Dose-Response Associations Between Number and Frequency of Substance Use and High-Risk Sexual Behaviors Among HIV-Negative Substance-Using Men Who Have Sex With Men (SUMSM) in San Francisco

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Abstract

We evaluated the relationship between frequency and number of substances used and HIV risk [ie, serodiscordant unprotected anal intercourse (SDUAI)] among 3173 HIV-negative substance-using MSM. Compared with nonusers, the adjusted odds ratio (AOR) for SDUAI among episodic and at least weekly users, respectively, was 3.31 [95% confidence interval (CI), 2.55 to 4.28] and 5.46 (95% CI, 3.80 to 7.84) for methamphetamine, 1.86 (95% CI, 1.51 to 2.29) and 3.13 (95% CI, 2.12 to 4.63) for cocaine, and 2.08 (95% CI, 1.68 to 2.56) and 2.54 (95% CI, 1.85 to 3.48) for poppers. Heavy alcohol drinkers reported more SDUAI than moderate drinkers [AOR, 1.90 (95% CI, 1.43 to 2.51)]. Compared with nonusers, AORs for using 1, 2, and ≥ 3 substances were 16.81 (95% CI, 12.25 to 23.08), 27.31 (95% CI, 18.93 to 39.39), and 46.38 (95% CI, 30.65 to 70.19), respectively. High-risk sexual behaviors were strongly associated with frequency and number of substances used.

Keywords

HIV; MSM; sexual risk behaviors; substance use; alcohol use; methamphetamine; cocaine; poppers

BACKGROUND

Men who have sex with men (MSM) account for roughly 4% of the US male population, yet comprised 79% of all HIV diagnoses among men in 2011.[1,2] Substance use— including predominantly noninjection substances such as alcohol, cocaine, methamphetamine, poppers (amyl nitrites), ecstasy—has been associated with HIV transmission and acquisition, among MSM.[3,4] Substance use is more prevalent among MSM than among the general population,[5–7] and many MSM engage in substance use with sex.[6] In the US National HIV Behavioral Surveillance survey, 42% of the MSM reported past year substance use, 74% of whom reported substance use before or during sex.[6] Acute effects of substance use can include altered cognition, impaired judgment, and increased sexual desire that are postulated to contribute to risk-taking behaviors among substance-using MSM (SUMSM).[3,8,9] These effects are particularly seen with cocaine, poppers, methamphetamine, and binge drinking, each of which have been independently associated with behavioral outcomes that increase HIV risk, including unprotected sex, multiple sex partners, and HIV-serodiscordant partners.[3,9–14] Heavy alcohol, methamphetamine, and poppers use have also been attributed to HIV seroconversion in 2 large longitudinal MSM studies.[12,13]

Many SUMSM use substances recreationally and less than weekly (ie, "episodically").[4,10] However, most research evaluating HIV risk has not distinguished between episodic users and at least weekly users.[4,10] In addition, many SUMSM are polysubstance users, defined as using more than 1 substance simultaneously or sequentially during a discrete period of time, yet most research focuses on the relationship between an individual class of substance and HIV risk.[10,15–17] To address these gaps in literature, we tested the hypothesis that increasing frequency of substance use and greater number of substances used before or during sex increases the likelihood of engaging in serodiscordant unprotected anal intercourse (SDUAI).

METHODS

Study Sample

We conducted a cross-sectional survey of HIV-negative SUMSM (age 18 or older) from March 2009 to May 2012 as part of screening for a subsequent mixed-methods study— with qualitative and randomized controlled trial phases—to adapt the Personalized Cognitive Counseling HIV prevention intervention for SUMSM (Project ECHO).[18,19] Recruitment was conducted using print advertisements, MSM-specific web sites, and active field recruitment in MSM venues and events. Study protocol was approved by the Committee on Human Research, University of California, San Francisco; Centers for Disease Control and Prevention investigators did not interact with study participants.

