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Authors

Okafor, Chukwuemeka N
Hucks-Ortiz, Christopher
Hightow-Weidman, Lisa B
et al.

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Associations between Self-Reported Substance Use Behaviors and PrEP Acceptance and Adherence among Black MSM in the HPTN 073 Study

Chukwuemeka N Okafor[1], Christopher Hucks-Ortiz[2], Lisa B Hightow-Weidman[3], Manya Magnus[4], Lynda Emel[5], Geetha Beauchamp[5], Irene Kuo[4], Craig Hendrix[6], Kenneth H Mayer[8], & Steve Shoptaw[7]

[1]Department of Public Health, Baylor University, Waco, TX

[2] CommonSpirit Health, Dignity Health, CARE Clinic, St. Mary Medical Center, Long Beach, CA

[3]Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

[4]Department of Epidemiology, George Washington University, Washington, DC

[5]Statistical Center for HIV/AIDS Research & Prevention, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA

[6]Department of Medicine (Clinical Pharmacology), Johns Hopkins University, Baltimore, MD

[7]Department of Family Medicine, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA

[8]The Fenway Institute, Fenway Health and Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA

Corresponding Author: Chukwuemeka N Okafor, PhD

UNITED STATES

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Abstract

Background: Preexposure prophylaxis (PrEP) is efficacious for HIV prevention. Black Men who have Sex with Men (MSM) accounted for the largest proportion of new HIV diagnoses in the U.S relative to other racial/ethnic groups. Black MSM who use substances are at an increased risk for HIV infection and are ideal candidates for PrEP, but barriers to maintaining PrEP adherence remain a concern. We assessed whether substance use behaviors are associated with initiation and adherence to PrEP among a sample of Black MSM in the U.S.

Methods: Data for this analysis comes from the HIV Prevention Trails Network Study 073 (HPTN 073). Substance use behaviors – including alcohol, marijuana, poppers (i.e. alkyl nitrites) and stimulants (i.e. methamphetamine/cocaine use) including use of these substances before/during condomless anal intercourse (CAI) – were assessed longitudinally via self-report. PrEP adherence was assessed by pharmacological testing in blood. Generalized estimating equations were used to evaluate association between substance use behaviors and PrEP initiation and adherence.

Results: Among 226 HIV-negative Black MSM, the majority (60%) were 25+ years of age. Most of the substance use behaviors, were not significantly associated with PrEP initiation or adherence. However, stimulant use before/during CAI was significantly associated with lower odds of PrEP adherence (Adjusted odds ratio=0.21, 95% confidence interval=0.07, 0.61; p=<0.01).

Conclusions: These findings suggest that PrEP adherence is feasible among Black MSM who use substances. However, Black MSM who engage in stimulant use before/during CAI may present a unique group for additional study and support with enhanced behavioral health and support services.

Keywords: HIV; Pre-exposure prophylaxis; adherence; Black men who have sex with men

Introduction

In 2018, Black Men who have Sex with Men (Black MSM) accounted for the largest proportion of new HIV diagnosis (38%) relative to Hispanic (30%) or white (25%) MSM in the United States [1]. Tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) combined with emtricitabine (FTC) for HIV pre-exposure prophylaxis (PrEP) is efficacious in preventing acquisition of HIV among at-risk MSM and transgender women [2–4]. The efficacy of PrEP depends on maintaining protective levels of adherence [5,6]. Substance use, particularly stimulant and alcohol use, is common among some MSM [7–10] , and is associated with HIV sexual transmission behaviors [10,11] and HIV acquisition [12]. Therefore, MSM who use substances could benefit from PrEP. but decreased adherence presents a concern [13–15]. Moreover, the relationship between substance use and PrEP adherence remains unclear.

In the iPrEx open label extension study, participants who used stimulants had a fivefold greater odds of sub-optimal PrEP adherence compared to non-users, but no association with binge drinking was found [16]. In other studies, stimulant and alcohol use decreased PrEP adherence [17,18]. Some studies have not found significant differences in PrEP adherence among MSM who use alcohol and marijuana [9,15,19,20]. At week 4 of a recent longitudinal study of MSM,

participants who used stimulants and who reported condomless anal intercourse (CAI) with multiple partners had significantly decreased PrEP adherence, but over the 48-week follow-up period, PrEP adherence increased [8].

