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ORIGINAL PAPER

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

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Abstract We examined how drugs, high-risk sexual behaviors, and socio-demographic variables are associated with recent HIV infection among men who have sex with men (MSM) in a case–control study. Interviewers collected risk factor data among 111 cases with recent HIV infection, and 333 HIV-negative controls from Chicago and Los Angeles. Compared with controls, cases had more unprotected anal intercourse (UAI) with both HIV-positive and HIV-negative partners. MSM with lower income or prior sexually transmitted infections (STI) were more likely to be recently HIV infected. Substances associated with UAI included amyl nitrate ("poppers"), methamphetamine, Viagra® (or similar PDE-5 inhibitors), ketamine, and gamma hydroxybutyrate (GHB). Cases more frequently used Viagra®, poppers, and methamphetamine during UAI compared with controls. In multivariate analysis, income, UAI with HIV-positive partners, Viagra®, and poppers remained associated with recent HIV seroconversion. Better methods are needed to prevent HIV among MSM who engage in high-risk sex with concurrent drug use.

Keywords Recent HIV infection · Men who have sex with men · Drug use · Viagra® · Poppers · Methamphetamine · Sexual risk behavior

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Introduction

Based on data from 33 states, 18,296 men who have sex with men (MSM) and 1,324 MSM who inject drugs accounted for 71% of male adults and adolescents, and 53% of all persons who received an HIV/AIDS diagnosis during 2005 in the United States (CDC 2007). In a study conducted in five cities between June 2004 and April 2005, HIV seroprevalence rates among urban MSM ranged from 18% to 40%, and seroincidence rates were 1.2–8.0% per year (CDC 2005). Approximately 60% of men living with HIV/AIDS are thought to have been infected via male-to-male sex (CDC 2007). Use of alcohol or other substances has been linked to sexual risk-taking behavior among MSM (Chesney et al. 1998; Colfax et al. 2005; Drumright et al. 2006a, b; Halkitis et al. 2005; Leigh and Stall 1993; Newman et al. 2004; Ostrow et al. 1993; Purcell et al. 2005a, b; Purcell et al. 2001; Stall and Purcell 2000; Stall et al. 2001; Thiede et al. 2003).

Methamphetamine is commonly used in conjunction with sexual risk-taking (Buchacz et al. 2005; Hirshfield et al. 2004; Molitor et al. 1998; Paul et al. 2005; Shoptaw et al. 2005; Thiede et al. 2008). In a longitudinal study of urban MSM, Koblin and her colleagues (Koblin et al. 2006) reported that use of amphetamines nearly doubled a study participant's chance of HIV seroconversion (hazard ratio of 1.96), but use of marijuana, poppers, hallucinogens, or cocaine or crack were not associated with seroconversion in multivariate analyses. Research has highlighted the risk-augmenting roles of other substances among MSM, including amyl nitrates or "poppers," (Buchbinder et al. 2005) and PDE-5 inhibitors such as Viagra® (Chu et al. 2003; Kim et al. 2002; Loeb 2004; Purcell et al. 2005a, b; Paul et al. 2005; Romanelli and Smith 2004; Swearingen and Klausner 2005).

Other studies have investigated varied combinations of drugs used in conjunction with sex among MSM (Mansergh et al. 2006; McNal and Remafedi 1999; Patterson et al. 2005; Plankey et al. 2007). Drugs may be used as precursors to sex or during sex and some individuals combine methamphetamine, poppers, PDE-5 inhibitors, and other substances (Catania et al. 2001; Patterson et al. 2005; Paul et al. 2005; Romanelli and Smith 2004). Concurrent use of multiple drugs may have complex and often harmful physiological or cognitive side effects, and enhance the likelihood of rapid partner change, and unprotected anal sex with serostatus unknown or HIV-seropositive partners (Chu et al. 2003; Kim et al. 2002; Loeb 2004). Purcell et al. (2005a, b) found that HIV-seropositive MSM who used Viagra® were more likely to have unprotected anal insertive or anal receptive sex, regardless of partner serostatus, compared with seropositive MSM who did not use Viagra®. Many substances impair judgment and memory, and reduce behavioral inhibitions, which in turn may increase HIV exposure and transmission (Kim et al. 2002). MSM report that they mix drugs to obtain a better "high," enhance sexual pleasure, increase their perceived energy level, take the edge off methamphetamine, or compensate for erectile problems associated with methamphetamine use (Patterson et al. 2005).

While it is clear that non-injection substance use may be an important contributor to on-going high HIV incidence and prevalence among MSM in the United States, it often has been challenging for studies with cross-sectional designs to ascertain how use of specific drugs is related to HIV seroincidence among MSM, especially when controlling for sex behaviors and other potential HIV risk factors (Koblin et al. 2006; Plankey et al. 2007). Also, many prior investigations have used data from samples that included mixtures of individuals who recently acquired HIV, pooled together with others who had been infected in the distant past. It also has been difficult to unambiguously determine whether use of a specific drug is associated with existing HIV prevalence, or is a risk factor for acquisition of new infection. However, advances in HIV testing have made it easier to distinguish individuals with evidence of recent HIV infection from persons infected at an unknown time in the past (Janssen et al. 1998; Kothe et al. 2003; Rawal et al. 2003). By using these assays, it is possible to design studies that can identify factors associated with recent HIV infection (Thiede et al. 2008).

