

# Associations Between Substance Use, Erectile Dysfunction Medication and Recent HIV Infection Among Men Who have Sex with Men

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Published online: 7 December 2007  
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**Abstract** We conducted a case-control study to compare illicit substance and erectile dysfunction medication (EDM) use between recently HIV-infected and uninfected men who have sex with men (MSM). Eighty-six recently (previous 12 months) HIV-infected MSM (cases) and 59 MSM who recently tested HIV-negative (controls) completed computer-assisted self-interviews. There were no statistical differences in demographics or number of sexual partners by HIV status. Cases were more likely than controls to report methamphetamine or nitrite use, but not EDM, gamma hydroxybutyrate, 3,4 methylenedioxymethamphetamine, cocaine, or marijuana use, in the previous 12 months and with their last three sexual partners in multivariate logistic regression models. Use of nitrites and amphetamine may increase HIV risk among MSM.

**Keywords** HIV · Primary infection · Recent infection · MSM · Drug use · Substance use · Methamphetamine · Volatile nitrites · Sildenafil · Erectile dysfunction medication

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## Introduction

Longitudinal studies have demonstrated associations between HIV seroconversion and use of illicit substances, including amphetamine (Burcham et al. 1989; Chesney et al. 2005; Koblin et al. 2006; PageShafer et al. 1997; Plankey et al. 2007), volatile nitrites (Buchbinder et al. 2005; Burcham et al. 1989; Chesney et al. 2005; Ostrow et al. 1995; Plankey et al. 2007), and cocaine (Chesney et al. 2005; Ostrow et al. 1995; Plankey et al. 2007). However, relatively few studies have examined substance use in the context of sexual activity. In a recent longitudinal study of men who have sex with men (MSM) in six metropolitan cities in the United States (U.S.), use of illicit substances during sexual activity was associated with HIV seroconversion (Koblin et al. 2006), but associations were not examined by substance type. Another cross-sectional study of MSM from seven U.S. cities examined associations between HIV prevalence and crack cocaine use during sexual activity in the previous 6 months (Harawa et al. 2004), finding no association between substance use and HIV status. However, HIV-infected individuals were not incident cases, therefore temporality between substance use and infection could not be established.

Other studies among MSM have demonstrated associations between unprotected anal intercourse (UAI) and illicit substance use, including use of methamphetamine or amphetamine (Celentano et al. 2006; Chmiel et al. 1987; Colfax et al. 2001, 2005; Hirshfield et al., 2004a, b; Molitor et al. 1998; Rusch et al. 2004; Waldo et al. 2000), volatile nitrites (Choi et al. 2005; Clutterbuck et al. 2001; Ekstrand et al. 1999; Hirshfield et al. 2004a, b; Mulry et al. 1994; Ostrow et al. 1993; Strathdee et al. 1998; Waldo et al. 2000; Woody et al. 1999), 3,4 methylenedioxymethamphetamine (MDMA) (Choi et al. 2005; Klitzman et al.

2000, 2002; Lee et al. 2003; Rusch et al. 2004; Waldo et al. 2000), gamma hydroxybutyrate (GHB) (Rusch et al. 2004), and ketamine (Rusch et al. 2004). Additionally, recent studies have demonstrated cross-sectional associations between erectile dysfunction medication (EDM) use and UAI (Chu et al. 2003; Hirshfield et al. 2004a; Kim et al. 2002; Mansergh et al. 2006; Paul et al. 2005; Sanchez and Gallagher 2006) and use of other illicit substances (Chu et al. 2003; Crosby and DiClemente 2004; Purcell et al. 2005; Paul et al. 2005; Sanchez and Gallagher 2006). However, some have suggested that associations between substance use and HIV risk behaviors are confounded by personality traits, such as impulsivity (Hayaki et al. 2006; Mccoul and Haslam 2001) and sensation seeking (Kalichman et al. 1996). Additionally, an event-based analysis of drug use and UAI among MSM did not demonstrate an association when using diaries to record sexual events occurring just after substance use (Gillmore et al. 2002), however all substances were collapsed into one measure in the analyses. Comparisons between associations of HIV infection with any substance use vs. associations with substance use during sexual activity may help to elucidate the true relationship between substance use and HIV risk. Using a case-control design, we compared reports of any substance use, regardless of sexual activity, in the previous year and substance use during sexual activity with the last three partners between recently HIV-infected and uninfected MSM to determine which substances may be associated with recent HIV infection.