Thus, the relationship between substance use and PrEP adherence appears complex and consideration of both the substance used (e.g., alcohol vs. stimulants) and the context of use (e.g., before/during CAI) is warranted. While substance use, particularly stimulant use, before/during sex has been shown to confer an increased risk of HIV acquisition [21], to date, this has not been fully examined with regard to PrEP adherence[15–20,22].. Additionally, most studies have not specifically assessed PrEP adherence among Black MSM, even though they have significantly lower adherence to PrEP than their white counterparts [15,24,25]. Therefore, the objective of this analysis was to determine whether substance use behaviors, including substance use before/during condomless anal intercourse (CAI) is associated with PrEP initiation and biologically confirmed PrEP adherence among a multi-city sample of Black MSM in the U.S.

Methods

Participants

Data for this analysis comes from the HPTN 073 study. Detailed description of study procedures for HPTN 073 are published elsewhere [20,26]. Briefly, HPTN 073 enrolled 226 HIV-negative Black MSM between August 2013 and September 2014 in three U.S. cities: Los Angeles, California; Washington DC; and Chapel Hill, North Carolina. Eligibility criteria included: 18+ years of age, African American/Black (Men who were African, Afro-Caribbean, Afro-Latino or other also eligible), assigned male sex at birth, HIV-negative and self-report of at

least one of the following: condomless anal intercourse (CAI) with a male partner, anal intercourse with more than 3 male partners, exchanging any anal sex with a male partner for money, gifts, shelter or drugs, anal sex with a male partner while using drugs or alcohol or being diagnosed with a sexually transmitted infection (STI) and having a male sex partner in the past 6 months. Following the baseline visit, study visits occurred at weeks 4, 8, and 13 and quarterly thereafter for up to 52 weeks. Institutional review boards at the respective study sites approved the study.

Measures

Outcomes: PrEP Initiation and Adherence

PrEP initiation. Participants were offered and could initiate PrEP at any time during the study from enrollment to 48 weeks. We defined PrEP initiation as the self-reported date the participant took the first dose.

PrEP adherence. Adherence was determined by pharmacological testing of two types of participant specimens: plasma and peripheral blood mononuclear cells (PBMCs). The levels of tenofovir (TFV) and FTC in plasma and FTC triphosphate and TFV diphosphate in lysed PBMCs were assessed at Week 26 and Week 52 (midpoint and end of the study) [2]. PrEP adherence was defined as those who met the 90% sensitivity threshold for ≥4 doses of FTC/TDF per week – consistent with protective levels in the iPrEx study [6] – from any of the two samples types (Plasma and PBMC) related to measurements of ≥4.2 ng/mL for TFV and ≥4.6 ng/mL for FTC in plasma and 9.9 fmol/10^6 for TFV diphosphate and 0.4 fmol/10^6 for FTC triphosphate in PBMCs[27].

Predictors:

Substance use behaviors.

At baseline and each follow-up study visit, participants self-reported their frequency of alcohol, marijuana, inhaled nitrates (poppers), cocaine (crack and powder) and methamphetamine use in the past three months. In addition, for each substance used, participants self-reported whether use occurred within 2 hours before/during CAI. Because of small counts in some frequency categories, we operationalized each substance use in two ways; any substance use and substance use before/during CAI (yes/no).

Covariates:

Sociodemographic. Participants completed questions asking about study site, age and educational attainment. Incarceration was defined as having ever spent ≥1 night in a jail, detention facility or prison. *Depression symptoms* was measured using the brief version of the Center for Epidemiologic Depression scale, with a cut-off score of 10 or more was used to categorize participants as having significant levels of depressive symptoms [28]. *Relationship* items included currently in a relationship with a primary/main male partner. *Sexual behavior* variable included CAI with a HIV-positive/unknown casual male partner in the past three months. *Baseline STI* diagnosis was defined as any diagnosis of syphilis, chlamydia trachomatis and Neisseria gonorrhea at the enrollment visit.