The purpose of this paper is to evaluate whether specific drugs (including methamphetamine, poppers, PDE-5 inhibitors such as Viagra®, and other substances) used in conjunction with sex may be associated with recent HIV seroconversion among MSM after controlling for other known HIV risk factors, such as engaging in UAI or having a history of other sexually transmitted infections (STI). Data were obtained as part of the "Context of HIV Infection Project" (CHIP), sponsored by the federal Centers for Disease Control and Prevention (CDC). The study was carried out in partnership with the local health departments in Chicago and Los Angeles.

Methods

Study Design, Eligibility and Recruitment

Our sample was drawn from the population of adult males residing in Chicago or Los Angeles, and was limited to biological males who reported ever having sex with another male regardless of their self-identified sexual orientation or gender identity (gay, bisexual, transgender, etc.). We used a matched retrospective case–control study design to identify risk factors associated with acquiring recent HIV infection among the MSM participants (Schlesselman 1982). To efficiently maximize statistical power, three controls residing in the same city were matched to each case. All cases and controls were recruited from the same set of HIV testing locations within each city, which included public HIV testing sites, STI clinics, public and private clinics, hospitals, community-based organizations, and prisons/jails. MSM participants with evidence of recent HIV infection served as the cases, and HIV-seronegative participants were controls. In addition to being an MSM, other case inclusion criteria were that the man was $\geq$ 18 years of age, received their HIV test from participating facilities, and had evidence of recent HIV seroconversion by either having a positive HIV test combined with a non-reactive HIV-1 LS-EIA (less sensitive enzyme immunoassay; Vironostika-LS EIA; bioMérieux, Raleigh, NC) (Janssen et al. 1998; Kothe et al. 2003; Rawal et al. 2003), or by having an otherwise verified HIV-negative test within 12 months prior to their current positive test. MSM who had evidence of acquiring HIV in the more distant past were not classified as "recent," and were

not eligible to be cases in our study. Controls met identical eligibility criteria, except they had an HIV-seronegative test result at the time of enrollment. Written informed consent was obtained prior to data collection, and financial reimbursement was provided to help compensate participants for their time (reimbursements ranged from $50 to $90 per respondent, depending upon the city and data collection components completed). After screening potential study participants, a total of 444 eligible MSM were recruited for this study. They included 111 MSM cases classified with recent HIV seroconversion, along with 333 HIV-seronegative MSM controls.

Data Collection and Variables Used

HIV serostatus was documented for each case and control, and served as our primary outcome measure. Data on potential risk factors were obtained from all study participants via a structured responses questionnaire administered by trained staff during face-to-face interviews. It assessed the respondents' socio-demographic characteristics; sexual behaviors; alcohol or drug use patterns; STIs; access to healthcare; and HIV testing and counseling experiences. The questionnaire was administered during an appointment that was scheduled after the respondents had learned their HIV test results and had received post-test counseling. Responses were entered into a computer database and verified for accuracy prior to analysis.

Sex risk was characterized as the reported number of HIV-positive and HIV-negative partners with whom respondents recalled having had unprotected anal intercourse (UAI) in the 6 months prior to receiving their HIV test result. Anal intercourse could include being the receptive partner, penetrative partner, or both. Among respondents who reported a history of having one or more STIs in their lifetime (excluding HIV), we assessed the total number of STIs of any type previously diagnosed by their health-care provider. Drug and alcohol risk factors include reported alcohol, poppers, methamphetamine, ketamine, GHB, Viagra®, marijuana, cocaine, ecstasy, LSD, or heroin use by the respondent at least once during UAI in the past 6 months prior to their HIV diagnosis.

Statistical Analysis

We compared socio-demographic characteristics, sexual risk behavior, and drug use while having UAI of recently HIV-infected cases versus HIV-negative controls using Fisher's exact test. Drug use correlations were estimated using Kendall's tau-b coefficient. Statistically significant variables in univariate analyses ($P < .05$) were retained for subsequent multivariate analysis after we examined collinearity among them by computing Nagelkerke's pseudo R-squared and variance inflation factor scores (VIF) (Kleinbaum 2002; Nagelkerke 1991). VIF values ranged from 1.09 to 1.63 for the socio-demographic, sex risk behavior, and drug use during UAI variables, which indicated that although collinearity existed, it was not enough of a problem to preclude use of these variables to develop reliable logistic regression models with statistically significant estimates. To calculate adjusted odds ratio estimates and 95% confidence intervals [CI], these variables were entered into multivariate conditional logistic regression models to determine which were independently associated with recent HIV infection, while simultaneously adjusting for the other covariates. Wald statistics and their corresponding p-values were computed to assess the statistical significance for the adjusted odds ratios and regression coefficients in the models, using a cut-off $P < .05$. To help verify the consistency of the results, multiple alternative models were developed and compared. This allowed us to examine different plausible combinations of covariates, as well as to highlight the associations of specific drugs with recent HIV seroconversion after controlling for other variables. To assess the overall goodness-of-fit of these models, likelihood ratio tests were calculated for the joint statistical significance of the covariates included in each model compared with the null, with a cut-off $P < .05$. Models were rejected if they did not meet these criteria. All the models presented in this paper are statistically rigorous and met these criteria; they also parsimoniously reflect the substantive conclusions obtained from examining our larger set of alternative models. Analyses were conducted using SPSS software, version 14.0 (Chicago, IL).

