

Individual and Poly-Substance use and Condomless Sex Among HIV-Uninfected Adults Reporting Heterosexual Sex in a Multi-Site Cohort

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Abstract

BACKGROUND: We analyzed the association between substance use (SU) and condomless sex (CS) among HIV-negative adults reporting heterosexual sex in the Seek, Test, Treat, and Retain (STTR) consortium. We describe the impact of SU as well as person/partner and context-related factors on CS, identifying combinations of factors that indicate the highest likelihood of CS.

METHODS: We analyzed data from four US-based STTR studies to examine the effect of SU on CS using two SU exposures: 1) current SU (within 3 months) and 2) SU before/during sex. Adjusted individual-study, multivariable relative risk regression was used to examine the relationship between CS and SU. We also examined interactions with type of sex and partner HIV status. Pooled effect estimates were calculated using traditional fixed-effects meta-analysis.

RESULTS: We analyzed data for current SU (n=6781; 82% men, median age=33 years) and SU before/during sex (n=2915; 69% men, median age=40 years). For both exposure classifications, any SU other than cannabis increased the likelihood of CS relative to non-SU (8-16%, p-values<0.001). In the current SU group, however, polysubstance use did not increase the likelihood of CS compared to single-substance use. Cannabis use did not increase the likelihood of CS, regardless of frequency of use. Type of sex was associated with CS; those reporting vaginal and anal sex had a higher likelihood of CS compared to vaginal sex only for both exposure classifications (18-21%, p<0.001). Current SU increased likelihood of CS among those reporting vaginal sex only (9-10%, p<0.001); results were similar for those reporting vaginal and anal sex (5-8%, p <0.01). SU before/during sex increased the likelihood of CS among those reporting vaginal sex only (20%; p<0.001) and among those reporting vaginal and anal sex (7%; p=0.002). Single- and poly-SU before/during sex increased the likelihood of CS for those with exclusively HIV-negative partners (7-8%, p£0.02), and for those reporting HIV-negative and HIV-status unknown partners (9-13%, p£0.03).

CONCLUSION: Except for cannabis, any SU increased the likelihood of CS. CS was associated with having perceived HIV-negative partners and with having had both anal/vaginal sex.

Background

In the United States, sexually transmitted infections (STIs) are increasing;(1) STIs including HIV disproportionately affect socially and economically marginalized populations(2) including African-Americans, Latinos, men who have sex with men (MSM), including bisexual men that also have sex with women, transgender women, those currently or formerly incarcerated, and younger adults.(3–10) Beyond abstinence, condoms are the most effective means of preventing STIs. The use of intoxicants prior to sex is a well-known barrier to condom use, (11–13) and substance use (SU) is common among many of the populations at greatest risk for contracting STIs/HIV. (14–16)

Much heterogeneity exists among studies in the strength of associations between SU and condomless sex (CS), particularly between those studies with different methodologies and recall periods.(17–20) The

literature suggests global (general, not necessarily concurrent) associations between alcohol consumption, CS, and HIV risk, however, such studies do not establish a causal relationship; more rigorous multiple event-level analyses provide the temporal sensitivity to assess causality, from which there have been mixed findings.(18) Additionally, the association of SU with CS has been found to vary substantially by gender and partner characteristics,(21) HIV status,(22) nature of relationship (i.e. primary vs. casual vs. transactional), (23) substance type,(11, 23–27) number of substances used,(28) combination of substances used, (22, 29) and pattern of substance use.(11, 23)

To better understand the relationship between SU and CS, we analyzed CS among heterosexual individuals in the context of SU, derived from the harmonized dataset of the National Institute of Drug Abuse (NIDA) Seek, Test, Treat, and Retain (STTR) HIV-prevention and treatment research initiative.(30) We describe the association between substance-related, person/partner related, and context-related factors and condom use. In the process we identify the combinations of factors that indicate the highest risk of CS, and hence potential for STI transmission. We hypothesize that a) persons who use multiple substances over the course of the reference period (polysubstance use) will be more prone to CS than single-substance users and non-users; b) persons who use any type of substance right before or during sex are at a higher risk of CS than persons who do not use substances before/during sex; and c) the degree of increased risk of CS in persons who use substances (PWUS) will vary depending on substance type and demographic factors (age, gender, race).