## Methods

### Selection of Cases

From May 2002 to February 2006, 200 people with recent HIV infection enrolled in the Acute Infection and Early Disease Research Program (AIEDRP) in San Diego, California, which has been described previously (Daar et al. 2001; Little et al. 1999). Recent infection occurred in the previous 12 months as determined by one of the following: (1) HIV seroconversion within the previous 12 months [negative HIV enzyme immunoassay (EIA) followed by positive EIA]; (2) presence of HIV RNA in plasma, but a negative EIA; or (3) results on a Western blot or detuned EIA that are consistent with early infection. Individuals who were screened for AIEDRP were recruited from local hospitals, physicians' offices, HIV testing and counseling sites, organizations and establishments that cater to MSM, friends, partners, and other AIEDRP participants. In medical care settings, a clinician or counselor may have informed patients about screening or they may have learned about AIEDRP through a brochure. In other

recruitment settings, participants would have been informed by word of mouth or a brochure.

At enrollment, participants were invited to respond to a computer-assisted self-interview (CASI), and 97% did so. Reasons for non-response included inability to speak English ( $n = 4$ ), withdrawing in the first week of study ( $n = 2$ ), and declining to complete the CASI ( $n = 1$ ). Among the remaining 193 respondents, 189 (98%) were men, 181 of whom (96%) reported sexual contact with another man in the previous 12 months. Cases ( $n = 86$ ) who were eligible for the current study had to (1) be enrolled in AIEDRP with recent HIV infection, (2) report sexual activity with other men in past 12 months, and (3) respond to the CASI between November 2003 and February 2006, at which time respondents were queried about their use of illicit substances and EDM in the previous 12 months and with their last three partners.

### Selection of Controls

HIV-seronegative controls were obtained from two sources. Sixty-eight MSM who were screened for AIEDRP, but were not infected with HIV, were invited to complete the CASI, and 66 (97%) did so. Additionally, 38 MSM who received negative EIA HIV tests from the counseling and testing clinics that referred the greatest number of MSM to AIEDRP completed the CASI. All HIV-negative MSM who reported symptoms consistent with acute HIV viremia were screened by HIV RNA, Western blot, and detuned EIA to rule out the possibility of acute HIV infection. Of the 104 HIV-negative MSM recruited from these two sources, 59 were eligible as controls for the current study because they responded to same questions as cases regarding substance and EDM use over the previous 12 months and with their last three partners.

### Data Collection

Prior to data collection, all participants completed informed consent and all study protocols were approved by the University of California, San Diego Institutional Review Board. Participants completed CASI within 3 weeks of their HIV diagnosis or last HIV-negative test. Respondents completed CASI in private and were queried about substance use, EDM use, and sexual behavior, including use of EDM or illicit substances at the time of sexual activity with their last three partners and any use in the previous 12 months. The CASI contained many questions pertaining to sexual activity. Participants were queried separately about the number of male and female

sexual partners they had in their lifetime and the previous 12, 3, and month prior to interview. Additionally, they were queried about their last three partners in detail including demographics, which assisted in establishing partner gender, substance use during sexual activity, number of sexual events, and the types of sexual activities that occurred including sexual positioning and condom use. EDM use was defined as use of any of the following medications: sildenafil citrate (Viagra<sup>®</sup>, Pfizer), tadalafil (Cialis<sup>®</sup>, Eli Lilly), and vardenafil hydrochloride (Levitra<sup>®</sup>, Bayer Pharmaceuticals, GlaxoSmithKlein, and Schering-Plough). Unfortunately, neither cases nor controls were queried about alcohol use.

### Analysis

Differences in demographics and sexual histories between cases and controls were compared using *t*-tests, Chi-square analysis, and univariate logistic regression. Associations between UAI and use of methamphetamine or nitrites among the last three partners were determined using generalized estimating equations (GEEs). Differences in the proportions of cases and controls reporting substance use were compared using univariate and multivariate logistic regression. In multivariate logistic regression models, each individual substance was analyzed in separate models while controlling for potential confounders. Interactions between EDM and methamphetamine or nitrite use were examined. For further examination of associations between recent HIV infection and methamphetamine and nitrites, an additional substance use variable that included use of both substances alone or together and use of substances other than methamphetamine or nitrites was created. Associations between this variable and HIV status were examined in multiply adjusted logistic regression models and potential interactions between nitrites and methamphetamine were examined. All analyses were conducted using STATA version 8.2 SE (STATA Corporation, College Station, TX, USA).