Data Collection

SUMSM expressing willingness to be screened for Project ECHO were surveyed by trained staff using a structured telephone questionnaire. Substance use frequency was collected for alcohol, methamphetamine, cocaine (either powdered or crack), and poppers. Situation-level data[20] on substance use during or within 2 hours before unprotected anal intercourse (UAI)

within the past 6 months were also collected for these substances and for marijuana, ecstasy, heroin, and erectile dysfunctions and nonprescription drugs. In addition, demographic characteristics, sexual behaviors, HIV testing history, and HIV serostatus of sexual partners from the past 6 months were collected.

Statistical Analysis

Our primary outcome was SDUAI, defined as an HIV-negative participant having unprotected anal sex with HIV-positive or unknown status partners.[4] Consistent with a previous study, self-reported substance use for cocaine, methamphetamine, and poppers was dichotomized to episodic (less than weekly) use and weekly or more frequent use; self-reported alcohol use was classified as heavy for those who reported drinking 4 or more drinks per day, and moderate for those who reported drinking less than 4 drinks.[4] Polysubstance use before or during UAI was calculated as the total number of the following substances taken before or during UAI: methamphetamine, cocaine, alcohol, poppers, crack, ecstasy, and heroin, categorized as using 0, 1, 2, or 3 or more. We conducted sensitivity analyses for polysubstance use including marijuana and erectile dysfunction drug use before or during UAI.

We used multivariable logistic models adjusting for age and race/ethnicity to examine the relationship between SDUAI and the frequency of cocaine, methamphetamine, poppers, and alcohol use and between SDUAI and the categories of polysubstance use. After fitting each model, we contrasted adjacent nonreference categories. We also conducted tests for log-linear trend across the ordered categories, and for departure from log-linear trend, using orthogonal contrasts, under the assumption that the categories are evenly spaced. We note that for the 3-category frequency variables, the test for trend is equivalent to the contrast between the first and third categories, whereas the test for departure assesses evidence for a quadratic pattern across all 3. Adjusted odds ratios (AOR) and Bonferroni-adjusted 95% confidence interval (CI) are reported.

RESULTS

Sample Characteristics

As shown in Table 1, the mean age of the 3173 SUMSM sampled was 33.8 years (SD = 10.5), and the sample was racially and ethnically diverse (51% white, 22% Latino/Hispanic, 10% black, 10% Asian and Pacific Islander, and 7% other/mixed race). Most participants (66%) were recruited in sites within the Castro neighborhood, which has the greatest concentration of MSM venues in San Francisco. Fifteen percent were recruited in sites outside of the Castro and 19% through passive recruitment materials.

HIV Testing and Sexual Behaviors

The majority of SUMSM (67%) reported HIV testing within the previous 6 months. Nearly all (98%) reported oral sex with male partners, 45% reported UAI at least once, 24% reported SDUAI, and 10% reported vaginal sex with women in the last 6 months.

Frequency and Patterns of Substance Use

Episodic substance use was more prevalent than at least weekly use for methamphetamine (12% vs. 6%), cocaine (27% vs. 5%), and poppers (27% vs. 8%). Heavy alcohol consumption was reported by 10%, whereas moderate consumption was reported by 84%. Any substance use before or during UAI was reported by 39%; 11% used 2 classes of substances before or during UAI, and 8% used 3 classes. The most common substances used before or during UAI were alcohol (28%), marijuana (18%), poppers (15%), erectile dysfunction drugs (8%), cocaine (8%), and methamphetamine (8%). Five percent reported current substance-use treatment.

Multivariable Analysis

For methamphetamine and cocaine, the odds of SDUAI increased with frequency of use (Figure 1A). Specifically, for methamphetamine use, both episodic [AOR, 3.31 (Bonferroni-adjusted 95% CI, 2.55 to 4.28)] and weekly [AOR, 5.46 (95% CI, 3.80 to 7.84)] use was higher risk than nonuse, and weekly was higher risk than episodic use [AOR, 1.65 (95% CI, 1.09 to 2.49)]. Similarly, for cocaine, both episodic [AOR, 1.86 (95% CI, 1.51 to 2.29)] and weekly [AOR, 3.13 (95% CI, 2.12 to 4.63)] users had higher odds of SDUAI than nonusers, and weekly use had higher odds than episodic use [AOR, 1.68 (95% CI, 1.12 to 2.54)]. Both tests for trend for methamphetamine and cocaine were highly statistically significant ($P < 0.001$). The trend was log-linear for cocaine ($P = 0.68$), but not for methamphetamine use ($P < 0.001$). The nonlinear pattern for methamphetamine use reflects smaller incremental effects associated with greater frequency (AOR, 1.65 for weekly vs. episodic compared with 3.31 for episodic vs. nonuse).