Methods

Seek, Test, Treat, and Retain (STTR) Data Collection and Harmonization Initiative

STTR is a consortium of research studies funded to develop and test interventions to improve HIV continuum of care outcomes in diverse populations.(31) Four US-based STTR studies contributed data to these analyses, two of which focused on populations involved with the criminal justice system and two of which focused on populations with lifestyle factors that put them at high risk of HIV acquisition or transmission (Table 1). We selected studies from the STTR consortium based on availability of illicit drug and alcohol use data, hereinafter referred to as substance use, and sexual risk behavior data. All participants ≥ 18 years of age who reported sexual activity were eligible for inclusion. Data were collected between 12/2011 and 06/2015.

Table 1
STTR studies included in analyses

Study	Geographic Location	Population	Current substance use	Substance use before/during sex	Reference Period	Participants Contributing Data
BCAP	Brooklyn, NY	Heterosexual individuals at high risk for HIV infection	Yes	Yes	30 days	2,133 (31.5)
BRIGHT	Baltimore City, MD & Providence, RI	Probationers/parolees	Yes	No	90 days	1,537 (22.7)
STAR	New York, NY	African-American substance-using men at risk for STI/HIV	Yes	Yes	30 days	768 (11.3)
STTR	Milwaukee County, WI	Detainees in the Wisconsin prison system detention center	Yes	No	90 days	2,343 (34.6)
TOTAL						6,781
Abbreviations: BCAP, Brooklyn Community Action Project; BRIGHT, Baltimore-Rhode Island Get HIV Tested; STAR, Seek, Test, and Retain; STTR, Seek, Test, Treat, and Retain.						

Data Sources

The STTR data repository integrates data from STTR studies, including clinical data such as standardized HIV-related information, as well as demographic, HIV transmission risk factors, and SU data obtained from enrollment interviews. All SU and CS variables focused on recent activity defined as the prior 1–3 months (timeframes were either 30 or 90 days). For studies including incarcerated participants, only non-incarcerated timeframes prior to incarceration were included. SU was included as a binary exposure (yes/no) for the following substances: binge alcohol (defined as ≥ 5 drinks per day for men and ≥ 4 for women), illicit opioids, cocaine/crack, methamphetamines/other stimulants, and other substances (e.g. hallucinogens, inhalants, barbiturates, synthetic drugs). Participants were also asked about the timing of SU (before/after), sexual activity, and condom use over the recall period. Two overall SU exposure variables were created for analysis: 1) Any SU during the reference period, hereinafter referred to as current substance use, and more specifically, 2) SU before or during sex. Main analyses did not include cannabis as our preliminary findings showed no association between cannabis and CS. We did, however, conduct sensitivity analyses including cannabis as an exposure. Each participant was categorized as either a non-user, a single-substance user, or a polysubstance user. SU before/during sex was included as

a binary exposure (yes/no) from two of the included studies (Table 1). The outcome, engagement in any CS during the recall period, was harmonized across studies as a binary variable (yes/no).

Statistical Analyses

Current Substance Use

We examined demographic characteristics (including age, gender, race/ethnicity, sexual orientation, and education) and HIV risk factors both overall and by SU category (Table 2). We used individual-study, multivariable relative risk regression with robust confidence intervals to examine the relationship between CS among single- and poly-substance users compared to non-users.⁽³²⁾ Final models included age, race/ethnicity, and gender. Pooled effect estimates were calculated using traditional fixed-effects meta-analysis because we did not believe naïve pooling was appropriate given the heterogeneity of the study populations.⁽³³⁾ Additional analyses stratified by type of sex (vaginal sex only or vaginal and anal sex) and by partner self-reported HIV status (HIV-negative partners only, HIV-status unknown partners only, or HIV-negative and HIV-status unknown partners) were also performed. We assessed interaction between type of sex and substance use category as well as partner(s)' self-reported HIV status and substance use category, however, we were not specifically powered to detect statistical interaction. Sensitivity analyses including cannabis as a substance were also conducted (data presented in Appendix).

