



THE ROLE OF POLY-SUBSTANCE USE IN HIGH-RISK SEX

Longitudinal Patterns of Methamphetamine, Popper (Amyl Nitrite), and Cocaine Use and High-Risk Sexual Behavior Among a Cohort of San Francisco Men Who Have Sex with Men

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ABSTRACT *Most prior studies examining drug use among men who have sex with men (MSM) have been cross-sectional or retrospective and have not determined whether periods of increased drug use are associated with high-risk sexual behavior at the individual level. In this article, we describe patterns of use of methamphetamines, poppers, and sniffed cocaine and sexual risk behavior among 736 San Francisco MSM enrolled in the EXPLORE study and followed for up to 48 months. In longitudinal analysis, use of methamphetamines, poppers, and sniffed cocaine declined during follow-up. However, compared with older participants, younger participants were more likely to increase their drug use over time. Results of conditional logistic regression demonstrated that high-risk sexual behavior was more common during reporting periods characterized by increased methamphetamine, poppers, or sniffed cocaine use. This within-person analysis found that compared with periods of no drug use, periods of both light drug use (less than weekly use of drugs) and heavier drug use (at least weekly use of at least one drug) were significantly associated with increased risk of engaging in unprotected anal sex with an HIV-positive or unknown-status partner. These results suggest that even intermittent, recreational use of these drugs may lead to high-risk sexual behavior, and that, to reduce and prevent risks of HIV, no level of use of these drugs should be considered “safe.” HIV prevention interventions should target MSM who report either light or heavy use of methamphetamines, poppers, and sniffed cocaine.*

KEYWORDS *Drug use, HIV, Men who have sex with men, Sexual risk behavior.*

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INTRODUCTION

Sexual risk behavior and HIV infection rates have been increasing among men who have sex with men (MSM) since the mid-1990s.^{1,2} Evidence points to corresponding high rates of drug use, suggesting that drug use may be contributing to higher levels of sexual risk behavior.³ The general relationship between noninjection drug use and HIV risk behavior has been well documented.⁴⁻¹¹ However, most studies examining the relationship between sexual risk behavior and drug use have been cross-sectional or retrospective. Although there are reports of increasing drug use among the general population,¹² trends in drug use among MSM have not been well documented and it is unclear whether short term changes in individual drug use are associated with corresponding changes in sexual risk behavior. Such an association would suggest the need for greater efforts to reduce drug use as a means of reducing risk of sexual transmission of HIV. This article documents longitudinal patterns of use of methamphetamines, poppers (amyl nitrites), and sniffed cocaine in a contemporary cohort of high-risk San Francisco MSM followed for up to 4 years. We focus on methamphetamines, poppers, and sniffed cocaine because these drugs are associated with high-risk sexual behavior.^{11,13,14} We also assess predictors of baseline use and changes in use of these drugs and examine whether increased use is associated with increases in sexual risk behavior.

METHODS

Study Population

The EXPLORE study is a trial of a randomized behavioral intervention among MSM to determine whether 10 individualized counseling sessions reduce HIV-infection rates compared with standard HIV testing and counseling. Details of the entire EXPLORE cohort have been previously described in detail¹⁵; this analysis is limited to San Francisco participants. From January 1999 to February 2001, eligible men in San Francisco who were HIV antibody-negative were recruited for the study. Men were eligible if they were 16 years of age or older and reported anal sex with one or more men in the past year, and excluded if they reported that they had been in a mutually monogamous relationship for 2 or more years with a known HIV antibody-negative male partner, or tested HIV-antibody positive at screening. San Francisco recruitment strategies included advertising; outreach on the street and at clubs, bars, bathhouses, sex clubs, health clubs; referrals from other cohort studies, current study participants, community agencies, and clinics.

Eligible men were then randomized to either the intervention (10 initial counseling sessions delivered over a 6-month period, followed by quarterly booster sessions) or the control arm (standard HIV testing and counseling).