Although the odds of SDUAI were elevated among popper users, we did not find strong evidence that risk increased with frequency of use. Compared with nonuse, both episodic [AOR, 2.08 (95% CI, 1.68 to 2.56)] and weekly [AOR, 2.54 (95% CI, 1.85 to 3.48)] use had increased odds of SDUAI, but episodic and weekly use were statistically similar [AOR, 1.22 (95% CI, 0.88–1.70)]. Although there was clear evidence for trend ($P < 0.001$), driven by the difference in SDUAI risk between weekly and nonusers, the pattern was nonlinear ($P = 0.009$), reflecting the similarity of episodic and weekly use.

Heavy alcohol users had higher odds of SDUAI than moderate users [AOR, 1.90 (95% CI, 1.43 to 2.51)], but not nonusers [AOR, 1.36 (95% CI, 0.87–2.13)]; accordingly, there was no clear evidence for linear trend ($P = 0.13$). Although the test for departure from trend suggested a U-shaped pattern ($P < 0.001$), moderate users and nonusers were statistically comparable [AOR, 0.72 (95% CI, 0.49 to 1.05)].

We found increasing odds of SDUAI with the number of substances reported. In particular, compared with those who did not use any substances before or during UAI, the AORs for SDUAI among MSM who used 1, 2, or 3 or more substances before or during UAI were 16.81 (95% CI, 12.25 to 23.08), 27.31 (95% CI, 18.93 to 39.39), and 46.38 (95% CI, 30.65 to 70.19), respectively (Figure 1B). The test for trend and all comparisons between adjacent categories were highly statistically significant ($P < 0.001$). However, the pattern was nonlinear ($P < 0.001$), reflecting smaller incremental effects of using more than 1 substance

[AOR, 1.62 (95% CI, 1.15 to 2.29) for 2 vs. 1, AOR, 1.70 (95% CI, 1.10 to 2.63) for 3 or more vs. 2] than the effect of using 1 vs. none (AOR, 16.81). Sensitivity analyses that included marijuana and erectile dysfunction drugs resulted in similar increased odds of SDUAI associated with greater number of substances used.

DISCUSSION

We found evidence that HIV risk among MSM increases with both the frequency of substance use and the numbers of substances used. For methamphetamine and cocaine, weekly users had higher odds of SDUAI than episodic users, who were in turn at higher risk than nonusers. Similarly, the odds of SDUAI increased across categories of the number of substances reported. For poppers, weekly and episodic use were similar, but both carried higher risk than nonuse. Finally, heavy alcohol users were more likely to report SDUAI than the moderate users.

Our results for cocaine, methamphetamine, and possibly poppers are comparable to previous studies observing dose–response associations for substance use and sexual risk among MSM.[3,4] Our findings for alcohol use, which in contrast did not suggest dose–response, were also consistent with other studies reporting that moderate alcohol users were at no higher HIV risk than nonusers, whereas observing that heavy drinking is associated with increased HIV risk.[14,21,22] Notably, we collected data on the amount of alcohol consumed, whereas data on frequency of use was collected for methamphetamine, cocaine, and poppers. Although consistent with extant literature, the heterogeneity in measures may explain the differences that we found between alcohol and substance use with respect to their impact on HIV risk.

