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Daily Marijuana Use Predicts HIV Seroconversion Among Black Men Who Have Sex with Men and Transgender Women in Atlanta, GA

Justin Knox[1,2] · Grace Hwang[3] · Adam W. Carrico[4] · Dustin T. Duncan[5] · Ryan J. Watson[6] · Lisa A. Eaton[6]

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Abstract

We evaluated whether different types of substance use predicted HIV seroconversion among a cohort of 449 Black men who have sex with men (MSM) and transgender women (TGW). A community-based sample was recruited in Atlanta, GA between December 2012 and November 2014. Participants completed a survey and were tested for STIs (Chlamydia and gonorrhoeae using urine samples and rectal swabs) at baseline. HIV testing was conducted at 12-months post enrollment. Multivariable binary logistic regression was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CI) for associations between substance use and HIV seroconversion. By 12-month follow-up, 5.3% (n = 24) of participants seroconverted. In multivariable analyses, daily marijuana use was positively associated with HIV seroconversion (aOR 3.07, 95% CI 1.11–8.48, P = 0.030). HIV incidence was high and daily marijuana use was associated with a more than threefold increased odds of HIV seroconversion among a community-based cohort of Black MSM and TGW.

Keywords HIV incidence · Marijuana · Substance use · Men who have sex with men (MSM) · Transgender women (TGW)

Resumen

Evaluamos si diferentes tipos de uso de sustancias predijeron la seroconversión del VIH entre una cohorte de 449 hombres que tienen sexo con hombres (HSH) y mujeres transgénero (TGW) de raza negra. Se reclutó una cohorte en la comunidad en Atlanta, GA, entre diciembre de 2012 y noviembre de 2014. Los participantes completaron una encuesta y se les hizo una prueba de infecciones de transmisión sexual (clamidia y gonorrea usando muestras de orina e hisopos rectales) al inicio del estudio. Los participantes completaron una prueba del VIH al final del estudio. Se utilizó la regresión logística binaria multivariable para estimar proporciones de probabilidades ajustadas (aOR) y los intervalos de confianza (CI) del 95% para las asociaciones entre el uso de sustancias y la seroconversión del VIH. A los 12 meses de seguimiento, 5,3% (n = 24) de los participantes se seroconvirtieron. En análisis multivariable, el consumo diario de marijuana se asoció positivamente con la seroconversión del VIH (aOR 3.07, 95% CI 1.11–8.48, P = 0.030). La incidencia del VIH fue elevada y el uso diario de marijuana se asoció con un aumento de más de 3 veces en las probabilidades de seroconversión del VIH entre una cohorte de HSH y TGW de raza negra reclutado por la comunidad.

✉ Justin Knox
justinryanknox@gmail.com

Grace Hwang
graceweihwang@gmail.com

Adam W. Carrico
a.carrico@miami.edu

Dustin T. Duncan
dd3018@cumc.columbia.edu

Ryan J. Watson
ryan.j.watson@uconn.edu

Lisa A. Eaton
lisa.eaton@uconn.edu

[1] Department of Psychiatry, Columbia University, 722 West 168th street, New York 10032, USA

[2] HIV Center for Behavioral Studies, New York State Psychiatric Institute, New York, USA

[3] Department of Sociomedical Sciences, Columbia University, New York, USA

[4] Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, USA

[5] Department of Epidemiology, Columbia University, New York, USA

[6] Department of Human Development and Family Sciences, University of Connecticut, Storrs, USA

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Introduction

In 2019, the United States (US) Department of Health and Human Services launched the Ending the HIV Epidemic initiative (EHE), the aims of which are to reduce new HIV infections in the US by 90% by 2030 by scaling up key HIV prevention and treatment strategies [1]. Under EHE, prioritization is given to 50 local areas that account for more than half of new HIV diagnoses, which includes Atlanta, GA, the site of the current study, as well as populations most heavily impacted by HIV, such as gay, bisexual and other cisgender men who have sex with men (MSM) and transgender women who have sex with men (TGW) [1]. According to the most recent National HIV Surveillance System Report, new HIV infections in the US decreased by 8% from 2015 to 2019, and much of this was a result of larger declines among MSM, particularly younger (ages 13–24) MSM [2].

Nevertheless, MSM still comprise the largest group living with HIV in the US, accounting for 75% of all new infections annually [3–5]. Stark racial disparities in new HIV infections exist among MSM, especially among Black MSM [4–8]. Black MSM account for one out of every four new HIV diagnoses [9]. Rates of HIV diagnoses among Black MSM have also varied by age, with increases observed specifically among young Black MSM, in contrast to decreases among other at-risk sub-populations during the same time period [10, 11]. The CDC estimates that, based on current rates of HIV infection, one in two Black MSM will be infected with HIV during their lifetime [10].