Results

Study Population

To better understand how our sample was similar or different from MSM in other U.S. cities, we compared the demographic composition of our sample of 444 MSM with a larger sample obtained through CDC's National HIV Behavioral Surveillance System (Sanchez et al. 2006). The national sample's data were gathered during a similar period (November 2003 through April 2005) as our study (February 2003 through March 2005). The national sample included 10,030 MSM aged $\geq$ 18 years, residing in 15 metropolitan statistical areas including Chicago and Los Angeles. In terms of race/ethnicity, there were no statistically significant differences except that our respondents more frequently described their race/ethnicity as "other" compared with the national sample (4% vs. 2%; $t_{(461)} = 2.30$, $P < .05$). In regard to age, there were no statistically significant differences except that our sample tended to include a slightly higher proportion of younger individuals

in the 18–24 year category compared with the national sample (26% vs. 22%; $t_{(478)} = 1.94$, $P < .06$). We also had fewer MSM in the 45–54 year age group (6% vs. 10%; $t_{(509)} = 3.68$, $P < .001$), and fewer older individuals $\geq$ 55 years (1% vs. 4%; $t_{(553)} = 4.06$, $P < .001$). No statistically significant differences were found for educational attainment between the two samples. To the extent that the national surveillance sample is typical of MSM at potential risk for HIV living in U.S. urban areas, and with respect to these specific variables, our study sample appears largely representative of the urban MSM population in the United States.

Table 1 shows no statistically significant differences between cases and controls for most socio-demographic variables, including age, employment status, race/ethnicity, or level of education. However, cases more often reported lower annual household income ($P < .01$, Fisher's exact test).

Sexual Risk Behavior, Drug Use, and Recent HIV Seroconversion

As also seen in Table 1, cases more frequently reported having one or more HIV-positive and HIV-negative partners with whom they had UAI in the past 6 months ($P < .01$, and $P < .05$, Fisher's exact test), and cases more often reported having one or more previously diagnosed STI ($P < .01$, Fisher's exact test). Overall, respondents frequently reported using alcohol (61.7%), poppers (28.8%), marijuana (25.9%), methamphetamine (15.8%), and Viagra® (15.3%). Except for alcohol and marijuana, cases more often used these substances during UAI compared with HIV-negative controls ($P < .01$, Fisher's exact test). Other drug use (GHB, ketamine, cocaine, ecstasy, LSD, and heroin) was infrequent.

Drug Use by Socio-demographic Characteristics and Recent HIV Status

Looking first at cases (Table 2), users of methamphetamine during UAI tended to be more common in Los Angeles, among whites, and among those with at least some college education (all these associations were statistically significant). Methamphetamine, ketamine- and GHB-using cases were more likely to report UAI with one or more HIV-seropositive and HIV-negative partners during the past 6 months. As with the methamphetamine pattern, Viagra® use during UAI among cases was more common in Los Angeles, and among whites, those with some college education, and those reporting UAI with one or more HIV-seropositive partners during the past 6 months. Likewise, cases that used poppers during UAI tended to be white, and to have had some college education. Table 2 also shows that controls who used alcohol during sex tended to be younger ($\leq$30 years of age); and more likely to have some college education. Controls who used methamphetamine during UAI tended to be from Los Angeles, worked part-time or less, tended to have UAI with partners they thought were HIV-negative, and had one or more previously diagnosed STI. GHB-using controls typically were white, and had one or more prior STI. Controls who reported Viagra® use during UAI generally were older MSM, white, had UAI with one or more HIV-seropositive partner in the past 6 months, and had one or more previous STI. Popper-using controls also tended to be white, and to have had one or more prior STIs.

Association among Drugs Used during UAI

Table 3 shows inter-correlations among the cases (matrix to upper right of diagonal) and controls (matrix to lower left of diagonal) for alcohol and the five drugs that were found significantly associated with recent HIV seroconversion in Table 1. Overall, the magnitudes of the associations shown in Table 3 tended to be larger among the cases compared with the controls, and MSM with recent HIV infection tended to report using a wider array of substances during UAI compared with HIV-negative controls.

Univariate and Multivariate Analyses

The first column in Table 4 shows unadjusted odds ratios for the three most commonly used drugs during UAI (methamphetamine, Viagra®, and poppers) that had statistically significant univariate associations. Unadjusted odds ratios also are shown for other socio-demographic and the two UAI variables (see Table 1 discussion). Statistically significant crude odds ratios shown in Table 4 include: annual household income less than $25,000 (OR = 1.79, 95% CI = 1.14, 2.83, $P < .01$), as well as methamphetamine use during UAI (OR = 3.13, 95% CI = 1.78, 5.52, $P < .001$), Viagra® use during UAI (OR = 4.51, 95% CI = 2.55, 8.02, $P < .001$), and popper use during UAI (OR = 3.14, 95% CI = 1.95, 5.07, $P < .001$) at least once in the last 6 months. UAI with one or more partners known to be HIV-negative (OR = 1.68, 95% CI = 1.07, 2.65, $P < .05$) as well as UAI with one or more HIV-positive partners (OR = 5.96, 95% CI = 2.80, 12.79, $P < .001$) in the past 6 months had strong crude associations with seroconversion.

