Substance Use and Sexual Risk: A Participant- and Episode-level Analysis among a Cohort of Men Who Have Sex with Men

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Prior reports associating substance use with sexual risk behavior have generally used summary measures and have not adjusted for participants' background levels of substance use. In this 1999–2001 US study (the EXPLORE study), the authors determined whether substance use during sex was independently associated with sexual risk during recent sexual episodes, as reported by 4,295 human immunodeficiency virus–negative men who have sex with men. The main outcome measure was serodiscordant unprotected anal sex (SDUA). The influence of participant-level characteristics was examined by using repeated-measures logistic models. In assessing the influence of episode-level predictors on SDUA, the influence of participant-level characteristics, including 6-month substance use, was removed by using conditional logistic regression, in effect making each participant his own control. The authors also adjusted for partner characteristics. Eleven percent of participants reported heavy alcohol use, 37% used poppers, 19% sniffed cocaine, and 13% used amphetamines. In the participant-level analysis, use of poppers, amphetamines, and sniffed cocaine as well as heavy alcohol use in the prior 6 months were independently associated with SDUA. In the conditional analysis, consumption of ≥6 alcoholic drinks or use of poppers, amphetamines, or sniffed cocaine just before or during sex was independently associated with SDUA. The authors concluded that programs aimed at preventing human immunodeficiency virus transmission should emphasize the influence of substance use during sex on increased risk behavior.

alcohol drinking; amphetamine; amyl nitrite; HIV; logistic models; risk factors; risk-taking; sexual behavior

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; SDUA, serodiscordant unprotected anal sex.

Noninjection substance use is highly prevalent among men who have sex with men (MSM) (1–4). These substances include alcohol, amphetamines, amyl nitrites (poppers), cocaine, and "club drugs" such as ecstasy (3,4-methylenedioxymethamphetamine (MDMA)) and gamma hydroxybutyrate (GHB) (5). A probability sample of urban

US MSM found that many participants reported using alcohol (85 percent) and noninjection drugs (51 percent) in the prior 6 months (6).

The general relation between noninjection substance use and human immunodeficiency virus (HIV) risk behavior has been reviewed previously (7). Many studies have found an association between sexual risk behavior and substance use, including amphetamines, poppers, alcohol, cocaine, and ecstasy (1, 8–15). Moreover, higher levels of substance use, including amphetamines and poppers, have been associated with increased risk of HIV infection (16).

The causal relations between substance use and sexual risk remain unclear. General associations between substance use and risk may be due to simple contextual effects, such as the effects of age and relationship status on both substance use and risk (2, 17). Personality disposition may also motivate people toward both substance use and risky behaviors (18). Substance use per se may enhance risk, independent of a person's stable characteristics, or interact with personal characteristics such that risk is increased. However, few studies have explicitly examined the effects of both background substance use and episode-specific use on sexual risk. Alcohol use has been examined most systematically in this context, with results generally indicating that global patterns of use are better predictors of sexual risk than are episode-specific measures (19–21). In contrast, some data indicate that episode-specific use of certain substances, including poppers, alcohol, and cocaine, relates to sexual risk behavior (15, 20–23). However, these analyses did not adjust for participants' background tendencies to use substances, potentially confounding the relation between episode-specific substance use and sex. If substance use induces risk because of stable individual differences, we would expect background use to emerge as the strongest predictor of risk. In contrast, if use during sex induces risk, we would expect episode-specific measures to predict risk beyond any effects of background variables.

We examined the relation between substance use and sexual activity by using baseline data from the EXPLORE trial, a randomized behavioral intervention for MSM. Information was gathered on substance use and sexual risk taking during the most recent sexual episode with each of up to three most recent partners as well as frequency of substance use over the past 6 months. The EXPLORE data provided a unique opportunity to determine the independent effects of substance use during specific sexual episodes, after removing the influence of background frequency of substance use.