Data analysis

We computed frequencies and percentages to describe the sociodemographic and substance use behaviors of the overall sample, stratified by PrEP initiation. The primary

independent variables were any substance use and use of these substances before/during CAI. The dependent variables were PrEP initiation and adherence. Baseline substance use behaviors were used to evaluate associations with PrEP initiation by week 26 (for those who had initiated PrEP) using logistic regression models. We used substance use behaviors at weeks 26 and 52 to evaluate associations with PrEP adherence at the same visits, using logistic regression models. These models were performed using generalized estimating equations [29], across 323 person-visits and specifying a compound symmetry correlation structure. Missing data ranged from 7% (for marijuana and stimulant use before/during CAI variables) to 8% (for alcohol and popper use before/during CAI variables). We used listwise deletion to handle missing data. We conducted all analyses with SAS version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Sample characteristics

The sample included 226 Black MSM, the majority of whom were 25 years of age or older (60%), 25% had a high school diploma or less, 48% reported less than $20,000 in annual income and nearly a third (31%) reported a history of incarceration.

Substance use behaviors and PrEP initiation.

Sixty-eight percent of the total sample (n=153), initiated PrEP at the enrollment visit, with an additional 25 (11%) initiating at a later visit [20]. In adjusted models, there was no statistically significant difference in PrEP initiation between participants self-reporting any substance use, including substance use before/during CAI compared to nonuse (Table 2).

Substance use behaviors and PrEP adherence.

Of the 178 participants who initiated PrEP, a blood sample for measurement of PrEP adherence was not available for 16 participants at Week 26 and 17 participants at Week 52, resulting in 323 visits with measured PrEP adherence available for analysis. Overall, of the men who initiated PrEP, 35% (64 of 178) and 36% (54 of 178) had levels consistent with protective levels at Week 26 and at Week 52, respectively. Furthermore, 25% (n=44) had levels consistent with protective levels at both study visits. In adjusted models, we found no statistically significant difference in PrEP adherence self-reported marijuana, popper, alcohol and stimulant use compared to nonuse. Similarly, there was no statistically significant difference in PrEP adherence in self-reported marijuana, popper and alcohol use before/during CAI compared to nonuse (Table 2). However, participants who self-reported stimulant use before/during CAI compared to those who did not, demonstrated a statistically significant lower odds of PrEP adherence (Adjusted odds ratio=0.21, 95% confidence interval=0.07, 0.62; p=<0.01; Table 2). This finding was consistent when data were analyzed separately by visit (data included in Supplemental Material,http://links.lww.com/QAI/B484). We then performed additional analysis to understand correlates of stimulant use before/during CAI. Among all factors that we assessed, only a history of incarceration was significantly and positively associated with stimulant use before/during CAI (OR=19.0, 95% CI: 4.7, 83.0; p=<0.001).

Discussion

In this analysis of Black MSM across three U.S. cities in a PrEP demonstration project, most substance use behaviors were not significantly associated with decreased odds of initiation

of PrEP or protective levels of PrEP adherence. However, we found that stimulant use before/during CAI was associated with decreased adherence to PrEP.

Our finding that Black MSM who engaged in stimulant use before/during CAI had decreased adherence to PrEP is novel. Our finding contrasts with that from O'Halloran *et al* (2019), who did not find a statistically significant association between *chemsex* and self-reported PrEP adherence [23]. Their study finding is different from ours because it was conducted among predominantly white MSM in England, PrEP adherence was self-reported, and their definition of *chemsex* included use of crystal meth, gamma-Hydroxybutyric acid/GHB or mephedrone use immediately prior to, or during sex. Our finding suggests that Black MSM who engage in stimulant use before/during CAI may comprise a unique group that could benefit from tailored prevention support regarding PrEP adherence. In *post-hoc* analysis, only previous incarceration history emerged as a significant predictor of stimulant use before/during CAI. This finding is particularly relevant for Black MSM, who have disproportionately higher rates of incarceration than their white counterparts [30,31]. An incarceration history can disrupt an individual's social and sexual network [32], exacerbate access to social determinants of health (e.g. employment and housing) linked to HIV risk behaviors [33,34] and reduced medication adherence[35]. Because this finding was observed from *post-hic analysis*, caution is needed in its interpretation, but certainly, additional investigations to understand the unique characteristics of Black MSM who engage in stimulant use before/during CAI is warranted. Alternatively, the relationship between Black MSM who use stimulants before/during CAI and lower PrEP adherence may be mediated by severity of stimulant use [36] and PrEP related stigma (i.e. rejection based on perception that PrEP use is suggestive of promiscuity or that they were HIV-positive) [37–40] which also warrants further investigation.