There are several plausible pathways by which alcohol and substance use may affect HIV risk.[3,8,22,23] Specifically, these practices have a myriad of biologic and cognitive effects that may increase sexual risk taking. Moreover, using different classes of substances together or in sequence may activate multiple risk pathways, synergistically increase risk behaviors, and thus, explain some of our findings.[3,8]

This study has limitations. First, the cross-sectional design limits our ability to make causal inferences. Also, self-reported measures for substance use and sexual risk behaviors may be subject to social desirability and/or recall biases. As with other nonrandomized observational studies, we cannot rule out the possibility of unmeasured confounders that may be associated with both substance use and HIV risk. In particular, these screener data did not include information on person-level characteristics, such as sensation seeking or risk-taking personalities, or extensive socio–demographic covariates.[24] In addition, we did not collect data on the amount of use for methamphetamine, cocaine, and poppers, limiting our ability to distinguish between binge and light episodic users. Finally, because our sample was limited to SUMSM from San Francisco, our findings may not be generalizable to other settings. For example, our study had higher substance-use rates relative to National HIV Behavioral Surveillance.[6] Additional studies are needed to further examine the putative additive effects of substance use based on data that permit event-level analyses and establish a strong temporal link between substance use and episodes of sexual risks.[20] Qualitative

studies of polysubstance users can help in determining which combinations of substances contribute to the greatest risk. Despite these limitations, given our large and diverse sample, our findings provide compelling evidence of a dose–response relationship between substance use frequency, increasing polysubstance use, and HIV risk.

In summary, we found that many SUMSM engage in SDUAI, and HIV risk was strongly associated with frequency of use and number of substances used before or during unprotected sex. This has several public health implications. SUMSM may benefit from strategies that build self-efficacy and promote skills for explicit HIV-serostatus communication with partners. Given the low rates of current self-help or substance-use treatment utilization among SUMSM in this sample, there is an urgent need to expand interventions beyond treatment settings and target existing evidence based–HIV prevention interventions to episodic users. Efforts similar to Project ECHO are needed to develop and evaluate HIV risk-reduction interventions adapted specifically for nondependent episodic SUMSM. Interventions that target SUMSM should also address a wider spectrum of substance-use patterns and increasing risks associated with polysubstance use.

ACKNOWLEDGMENTS

REFERENCES

1. Purcell DW, Johnson CH, Lansky A, et al. Estimating the population size of men who have sex with men in the United States to obtain HIV and syphilis rates. Open AIDS J. 2012; 6:98–107. [PubMed: 23049658]

2. CDC. HIV Surveillance Report, 2011. 2013; 23 Available at: http://www.cdc.gov/hiv/topics/surveillance/resources/reports/.

3. Drumright LN, Patterson TL, Strathdee SA. Club drugs as causal risk factors for HIV acquisition among men who have sex with men: a review. Subst Use Misuse. 2006; 41:1551–1601. [PubMed: 17002993]

4. Colfax G, Vittinghoff E, Husnik MJ, et al. Substance use and sexual risk: a participant- and episode-level analysis among a cohort of men who have sex with men. Am J Epidemiol. 2004; 159:1002–1012. [PubMed: 15128613]

5. SAMHSA. Results from the 2008 National Survey on Drug Use and Health: National Findings. Office of Applied Studies; Rockville, MD: 2009.

6. Sanchez T, Finlayson T, Drake A, et al. Human immunodeficiency virus (HIV) risk, prevention, and testing behaviors—United States, National HIV Behavioral Surveillance System: men who have sex with men, November 2003–April 2005. MMWR Surveill Summ. 2006; 55:1–16. [PubMed: 16826162]

7. Stall R, Paul JP, Greenwood G, et al. Alcohol use, drug use and alcohol-related problems among men who have sex with men: the Urban Men's Health Study. Addiction. 2001; 96:1589–1601. [PubMed: 11784456]

8. Colfax G, Guzman R. Club drugs and HIV infection: a review. Clin Infect Dis. 2006; 42:1463–1469. [PubMed: 16619161]

9. Colfax G, Santos GM, Chu P, et al. Amphetamine-group substances and HIV. Lancet. 2010; 376:458–474. [PubMed: 20650520]

10. Santos GM, Das M, Colfax GN. Interventions for non-injection substance use among US men who have sex with men: what is needed. AIDS Behav. 2011; 15(suppl 1):S51–S56. [PubMed: 21404011]

11. Greenwood GL, White EW, Page-Shafer K, et al. Correlates of heavy substance use among young gay and bisexual men: the San Francisco Young Men's Health Study. Drug Alcohol Depend. 2001; 61:105–112. [PubMed: 11137274]