Data Collection

At the enrollment visit and every 6 months thereafter, audio computer-assisted self-interview (ACASI) was used to collect data on alcohol and drug use and sexual behaviors. The interview assessed sexual behaviors with all HIV-positive, HIV-negative, and HIV-unknown-serostatus partners as well as drug use in the 6-months before enrollment. Depression was measured semiannually using a shortened version of the Center for Epidemiologic Studies Depression Scale (CES-D).¹⁶ Following the interviews, participants received HIV pretest counseling, and specimens were collected for HIV testing.

Statistical Analysis

The baseline composite drug-use variable was defined as any use of methamphetamines, poppers, or sniffed cocaine in the prior 6 months. In the longitudinal analysis, we defined increasing drug use in the following categories, with scores from 0 to 6: no use; no more than one drug less than once a week; no more than two drugs less than once a week; no more than three drugs less than once a week; no more than one drug at least once a week; no more than two drugs at least once a week; and three drugs at least weekly. These scores were used to calculate average drug usage per participant at each study visit, as well as change in drug usage over study visits.

The risk behavior outcome, serodiscordant unprotected anal sex (SDUA), was defined as self-reported insertive or receptive anal sex without a condom with either an HIV-positive partner or with a partner of unknown serostatus. These behaviors represent significant risk for HIV transmission.¹⁷

The depression indicator was calculated from a sum of 7 questions (as opposed to 20 on the full CES-D scale), where for each question, responses fell on a Likert scale of never or rarely, sometimes, often and mostly or always. We normalized the score based on the 20-question scale to reflect proportionately the same cut-point for clinically depressed. The modified index correlated 0.92 with the full CES-D scale, with an alpha reliability of .83.

Multiple logistic regression was used to examine demographic associations of any use of methamphetamines, poppers, and sniffed cocaine in the 6 months before enrollment. Mean levels of the ordinal measure of use of these drugs were plotted by visit. In addition, to examine how overall drug-use patterns might be affected by informative loss to follow-up, we plotted the results for subgroups based on the last visit; participants who seroconverted were not seen again after the last visit at which their infection was discovered. A proportional odds model was used to examine change in the 0–6 drug-use score from one visit to the next, grouped as decrease, no change, and increase; generalized estimating equations were used to account for the within-subject correlation of the repeated measures across time. Finally, to examine the influence of drug-use patterns on risk behavior, we used conditional logistic regression. This approach is appropriate when the focus is on within-subject comparisons; because each subject acts as his own control, the conditional approach eliminates the influence of between-participant predictors and accounts for within-subject correlations. Only participants who reported SDUA during at least one but not all visits contributed information to this analysis. The predictor of primary interest was the ordinal measure of drug use during the current 6-month period. The analysis is sensitive to within-participant increases in likelihood of reporting SDUA during 6-month periods when drug use is heavier or depression levels are higher, but does not reflect associations between SDUA and between-participant differences in average levels of drug use or chronic depression. The analyses were carried out in SAS[®] Version 8.2.

RESULTS

The primary EXPLORE study results did not demonstrate a statistically significant effect of the intervention on HIV infection rates compared with the control arm across all sites and have been previously reported, as have baseline characteristics of the entire cohort.^{15,19} In San Francisco, most EXPLORE participants were white, non-Latino, although nearly one third of the sample were non-white (Table 1). Most participants had college degrees, and more than two thirds reported an annual

TABLE 1. Baseline characteristics of San Francisco EXPLORE participants (n = 736)