Table 2
Demographic characteristics by substance use category – Current substance use

		Substance Category			
		Total	Non-PWUS ¹	Single-Substance User	Polysubstance User
N	N	6,781	3,292 (48.6)	2,222 (32.8)	1,267 (18.7)
Male	6,781	5,573 (82.2)	2,623 (79.7)	1,814 (81.6)	1,136 (89.7)
Age	6,781	33 (26–45)	32 (25–44)	34 (26–45)	37 (27–47)
Race/Ethnicity	6,781				
Black or African American		4,073 (60.1)	2,246 (68.2)	1,280 (57.6)	547 (43.2)
White		748 (11.0)	252 (7.7)	209 (9.4)	287 (22.7)
Hispanic or Latino		1,588 (23.4)	620 (18.8)	619 (27.9)	349 (27.6)
Other race		111 (1.6)	52 (1.6)	34 (1.5)	25 (2.0)
Two or more races		261 (3.9)	122 (3.7)	80 (3.6)	59 (4.7)
Sexual Orientation²	5,244				
Heterosexual/Straight		4,289 (81.8)	2,191 (90.1)	1,363 (77.8)	735 (69.3)
Homosexual/Gay/Lesbian/Queer/"Down-Lo"		62 (1.2)	13 (0.5)	22 (1.3)	27 (2.6)
Bisexual/Other		868 (16.6)	219 (9.0)	356 (20.3)	293 (27.6)

Data presented as median (IQR) or n (%) - percents may not sum to 100 due to rounding.

¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).

² Sexual orientation was not collected in one of the studies (BRIGHT).

³ Reference period for number of sex partners, unprotected sex, injection drug use, and substance use: past 30 or 90 days.

		Substance Category			
Refused/Missing		25 (0.5)	8 (0.3)	12 (0.7)	5 (0.5)
Education	6,781				
High school or less		5,270 (77.7)	2,587 (78.6)	1,710 (77.0)	973 (76.8)
Some college		1,351 (19.9)	635 (19.3)	456 (20.5)	260 (20.5)
College graduate or above		157 (2.3)	67 (2.0)	56 (2.5)	34 (2.7)
Refused/Missing		3 (< 0.1)	3 (0.1)	0	0
Risk Behaviors³	6,781				
<i>Number of sex partners</i>		1 (1-3)	1 (1-2)	2 (1-3)	2 (1-4)
<i>Unprotected sex</i>		5,435 (80.2)	2,528 (76.8)	1,845 (83.0)	1,062 (83.8)
<i>Injection Drug Use</i>					
Ever IDU		976 (14.4)	280 (8.5)	231 (10.4)	465 (36.7)
Recent IDU		355 (5.2)	-	64 (2.9)	291 (23.0)
Substance Use³	6,781				
Alcohol		4,142 (61.1)	1,116 (33.9)	1,946 (87.6)	1,080 (85.2)
Binge use		2,734 (40.3)	-	1,787 (80.4)	947 (74.7)
Cocaine/crack		907 (13.4)	-	107 (4.8)	800 (63.1)

Data presented as median (IQR) or n (%) - percents may not sum to 100 due to rounding.

¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).

² Sexual orientation was not collected in one of the studies (BRIGHT).

³ Reference period for number of sex partners, unprotected sex, injection drug use, and substance use: past 30 or 90 days.

	Substance Category			
Illicit opioids	917 (13.5)	–	178 (8.0)	739 (58.3)
Methamphetamine/stimulants	361 (5.3)	–	47 (2.1)	314 (24.8)
Cannabis	2,370 (35.0)	734 (22.3)	896 (40.3)	740 (58.4)
Other	628 (9.3)	–	103 (4.6)	525 (41.4)
Data presented as median (IQR) or n (%) - percents may not sum to 100 due to rounding.				
¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).				
² Sexual orientation was not collected in one of the studies (BRIGHT).				
³ Reference period for number of sex partners, unprotected sex, injection drug use, and substance use: past 30 or 90 days.				