MATERIALS AND METHODS

Study population

The EXPLORE study is a trial of a randomized behavioral intervention funded by the National Institutes of Health designed to determine whether 10 individualized counseling sessions reduce HIV infection rates compared with standard HIV testing and counseling. Details of EXPLORE study recruitment and enrollment procedures

have been described in detail previously (24). In brief, from January 1999 to February 2001, men who were HIV-antibody negative were recruited in six US cities: Boston, Massachusetts; Chicago, Illinois; Denver, Colorado; New York City, New York; San Francisco, California; and Seattle, Washington. Men were eligible if they were 16 years of age or older and reported having anal sex with one or more men in the past year. Men were 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. Recruitment strategies varied by city but included advertising; outreach on the street and at clubs, bars, bathhouses, sex clubs, health clubs, and video arcades; referrals from other cohort studies, current study participants, community agencies, and clinics; the Internet; and community forums, mailings, and a recruitment video.

Data collection

At the enrollment visit, audio computer-assisted self-interview was used to collect data on alcohol and substance use and on sexual behaviors. The interview assessed sexual behaviors with all HIV-positive, HIV-negative, and unknown-serostatus partners, as well as substance use (alcohol, marijuana, poppers, hallucinogens, sniffed cocaine, amphetamines, crack cocaine, smoked heroin, or any injection drug), in the 6 months prior to enrollment.

More detailed questions were asked about the most recent sexual episode with each of up to three most recent partners, including type of sex (unprotected receptive oral sex with ejaculation, receptive and insertive anal sex, protected and unprotected); quantity of alcohol used within 2 hours before or during sex; other substances used "immediately before or during sex" (marijuana, poppers, hallucinogens, sniffed cocaine, amphetamines, crack cocaine, smoked heroin, or any injection drug); age; and desirability of partner, type of relationship (primary/steady, nonprimary/casual), location of sex, and serostatus of partner. Participants were asked to report partner serostatus based on the following questions: "How many of your male sex partners were HIV positive?" "How many of your male sex partners told you they were HIV negative and you had no reason to doubt it?" and "How many of your male sex partners never told you their HIV status or told you they were negative and you have reason to doubt it?" Following the interviews, participants received HIV pretest counseling, and specimens were collected for HIV testing. Approximately 2 weeks after screening, participants received their test results and posttest counseling. Eligible men were then randomly assigned to either the intervention (10 counseling sessions) or control arm of the trial.

Our outcome, serodiscordant unprotected anal sex (SDUA), was defined as a report of either insertive or receptive anal sex without a condom with either an HIV-positive partner or a partner of unknown serostatus. These behaviors represent significant risk for HIV transmission (25). For each of up to three of the most recent partners the participant reported, this outcome was defined for the most

TABLE 1. Characteristics of EXPLORE study participants (n = 4,295), United States, 1999–2001

	Participants	
	No.	%
Age (years)		
16–25	814	19
26–35	1,823	42
36–45	1,159	27
≥46	499	12
Race/ethnicity		
White, non-Latino	3,112	72
Black, non-Latino	281	7
Latino	652	15
Other race/ethnicity	249	6
Participant educational level		
High school or less	407	9
Some college	1,129	26
College degree	1,534	36
Postcollege	1,223	28
Annual household income ($)		
<12,000	562	13
12,000–29,999	1,166	27
30,000–59,999	1,656	39
>60,000	904	21
Depressed	2,030	47
No. of male sex partners in the last 6 months		
0	42	1
1	306	7
2–5	1,382	32
6–9	750	17
≥10	1,812	42
No. of sexual episodes in the last 6 months*		
0	49	1
1	321	7
2	381	9
3	3,544	83
Substance use in the last 6 months		
Alcohol		
None	449	10
Light	2,004	47
Moderate	1,371	32
Heavy	453	11