12. Koblin BA, Husnik MJ, Colfax G, et al. Risk factors for HIV infection among men who have sex with men. AIDS. 2006; 20:731–739. [PubMed: 16514304]

13. Ostrow DG, Plankey MW, Cox C, et al. Specific sex drug combinations contribute to the majority of recent HIV seroconversions among MSM in the MACS. J Acquir Immune Defic Syndr. 2009; 51:349–355. [PubMed: 19387357]

14. Carey J, Mejia R, Bingham T, et al. Drug use, high-risk sex behaviors, and increased risk for recent HIV infection among men who have sex with men in Chicago and Los Angeles. AIDS Behav. 2009; 13:1084–1096. [PubMed: 18498049]

15. Mimiaga MJ, Reisner SL, Vanderwarker R, et al. Polysubstance use and HIV/STD risk behavior among Massachusetts men who have sex with men accessing Department of Public Health mobile van services: implications for intervention development. AIDS Patient Care STDS. 2008; 22:745–751. [PubMed: 18754704]

16. Grov C, Kelly BC, Parsons JT. Polydrug use among club-going young adults recruited through time-space sampling. Subst Use Misuse. 2009; 44:848–864. [PubMed: 19444726]

17. Halkitis PN, Palamar JJ, Mukherjee PP. Poly-club-drug use among gay and bisexual men: a longitudinal analysis. Drug Alcohol Depend. 2007; 89:153–160. [PubMed: 17267140]

18. Dilley JW, Woods WJ, Loeb L, et al. Brief cognitive counseling with HIV testing to reduce sexual risk among men who have sex with men: results from a randomized controlled trial using paraprofessional counselors. J Acquir Immune Defic Syndr. 2007; 44:569–577. [PubMed: 17310937]

19. Knight KR, Das M, Demicco E, et al. A roadmap for adapting an evidence-based HIV prevention intervention: personal cognitive counseling (PCC) for episodic substance-using men who have sex with men. Prev Sci. 2013 Epub ahead of print. DOI: 10.1007/s11121-013-0364-z.

20. Leigh BC, Stall R. Substance use and risky sexual behavior for exposure to HIV. Issues in methodology, interpretation, and prevention. Am Psychol. 1993; 48:1035–1045. [PubMed: 8256876]

21. Woolf SE, Maisto SA. Alcohol use and risk of HIV infection among men who have sex with men. AIDS Behav. 2009; 13:757–782. [PubMed: 18236149]

22. Vosburgh HW, Mansergh G, Sullivan PS, et al. A review of the literature on event-level substance use and sexual risk behavior among men who have sex with men. AIDS Behav. 2012; 16:1394–1410. [PubMed: 22323004]

23. Hahn JA, Woolf-King SE, Muyindike W. Adding fuel to the fire: alcohol's effect on the HIV epidemic in Sub-Saharan Africa. Curr HIV/AIDS Rep. 2011; 8:172–180. [PubMed: 21713433]