Substance Use Before/During Sex

We examined demographic and clinical characteristics by SU before/during sex. We used individual-study, multivariable relative risk regression with robust confidence intervals to examine the relationship between CS among PWUS before/during sex compared to those who did not. Final models included age, race/ethnicity, and gender. Again, pooled effect estimates were calculated using traditional fixed-effects meta-analysis.⁽³³⁾ Additional analyses of CS among PWUS before/during sex compared to those who did not were performed after stratifying by type of sex. We assessed interaction between type of sex and substance use before and during sex as well, with the same limitation as previously mentioned.

Results

Current Substance Use

Of the 6,781 sexually active participants in the pooled analyses, participant median age of participants was 33 years (interquartile range (IQR): 26–45), 82% were male, and the majority had a high school education or less (78%). Approximately half (52%) of the included participants reported substance use, with 19% reporting polysubstance use during the reference period (Table 2). PWUS differed on some demographic characteristics from non-users. Single- and poly-substance users, compared to non-users, reported more sexual partners on average and more often identified as something other than heterosexual, despite reporting heterosexual sex. Polysubstance users, compared to both non-users and single-substance users, were more likely to be male (90% vs. 80% and 82%, respectively), older (37 years vs. 32 and 34 years, respectively), and white (23% vs. 8% and 9%, respectively). The most commonly

reported substances among single-substance users was binge alcohol (80%), followed by illicit opioids (8%), cocaine/crack (5%), and other substances (5%). The most commonly reported substances among polysubstance users were binge alcohol (75%), followed by cocaine/crack (63%), illicit opioids (58%), and other substances (41%).

In regression analyses adjusted for demographic variables, PWUS were significantly more likely to engage in CS compared to non-users. Single-substance users were 8% more likely (95% confidence interval (CI): 5–11%, $p < 0.001$) to report recent CS and polysubstance users 9% more likely (95% CI: 5–13%, $p < 0.001$) to engage in this sexual risk behavior. A comparison of polysubstance users to single-substance users found no significant difference in likelihood of engaging in CS (RR = 1.02, 95% CI: 0.99–1.05, $p = 0.26$) (Table 3). There was no significant interaction by age and SU (results not shown). We performed this analysis for users of “hard” drugs only, classifying binge alcohol and cannabis use as substance non-users; the inference did not change (see Table 4).

Table 3
Substance use and CS – current substance use

	RR	95% CI	p-value
Current Substance Use			
Non-user ¹	Ref	–	–
Single-substance user	1.08	1.05–1.11	< 0.001
Polysubstance user	1.09	1.05–1.13	< 0.001
Single- vs. Poly-substance user	1.02	0.99–1.05	0.26
Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.			
Models adjusted for age, race/ethnicity, and gender.			
¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).			

Table 4
Substance use and CS – current substance use (hard drugs only)

	RR	95% CI	p-value
Current Substance Use			
Non-user ¹	Ref	–	–
Single-substance user	1.06	1.02–1.10	0.002
Polysubstance user	1.09	1.05–1.13	< 0.001
Single- vs. Poly-substance user	1.01	0.97–1.05	0.68
Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.			
Models adjusted for age, race/ethnicity, gender, and binge alcohol use.			
¹ Non-users included those without illicit drug use (any alcohol use and cannabis use was allowed).			

Type of sex was associated with CS, with participants reporting vaginal and anal sex 21% more likely (95% CI: 16–26%) to engage in CS compared to those reporting vaginal sex only ($p < 0.001$). Among participants having only vaginal sex, use of any substances was associated with a higher likelihood of CS compared to non-users, with single-substance users 9% more likely (95% CI: 5–14%, $p < 0.001$) and polysubstance users 10% more likely (95% CI: 5–15%, $p < 0.001$) to report CS. Among participants having both vaginal and anal sex, substance use also increased the likelihood of CS compared to non-users, with single-substance users 5% more likely (95% CI: 2–9%, $p = 0.004$) and polysubstance users 8% more likely (95% CI: 4–12%, $p < 0.001$) to report CS (Table 5). There was no significant interaction between type of sex and substance use category (results not shown).