Participant variables	Participants [n (%)]
Age (years)	
16–25	96 (13)
26–35	308 (42)
36–45	231 (31)
≥46	101 (14)
Race/ethnicity	
White, non-Latino	505 (69)
Black, non-Latino	51 (7)
Latino	115 (16)
Other race/ethnicity	65 (9)
Education	
High school or less	54 (7)
Some college	175 (24)
College degree	271 (37)
Post college	236 (32)
Annual household income (\$)	
\$<12,000	67 (9)
\$12,000–29,999	162 (22)
\$30,000–59,999	274 (37)
\$>60,000	233 (32)
Depressed	327 (45)
Number of male sex partners in last 6 months	
0	9 (1)
1	45 (6)
2–5	196 (27)
6–9	123 (17)
>10	362 (49)
Poppers	
Never	463 (63)
<1 time/week	219 (30)
≥1 time/week	51 (7)
Sniffed cocaine	
Never	590 (80)
<1 time/week	133 (18)
≥1 time/week	10 (1)
Methamphetamines*	
Never	563 (77)
<1 time/week	139 (19)
≥1 time/week	31 (4)

*Includes speed, crystal, and crank.

income of \$30,000/year or more. Nearly half of participants reported symptoms consistent with depression at baseline. Participants reported high levels of sexual activity, with nearly half reporting 10 or more partners in the prior 6 months. Popper use was reported by over one third of participants, with approximately one fifth reporting use of sniffed cocaine or methamphetamines. Few participants reported more than weekly use of any of these drugs at baseline.

Of the sociodemographic predictors of use of methamphetamines, poppers, or sniffed cocaine in the 6 months before enrollment, only one, being Latino, was nominally associated with baseline use: Latino men were significantly less likely than whites to use these drugs (OR = .63, 95% CI = .42–0.96, $P = .03$).

The mean composite drug use score over the completed visits was 0.99 (SD = 1.2, range 0–6). The average absolute change in the drug-use score from one visit to the next was 0.47 (SD = .57, range 0–4). In the proportional odds model, only younger age independently predicted changes in the composite drug-use score from one visit to the next, with men 25 years or younger somewhat more likely to increase their drug use compared to men 45 years or older (OR = 1.2, 95% CI = 1.0–1.5, $P = .05$).

Most (88%) San Francisco EXPLORE participants completed follow-up through their last planned visit. As shown in the Figure, mean values of the composite score measuring the use of methamphetamines, popper, or sniffed cocaine, declined slightly during follow-up, from about 1.0 at baseline to 0.75 by the 48-month follow up. Mean drug-use scores increased sharply among 38 men, or 5% of the cohort, who were last seen at the 6- or 24-month visits. There were no significant differences in mean number of drugs used by intervention versus control arm participants (data not shown).

Of the 736 participants, 386 (52%) reported engaging in SDUA during at least one follow-up visit, lower-risk behavior at another, and variability in drug use or depression across visits, and were therefore included in the conditional logistic analysis. Compared to other study participants, they were less educated, more likely to be depressed, and more likely to report multiple sex partners, as well as use of methamphetamines, poppers, or sniffed cocaine ($P < .05$ for all comparisons). This risk