### Results

The median age of the MSM ( $n = 145$ ) was 32 (Table 1). Most were white (72.4%), followed by Hispanic (15.2%), African American (6.2%), and Asian or Pacific Islander (4.1%). The median annual income was \$30,000, and nearly half completed college (49.7%). More participants were recruited in 2005/2006 than in 2003/2004. The median number of sexual partners reported was 24 (mean 41.2) in the previous 12 months and 6 (mean 12) in the previous 3 months. UAI with any of the last three partners

was reported by 88.3% of MSM, with 11.7% reporting no UAI, 16.6% reporting insertive UAI only, 22% reporting receptive UAI only, and 49.7% reporting both insertive and receptive UAI with any of the last three partners.

There were no significant differences between cases and controls by demographics or number of sexual partners (Table 1). However, cases were significantly less likely to have been recruited in 2005/2006 than controls. Although cases and controls reported UAI with their last three partners in similar proportions, cases were more likely to report UAI with more of their last three partners ( $p = 0.04$ ). A greater proportion of cases than controls reported having UAI with more than one of their last three partners (62.8% vs. 40.7%, respectively,  $p = 0.01$ ).

Any illicit substance use was reported by 71.7% of MSM in the previous 12 months and 71.7% with any of their last three partners (Table 1). In the previous 12 months, marijuana use was most commonly reported (62.8%), followed by volatile nitrites (57.9%), methamphetamine (52.4%), EDM (46.2%), cocaine (32.4%), MDMA (32.4%), and GHB (32.4%). With participants' last three partners, volatile nitrites were most commonly reported (44.8%), followed by methamphetamine (37.9%), marijuana (33.8%), EDM (23.5%), GHB (19.3%), cocaine (14.5%), and MDMA (11.7%). Polydrug use (i.e., use of more than one substance) was also commonly reported. Illicit substance use was reported by a greater proportion of cases than controls (Table 1), including volatile nitrites during sexual activity with their last three partners and nitrites, methamphetamine, and MDMA in the previous 12 months.

In multiply adjusted logistic regression models that examined one substance per model, use of methamphetamine or volatile nitrites with the last three partners (OR = 2.77 and 2.71, respectively) or over the previous 12 months (OR = 2.33 and 3.31, respectively) was reported more frequently among cases than controls (Table 2). There were no significant differences between cases and controls with regard to use of MDMA, ketamine, GHB, cocaine, marijuana, or EDM in the previous 12 months or with their last three partners.

Unprotected anal intercourse was consistently reported by a greater proportion of MSM who used either methamphetamine or nitrites with each of the last three partners (Fig. 1). In GEEs, UAI was significantly associated with use of methamphetamine and nitrites (OR = 3.1,  $p < 0.01$  and 1.8,  $p = 0.01$ , respectively) across all three partners regardless of case-control status while controlling for partner type (main vs. all other types). When considering positioning for UAI in GEEs, methamphetamine was associated with UAI regardless of positioning (receptive OR = 2.4,  $p < 0.01$ ; insertive OR = 1.8,  $p = 0.02$ ), but nitrite use was only associated with receptive UAI