Table continues

TABLE 1. Continued

	Participants	
	No.	%
Marijuana		
Never	2,300	54
<1 time/week	1,349	31
≥1 time/week	637	15
Poppers (amyl nitrites)		
Never	2,717	63
<1 time/week	1,224	29
≥1 time/week	343	8
Hallucinogens†		
Never	3,258	76
<1 time/week	897	21
≥1 time/week	132	3
Sniffed cocaine		
Never	3,460	81
<1 time/week	723	17
≥1 time/week	103	2
Amphetamines‡		
Never	3,731	87
<1 time/week	464	11
≥1 time/week	88	2
Smoked crack cocaine		
Never	4,104	96
<1 time/week	149	3
≥1 time/week	33	1
Smoked heroin		
Never	4,252	99
<1 time/week	28	1
≥1 time/week	8	<1
Any injectable drugs	439	10

* Participants reported on their most recent episode with each of up to three of their most recent partners.
† Includes phencyclidine (PCP, "angel dust"), ketamine hydrochloride (Special K), lysergic acid diethylamide (LSD), ecstasy (3,4-methylenedioxymethamphetamine (MDMA)).
‡ Includes methamphetamine hydrochloride, "speed," "crystal," "crank."

unprotected receptive and serodiscordant unprotected insertive anal sex.

Statistical analysis

We used multipredictor logistic models to identify the independent predictors of SDUA during each of the three most recent sexual episodes reported by each participant. For participant-level predictors, including demographics and substance use over the past 6 months, the generalized estimating equations approach (26, 27) was used to account for correlation between the repeated outcomes for each partici-

recent episode of sex and was analyzed as a repeated-measures outcome. In two supplementary analyses, we also examined the SDUA outcome by the participant's sexual role, focusing in separate analyses on serodiscordant

pant. This approach is appropriate when the focus is on between-participant comparisons in terms of participant-level predictors that are constant across the three episodes. Background substance use was modeled as the average level of substance use over the previous 6 months. Specifically, average frequency of substance use was coded as never, less than once per week on average, or once per week or more on average. Alcohol use was coded as light (≤3 drinks/day on no more than 1–2 days/week), moderate (4–5 drinks/day on no more than 1–2 days/week, or 1–5 drinks/day on 3–6 days/week, or 1–3 drinks/day on a daily basis), or heavy (daily drinking of ≥4 drinks, or drinking ≥6 drinks on any day). Depression was evaluated by using a shortened version of the Center for Epidemiologic Studies Depression/National Institute of Mental Health scale (28).

To examine the independent influence of episode-level predictors, we used conditional logistic regression. This approach is appropriate when the focus is on within-participant comparisons. By making each subject his own control, the conditional approach eliminates the influence of between-participant predictors and accounts for within-subject correlation. Only those participants who report SDUA during one or two but not all of their three recent sexual episodes contribute information to this analysis; as in simpler applications, including McNemar's test, "concordant" observations are uninformative. The predictor of primary interest was substance use just before or during the sexual episode.

All analyses were carried out by using SAS software, version 8.2 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Table 1 describes demographic, sexual history, and substance use characteristics of study participants in the prior 6 months. Additional characteristics of the cohort have been described previously (24). Of the 4,295 participants enrolled, the median age was 34 years. The majority were White, non-Latino. Most participants had college degrees, and more than half reported an annual income of $30,000 or more. Nearly half reported symptoms consistent with depression. Participants reported high levels of sexual activity, with 59 percent reporting six or more partners in the prior 6 months; 83 percent reported on the maximum of three detailed, separate sexual episodes with their three most recent sexual partners.

As also shown in table 1, substance use in the prior 6 months was common, with 90 percent of participants reporting alcohol use; marijuana, poppers, and hallucinogens were the other most commonly used substances. Nearly one fifth of participants reported using sniffed cocaine and 13 percent amphetamines. Frequent, heavy alcohol use was reported by 11 percent of participants. Compared with the overall prevalence of substance use, substance use at least weekly was reported by a relatively small proportion of participants, with marijuana and poppers being the most commonly used drugs besides alcohol. Three percent or fewer reported weekly use of other substances.