Table 5
Substance use and CS among current PWUS by type of sex and partner(s)' HIV status

Current Substance Use	RR	95% CI	p-value
Type of Sex			
Vaginal sex only	Ref	--	--
Vaginal and anal sex	1.21	1.16–1.26	< 0.001
<i>Vaginal sex only</i>			
Non-user ¹	Ref	--	--
Single-substance user	1.09	1.05–1.14	< 0.001
Polysubstance user	1.10	1.05–1.15	< 0.001
Single- vs. Poly-substance user	1.01	0.96–1.05	0.81
<i>Vaginal and anal sex</i>			
Non-user ¹	Ref	--	--
Single-substance user	1.05	1.02–1.09	0.004
Polysubstance user	1.08	1.04–1.12	< 0.001
Single- vs. Poly-substance user	1.03	0.99–1.06	0.12
HIV Status of Partner			
HIV-negative partners only	Ref	--	--
HIV-unknown partners only	0.92	0.86–0.98	0.01
HIV-negative & HIV-unknown partners only	1.11	1.04–1.19	0.001
<i>HIV-negative partners only</i>			
Non-user ¹	Ref	--	--
Single-substance user	1.08	1.02–1.13	0.004
Polysubstance user	1.07	1.01–1.14	0.02
Single- vs. Poly-substance user	0.99	0.94–1.05	0.81

Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.

Models adjusted for age, race/ethnicity, and gender.

¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).

Current Substance Use	RR	95% CI	p-value
<i>HIV-unknown partners only</i>			
Non-user ¹	Ref	–	–
Single-substance user	1.04	0.95–1.13	0.39
Polysubstance user	0.97	0.88–1.07	0.57
Single- vs. Poly-substance user	0.94	0.85–1.03	0.20
<i>HIV-negative & HIV-unknown partners only</i>			
Non-user ¹	Ref	–	–
Single-substance user	1.09	1.01–1.18	0.03
Polysubstance user	1.13	1.06–1.20	<0.001
Single- vs. Poly-substance user	1.04	0.98–1.10	0.22
Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.			
Models adjusted for age, race/ethnicity, and gender.			
¹ Non-users included participants that reported no illicit drug use or binge alcohol use (non-binge alcohol use and cannabis use was allowed).			

Partner(s)' self-reported HIV status was also associated with CS, with an 8% lower likelihood (95% CI: 2–14%, p = 0.01) of CS among participants reporting HIV-status unknown partners only compared to exclusively HIV-negative partners and a 11% higher likelihood (95% CI: 4–19%, p = 0.001) of CS among participants reporting both HIV-negative and HIV-status unknown partners compared to exclusively HIV-negative partners. Substance use was significantly associated with higher likelihood of CS among participants reporting exclusively HIV-negative partners and participants reporting both HIV-negative and HIV-status unknown partners, but not among participants reporting HIV-status unknown partners only. Use of any substances increased the likelihood of CS by 8% (95% CI: 2–13%, p = 0.004) for single-substance users and 7% (95% CI: 1–14%, p = 0.02) for polysubstance users compared to non-users among participants reporting exclusively HIV-negative partners. Use of any substances increased the likelihood of CS by 9% (95% CI: 1–18%, p = 0.03) for single-substance users and 13% (95% CI: 6–20%, p < 0.001) for polysubstance users compared to non-users among participants reporting HIV-negative and HIV-status unknown partners (Table 5). There was no significant interaction between partner(s)' HIV status and substance use category (results not shown).

Substance Use Before or During Sex

Among participants (n = 2915) that had information on substance use before/during sex and CS during the reference period, median age was 40 (IQR: 28–49), 69% male, and most had high school education or less (77%). Just over half (52%) of the participants reported substance use before/during sex (Table 6).

Similar to what we observed with current PWUS, participants who used substances before/during sex reported more sexual partners on average and despite reporting heterosexual behavior more often identified as something other than heterosexual. Additionally, those who used substances before/during sex reported higher rates of use across all substance categories, had higher rates of injection drug use (6% vs. 1%), and tended to be male (84% vs. 54%) and Hispanic or Latino (47% vs. 33%). The most commonly reported substances used before/during sex were binge alcohol (65%), polysubstance use (57%), cocaine/crack (21%), and illicit opioids (18%).