**Table 1** Demographics, sexual history, and substance use by HIV status ( $n = 145$ )

	OR	95% CI	<i>p</i> -value	HIV-negative ( $n = 59$ ) % ( $n$ ) mean (median)	HIV-positive ( $n = 86$ ) % ( $n$ ) mean (median)	Total ( $n = 145$ ) % ( $n$ ) mean (median)
Age	1.01	0.98, 1.05	0.54	31.8 (32)	32.8 (33)	32.4 (32)
White ethnicity vs. all other	1.11	0.53, 2.32	0.78	71.2 (42)	73.3 (63)	72.4 (105)
Annual income	1.00	0.99, 1.01	0.27	\$37,214 (30K)	\$58,279 (32K)	\$49,707 (30K)
Completed college	0.65	0.34, 1.27	0.21	55.9 (33)	45.4 (39)	49.7 (72)
Recruited in 2005/2006 vs. 2003/2004	0.21	0.10, 0.48	<0.01	83.1 (49)	51.2 (44)	64.1 (93)
Male sex partners previous 12 months	1.00	0.99, 1.01	0.34	35.6 (20)	45.2 (25)	41.2 (24)
Male sex partners previous 3 months	1.01	0.98, 1.02	0.69	11.4 (6)	12.6 (6.5)	12.1 (6)
>1 Partner during sex past 12 months	2.00	0.98, 4.06	0.06	59.3 (35)	74.4 (64)	68.3 (99)
UAI with last three partners*						
0 of 3	REF			11.9 (7)	11.6 (10)	11.7 (17)
1 of 3	0.55	0.18, 1.68	0.29	47.5 (28)	25.6 (22)	34.5 (50)
2 of 3	1.49	0.48, 4.69	0.49	25.4 (15)	37.2 (32)	32.4 (47)
3 of 3	1.71	0.50, 5.91	0.40	15.3 (9)	25.6 (22)	21.4 (31)
Ever incarcerated	0.48	0.22, 1.06	0.07	30.5 (18)	17.4 (18)	22.8 (33)
<i>Use with last three partners</i>						
Methamphetamine	1.96	0.97, 3.96	0.06	28.2 (17)	44.2 (38)	37.9 (55)
Volatile nitrites	2.75	1.37, 5.52	<0.01	30.5 (18)	54.7 (47)	44.8 (65)
Marijuana	1.45	0.72, 2.99	0.30	28.8 (17)	37.2 (32)	33.8 (49)
GHB	1.93	0.79, 4.74	0.15	13.6 (8)	23.3 (20)	19.3 (28)
MDMA	1.75	0.58, 5.27	0.32	8.5 (5)	14.0 (12)	11.7 (17)
Cocaine	0.90	0.35, 2.30	0.83	15.3 (9)	14.0 (12)	14.5 (21)
Polydrug use	2.18	1.10, 4.31	0.03	35.6 (21)	54.7 (47)	46.9 (68)
Any drug use	2.10	1.01, 4.37	0.05	62.7 (37)	77.9 (67)	71.7 (104)
EDM	0.97	0.45, 2.13	0.95	23.7 (14)	23.3 (20)	23.5 (34)
<i>Any use in previous 12 months</i>						
Methamphetamine	1.98	1.01, 3.88	0.05	42.4 (25)	59.3 (51)	52.4 (76)
Volatile nitrites	3.82	1.90, 7.69	<0.01	39.0 (23)	70.9 (61)	57.9 (84)
Marijuana	1.45	0.73, 2.86	0.29	57.6 (34)	66.3 (57)	62.8 (91)
GHB	2.00	0.95, 4.20	0.07	23.7 (14)	38.4 (33)	32.4 (47)
MDMA	2.31	1.09, 4.91	0.03	22.0 (13)	39.5 (34)	32.4 (47)
Cocaine	1.02	0.50, 2.06	0.96	32.2 (19)	32.6 (28)	32.4 (47)
Polydrug use	3.65	1.76, 7.57	<0.01	50.9 (30)	79.1 (68)	67.6 (98)
Any drug use	5.79	1.79, 18.8	<0.01	78.0 (46)	95.4 (82)	88.3 (128)
EDM	1.46	0.75, 2.85	0.27	40.7 (24)	50.0 (43)	46.2 (67)

\* Test for trend  $p = 0.04$

(OR = 1.9,  $p = 0.01$ ; insertive OR = 1.2,  $p = 0.40$ ) after controlling for partner type. EDM use was not associated with UAI regardless of sexual positioning. Data on UAI with partners in general in the past 12 months were not available.