Table 2 shows univariate and multivariate associations of the participant-level variables shown in table 1 with SDUA.

Of the 11,715 sexual episodes reported, 1,867 (16 percent) were SDUA. In univariate analyses, we found that most substances were associated with high-risk sexual behavior; however, when adjusted for the other variables shown, only popper, amphetamine, and sniffed cocaine use and heavy alcohol consumption remained associated with SDUA. Older participants and those with less education and lower incomes were also more likely to report SDUA, as were depressed participants. In supplementary analysis, similar results were seen for both serodiscordant unprotected receptive and serodiscordant unprotected insertive anal sex, with the same patterns holding for the substance use associations (data not shown).

Of the 4,295 participants, 1,225 (29 percent) reported one or two episodes of SDUA and another lower-risk episode and were included in the conditional analysis. Compared with other study participants, those included were less likely to have at least a college degree and more likely to be depressed, have six or more sex partners, and report a greater number of sexual episodes in the past 6 months ($p < 0.001$ for all comparisons). This risk differential reflects the fact that, to be included in the analysis, participants had to report at least one episode of SDUA with one of their three most recent partners. There were no significant differences by age, race/ethnicity, or income.

Episode-specific variables, describing substance use and characteristics of sex partners for these participants, are shown in table 3. For more than one third of all episodes, participants reported consuming alcohol just before or during sex, with nearly one in 10 consuming at least six drinks. Thirty-one percent of sexual episodes involved using nonalcoholic substances, with marijuana, poppers, hallucinogens, and sniffed cocaine being the most common. Participants reported that over one third of episodes involved a partner consuming alcohol; nearly one fifth involved a partner using other substances. Most partners were nonsteady, with 46 percent of participants reporting only one sexual experience with the partner and most reporting having had sexual relations with the partner for less than a month.

Table 4 shows the results of the conditional logistic regression analysis of 3,597 sex episodes with up to the last three partners, of which 1,534 (43 percent) were SDUA episodes. For this model, alcohol was analyzed as the number of drinks consumed during the sexual episode. Other substances shown to be independently associated with SDUA in the participant-level analysis (amphetamines, sniffed cocaine, and poppers) were represented by a composite indicator for any use of these substances during the episode. Use of these substances just before or during sex was independently associated with SDUA, as was consumption of six or more alcoholic drinks just before or during sex. Partner use of alcohol or other drugs just before or during sex was also independently associated with SDUA, as was participants' reporting that their partners' drug use was "unknown." The risk of SDUA decreased with increasing partner age and for sex occurring outside of a house or apartment, including a hotel, dance club, or street, excluding sex clubs or baths.

We found similar results in conditional models examining substance use during sex and associations with serodiscordant unprotected receptive and serodiscordant unprotected

TABLE 2. Subject-level predictors of episodes of serodiscordant unprotected anal sex with up to the last three sex partners among 4,295 EXPLORE study participants, United States, 1999–2001