Findings showing that general substance use did not decrease PrEP adherence are consistent with findings from prior studies [5,15,24,41,42]. In addition, the current analysis further expands the literature by showing that alcohol, marijuana and popper use before/during CAI did not decrease PrEP adherence. These findings underscore that Black MSM who use these substances and who are candidates for PrEP can achieve protective levels of PrEP adherence.

Our analysis had some limitations. The sample was relatively small, especially for conducting separate analysis for some substance use type (i.e. crack/cocaine and methamphetamine). Relatedly, the multivariable models were adjusted for a limited set of covariates. We used PrEP adherence data from only two time-points. The sexual and substance use behavior data was collected via self-report. We did not assess frequency or route of use (e.g. injection vs. oral) of substances used. Generalizability of our findings to the broader community of Black MSM in the U.S is limited because our sample was recruited from just three cities in the US.

Conclusion

Among Black MSM in this study, alcohol, marijuana and popper use did not decrease initiation of or adherence to PrEP. Thus, Black MSM who use these substances and are candidates for PrEP, can attain protective levels of PrEP adherence, which should increase physician willingness to prescribe PrEP to this group. However, Black MSM self-reporting stimulant use before/during CAI, had decreased PrEP adherence. Preliminary findings suggest that indicators of structural determinants of health, such as incarceration history, were associated with using stimulant use before/during CAI and present a barrier to attaining the goal of ending

HIV in the U.S. The findings also suggest that enhanced behavioral health and social services to support MSM who use stimulants before/during CAI are warranted to ensure that they will optimally benefit from PrEP.

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Table 1. Characteristics of Black Men who have Sex with Men in the HPTN 073 Study at Enrollment							
			Initiated PrEP¶				
	Overall		Yes (n=178)		No (n=48)		*P*-value
	n	%	n	Row %	n	Row %	
Site							
GWU	75	33.2	60	80.0	15	20.0	<0.01
UCLA	76	33.6	51	67.1	25	32.9	
UNC AIDS	75	33.2	67	89.3	8	10.7	
Age (In years)							
<25	91	40.3	76	83.5	15	16.5	0.15
>=25	135	59.7	102	75.6	33	24.4	
Education							
HS or less	56	24.8	43	76.8	13	23.2	0.71
Some college or vocational school	93	41.2	72	77.4	21	22.6	
Two-year college or greater	77	34.1	63	81.8	14	18.2	
Employment							
Unemployed, disabled or other	61	27.0	40	65.6	21	34.4	0.01
Part time or self-employed	80	35.4	67	83.8	13	16.3	
Full time	85	37.6	71	83.5	14	16.5	
Ever incarcerated							
No	154	69.1	124	80.5	30	19.5	0.26
Yes	69	30.9	51	73.9	18	26.1	
Depression symptoms (CESD≥10)							
No	159	70.7	123	77.4	36	22.6	0.45
Yes	66	29.3	54	81.8	12	18.2	
Any primary male partners ‡							
No	148	66.7	117	79.1	31	20.9	0.90
Yes	74	33.3	58	78.4	16	21.6	
Condomless anal intercourse (CAI) with HIV+ or unknown casual male partner							
No	127	56.4	89	70.1	38	29.9	<0.01
Yes	98	43.6	88	89.8	10	10.2	