TGW also remain a population heavily impacted by HIV [11–14]; with stark racial disparities characterizing the epidemic among TGW in the US [12, 15]. For example, in a seroprevalence study of TGW in 3 US cities, there were three-fold more undiagnosed HIV infections in TGW of color compared to White TGW [15].

This HIV crisis among Black MSM and TGW in the US is most pressing in the Southeastern US, which is home to 21 of the 25 metropolitan areas with the highest prevalence of HIV [16]. HIV infection is hyper-endemic (sustained at levels of 15% or higher) among Black MSM and TGW in these areas [16]. In Atlanta, Georgia, the estimated prevalence of HIV is 46% among Black MSM, which is more than three times higher than the HIV prevalence among white MSM (13%) [17]. HIV incidence was nearly three times higher among Black MSM compared to white MSM, and was the highest among young (18–24 years) Black MSM [18].

Despite this increased burden and risk of HIV infection among Black MSM and TGW, with a focus in the US Southeast, very little research, thus far, has studied predictors of HIV incidence among samples of exclusively Black MSM and TGW. The Brothers Study (HPTN 061), a multi-site study of Black MSM and a limited number of Black TGW across the US with a site in Atlanta, GA, found that age and condomless receptive anal intercourse with HIV-positive or unknown status partners were independently associated with HIV seroconversion [19]. Among the uConnect cohort of 393 young (aged 16–29 years), Black MSM in Chicago, having at least one older (≥ 10 years older) sexual partner was the only predictor independently associated with HIV seroconversion [20]. Further research to understand predictors of HIV acquisition among Black MSM and TGW are urgently needed to inform HIV prevention interventions, including research on the potential role of substance use.

Other research among racially and ethnically diverse cohorts of MSM have shown specific types of substance use (e.g., stimulants, amyl nitrites) to be positively associated with HIV seroconversion [21–23]. Substance use could increase HIV infection though various behavioral and biological pathways. For example, past research suggests that substance use is associated with an increase in sexual risk behaviors (e.g., decreased condom use, increased number of sexual partners, increased likelihood of exchanging sex for money, goods, and/or services) [26–28]. Substance use has also been shown to amplify biological vulnerability through STI acquisition, as well as rectal inflammation and immune dysregulation [29, 30]. Taken together, these studies suggest that, while substance use does not account for racial disparities in HIV burden among sexual minorities [31], substance use might increase risk of HIV incidence within disparately impacted populations. Further research focused on the role of substance use in HIV infection among Black MSM and TGW is urgently needed, especially types of substance use that have been found to be highly prevalent among Black sexual minority groups, such as heavy drinking and marijuana use [32, 33].

Therefore, the objective of the current study was to examine substance use as a risk factor for HIV seroconversion in a cohort of Black MSM and TGW. We assessed whether different types of substance use were predictors of HIV seroconversion. Subsequently, we explored whether any associations between substance use and HIV seroconversion were independent of other sociodemographic characteristics, or attenuated by other HIV risk behaviors, including STI status. Finally, we stratified HIV seroconversion as a function of different age groups, given the observed disparities in HIV incidence [8, 9, 19], and explored these same relationships within different age categories.

Methods

Population

The data were drawn from a two-arm randomized controlled trial design to assess the effect of a sexual risk reduction

intervention for STI prevention among Black MSM and TGW in Atlanta, GA, USA metropolitan and surrounding areas between December 2012 and November 2014, which has been fully described previously [34]. The intervention was found to have no effect on biologically confirmed STI outcomes at long term follow ups (i.e., over 1 year) or HIV [34].

Potential study participants were enrolled via Lesbian, Gay, Bisexual, Transgender, Queer (LGBTQ) venues (such as bars), via dating applications (such as Grindr), and by posted fliers and word-of-mouth. Eligible participants were 18 years of age or older, assigned male gender at birth, identified as male or transgender female, reported HIV-negative or unknown serostatus, and had two or more male sex partners in the past year with at least one condomless anal sex act in the previous year. All participants included in this study were confirmed HIV-negative using an OraQuick ADVANCE Rapid HIV 1/2 Antibody Test at study enrollment, and then tested for HIV at 12-month post-enrollment using the same test. For these analyses, we include all participants who reported identifying as Black or African American and who tested for HIV at post-enrollment.