Conditional logistic regression was used to estimate adjusted odds ratios for these three drugs with seroconversion, while controlling for other socio-demographic and UAI variables. City of residence (Chicago versus Los Angeles) was controlled through the matched case–control design. To highlight the effects of the drugs used during UAI when adjusting for different sets of covariates, three alternative models are shown in Table 4: Model 1 shows adjusted odds

Table 1 Socio-demographic characteristics, drugs used during UAI in past 6 months, and sexual risk behaviors of MSM by HIV seroconversion status (Chicago and Los Angeles, 2003–2005)

Variables	CHIP MSM sample (Total $N = 444$)						
	Total		Recent HIV + Men ($N = 111$)		HIV − Men ($N = 333$)		P[a]
	No.	%	No.	%	No.	%	
Matched groups							
Site							
Chicago	224	(50.5)	56	(50.5)	168	(50.5)	N/A
Los Angeles	220	(49.5)	55	(49.5)	165	(49.5)	
Socio-demographic							
Age category							
>30	233	(52.5)	64	(57.7)	169	(50.8)	NS
≤30	211	(47.5)	47	(42.3)	164	(49.2)	
Work situation/past 6 months							
Fulltime	241	(54.3)	67	(60.4)	174	(52.3)	NS
Less than full time	203	(45.7)	44	(39.6)	159	(47.7)	
Household income							
<$25,000	190	(43.3)	60	(54.1)	130	(39.6)	<.01
≥$25,000	249	(56.7)	51	(45.9)	198	(60.4)	
Race/ethnicity							
White/Caucasian	187	(42.1)	48	(43.2)	139	(41.7)	NS
Hispanic/Latino	120	(27.0)	29	(26.1)	91	(27.3)	
Black/African American	74	(16.7)	21	(18.9)	53	(15.9)	
Asian/Asian American	21	(4.7)	5	(4.5)	16	(4.8)	
Other	42	(9.5)	8	(7.2)	34	(10.2)	
Education							
Some college or more	315	(71.1)	77	(70.0)	238	(71.5)	NS
Less than college	128	(28.9)	33	(30.0)	95	(28.5)	
Respondent sex risk behaviors[b]							
No. HIV − partners UAI (past 6 months)							
None	235	(52.9)	48	(43.2)	187	(56.2)	<.05
1 or More	209	(47.1)	63	(56.8)	146	(43.8)	
No. HIV + partners UAI (past 6 months)							
None	407	(91.7)	88	(79.3)	319	(95.8)	<.001
1 or More	37	(8.3)	23	(20.7)	14	(4.2)	
Number of prior STIs (≥ 1)							
Yes	216	(48.6)	70	(63.1)	146	(43.8)	<.001
No	228	(51.4)	41	(36.9)	187	(56.2)	
Drug use at least once in past 6 months during UAI[c]							
Alcohol							
Yes	272	(61.7)	68	(61.3)	204	(61.8)	NS
No	169	(38.3)	43	(38.7)	126	(38.2)	
Methamphetamine							
Yes	70	(15.8)	32	(28.8)	38	(11.4)	<.001
No	373	(84.2)	79	(71.2)	294	(88.6)	
Ketamine							
Yes	8	(1.8)	7	(6.3)	1	(.3)	<.01
No	436	(98.2)	104	(93.7)	332	(99.7)	

Table 1 continued

Variables	CHIP MSM sample (Total $N = 444$)						
	Total		Recent HIV + Men ($N = 111$)		HIV − Men ($N = 333$)		P[a]
	No.	%	No.	%	No.	%	
GHB							
Yes	25	(5.7)	13	(11.7)	12	(3.6)	<.01
No	417	(94.3)	98	(88.3)	319	(96.4)	
Viagra							
Yes	68	(15.3)	36	(32.4)	32	(9.6)	<.001
No	376	(84.7)	75	(67.6)	301	(90.4)	
Poppers							
Yes	128	(28.8)	53	(47.7)	75	(22.5)	<.001
No	316	(71.2)	58	(52.3)	258	(77.5)	
Marijuana							
Yes	115	(25.9)	31	(27.9)	84	(25.2)	NS
No	329	(74.1)	80	(72.1)	249	(74.8)	
Cocaine							
Yes	50	(11.3)	15	(13.5)	35	(10.5)	NS
No	394	(88.7)	96	(86.5)	298	(89.5)	
Ecstasy							
Yes	22	(5.0)	7	(6.3)	15	(4.5)	NS
No	422	(95.0)	104	(93.7)	318	(95.5)	
LSD							
Yes	2	(.5)	0	(.0)	2	(.6)	NS
No	442	(99.5)	111	(100.0)	331	(99.4)	
Heroin							
Yes	4	(.9)	1	(.9)	3	(.9)	NS
No	440	(99.1)	110	(99.1)	330	(99.1)	

[a] Fisher's exact test

[b] Data on UAI with unknown serostatus partners not included (not available in dataset)

[c] 2 × 2 Table's sample sizes may not add to total due to missing values. "Past 6 months" refers to the period prior to receiving their HIV test result (either HIV-positive or HIV-negative)

ratios (AOR) for methamphetamine, Viagra®, and poppers during UAI, after controlling for the socio-demographic variables. Model 2 is the same as Model 1, except that it also adjusts for UAI with 1 or more HIV-*negative* partners during the past 6 months. Finally, Model 3 includes the same set of covariates as Model 1, but adds UAI with 1 or more HIV-*positive* partners in the past 6 months.