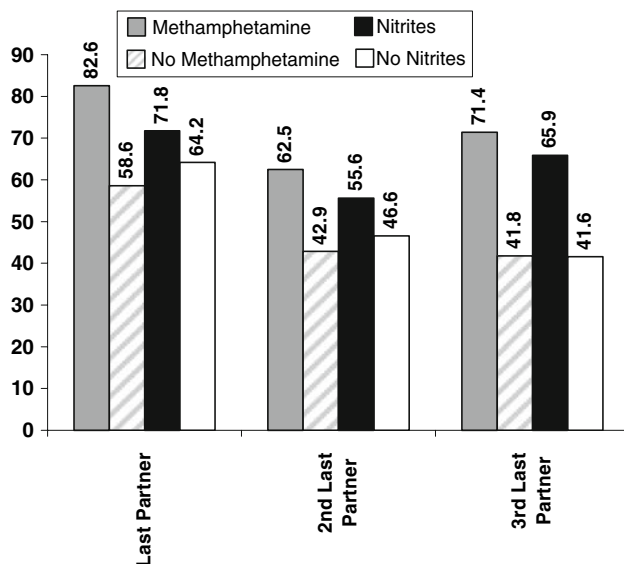
In multivariate models examining associations between HIV status and substance use as a single variable (i.e., no use vs. methamphetamine only vs. nitrites only vs. both nitrites and methamphetamine vs. other substances), cases were more likely to report use of nitrites (OR = 6.20,

$p = 0.03$ ), or both methamphetamine and nitrites (OR = 8.26,  $p = 0.01$ ), but not methamphetamine alone in the previous 12 months as compared to controls (Table 3). Additionally, compared to controls, cases were more likely to report use of both methamphetamine and nitrites (OR = 3.23,  $p = 0.03$ ), but not use of each of these substances alone with their last three partners. No interactions between methamphetamine and nitrite use were observed in models examining use with the last three partners or use in the past 12 months.

**Table 2** Associations between HIV status and substance use ( $n = 145$ )

Substance	Use in the previous 12 months			Use with the last three partners		
	AOR <sup>a</sup>	95% CI	<i>p</i> -value	AOR <sup>a</sup>	95% CI	<i>p</i> -value
Methamphetamine	2.33	1.1, 5.2	0.04	2.77	1.2, 6.6	0.02
Volatile nitrites	3.31	1.5, 7.4	<0.01	2.71	1.2, 6.2	0.02
MDMA	1.89	0.8, 4.5	0.15	1.09	0.3, 3.8	0.89
Ketamine	2.41	0.8, 7.7	0.14	2.13	0.2, 10.0	0.58
GHB	1.69	0.7, 3.9	0.22	1.71	0.6, 4.9	0.32
Cocaine	0.93	0.4, 2.1	0.86	1.15	0.4, 3.4	0.80
Marijuana	1.49	0.7, 3.3	0.33	1.70	0.7, 3.9	0.22
EDM	1.02	0.5, 2.3	0.96	0.80	0.3, 2.0	0.63

<sup>a</sup> AOR adjusted odds ratio for age, number of male partners in the previous 12 months, sexual activity with more than one partner at one time in the previous 12 month period, UAI with more than one of the last three partners, history of imprisonment, and recruitment in the last 18 months of study vs. the first 18 months



**Fig. 1** Percent of methamphetamine or volatile nitrites users compared to non-users reporting UAI with the last three partners ( $n = 145$ ). Asterisk indicates Associations between UAI and substance use calculated across all three partners using generalized estimating equations and controlling for partner type. GEE analyses indicate significant associations between methamphetamine use and UAI across the last three partners (OR = 3.1; 95% CI: (1.9, 5.0);  $p < 0.01$ ) and nitrite use and UAI across the last three partners (OR = 1.8; 95% CI: (1.1, 2.9);  $p = 0.01$ )

## Discussion

We found significant associations between recent HIV infection and nitrite use and recent HIV infection and methamphetamine use regardless of whether these substances were used during sexual activity with the last three partners or at any time during the previous 12 months. Additionally, cases were more likely to report UAI with

more than one of their last three partners than controls. UAI was associated with use of methamphetamine or nitrites with the last three partners regardless of case-control status, suggesting that use of these substances may increase the likelihood of UAI. Use of methamphetamine and nitrites in combination were most strongly associated with recent HIV infection. These associations persisted even though there were very few differences between recently HIV-infected MSM and those who recently tested HIV-negative. Additionally, there were no significant associations between HIV status and EDM use.