Procedures

All study procedures were conducted at a community-based research site. Participants completed a computerized assessment and STI testing at baseline. Interview questions solicited information on sociodemographic characteristics, substance use and HIV risk behaviors. Nucleic acid amplification testing (NAAT) was conducted to test participants for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using self-collected samples of urine and rectal swabs [35]. HIV testing was performed at baseline and 12-month post-enrollment using the OraQuick ADVANCE Rapid HIV 1/2 Antibody Test. Participants were compensated $45 for each assessment. Baseline data from all participants was used to predict HIV seroconversion by 12-months. All study protocols received Institutional Review Board approval and the trial was registered in the clinical trials registry, clinicaltrials.gov (NCT02128594). All participants provided written informed consent.

Measures

HIV seroconversion was defined as a positive test at the 12-month study assessment point using an OraQuick ADVANCE Rapid HIV 1/2 Antibody Test.

Substance use was determined by asking participants how often in the past 3 months they had used: marijuana, stimulants (crack, cocaine, or methamphetamine), poppers (nitrile inhalants), erectile dysfunction medications regardless of a prescription, any injection drugs, or other drugs. Responses were dichotomized to used at least once in the past 3 months and never used in the past 3 months, except for marijuana use, which was the most prevalent form of substance use, and was thus dichotomized to daily use and less than daily use. Alcohol use was assessed using the 3-item Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) [36, 37]. The AUDIT-C consists of three items on drinking quantity and frequency, including binge drinking; an AUDIT-C score of ≥ 4 was considered indicative of unhealthy alcohol use [38, 39].

HIV risk behaviors were determined by asking participants whether (yes/no) they had, in the past 3 months: engaged in substance use (drugs or alcohol) before or during sex and engaged in group sex. In addition, participants reported the number of male sex partners and number of condomless sex acts they had in the past 3 months. Finally, participants were asked if they ever tested for HIV outside of the study (yes/no), and if they were currently taking PrEP (yes/no). *Chlamydia trachomatis* and *Neisseria gonorrhoeae* results were categorized as a composite of any baseline rectal or urine STI (yes/no).

Participants also reported on age, gender identity, sexual orientation, relationship status, education, income, and symptoms of depression (using the 10-item Center for Epidemiological Studies Depression Scale Revised (CES-D) [40], ≥ 10 was used as cut-off, Cronbach's $\alpha = 0.82$).

Statistical Analyses

We summarized sociodemographic characteristics, substance use, and HIV risk behaviors and compared the distribution of these factors by HIV seroconversion using χ^2, Fisher's exact, and Wilcoxon tests. For multivariable analyses, all sociodemographic characteristics were controlled for, except for age category, which was conceptualized as an effect modifier because of previously reported variation in HIV seroconversion rates by age among Black MSM [8, 9, 19]. Initially, all types of substance use were entered into a binary logistic regression model with HIV seroconversion as the outcome to estimate odds ratios (OR), and 95% confidence intervals (CI). Any type of substance use associated with HIV seroconversion at $P < 0.20$ was then included in a multivariable model to estimate adjusted odds ratios (aOR) and 95% CI. Subsequently, HIV risk behaviors were entered into these multivariable models, one at a time, and the extent to which they attenuated the relationship between substance use and HIV seroconversion was evaluated by the change in the aOR due to the addition of the covariate. Factors that attenuated the aOR by $\geq 5\%$, were considered meaningful explanatory variables [41]. Supplementary analyses stratified by age category were run to assess predictors of HIV seroconversion within age categories. Statistical tests were

2-sided and $P < 0.05$ was considered statistically significant. SAS 9.4 was used for all statistical analyses.

Results

Sample Characteristics

Table 1 shows baseline sample characteristics, overall and by HIV conversion. Most participants were MSM (93.7%), and a proportion (7.3%) were TGW. There was a fairly even distribution among age categories. Fewer than half (47.7%) were employed. One in four (25.9%) had an annual income of less than $20,000. One in four (24.9%) were homeless. Nearly half (49.0%) screened positive for symptoms of depression.

HIV Seroconversion

By 12-months follow-up, 5.3% of participants (n = 24) had seroconverted. By age group, 10.4% (n = 13) of 18–24-year-olds seroconverted, 7.3% (n = 8) of 25–29-year-olds, 1.6% (n = 1) of 30–39-year-olds seroconverted, and 1.0% (n = 2) of participants who were 40 years of age and older.