Table 6
Demographic characteristics among those using substances before or during sex

		Substance Use Before/During Sex		
		Total	No	Yes
N	N	2,915	1,397(47.9)	1,518 (52.1)
Male	2,915	2,021 (69.3)	758 (54.3)	1,263 (83.2)
Age	2,915	40 (28–49)	37 (26–48)	41 (29–49)
Race/Ethnicity	2,915			
Black or African American		1,701 (58.4)	912 (65.3)	789 (52.0)
White		0	0	0
Hispanic or Latino (alone or in combination with race)		1,169 (40.1)	460 (32.9)	709 (46.7)
Two or more races		45 (1.5)	25 (1.8)	20 (1.3)
Sexual Orientation	2,915			
Heterosexual/Straight		2,002 (68.7)	1,168 (83.6)	834 (54.9)
Homosexual/Gay/Lesbian/ Queer/Down-Lo		55 (1.9)	13 (0.9)	42 (2.8)
Bisexual/Other		843 (28.9)	212 (15.2)	631 (41.6)
Refused/DK/Missing		15 (0.5)	4 (0.3)	11 (0.7)
Education	2,915			
High school or less		2,251 (77.2)	1,084 (77.6)	1,167 (76.9)
Some college		572 (19.6)	278 (19.9)	294 (19.4)
College graduate or above		91 (3.1)	34 (2.4)	57 (3.8)
Refused/DK/Missing		1 (< 0.1)	1 (0.1)	0

Data presented as median (IQR) or n (%) - percents may not sum to 100 due to rounding.

¹ Reference period for number of sex partners, unprotected sex, injection drug use, and substance use: past 30 days.

		Substance Use Before/During Sex		
Risk Behaviors¹	2,915			
<i>Number of sex partners</i>		2 (1–3)	1 (1–2)	2 (1–3)
<i>Unprotected sex</i>	2,425 (83.2)		1,110 (79.5)	1,315 (86.6)
<i>Injection Drug Use</i>				
Ever IDU	371 (12.7)		116 (8.3)	255 (16.8)
Recent IDU	92 (3.2)		8 (0.6)	84 (5.5)
Substance Use¹	2,915			
Alcohol	2,133 (73.2)		812 (58.1)	1,321 (87.0)
Binge use	1,419 (48.7)		437 (31.3)	982 (64.7)
Cocaine/crack	334 (11.5)		19 (1.4)	315 (20.8)
Illicit opioids	285 (9.8)		17 (1.2)	268 (17.7)
Methamphetamine/stimulants	73 (2.5)		10 (0.7)	63 (4.2)
Cannabis	899 (30.8)		192 (13.7)	707 (46.6)
Other	180 (6.2)		19 (1.4)	161 (10.6)
Poly	1,039 (35.6)		175 (12.5)	864 (56.9)
Data presented as median (IQR) or n (%) - percents may not sum to 100 due to rounding.				
¹ Reference period for number of sex partners, unprotected sex, injection drug use, and substance use: past 30 days.				

In regression analyses adjusted for demographic variables, substance use before/during sex was significantly associated with CS, with a 16% increased likelihood (95% CI: 12–20%, $p < 0.001$) of CS compared to participants that did not use substances during sex (Table 7). The association between substance use during/before sex and CS did not change across age levels (results not shown). There was no significant interaction by age and substance use before/during sex (results not shown).

Table 7
Substance use and CS – Substance Use Before or During Sex

Substance Use Before/During Sex	RR	95% CI	p-value
No	Ref	--	--
Yes	1.16	1.12–1.20	<0.001
Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.			
Models adjusted for age, race/ethnicity, and gender.			

Again, type of sex was associated with CS, with an 18% higher likelihood (95% CI: 11–26%, $p < 0.001$) of CS among participants reporting vaginal and anal sex compared to vaginal sex only. Among participants having only vaginal sex, consumption of one or more substances during sex increased the likelihood of CS by 20% (95% CI: 12–29%, $p < 0.001$). Among participants having both vaginal and anal sex, consumption of one or more substances during sex increased the likelihood of CS by 7% (95% CI: 3–11%, $p = 0.002$) (Table 8). There was no significant interaction between type of sex and substance use before/during sex (results not shown).