Participant variable	Univariate OR* for SDUA*	95% CI*	p value	Multivariate OR for SDUA	95% CI	p value
Age (years)						
16–25	Reference					
26–35	1.0	0.9, 1.2	0.9	1.2	1.0, 1.5	0.03
36–45	1.0	0.8, 1.2	1.0	1.3	1.1, 1.6	0.01
≥46	1.0	0.8, 1.3	0.8	1.4	1.1, 1.9	0.004
Race/ethnicity						
White, non-Latino	Reference					
Black, non-Latino	1.0	0.8, 1.3	0.9	1.0	0.7, 1.2	0.7
Latino	1.1	0.9, 1.3	0.2	1.0	0.9, 1.2	0.8
Other race/ethnicity	0.9	0.7, 1.2	0.6	1.0	0.7, 1.3	0.8
Educational level						
High school or less	2.0	1.6, 2.5	<0.0001	1.8	1.5, 2.3	<0.0001
Some college	1.5	1.3, 1.8	<0.0001	1.4	1.2, 1.7	<0.0001
College degree	1.2	1.0, 1.4	0.04	1.2	1.0, 1.3	0.07
Postcollege	Reference					
Annual household income ($)						
<12,000	1.5	1.2, 1.9	<0.0001	1.3	1.0, 1.7	0.03
12,000–29,999	1.4	1.2, 1.7	0.0001	1.3	1.1, 1.6	0.005
30,000–59,999	1.3	1.1, 1.5	0.003	1.3	1.1, 1.5	0.007
>60,000	Reference					
Depressed	1.5	1.3, 1.7	<0.0001	1.3	1.2, 1.5	<0.0001
No. of male sex partners in the last 6 months						
1	Reference					
2–5	1.1	0.7, 1.5	0.8	1.0	0.7, 1.5	0.9
6–9	1.1	0.8, 1.6	0.6	1.1	0.8, 1.5	0.7
≥10	1.5	1.0, 2.1	0.03	1.3	0.9, 1.9	0.11
Substance use in the last 6 months						
Alcohol						
None	Reference					
Light	0.9	0.7, 1.1	0.3	1.0	0.8, 1.2	0.7
Moderate	1.0	0.8, 1.2	0.9	1.0	0.8, 1.2	1.0
Heavy	1.7	1.3, 2.2	<.0001	1.4	1.1, 1.8	0.02

Table continues

insertive anal sex. There were significant associations with both outcomes for reporting six or more drinks just before or during sex as well as use of sniffed cocaine, poppers, or amphetamines during sex, adjusting for the same variables as shown in table 4 (data not shown).

DISCUSSION

Among this large cohort of urban, HIV-negative MSM, we found that heavy alcohol use and use of poppers, amphetamines, or sniffed cocaine in general, as well as specifically just before or during sex, were significantly associated with increased risk of having unprotected anal sex with an HIV-positive or unknown-serostatus partner. Our findings support prior analyses of the association between substance use and high-risk sex and clarify the role of use during sexual episodes. We were able both to directly link the timing of substance use to sexual activity and, through our conditional logistic regression analysis, to fully control for or condition on participant baseline characteristics, including participants' overall tendencies to use substances. This analysis therefore represents a stringent test of the hypothesis that use

TABLE 2. Continued

Participant variable	Univariate OR for SDUA	95% CI	*p* value	Multivariate OR for SDUA	95% CI	*p* value
Marijuana						
Never	Reference					
<1 time/week	1.2	1.0, 1.3	0.01	1.0	0.8, 1.1	0.7
≥1 time/week	1.2	1.0, 1.4	0.02	0.9	0.7, 1.0	0.1
Poppers (amyl nitrites)						
Never	Reference					
<1 time/week	1.5	1.3, 1.7	<0.0001	1.3	1.2, 1.5	<0.0001
≥1 time/week	1.5	1.2, 1.8	0.0001	1.2	1.0, 1.5	0.1
Hallucinogens†						
Never	Reference					
<1 time/week	1.2	1.1, 1.4	0.006	1.0	0.8, 1.1	0.6
≥1 time/week	1.7	1.3, 2.3	0.0003	0.9	0.6, 1.4	0.8
Sniffed cocaine						
Never	Reference					
<1 time/week	1.5	1.3, 1.7	<0.0001	1.2	1.0, 1.4	0.04
≥1 time/week	2.7	2.0, 3.6	<0.0001	1.7	1.2, 2.5	0.004
Amphetamines‡						
Never	Reference					
<1 time/week	1.7	1.5, 2.0	<0.0001	1.4	1.2, 1.7	0.0008
≥1 time/week	2.9	2.1, 4.0	<0.0001	2.0	1.3, 3.1	0.0008
Smoked crack cocaine						
Never	Reference					
<1 time/week	1.6	1.2, 2.2	0.001	0.9	0.7, 1.3	0.7
≥1 time/week	2.4	1.4, 4.0	0.001	1.4	0.8, 2.6	0.2
Smoked heroin						
Never	Reference					
<1 time/week	1.4	0.7, 2.8	0.3	0.7	0.3, 1.4	0.3
≥1 time/week	0.6	0.1, 4.4	0.6	0.3	0.0, 2.2	0.2
Any injectable drugs	2.6	1.4, 5.0	0.004	1.5	0.8, 3.1	0.2

∗ OR, odds ratio; SUDA, serodiscordant unprotected anal sex; CI, confidence interval.