Substance Use and HIV Seroconversion

Table 2 shows baseline prevalence of substance use, overall and by HIV seroconversion. One in ten (10.5%) participants had an AUDIT-C score of 4 or more, an indicator of unhealthy drinking. Among all participants, 52.3% reported any marijuana use (data not shown in Table), with 11.8% reporting daily marijuana use, 26.5% reporting stimulant

Table 1 Sociodemographic characteristics and HIV seroconversion among n = 449 Black men who have sex with men (MSM) and transgender women (TGW) in Atlanta, GA, 2012–2014

	All participants (n = 449)		HIV − (n = 425)		HIV+ (n = 24)		χ^2	
	%	*N*	*Row %*	*N*	*Row %*	*N*	*Value*	*p*
Gender							0.036	0.85
Men who have sex with men (MSM)	92.7%	416	94.7%	394	5.3%	22		
Transgender women (TGW)	7.3%	33	93.9%	31	6.1%	2		
Age range (years)							13.806	0.007 [a]
18–24	27.8%	125	89.6%	112	10.4%	13		
25–29	24.3%	109	92.7%	101	7.3%	8		
30–39	14.0%	63	98.4%	62	1.6%	1		
40+	33.9%	152	98.7%	150	1.3%	2		
Sexual orientation							0.787	0.55
Homosexual/gay or bisexual	85.5%	382	94.2%	360	5.8%	22		
Heterosexual	14.5%	65	96.9%	63	3.1%	2		
Education							0.264	0.61
Less than college	36.7%	165	93.9%	155	6.1%	10		
Some college or more	63.3%	284	95.1%	270	4.9%	14		
Current employment status							1.158	0.33
Disability/unemployed/other	52.3%	235	95.7%	225	4.3%	10		
Employed/student	47.7%	214	93.5%	200	6.5%	14		
Annual income							0.011	0.92
> $20,000	74.1%	329	94.5%	311	5.5%	18		
≤ $20,000	25.9%	115	94.8%	109	5.2%	6		
Current housing stability							0.229	0.63
Stable/permanent	75.1%	337	94.4%	318	5.6%	19		
Homeless	24.9%	112	95.5%	107	4.5%	5		
Current relationship status							2.970	0.085
In a relationship	27.8%	125	97.6%	122	2.4%	3		
Not in a relationship	72.2%	324	93.5%	303	6.5%	21		
Depression (CES-D Score ≥ 10)							1.340	0.25
No	51.0%	228	93.4%	213	6.6%	15		
Yes	49.0%	219	95.9%	210	4.1%	9		

[a]Denotes statistical significance at an α = 0.05

Table 2 Bivariate and multivariable associations between substance use and HIV seroconversion among n = 449 Black men who have sex with men (MSM) and transgender women (TGW) in Atlanta, GA, 2012–2014

	All Participants (n = 449)		HIV− (n = 425)		HIV+ (n = 24)		χ^2		Multivariable[a]		
	%	*N*	*Row %*	*N*	*Row %*	*N*	*Value*	*p*	aOR	95% CI	*P*
Positive AUDIT score (≥ 4)							0.145	0.70			0.56
No	10.5%	47	91.5%	43	8.5%	4			Reference		
Yes	89.5%	401	95.0%	381	5.0%	20			1.29	0.54–3.09	
Daily marijuana use							4.241	0.039[b]			0.030[b]
No	88.2%	396	95.5%	378	4.5%	18			Reference		
Yes	11.8%	53	88.7%	47	11.3%	6			3.07	1.11–8.48	
Stimulants (cocaine, crack, methamphetamine)							1.065	0.30			0.53
No	74.4%	334	94.0%	314	6.0%	20			Reference		
Yes	25.6%	115	96.5%	111	3.5%	4			0.68	0.21–2.23	
Poppers							2.412	0.25			
No	91.3%	410	94.1%	386	5.9%	24					
Yes	8.7%	39	100.0%	39	0.0%	0					
Erectile dysfunction medications							3.035	0.061			
No	89.3%	401	94.0%	377	6.0%	24					
Yes	10.7%	48	100.0%	48	0.0%	0					
Other drugs							0.138	0.71			0.84
No	81.2%	381	94.5%	341	5.5%	20			Reference		
Yes	18.8%	88	95.5%	84	4.5%	4			1.13	0.35–3.64	
Any injection drug use							0.460	0.50			
No	98.2%	441	94.6%	417	5.4%	24					
Yes	1.8%	8	100.0%	8	0.0%	0					

[a]Types of substance use with no seroconversions were not included in the multivariable model because they interfered with model convergence

[b]Denotes statistical significance at an $\alpha = 0.05$

use, and 8.7% reporting use of poppers. Furthermore, 10.7% of participants reported use of erectile dysfunction medications (EDM), 1.8% reported any injection drug use, and 18.8% reported other drug use.

In bivariate analysis, 11.3% of participants who reported daily marijuana use seroconverted compared to 4.5% of participants who did not report daily marijuana use, a difference that was statistically significant ($P = 0.039$). In multivariable analysis including all types of substance use, daily marijuana use remained positively associated with HIV seroconversion (aOR 2.85, 95% CI 1.07–7.61, $P = 0.036$). No other type of substance use was associated with HIV seroconversion.