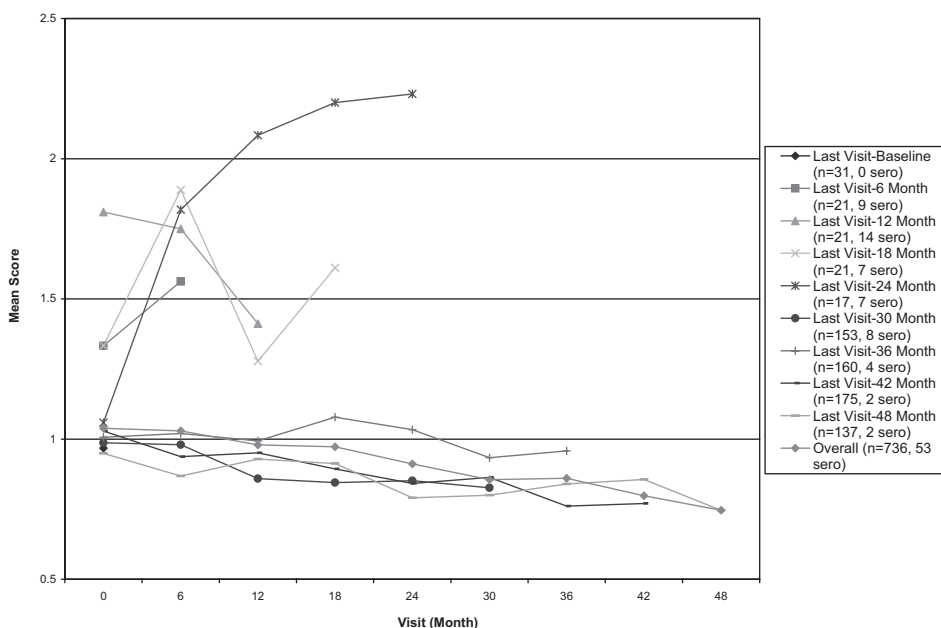


FIGURE. Mean substance use score (based on 0–6 score) of composite substance use variable for San Francisco EXPLORE participants, by last study visit, including participants terminated due to HIV seroconversion (sero). See methods in text for details on how score was calculated.

TABLE 2. Drug use as predictor of serodiscordant unprotected anal sex (SDUA) by conditional logistic regression analysis, among San Francisco EXPLORE participants (n = 386)

Composite drug use score	Definition	OR for SDUA (95% CI)	P value
0	No drug use	Reference	
1	One drug used <1 week	1.5 (1.1–1.9)	.005
2	Two drugs used <1 week	3.2 (2.2–4.7)	<.0001
3	Three drugs used <1 week	2.8 (1.6–4.9)	.0002
≥4	At least one drug used weekly	2.2 (1.5–3.4)	.0002

Drugs included use of methamphetamines, poppers, or sniffed cocaine. The model also adjusted for symptoms of depression, which were not significantly associated with SDUA (OR 1.2, 95% CI = .95–1.5, $P = .13$).

differential reflects the fact that participants had to report at least one period during which they reported SDUA, as well as variability in either drug use or depression across visits. There were no significant differences by age, race/ethnicity, or income.

As shown in Table 2, participants were significantly more likely to report SDUA during 6-month reporting periods characterized by higher composite drug-use scores, after controlling for current depression levels. However, a nonlinear response was apparent, with nominally lower odds ratio point estimates for scores of 3 and ≥4 than for a score of 2. Reporting of depression symptoms was not significantly associated with increased risk of SDUA.

DISCUSSION

To our knowledge, this is the first report on longitudinal patterns of methamphetamine, popper, and cocaine use among a cohort of high-risk MSM. With the exception of relatively few men who increased their use of drugs before leaving the trial early, we found that drug use declined, on average, over the duration of the trial. However, among participants included in the conditional logistic analysis, episodic use of methamphetamines, poppers, or sniffed cocaine was strongly associated with high-risk sexual behavior.

At baseline, the frequency of the use of methamphetamines, poppers, and sniffed cocaine was similar to that reported in results from population-based studies of MSM.²⁰ Our finding that Latino participants were less likely to report use of these drugs compared with white participants is consistent with other studies.^{3,21} These findings reinforce the importance of recognizing that drug-use patterns vary among racial/ethnic groups of MSM, and that HIV prevention interventions need to be tailored accordingly.

We found no difference in drug-use patterns among San Francisco EXPLORE participants assigned to the intervention versus standard arm. This finding should be interpreted with caution with regard to whether behavioral interventions can influence drug use. The EXPLORE study did not target drug users, and reducing drug use was not a primary study outcome. Although some components of the intervention addressed drug use, building interpersonal and communication skills were emphasized; it is possible that a more direct approach to dealing with drug use, such as providing participants with components of substance-use treatment programs, could significantly reduce drug use among the MSM population.

In view of the fact that the EXPLORE intervention did not affect drug use among San Francisco participants, increasing average levels of drug use might have

been expected in the cohort, given the high rates of baseline use reported in this and other studies of MSM.^{11,22} The decreases in the overall mean score were not explained by selective loss to follow-up of men who increased their drug use just before leaving the study, because increasing average use was only evident in two small subgroups who left the study after the 6- or 24-month visits, and was not reflected in the other subgroups who left the study early. There are other possible explanations for this finding. Participants in both arms of the study received HIV testing and counseling semiannually; it is possible that the counseling had the effect of reducing drug use among participants in both study arms. It is also possible that men who were increasing their drug use were less likely to enroll in the study.