Table 8
Substance use and CS by type of sex– Substance Use Before or During Sex

Substance Use Before/During Sex	RR	95% CI	p-value
Type of Sex			
Vaginal sex only	Ref	--	--
Vaginal and anal sex	1.18	1.11-1.26	<0.001
<i>Vaginal sex only</i>			
No	Ref	--	--
Yes	1.20	1.12-1.29	<0.001
<i>Vaginal and anal sex</i>			
No	Ref	--	--
Yes	1.07	1.03-1.11	0.002

Abbreviations: CI, confidence interval; CS, condomless sex; RR, relative risk.

Models adjusted for age, race/ethnicity, and gender.

Sensitivity Analyses with Cannabis

Sensitivity analyses found that cannabis was not associated with CS when used in the absence of other substances (RR = 0.99, 95% CI: 0.94–1.04, p = 0.61) (Appendix Table 1). Additionally, even with increasing frequency of use, cannabis was not associated with engagement in CS (RR range = 1.00-1.05, p-value range: 0.24–0.92) (Appendix Table 2).

Discussion

In this large, cross-sectional study with a diverse sample of substance-using HIV-uninfected adults reporting heterosexual sex, we note several key findings. The use of alcohol, cocaine/crack, methamphetamine/stimulants, and/or illicit opioids, but not cannabis, was associated with CS relative to non-substance use. This was true of both ‘current’ substance use (in either the previous 30 or 90 days), as well as substance use before/during sex. Current polysubstance use also increased CS risk, though not more so than single-substance use. The lack of excess risk among polysubstance compared to single-substance users does not align with findings from a large study of HIV-uninfected MSM(28), however prevalence of substance use in our study was generally much lower than in the MSM cohort and different analysis methodologies were utilized, both of which might account for this discrepancy. Before or during sex, any substance use, with the exception of cannabis, increased CS. Notably, age did not modify the effect between SU and increased risk of CS. The finding that most substances increase CS differs from that of a recent systemic review of substance administration studies, which found alcohol to be independently associated with sexual risk behavior, that cocaine increased it, and cannabis decreased it. (27)

Important here is the strong correlation between concurrency in sexual and drug use risk. Previous studies using a variety of methods inconsistently show a temporal relationship between concurrent drug/alcohol use and sexual risk,⁽³⁴⁾ likely due to pitfalls in collection methods. Timeline follow-back, with 14- or 30-day recall, is fraught with recall bias.⁽³⁵⁾ Daily diaries are constrained because entries are not made in near real-time and do not measure intentions before events occur.⁽³⁶⁾ Newer event-level methods, like ecological momentary assessment,^{(37),(38)} may further disentangle this association.

Cannabis use did not increase the risk of CS, neither in the context of ‘current use’ nor before/during sex. Frequency of cannabis use did not change CS risk. While a similar lack of effect has been observed in several other studies of adolescents, young adults, and MSM, (34, 39–43) other studies have found the opposite.(44–50) Several wide-ranging factors may be driving differences in findings; these include population-level factors (e.g., age, gender, sexual orientation); social factors (e.g., relationship type and duration, power dynamics surrounding sexual behavior, and the role of intentionality to use condoms in the context of cannabis use); factors specific to cannabis and its use itself (e.g., drug potency, dependency, tolerance to its effects); study design factors, such as social desirability bias from particular data collection methods. More research, ideally a meta-analytic review, or a large representative sample of the whole source population with careful sub-group testing is needed to help reconcile discrepancies between findings.

Due to mixed findings of a correlation between cannabis use and CS in the wider literature, findings here are restricted to an older population than previously reported. Our relatively mature adult cohort, many of whom represent highly marginalized populations and have long histories of cannabis and other substance use, may have developed a tolerance to the effects of cannabis. Frequent cannabis users have shown an increased tolerance to its impairing effects,(51) even when also intoxicated by alcohol;(52) members of our cohort may have developed an ability to function under its influence or under that of multiple combined substances. Results may differ among less-experienced users such as youth/adolescents, for whom the effects of cannabis have been found to be particularly detrimental to brain function.(53, 54) Due to the ambiguity of cannabis's role in CS across populations relative to other non-cannabis substances, we recommend that future analyses of poly-substance impact on CS analyze cannabis use independently from other grouped substances in order to avoid potentially underestimating the impact of non-cannabis substances.