† Includes phencyclidine (PCP, "angel dust"), ketamine hydrochloride (Special K), lysergic acid diethylamide (LSD), ecstasy (3,4-methylenedioxymethamphetamine (MDMA)).

‡ Includes methamphetamine hydrochloride, "speed," "crystal," "crank."

of substances during sex directly enhances the likelihood of risky sex, independent of other participant variables that may confound this relation. In addition, our episode-level analysis controlled for many partner characteristics, providing strong evidence that substance use contributes to increased risk behavior independent of many partner-level variables, including attractiveness and relationship type.

Although we were unable to determine the mechanisms through which substance use increases sexual risk, several possibilities warrant consideration. A key mechanism may be that being intoxicated "disinhibits" a participant to have sex—including unprotected sex—with an HIV-positive or unknown-serostatus partner. Substance use may also decrease safer-sex skills, such as the ability to use condoms

properly. This interpretation is supported by other data showing that alcohol consumption and amphetamine use are associated with condom failure (29). In a corollary perspective, popper use facilitates anal sex by increasing tactile sensitivity and relaxing sphincter tone, which may lead to more unprotected anal sex because of increased partner receptivity. Thus, the immediate effect of alcohol or drugs on risk may be due to pharmacologic effects that simultaneously disrupt basic safety behaviors and facilitate some risky activities.

We should note that the effect on sexual risk of substance use during sexual episodes is not incompatible with a "person"-based perspective on risk. Thus, some participants may intentionally use substances to reduce anxiety about

TABLE 3. Episode-specific variables for EXPLORE study participants who reported at least one episode of serodiscordant unprotected anal sex and at least one additional lower-risk episode, United States, 1999–2001*

Behavior	Episodes	
	No.	%
Participant alcohol use just before or during sex		
None	2,135	59
1–2 drinks	420	12
3–5 drinks	730	20
≥6 drinks	307	9
Participant substance use just before or during sex		
Marijuana	337	9
Poppers (amyl nitrite)	310	9
Hallucinogens	160	4
Sniffed cocaine	133	4
Amphetamines	121	3
Smoked crack cocaine	35	1
Smoked heroin	1	<1
Any injectable drugs	27	1
Partner characteristics		
Partner consumption of alcohol just before or during sex		
No	1,449	40
Yes	1,272	35
Unknown	876	24
Partner use of other drugs immediately before or during sex		
No	1,907	53
Yes	613	17
Unknown	1,077	30

Table continues

TABLE 3. Continued

Behavior	Episodes	
	No.	%
Partner age (years)		
16–25	732	21
26–35	1,762	51
36–45	779	23
>45	179	5
Partner type		
Primary	489	14
Steady, nonprimary	736	20
Nonsteady	2,371	66
Partner attractiveness		
Attractive enough	1,498	42
Very desirable	1,206	34
Extremely desirable	881	25
Length of time having sex with partner		
>6 months	567	16
1–6 months	823	23
<1 month	2,190	61
Location of sex with partner		
House or apartment	2,606	72
Sex club or bath	384	11
Other†	606	17
No. of times had sex with partner in the past 6 months		
1	1,658	46
2–5	1,153	32
≥6	779	22

* 1,225 participants, 3,597 total episodes.
† Includes hotel, bar, dance club, porn theater, video arcade, or other public place, including the street.

having sex and/or the potential for disease transmission, leading to higher risk behavior than may have occurred in the absence of substance use (30). In this light, there may be stable individual differences in the substance use–risk linkage that operate on an episode-by-episode basis. Our data did not measure alcohol/drug expectancies or other attitude constructs, so we were not able to test this hypothesis. Given that expectancies or attitudes may be important "access points" for behavioral interventions, further studies should examine both cognitive variables and episodic use to test or clarify the interaction of these classes of variables.