Although average levels of use of methamphetamines, poppers, or sniffed cocaine did not increase over the duration of the trial, younger MSM were more likely to report increasing use of these drugs. Given the high rates of drug use reported by young MSM, with up to 66% reporting illicit drug use in the prior 6 months,³ and their high risk for HIV infection,²³ these findings substantiate the need for HIV prevention interventions that reach and engage young drug-using MSM, and for HIV prevention programs targeting young MSM to stress the link between drug use and sexual risk behavior. Intervening among younger populations presents many challenges, but present opportunities to reduce sexual and drug-use behavior in early adulthood, thereby preventing the long-term sequelae of these risky behaviors. At least one intervention has been shown to be effective in reducing HIV risk and drug use among younger persons.²⁴

The within-participant evidence for increases in high-risk sexual behavior during reporting periods characterized by increased use of methamphetamine, poppers, or sniffed cocaine suggests that, to reduce and prevent HIV, no level of use of these drugs should be considered “safe”. There was no dose–response for drug use scores above 2, indicating that even intermittent, recreational use of these drugs is associated with high-risk sexual behavior.

We found no statistically significant association with depression and SDUA, after adjusting for changes in drug use. This finding is consistent with other studies.²⁵ Note, however, that the conditional analysis was sensitive only to an association between changes in depression status and SDUA, and was not designed to detect an association between chronic depression and high-risk sexual behavior.

There are some limitations to this analysis. Although we found that periods of drug use were associated with higher risk behavior, we cannot conclude that there is causal relationship between drug use and high-risk sex. It is possible that drug use and sexual risk were not temporally related; this analysis did not examine event-specific data to determine whether drugs were used during sex, although our previous analysis of EXPLORE baseline data found a strong relationship between drug use during sexual activity and risk behavior.¹³ It is also possible that substance use and sexual risk are markers for social instability or other unmeasured factors that could confound the associations found here. In addition, participants were recruited from a variety of venues, but did not constitute a population-based cohort. Drug use was not a criterion for trial participation; and although the data may be more likely to represent drug-use patterns among sexually active, high-risk MSM, large numbers of heavier users were not included in the sample. This analysis was limited to San Francisco EXPLORE participants; drug-use patterns in other areas of the country may differ among MSM populations. Although behavioral data were collected with audio computer-assisted self-interview, which has been shown to increase reporting of

socially undesirable behaviors compared with interviewer-administered questionnaires,²⁶ participants may still have underreported their drug use or sexual risk behavior.

In conclusion, this analysis found that EXPLORE participants reported using methamphetamines, poppers, or sniffed cocaine a mean of less than once a week upon trial enrollment. Although mean levels of drug use among participants as measured by a composite score declined slightly over the duration of the trial, participants were at increased risk of engaging in high-risk sexual behavior during the periods they reported increased drug use. These findings suggest that HIV prevention interventions to reduce intermittent as well as heavy methamphetamine, popper, and sniffed cocaine use among MSM may be effective in reducing sexual transmission of HIV as well.