HIV Risk Behaviors and HIV Seroconversion

Table 3 shows baseline prevalence of HIV risk behaviors, overall and by HIV seroconversion. Most participants had tested for HIV (84.2%) and had engaged in substance use before having sex (78.0%). A considerable portion of the sample had sex in exchange for goods (29.9%), had engaged in group sex (26.3%), and had a laboratory-confirmed STI (12.7%). Five participants (1.1%) were currently taking PrEP.

In bivariate analysis, 14.0% of participants with a laboratory-confirmed STI seroconverted compared to 4.5% of participants who did not, a difference that was statistically significant ($P = 0.002$). No other HIV risk behaviors were associated with HIV seroconversion. In multivariable analysis, having a laboratory-confirmed STI was positively associated with HIV seroconversion (aOR 3.11, 95% CI 1.22–7.96, $P = 0.018$).

Daily Marijuana Use and HIV Seroconversion: Behavioral and Biological Explanatory Factors

Daily marijuana use was positively associated with HIV seroconversion (aOR 3.07, 95% CI 1.11–8.48, $P = 0.030$). As the only type of substance use positively associated with HIV seroconversion, we explored whether the association between daily marijuana use and HIV seroconversion was attenuated by other HIV risk behaviors (see Fig. 1). The association between daily marijuana use and HIV

Table 3 Bivariate and multivariable associations between HIV-related behaviors and HIV seroconversion among n = 449 Black men who have sex with men (MSM) and transgender women (TGW) in Atlanta, GA, 2012–2014

	All Participants (n = 449)		HIV− (n = 425)		HIV+ (n = 24)		χ^2		Multivariable [a]		
	%	*N*	*Row %*	*N*	*Row %*	*N*	*Value*	*p*	aOR	95% CI	*P*
Tested for HIV (ever)							0.014	0.78			0.79
No	15.8%	71	94.4%	67	5.6%	4			Reference		
Yes	84.2%	378	94.7%	358	5.3%	20			1.17	0.37–3.69	
	SD	Mean	SD	Mean	SD	Mean					
Number of male sex partners	3.9	4.5	3.8	4.6	4.1	3.0	0.36	0.71	1.01	0.93–1.10	0.81
Number of condomless sex acts	5.8	12.7	5.9	13.0	3.9	3.8	2.03	0.047	0.98	0.92–1.05	0.55
	%	*N*	*Row %*	*N*	*Row %*	*N*					
Substance use before sex							0.022	0.88			0.58
No	22.0%	99	94.9%	94	5.1%	5			Reference		
Yes	78.0%	350	94.6%	331	5.4%	19			0.78	0.31–1.92	
Had sex in exchange for goods							0.289	0.59			0.91
No	70.1%	312	94.2%	294	5.8%	18			Reference		
Yes	29.9%	133	95.5%	127	4.5%	6			0.94	0.33–2.69	
Engaged in group sex							1.223	0.27			0.42
No	73.7%	330	93.9%	310	6.1%	20			Reference		
Yes	26.3%	118	96.6%	114	3.4%	4			0.63	0.21–1.93	
Current PrEP use							0.285	1.000			0.82
No	98.9%	444	94.6%	420	5.4%	24			Reference		
Yes	1.1%	5	100.0%	5	0.0%	0			1.45	0.06–34.16	
Any sexually transmitted infections							9.744	0.002[b]			0.018[b]
No	87.3%	392	95.9%	376	4.1%	16			Reference		
Yes	12.7%	57	86.0%	49	14.0%	8			3.11	1.22–7.96	

[a]Multivariable analyses controlled for all sociodemographic characteristics, except for age category, which was conceptualized as an effect modifier

[b]Denotes statistical significance at an $\alpha = 0.05$

seroconversion was attenuated when accounting for having a laboratory-confirmed STI (reduction in aOR 5.3%), although the association remained statistically significant ($P = 0.042$). The association between daily marijuana use and HIV seroconversion was not attenuated when accounting for any other HIV risk behavior.

Supplementary Analyses

We assessed the prevalence of daily marijuana use and its association with HIV seroconversion among the different age categories (Table 4). To summarize, daily marijuana use was considerable in each age category (18.4%, 13.8% and 15.9%, respectively) except for 40 years of age and older (3.3%). Daily marijuana use was positively associated with HIV seroconversion in all age groups except among participants who were 40 years of age and older, although no associations achieved statistically significance. No baseline sociodemographic characteristics or other HIV risk behaviors were associated with HIV seroconversion within any age category.

Discussion

Among our community-based cohort of Black MSM and TGW with recent HIV risk behavior in the Atlanta metropolitan and surrounding areas, HIV incidence was high: 5.3% of participants (24 out of 449 individuals) seroconverted over the course of the one-year study. Daily marijuana use was associated with a more than threefold increased odds of HIV seroconversion. This association was not explained by other HIV risk behaviors, although it was attenuated when controlling for laboratory-confirmed STI. No other types of drug use predicted HIV seroconversion.