Model 1 in Table 4 indicates that reported methamphetamine use at least once during UAI in the past 6 months was no longer significantly associated with HIV seroconversion after adjusting for the other covariates. However, employment situation, household income, Viagra® use during UAI, and poppers use during UAI remained statistically significant variables in Model 1. The crude effect of methamphetamine disappears.

Model 2 presents the association of all three substances at least once during UAI in the past 6 months with HIV status while controlling for UAI with HIV-negative partners (Table 4). In this scenario, Viagra® and poppers continue to remain associated with recent HIV infection after controlling for UAI with HIV-negative partners, and the socio-demographic covariates (age, employment, income, race/ethnicity, and education. However, the magnitude of the AOR for Viagra® (AOR = 2.56, 95% CI = 1.15, 5.70, $P < .01$) and poppers (AOR = 2.04, 95% CI = 1.07, 3.85, $P < .05$) decrease compared with their unadjusted OR (see point estimates and CI above, 4.51 and 3.14, respectively). Household income remained statistically significant in Model 2 (AOR = 2.05, 95% CI = 1.10, 3.81, $P < .05$). Model 3 shows the AOR for methamphetamine, Viagra® and poppers while adding UAI with one or more HIV-positive partners. In this final model, the AOR for Viagra® and poppers (AOR = 2.16, 95% CI = .96, 4.90, $P < .06$ vs. AOR = 1.87, 95% CI = .99, 3.52,

Table 2 Socio-demographic characteristics of MSM by drugs Use during UAI in the past 6 months and by HIV seroconversion status (Chicago and Los Angeles, 2003–2005)

Variables	No. (%) of CHIP MSM sample ($N = 444$)[a]											
	Recent HIV + Men ($N = 111$)						HIV − Men ($N = 333$)					
	Alcohol No. (%)	Meth. No. (%)	Ketamine No. (%)	GHB No. (%)	Viagra No. (%)	Poppers No. (%)	Alcohol No. (%)	Meth. No. (%)	Ketamine No. (%)	GHB No. (%)	Viagra No. (%)	Poppers No. (%)
Socio-demographics												
Site												
Chicago	33(58.9)	11(19.6)*	1(1.8)	4(7.1)	12(21.4)**	29(51.8)	103(62.0)	13(7.8)*	1(.6)	8(4.8)	19(11.3)	43(25.6)
Los Angeles	35(63.6)	21(38.2)	6(10.9)	9(16.4)	24(43.6)	24(43.6)	101(61.6)	25(15.2)	0(0)	4(2.4)	13(7.9)	32(19.4)
Age category												
>30	41(64.1)	20(31.3)	4(6.3)	5(7.8)	24(37.5)	33(51.6)	93(56.0)*	22(13.1)	0(0)	7(4.2)	24(14.2)**	36(21.3)
≤30	27(57.4)	12(25.5)	3(6.4)	8(17.0)	12(25.5)	20(42.6)	111(67.7)	16(9.8)	1(.6)	5(3.0)	8(4.9)	39(23.8)
Work situation												
Full-time	43(64.2)	18(26.9)	3(4.5)	7(10.4)	23(34.3)	31(46.3)	108(62.8)	14(8.1)*	0(0)	7(4.1)	14(8.0)	38(21.8)
Part-time/ less	25(43.2)	14(31.8)	4(9.1)	6(13.6)	13(29.5)	22(50.0)	96(60.8)	24(15.1)	1(.6)	5(3.1)	18(11.3)	37(23.3)
Household Income												
<$25,000	39(65.0)	18(30.0)	5(8.3)	5(8.3)	20(33.3)	27(45.0)	75(57.7)	19(14.6)	0(0)	3(2.3)	11(8.5)	26(20.0)
≥$25,000	29(56.9)	14(27.5)	2(3.9)	8(15.7)	16(31.4)	26(51.0)	128(65.6)	18(9.1)	1(.5)	9(4.6)	21(10.6)	49(24.7)
Race/ethnicity												
White	33(68.8)	20(41.7)**	5(10.4)	10(20.8)	22(45.8)**	29(60.4)**	90(65.2)	16(11.6)	1(.7)	9(6.6)*	21(15.1)**	41(29.5)**
Other	35(55.6)	12(19.0)	2(3.2)	3(4.8)	14(22.2)	24(38.1)	114(59.4)	22(11.3)	0(0)	3(1.5)	11(5.7)	34(17.5)
Education												
<College	17(51.5)	4(12.1)**	1(3.0)	2(6.1)	3(9.1)***	10(30.3)*	50(53.2)*	11(11.6)	0(0)	1(1.1)	7(7.4)	18(18.9)
≥College	50(64.9)	28(36.4)	6(7.8)	11(14.3)	33(42.9)	42(54.5)	154(65.3)	27(11.4)	1(.4)	11(4.7)	25(10.5)	57(23.9)
Sex risk behaviors												
HIV − partners UAI												
No	26(38.2)	6(18.8)***	2(28.6)	4(30.8)	9(25.0)**	16(30.2)**	97(47.5)***	15(39.5)*	0(0)	4(33.3)	12(37.5)*	32(42.7)**
Yes	42(61.8)	26(81.3)	5(71.4)	9(69.2)	27(75.0)	37(69.8)	107(52.5)	23(60.5)	1(100)	8(66.7)	20(62.5)	43(57.3)
HIV + partners UAI												
No	51(64.6)	17(21.5)***	3(3.8)*	3(3.8)***	23(29.1)*	35(44.3)	136(71.2)	27(14.2)	1(.5)	8(4.2)	21(11.0)**	53(27.7)
Yes	13(56.5)	14(60.9)	4(17.4)	9(39.1)	12(52.2)	15(65.2)	8(57.1)	4(28.6)	0(0)	2(14.3)	7(50.0)	5(35.7)
No. Prior STIs (≥1)												
Yes	41(58.6)	24(34.3)	7(10.0)	10(14.3)	26(37.1)	38(54.3)	90(62.5)	25(17.1)**	1(.7)	10(6.8)**	22(15.1)**	45(30.8)**
No	27(65.9)	8(19.5)	0(0)	3(7.3)	10(24.4)	15(36.6)	114(61.3)	13(7.0)	0(0)	2(1.1)	10(5.3)	30(16.0)