The results of this study are consistent with earlier studies. Among six studies that examined associations between HIV seroconversion and use of specific substances, five found significant associations between nitrite use during follow-up and HIV seroconversion (Buchbinder et al. 2005; Burcham et al. 1989; Chesney et al. 2005; Ostrow et al. 1995; Plankey et al. 2007), whereas two found no such association (Koblin et al. 2006; PageShafer et al. 1997). In the six studies that examined amphetamine use, five demonstrated significant associations between amphetamine use and HIV seroconversion (Burcham et al. 1989; Chesney et al. 2005; Koblin et al. 2006; PageShafer et al. 1997; Plankey et al. 2007). However, the remaining study only found such associations prior to adjusting for confounding (Buchbinder et al. 2005). Consistent with two earlier studies (Burcham et al. 1989; Koblin et al. 2006), we did not observe a significant association between recent HIV infection and cocaine use. In contrast, three longitudinal studies (Chesney et al. 2005; Ostrow et al. 1995; Plankey et al. 2007) reported significant associations between HIV seroconversion and cocaine use. These differences may be due in part to substance use trends by year or geographic region, or social–sexual networks surrounding use of certain substances. Additionally, we may have failed to detect an association due to insufficient



**Table 3** Adjusted odds ratios for associations between HIV status and use of methamphetamine, volatile nitrites, a combination of methamphetamine and volatile nitrites, and other substance use controlling for age, number of male partners in the previous12 months, sexual activity with more than one partner at one time in the previous 12 month period, UAI with more than one of the last three partners, history of imprisonment, and recruitment in the last 18 months of study vs. the first 18 months ( $n = 145$ )

	Previous 12 months			Last three partners		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Substances used						
None	REF			REF		
Methamphetamine only	3.42	0.60, 19.4	0.16	3.45	0.69, 17.2	0.13
Volatile nitrites only	6.20	1.20, 32.2	0.03	2.72	0.77, 9.61	0.12
Methamphetamine and volatile nitrites	8.26	1.86, 36.7	0.01	3.23	1.12, 9.34	0.03
Other substances	2.80	0.60, 13.2	0.19	0.89	0.29, 2.70	0.84
UAI with >1 partner among last three	2.68	1.18, 6.10	0.02	2.66	1.16, 6.07	0.02
Age	1.00	0.96, 1.05	0.91	1.00	0.96, 1.05	0.85
Imprisonment	0.24	0.09, 0.67	0.01	0.23	0.08, 0.63	<0.01
Number of male partners in the previous 12 months	1.00	0.99, 1.01	0.55	1.00	0.99, 1.01	0.85
>1 Partner during sex past 12 months	1.44	0.06, 3.45	0.41	1.68	0.69, 4.08	0.25
Recruitment in the last 18 months (vs. the first)	0.19	0.08, 0.49	<0.01	0.15	0.06, 0.38	<0.01

power, as a greater proportion of MSM reported cocaine use in previous studies (Chesney et al. 2005; Ostrow et al. 1995; Plankey et al. 2007). On the other hand, substances that have consistently shown no association with HIV seroconversion, such as marijuana (Burcham et al. 1989; Chesney et al. 2005; Koblin et al. 2006; Ostrow et al. 1995; PageShafer et al. 1997), were not associated with incident HIV infection in this study.

In addition to finding associations between recent HIV infection and methamphetamine or nitrite use, we also found associations between UAI and methamphetamine or nitrite use across the last three partners. These data suggest that methamphetamine or nitrite use during sexual activity may increase the risk of HIV through increasing the likelihood of UAI with high-risk partners. Previously, we demonstrated associations between UAI and methamphetamine use among recently infected MSM in this population using the individual as his own control (Drumright et al. 2006), thereby controlling for unmeasured factors (e.g., personality) that may confound associations.

When examined as a single substance use variable that included use of methamphetamine alone, nitrites alone, both methamphetamine and nitrites, or other substances, methamphetamine was not associated with HIV status. There are some potential explanations for the discrepancy between these findings and those demonstrating an association between recent HIV infection and methamphetamine in this study. The number of MSM reporting methamphetamine use only was small [( $n = 13$  with last three partners (9%),  $n = 17$  in previous 12 months (12%)]. The sample size was larger for nitrite use and even larger for use of both methamphetamine and nitrites, pointing to a

potential lack of power when stratifying by use of more than one substance. Additionally, it may be possible that individuals who practice polydrug use are more likely to engage in riskier sexual behaviors such as UAI (Colfax et al. 2005; Ostrow et al. 1993; Patterson et al. 2005), and use of nitrites and methamphetamine together could be representative of polydrug use in this sample. We recommend examining reasons for increased HIV risk among polydrug using MSM in future studies with larger sample sizes.

