s defined	as at least	once per da

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Table 2

Adjusted RDS-weighted logistic regression models of selected characteristics with odds of seroconversion,¹ uConnect

	Network Model		PrEP Model	
	(n :	= 326)	(n	= 304)
Characteristic	OR	95% CI	OR	95% CI
Recent network members	12.96**	5.69-29.50	-	-
Long-term network members	0.74	0.14-3.82	-	-
Total network members	1.22*	1.01-1.46	8.91 **	4.53-17.52
HIV-negative network members	-	-	0.14**	0.07-0.26
PrEP users in network	-	-	0.44*	0.20-0.96
Condomless sex ²				
Never	Ref	-	Ref	-
1 time	-	-	0.51	0.16-1.63
Employment				
>30 hours	Ref	-	Ref	-
<30 hours	1.37	0.23-8.19	1.87	0.27-13.00
Unemployed	3.25	0.76–16.38	5.27*	1.19–23.41
Have health coverage				
No	Ref	-	Ref	-
Yes	4.15*	1.11-15.53	2.64	0.85-8.16
Current student				
No	Ref	-	Ref	-
Yes	0.77	0.31-1.92	0.76	0.37-1.54
In a relationship ²				
No	Ref	-	Ref	-
Yes	0.79	0.24-2.65	0.76	0.25-2.36
Marijuana use ³				
Never	Ref	-	Ref	-
Intermittent	0.42	0.08-2.40	0.42	0.10-1.77
Heavy	0.12*	0.02-0.72	0.08 **	0.02-0.41
Other Substance Use ⁴				
None	Ref	-	Ref	-
One other substance	5.63*	1.44-22.02	4.96*	1.33–18.54

Abbreviations: OR = odds ratio; CI = confidence interval; PrEP = pre-exposure prophylaxis;

^IDefined as HIV seropositive with previous HIV seronegative in a prior wave.

 2 In the past 12 months

 $^{\mathcal{S}}$ Intermittent use is defined as less than and including weekly use; heavy use is defined as at least once daily.

 ${}^{4} Includes the use of ecstasy/molly/E, marijuana, cocaine/crack, heroin, psychedelics, methamphetamines, prescription drugs$

* p <0.05;

*** p <0.001