Baseline any STI diagnosis							
No	194	85.8	150	77.3	44	22.7	0.19
Yes	32	14.2	28	87.5	4	12.5	
Marijuana use ǂ							
No	113	50.7	88	77.9	25	22.1	0.82
Yes	110	49.3	87	79.1	23	20.9	
Marijuana use before/during CAI ǂ							
No	183	82.1	142	77.6	41	22.4	0.49
Yes	40	17.9	33	82.5	7	17.5	
Popper use ǂ							
No	183	82.1	140	76.5	43	23.5	0.12
Yes	40	17.9	35	87.5	5	12.5	
Popper use before/during CAI ǂ							
No	197	88.3	154	78.2	43	5	
Yes	26	11.7	21	80.8	21.8	19.2	0.76
Alcohol use ǂ							
No	24	11.7	17	70.8	7	29.1	0.33
Yes	199	88.3	158	79.4	41	20.6	
Alcohol use before/during CAI ǂ							
No	137	61.4	103	75.2	34	24.8	0.13
Yes	86	38.6	72	83.7	14	16.3	
Stimulant use ǂ							
No	188	84.3	148	78.7	40	21.3	0.83
Yes	35	15.7	27	77.1	8	22.9	
Stimulant use before/during CAI ǂ							
No	204	91.5	159	77.9	45	22.1	0.52
Yes	19	8.5	16	84.2	3	15.8	

Note: ¶153 initiated PrEP at the enrollment visit, with an additional 25 initiating at a later visit; GWU, George Washington University; UCLA, University of California, Los Angeles; UNC AIDS, University of North Carolina Center for AIDS Research; CESD, Center for Epidemiologic Studies Depression Scale; STI, Sexually Transmitted Infection; CAI= Condomless anal intercourse; Stimulant use defined as methamphetamine/cocaine use ǂ past three months;

Table 2. Results of Logistic and GEE Models of Unadjusted and Adjusted Associations between Substance use Behaviors and PrEP Initiation and Adherence				
	PrEP Initiation (N=178/226) †		**PrEP Adherence (118/323) ⁑**	
Any substance use[π]				
	OR[¶]	**aOR‖**	**OR[¶]**	**aOR‡**
Marijuana use				
No	Ref.	Ref.	Ref.	Ref
Yes	1.30 (0.67, 2.53)	0.91 (0.42, 1.95)	0.64 (0.38, 1.108	0.79 (0.44, 1.44)
Popper use				
No	Ref.	Ref.	Ref.	Ref.
Yes	2.35 (0.85, 6.50)	1.32 (0.44, 3.95)	1.60 (0.93, 2.72)	1.75 (0.90, 3.25)
Alcohol use				
No	Ref.	Ref	Ref	Ref
Yes	1.28 (0.48, 3.39)	1.01 (0.32, 3.21)	0.96 (0.59, 1.54)	1.00 (0.56, 1.78)
Stimulant use				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.30 (0.52, 3.21)	1.26 (0.46, 3.47)	0.46 (0.21, 1.03)	0.54 (0.17, 1.12)
Substance use before/during condomless anal intercourse (CAI) [π]				
Marijuana use before/during CAI				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.61 (0.64, 3.98)	0.89 (0.30, 2.62)	1.37 (0.75, 2.52)	1.74 (0.79, 3.85)
Popper use before/during CAI				
No	Ref.	Ref.	Ref.	Ref.
Yes	1.32 (0.45, 3.80)	0.54 (0.16, 1.81)	1.52 (0.79, 2.91)	1.52 (0.76, 3.03)
Alcohol use before/during CAI				

No	Ref.	Ref.	Ref.	Ref.
Yes	1.94 (0.94, 3.97)	1.41 (0.61, 3.25)	1.32 (0.79, 2.23)	1.25 (0.69, 2.29)
Stimulant use before/during CAI				
No	Ref.	Ref.	Ref.	Ref.
Yes	2.46 (0.65, 9.24)	2.19 (0.52, 9.21)	0.37 (0.17, 0.82)*	0.21 (0.07, 0.62)*

†N represents among participants; logistic regression models was used to assess the association between substance use behaviors and PrEP initiation;

⁑ N represents across person-visits, generalized estimating equations was used to conduct logistic regression models to evaluate the association between substance use behaviors and PrEP adherence across 323 study visits; ¶ Adjusted for study site only; ‖Adjusted for study site, age, education, condomless anal intercourse with HIV+/unknown status partner and any sexually transmitted infection diagnosis at baseline; ‡ Adjusted for study site, age, education and any sexually transmitted infection diagnosis at baseline ᶖ Models were run separately; CAI= Condomless anal intercourse, Stimulant use defined as methamphetamine or cocaine use; All substance use variables were in the past three months; OR=odds ratio, aOR=adjusted odds ratio, *p<0.01;