We found that having exclusively HIV-negative partner/s increased the likelihood of CS. Having exclusively HIV-status unknown partners did not, even in the event-level context of substance use. Assuming that not knowing a partner's HIV status implies less overall familiarity with the partner, a possible explanation for this finding is that lower partner familiarity is associated with increased condom use, perhaps indicative of greater concern or consciousness for potential HIV/STI transmission risk and/or pregnancy risk. Conversely, the higher rate of CS observed among those with exclusively HIV-negative partners may in part reflect practices within long-term and/or perceivably monogamous partnerships in which STI/HIV transmission is thought to be of low concern, diminishing the felt need to use condoms. Among those with a mix of HIV-status unknown and HIV-negative partners, CS was also higher. However, with this group, we lacked data regarding with which partners (HIV-negative or HIV-status unknown) condoms were and were not used. Our findings among those with partner/s of exclusive serostatus (all negative or all unknown) suggest that the high rate of CS among those with both types of partners is driven primarily by the low condom use observed between HIV-negative partners.

Based on these findings, it may be advisable for HIV/STI prevention efforts as well as care providers to assess HIV/STI transmission risk among those with exclusively HIV-negative partners, particularly non-cannabis using PWUS, and to assess HIV/STI transmission risk and prevention practices among those reporting any partners for whom HIV/STI status is unknown. Of concern, we found that CS was more likely to occur among those having anal sex in addition to vaginal sex, compared to those reporting exclusively vaginal sex; substance use increased likelihood of CS for both of these groups. This has particularly strong implications for HIV transmission risk, given the higher risk of infection known to occur in anal compared to vaginal sex, underscoring the need to identify such risk behaviors, including current substance use, at point-of-care. It is also essential that gender dynamics and sexual power be considered with sensitive instrumentation and interventions for those who might report lack of personal agency for protection, so that interventions could address these differentials and help empower participants with more at-risk behaviors. Finally, we note that participant age did not have an effect on likelihood of CS, neither for current PWUS nor those who used before/during sex, indicating a need to address sexual risk behavior across the life span.

Strengths

A strength of our study is its sample size demographic and geographic diversity of participants.

Limitations

We note that study sites did not use uniform time frames in their measures. Additionally, because different studies used different instruments, collection of covariates differed by study and not all potential confounders had data available. Because the data were cross-sectional, only associations and not causation could be determined. While we used CS as our outcome, we cannot infer any increased level of developing a STI, especially since the populations is older than traditional populations at risk for most bacterial STIs. We note that because nuanced data was not available on partner serosorting, condom use behavior lacked context. We also note that HIV negative serostatus was based on participant self-report, not testing. In addition, this paper focuses on condomless sex. However, clearly there are other approaches to address in order to reduce HIV/STI transmission, including the use of pre-exposure prophylaxis, needle exchange programs for injection drug users.

Conclusion

With the exception of cannabis, any substance use was associated with an increased likelihood of engaging in CS, whether used in the past 30–90 days, or before/during sex. Polysubstance use, however, relative to single substance use, did not further elevate this risk. Higher frequency of cannabis use did not increase the risk of CS. Future studies of the impact of substance use on behavior should consider analyzing cannabis use independently from other substances. For non-cannabis-using PWUS, CS was higher for participants with exclusively HIV-negative partners and for those reporting both anal and vaginal sex in the past 30 or 90 days. Conversely, participants reporting exclusively HIV-status unknown partners in the same reference period did not have a higher risk of CS. STI prevention efforts among non-cannabis-using PWUS should not overlook STI risk assessment for those reporting HIV-negative partners.

Declarations

Ethics approval and consent to participate

Human subject research approval for this research was obtained via the each associated institution's Institutional Review Board:

- BCAP, New York University
- BRIGHT, Friends Research Institute
- STAR, Columbia University
- STTS, University of Wisconsin-Milwaukee

Informed consent was obtained by all study participants.

Consent for publication

Not applicable.

Availability of data and materials

Not currently available. However, a data set has been prepared for NIDA based repository and availability is pending.

Competing interests

1. Springer received consultation payment from Alkermes Inc for scientific expertise consulting. No other disclosures.

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