24. Newcomb ME, Clerkin EM, Mustanski B. Sensation seeking moderates the effects of alcohol and drug use prior to sex on sexual risk in young men who have sex with men. AIDS Behav. 2011; 15:565–575. [PubMed: 20960048]
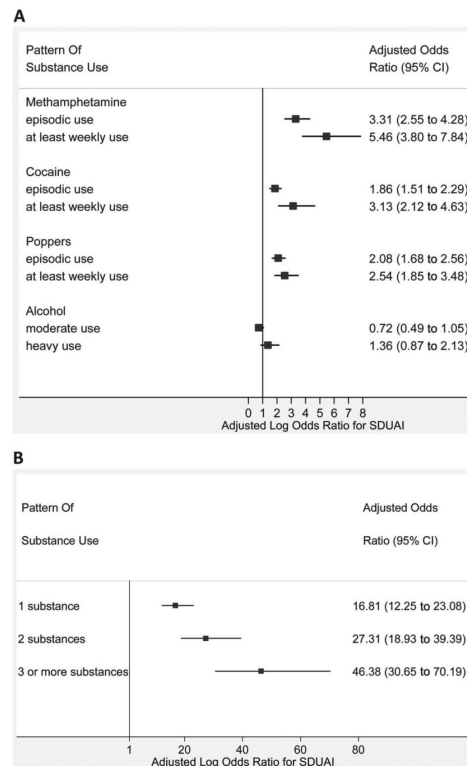
FIGURE 1.
Multivariable logistic regression of SDUAI and substance use patterns among HIV-negative SUMSM surveyed, San Francisco, CA, 2009–2012. A, Substance use frequency and SDUAI. 95% CIs are Bonferonni adjusted. Referent group = substance users who did not report using (top to bottom) methamphetamine, cocaine, poppers, or alcohol, respectively. Episodic use = less than weekly use. Moderate alcohol use = less than 4 drinks per day; heavy alcohol use = 4 or more drinks per day. Models adjusted for age and race/ethnicity. [Compared with episodic users, the AOR for SDUAI among at least weekly users of methamphetamine, cocaine, and poppers was 1.65 (Bonferroni-adjusted 95% CI, 1.09 to 2.49) 1.68 (95% CI, 1.12 to 2.54), and 1.22 (95% CI, 0.88 to 1.70), respectively. Compared with moderate alcohol users, the AOR for SDUAI among heavy alcohol users was 1.90 (95% CI, 1.43 to 2.51)]. Panel B: Number of substances used before or during UAI and SDUAI. 95% CIs are Bonferonni adjusted. Referent group = substance users who reported not using any substances before or during UAI. Number of substances = any combinations of the following substances: methamphetamine, cocaine, alcohol, poppers, crack, ecstasy, and heroin (sensitivity analyses that included marijuana and erectile dysfunction drug use resulted in similar trends showing an increase in risk associated with greater number of substances used). Model adjusted for age and race/ethnicity. [SDUAI AOR among those who use 2 vs. 1 and 3 or more vs. 2 substances before or during UAI were 1.62 (95% CI, 1.15 to 2.29) and 1.70 (95% CI, 1.10 to 2.63), respectively].

TABLE 1

Characteristics of HIV-Negative SUMSM Surveyed, San Francisco, CA, 2009–2012

Demographics[*]	N (%)
Age, mean (SD)	33.8 (10.5)
Race/ethnicity	
White	1624 (51)
Black	321 (10)
Latino/Hispanic	703 (22)
Asian and Pacific Islander	302 (10)
Other	223 (7)
HIV test history	
Last HIV test	
Less than 6 months ago	2140 (67)
6 months to less than 1 year	616 (19)
Over 1 year ago	412 (13)
Never	5 (<1)
Sexual behaviors	
Oral sex with male partners	3097 (98)
UAI with male partners	1425 (45)
UAI with male partners with HIV-serodiscordant status (SDUAI)	750 (24)
Vaginal sex with female partners	315 (10)
Substance use frequency[†]	
Methamphetamine	
Less than weekly	389 (12)
At least weekly	178 (6)
Cocaine (powdered or crack)	
Less than weekly	863 (27)
At least weekly	157 (5)
Poppers	
Less than weekly	854 (27)
At least weekly	264 (8)
Alcohol	
Less than 4 drinks per day	2657 (84)
4 or more drinks per day	330 (10)
Substance use before or during UAI	
Any alcohol/substance use	1246 (39)
Alcohol	887 (28)
Marijuana	577 (18)
Poppers	460 (15)
Erectile dysfunction drugs (eg, Viagra, Levitra, Cialis)	264 (8)
Cocaine	255 (8)
Methamphetamine	245 (8)

Demographics[*]	N (%)
Ecstasy	162 (5)
Crack	89 (3)
Heroin	28 (<1)
Number of substance uses before or during UAI[‡]	
None	2029 (64)
1 substance	565 (18)
2 substances	319 (10)
3 or more substances	260 (8)
Substance use treatment	
Currently in substance use treatment/self-help	159 (5)

[*] Telephone screen interviews did not collect extensive socio-demographic characteristics such as education, income, and other covariates.

[†] Data on frequency of use only collected for cocaine, methamphetamine, poppers, and alcohol in telephone questionnaire.

[‡] Any combinations of the following substances: methamphetamine, cocaine, alcohol, poppers, crack, ecstasy, and heroin.