This level of HIV incidence is higher than what was reported among Black MSM in HPTN 061, where a 3.0% HIV incidence rate (95% CI 2.0–4.4%) was observed [19].

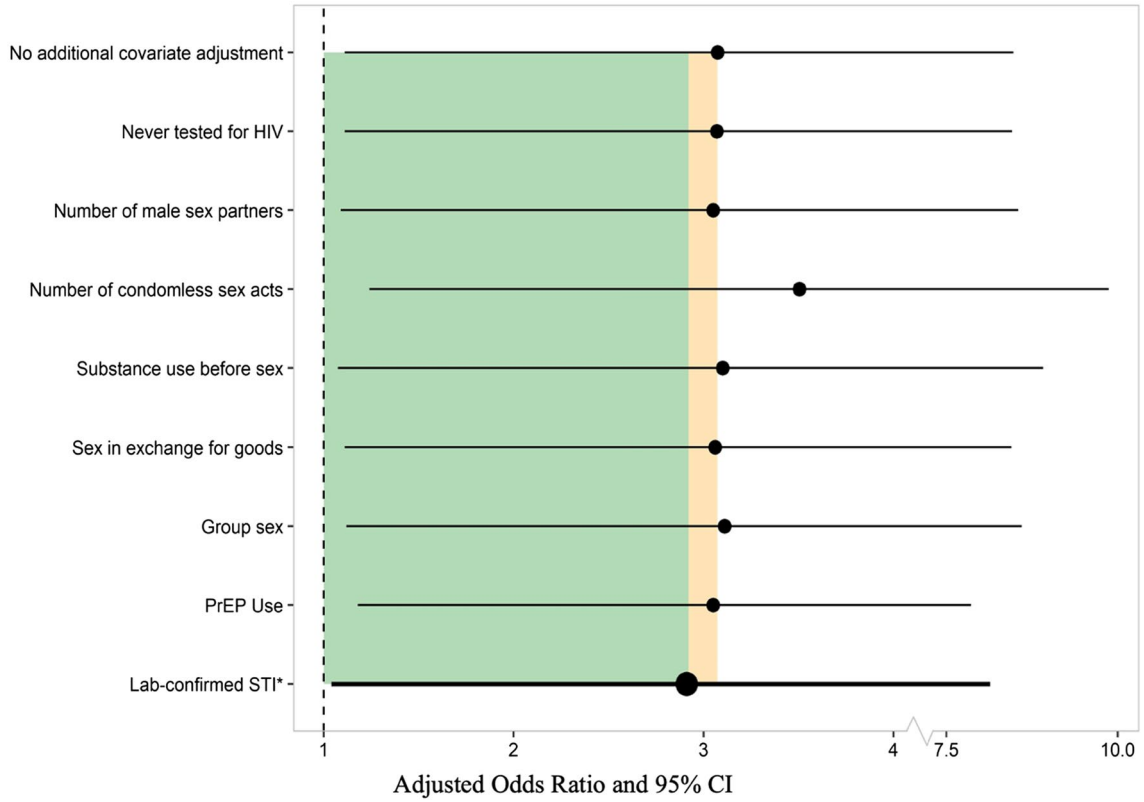

Fig. 1 Adjusted odds ratios for daily marijuana use and HIV seroconversion from multivariable models in a community-based sample of n = 449 black MSM and TGW, Atlanta, 2012–2014. a. Yellow region indicates covariate-adjusted OR for daily marijuana use and HIV seroconversion that are between 0 and 5% less than the aOR for everyday marijuana use with just sociodemographic adjustment, whereas green region indicates covariate-adjusted OR that are more than 5% less, indicating meaningful attenuation of the association between daily marijuana use and HIV seroconversion. b. The one factor that meaningfully attenuated the association between daily marijuana use and HIV seroconversion (laboratory-confirmed STI), is indicated in bold with an asterisk after its label. C. Even after adjustment by each covariate, daily marijuana use remains significantly associated with HIV seroconversion

Table 4 Bivariate associations between everyday marijuana use among age categories of n = 449 Black men who have sex with men (MSM) and transgender women (TGW) in Atlanta, GA, 2012–2014