Note: drug use was defined as having used any drug with sex at least once in the past 6 months prior to the HIV test/diagnosis. Percentages correspond to "Yes" responses from total number of participants in that particular variable category.

[a] 2 × 2 Table's sample sizes may not add to total due to missing values. Data on UAI with unknown serostatus partners not included (not available in dataset)

* $P < .05$; ** $P < .01$; *** $P < .001$, Fisher's exact test

Table 3 Correlations of drugs used at least once during UAI in the past 6 months among MSM with recent HIV infection ($N = 111$; top matrix) and HIV-negative MSM ($N = 333$; bottom matrix) in Chicago and Los Angeles, 2003–2005

Variables	1	2	3	4	5	6
1. Alcohol		.01	.05	.06	.19*	.20*
2. Methamphetamine	.05		**.40****	**.57****	**.45****	**.38****
3. Ketamine	.04	.15**		**.48****	.13	.19*
4. GHB	.05	**.48****	.28**		.28**	.26**
5. Viagra (Viagra®)	.11*	**.34****	.16**	**.38****		**.41****
6. Poppers	.23**	.21**	.10	.28**	.21**	

Note: Non-parametric Kendall's tau-b was estimated for dichotomous variables. Moderate associations >.30 are highlighted in bold for visual emphasis

* $P < .05$; ** $P < .01$, rank independence test

$P < .06$ respectively) closely approached statistical significance. Household income (AOR = 2.10, 95% CI = 1.12, 3.91, $P < .01$) and the UAI with HIV-seropositive partners (AOR = 3.01, 95% CI = 1.14, 7.92, $P < .01$) also are associated with seroconversion. Finally, we added the history of having one or more sexual transmitted infections (STIs) variable to all three models, but it was not associated with recent HIV seroconversion after adjusting for the other variables (data not shown in Table 4).

Discussion

In our case–control study, we examined how drug use and sexual risk behaviors were associated with recent HIV seroconversion among MSM in Chicago and Los Angeles. Our sample likely was typical of higher-risk MSM who seek services at common HIV testing venues. Many of our participants were relatively well-educated, but low-to-medium income individuals, with diverse racial/ethnic backgrounds. Our sample tended to be slightly younger than a contemporaneous HIV behavioral surveillance sample of urban MSM throughout the United States (Sanchez et al. 2006). Consistent with many prior studies, our investigation documented high use of drugs during UAI by MSM,

Table 4 Crude and adjusted odds ratios for variables associated with recent HIV seroconversion among MSM ($N = 444$) (Chicago and Los Angeles, 2003–2005)

Risk factors (higher risk category listed)	Crude OR (95% CI)	Model 1[a] Adjusted OR (95% CI)	Model 2[a] Adjusted OR (95% CI)	Model 3[a] Adjusted OR (95% CI)
Age				
>30	1.32 (.84–2.09)	1.17 (.70–1.95)	1.28 (.70–2.35)	1.24 (.66–2.30)
Work situation/past 6 months				
Full-time	1.39 (.88–2.21)	**1.81 (1.08–3.04)***	1.73 (.94–3.19)	1.78 (.97–3.29)
Household income				
<$25,000	**1.79 (1.14–2.83)****	**2.00 (1.18–3.37)****	**2.05 (1.10–3.81)***	**2.10 (1.12–3.91)****
Race/ethnicity				
White	1.06 (.67–1.68)	.80 (.48–1.33)	1.02 (.54–1.92)	.89 (.47–1.68)
Education				
Less than College	1.07 (.67–1.77)	1.18 (.66–2.11)	1.09 (.55–2.17)	1.24 (.62–2.49)
HIV-negative UAI partners (past 6 months)				
1 or More	**1.68 (1.07–2.65)***	Not included	1.72 (.92–3.19)	Not included
HIV-positive UAI partners (past 6 months)				
1 or More	**5.96 (2.80–12.79)*****	Not included	Not included	**3.01 (1.14–7.92)****
Methamphetamine use during UAI (past 6 months)				
Yes	**3.13 (1.78–5.52)*****	1.66 (.84–3.29)	1.00 (.45–2.19)	.95 (.42–2.16)
Viagra use during UAI (past 6 months)				
Yes	**4.51 (2.55–8.02)*****	**3.02 (1.54–5.93)****	**2.56 (1.15–5.70)****	2.16 (.96–4.90)[†]
Poppers use during UAI (past 6 months)				
Yes	**3.14 (1.95–5.07)*****	**1.90 (1.13–3.22)***	**2.04 (1.07–3.85)***	1.87 (.99–3.52)[†]