Clearly, interventions are needed that target the use of substances during sex. These results suggest that such interventions should focus not only on sexual risk but also on substance use itself, given that the simple presence of alcohol or drugs during a sexual episode was associated with SDUA. Studies have reported that sexual risk behavior declines among MSM who seek treatment for substance use, although these data are largely from observational studies

(31). Sporadic substance use during sexual activity was a common pattern in this cohort, including use of substances such as amphetamines and cocaine that can lead to dependency. This finding suggests that interventions may need to be developed to prevent sporadic users from becoming chemically dependent.

The relatively low frequency of heavy substance use in this cohort suggests that traditional treatment interventions based on addiction/dependent treatment models may be less useful than interventions that more directly address the effect of episodic use on sexual and other risks. Such programs should be designed to reduce directly substance use during sex and should address indirect processes such as degradation of safer sex skills when high.

A notable exception to participants' relatively low, intermittent patterns of substance use is alcohol: approximately one out of 10 men was a heavy user. Alcohol was also the most commonly used substance just before or during sex. The role of alcohol in promoting high-risk sexual activity has been controversial, with some but not all studies

TABLE 4. Univariate and multivariate conditional logistic regression analysis of episode-level predictors of episodes of serodiscordant unprotected anal sex with up to the last three sex partners in the EXPLORE study, United States, 1999–2001*

Variable	Univariate OR† for SDUA	95% CI†	p value	Multivariate OR for SDUA	95% CI	p value
Participant alcohol use just before or during sex						
None	Reference					
1–2 drinks	1.2	0.9, 1.6	0.1	1.0	0.7, 1.4	1.0
3–5 drinks	1.7	1.3, 2.1	<0.0001	1.2	0.9, 1.7	0.2
≥6 drinks	3.3	2.3, 4.7	<0.0001	2.4	1.6, 3.7	<0.0001
Participant substance use just before or during sex						
Poppers (amyl nitrites), snorted or sniffed cocaine, or amphetamines	1.9	1.4, 2.5	<0.0001	1.5	1.1, 2.0	0.02
Partner consumption of alcohol just before or during sex						
No	Reference					
Yes	1.8	1.5, 2.1	<0.0001	1.3	1.0, 1.7	0.03
Unknown	1.8	1.4, 2.2	<0.0001	1.2	0.9, 1.6	0.2
Partner use of other drugs immediately before or during sex						
No	Reference					
Yes	2.0	1.6, 2.4	<0.0001	1.5	1.2, 2.0	0.002
Unknown	1.8	1.4, 2.1	<0.0001	1.6	1.2, 2.0	0.0005
Partner age (years)						
16–25	Reference					
26–35	0.8	0.7, 1.0	0.06	0.8	0.7, 1.0	0.04
36–45	0.7	0.6, 0.9	0.01	0.7	0.6, 1.0	0.02
>45	0.7	0.4, 1.0	0.04	0.7	0.5, 1.1	0.2
Partner type						
Primary	Reference					
Steady, nonprimary	1.2	1.0, 1.6	0.1	1.2	0.9, 1.6	0.3
Nonsteady	1.5	1.2, 1.8	0.0002	1.3	1.0, 1.8	0.11
Partner attractiveness‡						
Attractive enough	Reference					
Very desirable	0.9	0.8, 1.1	0.5			
Extremely desirable	1.0	0.8, 1.2	0.9			
Location of sex with partner						
House or apartment	Reference					
Sex club or bath	1.5	1.1, 2.0	0.01	1.1	0.8, 1.5	0.7
Other§	0.9	0.7, 1.1	0.3	0.8	0.6, 1.0	0.04
No. of times had sex with partner in the past 6 months						
1	Reference					
2–5	1.0	0.8, 1.2	1.0	1.2	1.0, 1.5	0.1
≥6	0.8	0.6, 0.9	0.007	1.2	0.8, 1.6	0.4

* A total of 1,225 participants reporting 3,597 sexual episodes, of which 1,534 were serodiscordant unprotected anal sex (SDUA).