	%	*N*	*Row %*	*N*	*Row %*	*N*	Fisher's	*p*
Participants 18–24 years old	Total (n = 125)		HIV− (n = 112)		HIV+ (n = 13)		0.088	1.000
No	81.6%	102	89.2%	91	10.8%	11		
Daily marijuana use	18.4%	23	91.3%	21	8.7%	2		
Participants 25–29 years old	Total (n = 109)		HIV− (n = 101)		HIV+ (n = 8)		4.100	0.078
No	86.2%	94	94.7%	89	5.3%	5		
Daily marijuana use	13.8%	15	80.0%	12	20.0%	3		
Participants 30–39 years old	Total (n = 63)		HIV− (n = 62)		HIV+ (n = 1)		5.385	0.16
No	84.1%	53	100.0%	53	0.0%	0		
Daily marijuana use	15.9%	10	90.0%	9	10.0%	1		
Participants 40 + years old	Total (n = 152)		HIV− (n = 150)		HIV+ (n = 2)		0.069	1.000
No	96.7%	147	98.6%	145	1.4%	2		
Daily marijuana use	3.3%	5	100.0%	5	0.0%	0		

Supplementary analyses table

Both studies used recent HIV risk behavior as part of the inclusion criteria, although the criteria were slightly different (our study required that men report having two or more male sex partners in the past year with at least one condomless anal sex act in the previous year, whereas HPTN 061 included men who reported having at least one condomless anal sex act with a man in the previous 6 months). The observed level of HIV incidence in this study is lower than what was reported among Black MSM in the uConnect study, where HIV incidence was 8.5 cases per 100 PY (95% CI 6.0–11.9). Notably, though, the uConnect study was among Black MSM aged 16–29 years. Variation in results between the current study and others might also be due to distinct local context. Previous research has documented notable geographical differences in patterns of substance use [42], substance use disorder among individuals enrolled in HIV services [43, 44], and new HIV diagnoses among MSM [16, 45]. Geographic variation in trends in HIV prevalence among people who inject drugs have been shown to reflect policy differences, such as harm reduction approaches (e.g., needle exchange services) being more widely adopted in large Eastern and Midwestern metropolitan areas [46]. Relevant to the current study, Georgia has not yet acted to expand Medicaid coverage [47], which has been shown to be associated with improved outcomes for other health conditions [48], including a decline in new HIV diagnoses [49], and uptake of PrEP among high-risk populations for HIV infection [50]. Further research should explore the generalizability of these findings to other settings.

We also observed increased HIV incidence among younger Black MSM and TGW, which was also observed in HPTN 061 [19], and which aligns with HIV surveillance data that shows elevated HIV incidence among young Black MSM [8, 9]. Also, having a laboratory-confirmed STI was associated with a more than threefold increased odds of HIV seroconversion, a long-standing a well-documented risk factor for HIV infection among MSM [51, 52].

The observed association between frequent marijuana use and HIV seroconversion is novel in that, prior research with predominantly white MSM has found that stimulants, amyl nitrites, and erectile dysfunction medications are associated with faster HIV incidence but not marijuana use [21–23]. There are multiple potential pathways through which marijuana use could contribute to HIV incidence. Marijuana use could potentially contribute to increases in HIV risk behaviors, as has been shown with other types of substance use [53], including among Black MSM [54, 55]. Any marijuana use has previously been associated with participation in HIV risk behaviors among Black MSM [56], and heavy marijuana use has been associated with being HIV positive and unaware of one's status among Black MSM [57]. In contrast, our results suggest that HIV risk behaviors did not attenuate the increased level of HIV incidence among daily marijuana users. Alternatively, heavy marijuana use among Black MSM has been found to increase the number of connections to other Black MSM in a HIV transmission cluster, suggesting that heavy marijuana use could expose Black MSM to social networks with increased risk of HIV exposure [58]. We were not able to explore this particular hypothesis with these data. Future research should consider focusing on Black MSM and TGW who are at risk for HIV and who use marijuana frequently. This research could also measure marijuana use with more granularity, including modes (e.g., vaping, smoking blunts, edibles) and quantity of use.

Marijuana use could also contribute to HIV incidence by increasing biological vulnerability to HIV infection. Other substance use has been shown to amplify biological vulnerability for HIV/STI acquisition, through rectal inflammation and immune dysregulation [29, 30]. However, marijuana use has been shown to have a beneficial biological impact on systemic inflammation [59–62]. Polysubstance use may also be particularly important with regards to this biological vulnerability, although it is much less studied [63–66], including in our analyses. Our finding that laboratory-confirmed STI was found to reduce the association between daily marijuana use and HIV incidence suggests that this is a plausible mechanism. Integrated bio-behavioral research into how marijuana use might contribute to biological vulnerability to HIV infection is urgently needed, including in the context of PrEP use, other STIs, and sexual behavior.