* $P < .05$; ** $P < .01$; *** $P < .001$ chi-square test. Statistically significant associations highlighted in bold. [†] $P < .06$ for these two AOR

[a] These three models are intended to highlight the effects of methamphetamine, Viagra, and poppers when alternative sets of covariates are simultaneously included and adjusted for

Model 1: Both UAI variables are excluded

Model 2: Includes UAI with 1 or more HIV-*negative* partners during the past 6 months

Model 3: Includes UAI with 1 or more HIV-*positive* partners during the past 6 months

particularly among MSM with recent HIV infection, in the 6 months prior to their HIV diagnosis. Methamphetamine, Viagra®, and popper use appeared especially frequent, although other drugs such as ketamine and GHB also were associated with HIV seroconversion at the crude level. Not surprisingly, and as in prior research, our data re-emphasize that MSM who engage in high-risk sexual behaviors, such as UAI with an HIV-seropositive partners, appear to be at much greater risk for HIV infection.

A troubling aspect of our results concerns the on-going high rates of substances used during UAI. Both HIV-seronegative controls and seropositive cases use a diverse range of substances, and both cases and controls reported UAI while under their influence. Our cases and controls were drawn from MSM that had personally decided to seek HIV testing, perhaps because they correctly perceived themselves as engaging in high-risk sex and drug-related activities.

However, not all subgroups tended to use the same types or combinations of substances. For example, methamphetamine and Viagra® use during UAI tended to be more prominent among HIV-positive MSM in Los Angeles compared with HIV-positive MSM in Chicago. White MSM, regardless of their HIV serostatus, reported greater use of Viagra® and poppers with sex compared with other ethnic/racial groups, which is a pattern noted in other studies (Hirshfield et al. 2004; Stall and Purcell 2000). Some other substances, such as alcohol or marijuana, were frequently used during UAI, but there were no differences in usage between cases and controls (Stall et al. 2001, 2003).

Because substance use is not evenly distributed by socio-demographic subgroup or by city, we speculate that if our study had been conducted elsewhere, we might have observed different drug use-related risk factors associated with recent HIV seroconversion. In prior studies of substance use among MSM, it has not been easy to determine whether non-IDU drug use itself was directly linked with increased risk of becoming infected with HIV, or if it was a proxy indicator of other high-risk sexual behaviors (such as UAI) that more directly may lead to viral exposure or transmission (Paul et al. 2005; Plankey et al. 2007; Rosen et al. 2006; Shoptaw and Reback 2007; Strathdee and Sherman 2003). Analyses are further complicated because some substances (most obviously PDE-5 inhibitors such as Viagra®) may be consciously used by MSM to facilitate high-risk sexual behaviors (Rosen et al. 2006).

Because of the complex relationships between sex behaviors, drug use, and socio-demographic characteristics, we attempted to disentangle the relative effects of these variables on HIV seroconversion through development and comparison of a series of alternative logistic regression models. Several interesting findings emerged. First, regardless of the set of covariates that were controlled for in the different models, annual income consistently remained a statistically significant factor associated with recent HIV seroconversion. Lower income MSM were at elevated risk, even after adjusting for all the other socio-demographic, drug use, and UAI variables. Given that our sample's median income was approximately $25,000 per year, it is very easy to imagine that many of the MSM in our sample faced serious economic challenges due to high cost of living in Chicago and Los Angeles. Men with the lowest incomes also were more likely to be HIV infected compared with higher-income respondents.

As in numerous prior studies, we observed strong crude associations between HIV seroconversion and drug use during high-risk UAI, particularly for methamphetamine, Viagra®, and poppers. Not only were recently infected MSM more frequent users of drugs during sex, they also used a wider array of substances. However, several more interesting findings appeared after we examined adjusted odds ratios. First, the initial strong crude association between methamphetamine and HIV seroconversion disappeared in all our multivariate models. This likely is because methamphetamine users tended to engage in more unprotected anal sex with HIV-seropositive partners. In essence, methamphetamine use was a proxy marker for persons engaged in the highest risk sexual activities, which in turn put them at direct risk for HIV infection. For similar reasons, the adjusted associations for popper and Viagra® use with seroconversion declined compared with initially high crude associations, but not to the same extent as for methamphetamine.

Our findings are consistent with other studies. For example, after adjusting for similar covariates in a longitudinal cohort study, Plankey et al. (2007) observed decreases in the magnitudes of association of methamphetamine and popper use with HIV seroconversion among MSM, although the adjusted associations retained statistical significance, probably because they had a much larger sample which would enhance statistical power for detecting small associations ($n = 4{,}003$). Likewise, Celentano et al. (2006) reported modest magnitudes of association (ORs = 1.2–1.9) between unprotected insertive or receptive anal sex while under the influence of alcohol, marijuana, amphetamines, poppers, or cocaine at least once during a 6 month recall period among MSM aged 15–22 years from the Young Men's Survey. In a review of 14 MSM studies, Swearingen and Klausner (2005) found that use of PDE-5 inhibitors like Viagra® was associated with increased chances of UAI with partners of unknown or serodiscordant status (OR range = 2.0–5.7), as well as being associated with increased chances of STI and HIV infection (OR range = 1.92–2.5).