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REFERENCES

1. Katz MH, Schwarcz SK, Kellogg TA, et al. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health*. 2002;92:388–394.
2. Catania JA, Osmond D, Stall RD, et al. The continuing HIV epidemic among men who have sex with men. *Am J Public Health*. 2001;91:907–914.
3. Thiede H, Valleroy LA, MacKellar DA, et al. Regional patterns and correlates of substance use among young men who have sex with men in 7 US urban areas. *Am J Public Health*. 2003;93:1915–1921.
4. Crosby GM, Stall RD, Paul JP, Barrett DC. Substance use and HIV risk profile of gay/bisexual males who drop out of substance abuse treatment. *AIDS Educ Prev*. 2000;12:38–48.
5. Diaz RM, Stall RD, Hoff C, Daigle D, Coates TJ. HIV risk among Latino gay men in the southwestern United States. *AIDS Educ Prev*. 1996;8:415–429.
6. Page-Shafer K, Veugelers P, Moss AR, Strathdee S, Kaldor JM, van Griensven GJ. Sexual risk behavior and risk factors for HIV-1 seroconversion in homosexual men participating in the Tricontinental Seroconverter Study, 1982–94. *Am J Epidemiol*. 1997;146:531–542.
7. Woody GE, Donnell D, Seage GR, et al. Non-injection substance use correlates with risky sex among men having sex with men: data from HIVNET. *Drug Alcohol Depend*. 1999;53:197–205.

8. Stall R, Ekstrand M, Pollack L, McKusick L, Coates TJ. Relapse from safer sex: the next challenge for AIDS prevention efforts. *J Acquir Immune Defic Syndr*. 1990;3:1181–1187.
9. Frosch D, Shoptaw S, Huber A, Rawson RA, Ling W. Sexual HIV risk among gay and bisexual male methamphetamine abusers. *J Subst Abuse Treat*. 1996;13:483–486.
10. Ostrow DG, Beltran ED, Joseph JG, DiFranceisco W, Wesch J, Chmiel JS. Recreational drugs and sexual behavior in the Chicago MACS/CCS cohort of homosexually active men. Chicago Multicenter AIDS Cohort Study (MACS) /Coping and Change Study. *J Subst Abuse*. 1993;5:311–325.
11. Purcell DW, Parsons JT, Halkitis PN, Mizuno Y, Woods WJ. Substance use and sexual transmission risk behavior of HIV-positive men who have sex with men. *J Subst Abuse*. 2001;13:185–200.
12. Kissin WBJ. *The DAWN Report: Drug Abuse Warning Network*. Office of Applied Studies. Substance Abuse and Mental Health Services Administration. Washington, DC: Department of Health and Human Services; 2003.
13. 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.
14. Gorman EM, Barr BD, Hansen A, Robertson B, Green C. Speed, sex, gay men, and HIV: ecological and community perspectives. *Med Anthropol Q*. 1997;11:505–515.
15. Koblin BA, Chesney MA, Husnik MJ, et al. High-risk behaviors among men who have sex with men in 6 US cities: baseline data from the EXPLORE Study. *Am J Public Health*. 2003;93:926–932.
16. Radloff L. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–411.
17. Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol*. 1999;150:306–311.
18. Ross CE, Mirowsky J. Components of depressed mood in married men and women. The Center for Epidemiologic Studies' Depression Scale. *Am J Epidemiol*. 1984;119:997–1004.
19. The EXPLORE Study Team. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet*. 2004;364:41–50.
20. 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.
21. Kann L, Kinchen SA, Williams BI, et al. Youth Risk Behavior Surveillance—United States, 1999. State and local YRBSS coordinators. *J Sch Health*. 2000;70:271–285.
22. 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.
23. Valleroy LA, MacKellar DA, Karon JM, et al. HIV prevalence and associated risks in young men who have sex with men. Young Men's Survey Study Group. *JAMA*. 2000;284:198–204.
24. Rotheram-Borus MJ, Swendeman D, Comulada WS, Weiss RE, Lee M, Lightfoot M. Prevention for substance-using HIV-positive young people. Telephone and in-person delivery. *J Acquir Immune Defic Syndr*. 2004;37:S68–S77.
25. Crepaz N, Marks G. Are negative affective states associated with HIV sexual risk behaviors? A meta-analytic review. *Health Psychol*. 2001;20:291–299.
26. Metzger DS, Koblin B, Turner C, et al. Randomized controlled trial of audio computer-assisted self-interviewing: utility and acceptability in longitudinal studies. HIVNET Vaccine Preparedness Study Protocol Team. *Am J Epidemiol*. 2000;152:99–106.