Surprisingly, we did not observe significant associations between EDM use and HIV status. Previous cross-sectional studies of MSM have demonstrated associations between sildenafil use and serodiscordant UAI (Brewer et al. 2006; Chu et al. 2003; Kim et al. 2002; Mansergh et al. 2006), and between sildenafil use and HIV prevalence (Chu et al. 2003; Paul et al. 2005; Sanchez and Gallagher 2006). However, recently infected and uninfected MSM in our cohort reported EDM use in similar proportions, suggesting that EDM use alone may not be a risk factor for HIV infection. This lack of association could be due to use of EDMs for various reasons including experimental one-time use, to assist in maintaining an erection while using condoms, or for higher risk sexual activity such as combining use with illicit substances. Additionally, only about half of MSM who reported EDM use in the previous year reported use with any of their last three partners, indicating infrequent use. In a recent study of risk factors for syphilis among MSM, sildenafil (Viagra) use in combination with methamphetamine, but not alone was associated with increased risk of syphilis (Wong et al. 2005), suggesting that associations between UAI and EDM use may be

confounded by other substance use. In our study there were no interactions between use of EDM and other substances with respect to HIV status.

Although efforts were made to minimize limitations, some may persist. When collecting data on socially sensitive information, there may be a non-differential bias in under-reporting sensitive behaviors. For this reason, CASI was used for data collection as it has been shown to increase reporting of socially sensitive information (Ghanem et al. 2005; Hewitt 2002; Kurth et al. 2004; Perlis et al. 2004; Rogers et al. 2005; Simoes et al. 2006) and may increase validity (Murphy et al. 2000; Paschall et al. 2001; van Griensven et al. 2006). Additionally, interviews were conducted after HIV diagnosis, which may increase the risk of recall bias wherein cases are more likely to overestimate exposure (Schlesselman 1982). Such bias was minimized by keeping participants unaware of the research questions. With any case-control study there is a concern that cases and controls differ with regard to factors that were not studied, however our cases and controls were comparable by demographics and sexual histories. Since this study was conducted in San Diego and only included MSM who were at high-risk for HIV, it may not be generalizable to all MSM.

Although our overall sample size was smaller than previous studies, this study reports on a greater number of recently HIV-infected MSM and demonstrates associations not only between recent HIV infection and substance use during the time period of infection, but also between recent HIV infection and substance use during sexual activity. This study provides evidence that use of methamphetamine or nitrites during sexual activity could increase the risk of HIV acquisition among MSM through potentially increasing UAI. These data are supported by other recent studies that indicate that MSM may be more likely to have UAI with serodiscordant partners when using nitrites (Brewer et al. 2006; Colfax et al. 2001) and methamphetamine (Brewer et al. 2006; Colfax et al. 2001; Morin et al. 2005). Additionally, this is the first case-control study that we are aware of that examines EDM use as a risk factor for recent HIV infection, demonstrating no significant associations. EDM use may be more likely to be associated with insertive anal intercourse than receptive (Mansergh et al. 2006), which may not carry as high of a risk for HIV acquisition as receptive anal intercourse (Buchbinder et al. 2005; Burcham et al. 1989; Koblin et al. 2006; PageShafer et al. 1997); however we did not observe greater likelihood of insertive anal intercourse or UAI with EDM use alone or in combination with any other substance in this sample of MSM. Further investigation into reasons for EDM use and variation in HIV risk among MSM by different patterns of usage is warranted.

**Acknowledgments** The authors would like to acknowledge and thank Tari Gilbert, Jacqui Pitt, Paula Potter, Joanne Santangelo, and the University of California, San Diego Antiviral Research Center staff for their support in data collection; and W. Susan Cheng for her assistance in data collection and management. Most of all we would like to thank our participants for volunteering for this study. Funding for this study was provided by: the National Institutes of Allergy and Infectious Diseases, grant # AI43638 (The Southern California Primary Infections Program) and grant # 5 T32 AI07384 (AIDS Training Grant); and the Universitywide AIDS Research Program, grant # ID01-SDSU-056; grant # IS02-SD-701; grant # D03-SD-400; and grant # F06-SD-258.

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