Taken together, our findings suggest that use of substances—particularly PDE-5 inhibitors like Viagra® or poppers—during anal intercourse likely is associated with

elevated odds of recent HIV seroconversion. The link between drug use and high-risk sex might be thought of as an example of a "syndemic," or cluster, of co-occurring risk-behaviors and health problems (Shoptaw and Reback 2007; Stall and Purcell 2000; Stall et al. 2003). Drug use may facilitate sexual risk-taking behaviors, which in turn directly exposes MSM to HIV; these patterns may be especially pronounced among low-income MSM. In addition, for some groups of MSM, both substance use and sexual risk-taking may be associated with other underlying variables such as sensation seeking (Benotsch et al. 2005; Mustanski 2008). Further studies are needed to explore how these or other proximate and underlying determinants may be associated with recent HIV seroconversion among MSM living in different conditions (Boerma and Weir 2005; MacDonald et al. 2008).

Limitations to our investigation should be noted. First, it is possible that persons with recent HIV infection occasionally may be misclassified by the LS-EIA assay (Kothe et al. 2003; Rawal et al. 2003). Second, some respondents may have had difficulty in accurately recalling past events, including some that may have occurred while they were under the influence of one or more substances. However, these limitations are mitigated because these types of misclassification would be non-differential or random, which would bias our odds ratio magnitudes toward the null (Schlesselman 1982). In other words, our findings are statistically conservative. A strength of our sample is that it is comparable to urban MSM living elsewhere in the United States engaging in high-risk sex (Sanchez et al. 2006). But our findings may not be applicable to persons with non-recent HIV infection, recently-infected persons who have not sought HIV testing services, or uninfected MSM who do not seek testing. We found variation in drug use by city and socio-demographic subgroups, which would affect generalizability to other MSM groups elsewhere who use other drugs. Despite these limitations, our use of case–control methods provided an excellent opportunity for controlling for confounders, as well as for exploring associations between high risk behaviors and recent HIV infection. Another strength was that we successfully developed several statistically reliable multivariate models that provided internally consistent substantive results, and our findings complement and augment prior related research.

Future research should explore how use of Viagra®, poppers, methamphetamine, or other combinations of drugs affect the risk of HIV infection among MSM (Drumright et al. 2006a, b; Plankey et al. 2007). Viagra® commonly is used to counter the undesirable effects of other drugs (Celentano et al. 2006; Purcell et al. 2005a, b; Strathdee and Sherman 2003). Viagra® and popper users may have anal sex for longer periods with more partners, thereby increasing their chance for HIV viral exposure. An unintended consequence is that effects of some drugs may enhance mucosal susceptibility or facilitate anal trauma, making HIV infection upon exposure more likely. Moreover, use of stimulants may increase arousal, as well as contribute to behavioral disinhibitions, poor decision-making, or other cognitive states (e.g., perceived escape from HIV-related or general life stressors). This may preclude safety concerns, such as condom use or avoiding sex with HIV-seropositive partners (Giancola and Tarter 1999; McKirnan et al. 1996; Plankey et al. 2007).

Several important public health implications can be drawn from our study. In addition to assisting some MSM in reducing their high-risk sex behaviors, there is a clear need to encourage primary care physicians and other HIV prevention providers to screen MSM clients for use of Viagra®, methamphetamines, or poppers. These substances may be proxy indicators of a patient engaging in high-risk sexual behaviors that greatly elevate their risk for HIV or STI, as well as having other potential harmful health effects. Assessment of substance use during client intake and clinical care may help prioritize clients who require more intensive, individualized counseling or substance use treatment (Mausbach et al. 2007; Sanchez and Gallagher 2006). Similar efforts are needed at the population level in behavioral surveillance systems at national, state, or local levels. Greater integration of drug use topics into HIV risk reduction interventions is needed along with more attention to the drug use in the context of sexual risk practices (Herbst et al. 2005). Integration of STI/HIV care with substance abuse education and treatment also is warranted (Hirshfield et al. 2004; Metzger and Navaline 2003; Metzger et al. 1998). Drug treatment has been shown to decrease HIV risk and HIV infections, as well as significantly lower rates of drug use, drug-related behaviors, and HIV infections among drug users who remain in treatment programs (Gibson et al. 1999; Metzger et al. 1993; Metzger and Navaline 2003; Shoptaw et al. 2005). Efforts to better integrate this with HIV/STI screening and prevention would be beneficial. To further improve HIV prevention programs, it also is important to increase routine HIV testing for MSM because seropositive individuals who are aware of their serostatus often reduce their sexual risk behaviors, and also to provide appropriately tailored prevention messages for both HIV-seropostive and seronegative populations (Chou et al. 2005; Fenton and Valdiserri 2006; Greenwald et al. 2006; Marks et al. 2005; Wolitski et al. 2006).

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