† OR, odds ratio; CI, confidence interval.

‡ Because these variables were not significant in univariate analysis, they were not included in the final multivariate model.

§ Includes hotel, bar, dance club, porn theater, video arcade, or other public place, including the street.

suggesting that alcohol use is associated with high-risk sexual behavior (32–35). Our findings suggest that, at a population level, alcohol use may be contributing to a greater proportion of high-risk sexual behaviors than any other substance, especially among those who have multiple drinks prior to having sex. Targeting HIV prevention to heavy alcohol users, including focusing on reducing the quantity of alcohol used in sexual settings, may be effective in reducing sexual risk.

In our episode-level analysis, we also found a relatively strong association between partner substance use and SDUA. The fact that this association was independent of participants' own substance use suggests that prevention strategies addressing substance use should include addressing whether partners are intoxicated during sexual encounters and suggestions for remaining safe in such settings. The association of participants not knowing whether their partners were on drugs during sex with SDUA is most likely a marker for familiarity with the partner or the partner's personality, or it may reflect participants' hesitation to answer the question definitively unless they specifically asked their partners about their substance use.

Although the focus of this analysis was to examine substance use and sexual risk behavior, we also found that the possibility of high-risk sex increased among participants with less education and lower incomes. These findings suggest that prevention programs should reemphasize the risk of unprotected sex with nonprimary partners and tailor prevention programs for less-educated MSM, especially those with no college education. While some studies have reported that depression is not associated with sexual risk behavior, our finding that depressive symptoms are independently associated with sexual risk, after controlling for substance use, supports directly addressing the mental health of MSM, through either counseling or pharmacologic treatment, as a potentially important HIV prevention strategy (36). Finally, although we found a small, but significant decrease in risk behavior with increasing *partner* age in the episode-level analysis, risk behavior increased with increasing *participant* age in the subject-level analysis, reinforcing the need to focus prevention efforts on MSM of all ages.

There are some limitations to our findings. Participants were recruited through a variety of venues but may not be representative of the general population of high-risk, HIV-negative MSM. Although behavioral data were collected by using an audio computer-assisted self-interview, which has been shown to increase reporting of socially undesirable behaviors compared with interviewer-administered questionnaires (37), participants may still have underreported their substance use or sexual risk behavior. In addition, episode-specific data were collected on only the three most recent sexual partners. It is possible that additional detailed data from more sexual episodes may have changed our results to the extent that people more likely to use substances during sex may also be more likely to report more sexual partners. Our effect sizes may therefore represent lower-bound estimates for the relation between substance use and sexual risk. Although our analysis was able to control for or remove the influence of multiple partner and participant

characteristics, other unmeasured episode-level variables may confound the relation between substance use and sex. We also did not measure use of some specific club drugs, including ketamine and gamma-hydroxybutyrate, and were therefore unable to measure their associations with risk behavior. Finally, baseline use of sildenafil citrate (Viagra; Pfizer Labs, New York, New York), which has been associated with risk behavior in prior studies (4, 38), was not assessed in this cohort.

HIV and other sexually transmitted diseases are increasing among gay and bisexual men (39, 40). HIV prevention programs need to increase awareness of the sexual risk associated with substance use. Inquiring about substance use during sexual activity should be emphasized as part of primary care delivered to MSM and as part of HIV testing and counseling procedures. MSM who report using substances just before or during sex should be made aware of the risk potential of that behavior, and they should have risk-reduction and treatment programs available for modifying this key risk precursor.

cial products, or organizations imply endorsement by the US Government.

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