One additional pathway through which marijuana use could contribute to HIV incidence is by negatively impacting PrEP uptake and adherence. PrEP was not associated with HIV seroconversion in our study, and it did not attenuate the association between daily marijuana use and HIV seroconversion, although very few participants were currently using PrEP. This is likely because data was collected in 2012–2014, while PrEP was approved by the FDA in 2012 [67]. PrEP awareness and utilization has been increasing in recent years [69–71], although concerns remain about PrEP uptake and adherence being sub-optimal among populations at risk [72–74], especially Black MSM and TGW [75–77]. Relationships between marijuana use and PrEP should continue to be explored further, particularly using more recent data, as PrEP uptake increases.

The strong association observed between frequent marijuana use and HIV seroconversion raises a critical issue because marijuana use, including frequent marijuana use, has been found to be prevalent in Black MSM [33, 78]. Furthermore, marijuana is already a large industry in the US, currently estimated at $8 billion per year [79], and it is greatly expanding, such that it is expected to triple by 2025 [80], because of increasing legalization. Thus far, 13 states have fully legalized cannabis for recreational use. Legalization of marijuana appears to increase the prevalence of

marijuana use among adults [81–84], as well as other types of substance use [85]. Marijuana legalization is also changing modes of use and the potency of products used [86]. These changing laws also seem to differentially impact sexual and gender minorities [33, 78]. While individuals can use marijuana without harm [87], and some report beneficial effects from use [88–91], many also experience negative health consequences [92, 93]. The potential contribution of marijuana to HIV transmission, and to racial disparities in HIV burden, is an area that merits further research.

There are limitations to this study. First, the use of self-reported substance use as the primary exposure would be stronger if it were confirmed using objective biomarker data. Participants likely under-reported their substance use, which research has shown that there are issues with the validity of self-reported substance use, including marijuana use, among Black MSM living in Atlanta, GA [94]. Under-reporting of substance use, however, likely would have biased any observed associations towards the null [95]. Furthermore, future researchers might consider using more robust measures of substance use beyond frequency of use, including measures that index problematic patterns of substance use. For example, the Cannabis Use Disorders Identification Test (CUDIT) can be used to screen for hazardous cannabis use [96]. Future researchers could also measure the context of substance use. For example, previous research has shown that the reasons that Black MSM engage in substance use, including marijuana use, are relevant to their sexual behavior [56, 97]. Assessing substance use more robustly in these ways would also allow future researchers to explore whether there are sub-groups with different risk profiles. Second, this sample was not intended to be representative of Black MSM and TGW in Atlanta, GA or other areas, thus also potentially limiting generalizability of the findings. Third, we used the same recruitment strategy for both MSM and TGW, and only 7.3% of study participants identified as TGW. We acknowledge that Black MSM and TGW are distinct populations [98, 99], with unique HIV prevention needs [100, 101]. Because relatively little research in this area has included TGW, particularly TGW of color, we felt that it was important to include them in the analyses. However, the study was under-powered to be able to assess possible differences between Black MSM and TGW, an area for future research that would require larger samples of TGW. Lastly, this paper is reporting data collected in 2012–2014 and future research should explore the generalizability of these findings using more recent data given the many changes in domestic policies that have since taken place, such as the previously mentioned changes in the legalization of marijuana and Medicaid expansion, as well as other changes related to substance-related healthcare services (e.g., in response to the opioid epidemic [102]) and ongoing advancements in HIV, prevention, detection and care.

Conclusions

Among a community-based sample of Black MSM and TGW living in the US Southeast, we observed a concerningly high level of HIV seroconversion, and that daily marijuana use was associated with more than triple the odds of HIV seroconversion. Further research is needed to determine the underlying mechanisms linking marijuana use and HIV seroconversion among these disparately impacted populations, including research with a more nuanced look at marijuana use (e.g., amounts of marijuana used, modes of marijuana use, potency of marijuana consumed). Findings also underscore the potential benefits of expanded efforts to encourage more frequent HIV testing as well as PrEP use among Black MSM and TGW who use marijuana frequently.

Author Contributions JK wrote the manuscript. GH served as the lead statistician. GH, AWC, DTD, RJW and LAE assisted with data interpretation and read drafts of the paper. LAE served as the principal investigator for the project.

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Data Availability The data underlying the results presented in the study are available upon request from Lisa Eaton, lisa.eaton@uconn.edu.

Code Availability The code used to achieve the results presented in the study is available upon request from Lisa Eaton, lisa.eaton@uconn.edu.

Declarations

Conflict of interest The authors have no conflicts of interest to declare.

Consent to Participate All participants provided written informed consent.

Consent for Publication The authors affirm that all participant signed informed consent regarding publishing their data.

Ethical Approval All study protocols received Institutional Review Board approval and the trial was registered in the clinical trials registry, clinicaltrials.gov (NCT02128594).

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