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Sexually transmitted infections among HIV-infected heavy drinkers in St. Petersburg, Russia

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Abstract

Objective—To estimate the prevalence and identify correlates of four sexually transmitted infections (STIs) among HIV-infected Russians reporting heavy alcohol use and recent unprotected sex.

Methods—This study was a cross-sectional analysis of baseline data from the HERMITAGE study. The primary outcome was any current STI, based on urine tests for *Neisseria gonorrhea*, Chlamydia trachomatis and Trichomonas vaginalis and serum testing for infection with *Treponema pallidum*. Data on potential demographic and behavioral predictors of STI were obtained from surveys administered at study entry.

Results—Of 682 participants, 12.8% (95% CI 10.3, 15.3) tested positive for at least one STI. In a multivariable model adjusted for gender, age and marital status, only sex trade involvement over the last three months was significantly associated with an increased odds of STI (AOR 2.00, 95% CI 1.13, 3.55).

Conclusions—Given that STIs were common in this HIV-infected cohort, and that few patient characteristics predicted STI, the current practice of screening HIV-infected Russians for syphilis alone merits reevaluation.

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Keywords

Sexually transmitted infection; HIV; risk behavior; alcohol drinking; Russia

Introduction

The HIV epidemic in Russia has expanded rapidly over the last decade and continues to grow, with an estimated 1 million HIV-infected people in 2010 (1). While the epidemic has been largely driven by injection drug use, the proportion of new infections attributed to sexual risk is increasing (2,3). This shift has drawn attention to the possible role of sexually transmitted infections (STIs) in facilitating the spread of HIV in the country. Russia experienced rising STI rates in the period preceding its HIV epidemic (4) and STIs are known to increase both susceptibility to HIV and the infectiousness of those with HIV (5, 6).

Studies outside Russia have demonstrated that STIs, particularly gonorrhea, chlamydia and syphilis, are prevalent in a number of HIV-infected subpopulations (7–12). However, there are few studies addressing STIs among HIV-infected Russians (12). Existing data derive from studies based on self-report of STI symptoms, or only a small number of HIV-infected participants (2,13). These limited data suggest that STIs may make a significant contribution to heterosexual transmission of HIV in Russia: For example, among 32 HIV infected intravenous drug users (IDU) in one study, 18 (56%) tested positive for infection with either *Chlamydia trachomatis* (herein referred to as chlamydia), *Neisseria gonorrhea (*gonorrhea), *Treponema pallidum (*syphilis), *Trichomonas vaginalis* (trichomoniasis) or HSV-2 (13). Data from a larger sample on the prevalence and correlates of STIs among those infected with HIV in Russia could inform clinical practice as to the appropriate role for STI screening for this group, which, according to national guidelines, is screened routinely only for syphilis, but not for other STIs.

The HERMITAGE (HIV Evolution in Russia - Mitigating Infection Transmission and Alcoholism in a Growing Epidemic) study provided an opportunity to investigate the prevalence and correlates of four STIs among 682 HIV-infected Russians. HERMITAGE is a randomized controlled trial of a behavioral intervention to reduce high risk sexual activity and substance use among HIV-infected heavy alcohol users who reported recent unprotected sex in St Petersburg. The current study was a cross-sectional, secondary analysis which investigated the prevalence of gonorrhea, chlamydia, syphilis and trichomoniasis at study entry, and examined which behaviors and demographic characteristics were associated with testing positive for one or more of these STIs.

Methods

Study Design and Participants

From October, 2007 through April, 2010, the HERMITAGE study recruited HIV-infected heavy drinkers who reported recent unprotected sex from five inpatient and outpatient HIV and substance use care sites in St. Petersburg, Russia. In the clinical settings, research associates approached patients, assessed eligibility, offered participation, and conducted assessments. At the non-clinical recruitment site, a needle exchange, research associates gave potential participants information on the study and referred them to one of the clinical sites for eligibility assessment.

Patients were eligible for inclusion in the study if they were 18 years of age or older; HIV infected; reported anal or vaginal sex without a condom in the past 6 months; and reported past 6 month National Institute on Alcohol Abuse and Alcoholism (NIAAA) “at risk”

drinking levels (defined as >14 drinks per week or >4 drinks on a single occasion for men, and >7 per week or >3 on a single occasion, for women), described as "heavy drinking" herein (14). Exclusion criteria included cognitive impairment, acute illness precluding participation, pending legal issues which could lead to incarceration, or ongoing efforts to conceive.

Procedure

After eligibility assessment, all participants provided written informed consent. Baseline data were collected via: (a) a face-to-face interview with a research associate and (b) a self-administered questionnaire for particularly sensitive questions (e.g. about sexual victimization). A medical chart review was performed for participants recruited from medical settings. All participants were asked to provide a urine and blood sample for STI screening at the baseline assessment. Those testing positive for an STI at baseline were offered treatment.

Interviews were conducted in Russian. Participants were compensated 200 rubles, the equivalent of approximately seven U.S. dollars, for the baseline assessment and received 30 condoms. The HERMITAGE study was approved by the Institutional Review Boards of Boston Medical Center and St Petersburg Pavlov State Medical University.

Measures

Outcome measures—The primary outcome of the current study was a diagnosis of one or more STIs (gonorrhea, chlamydia, trichomoniasis and/or syphilis) based on biologic testing at study entry. Urine specimens were tested for *Neisseria gonorrhea*, *Chlamydia trachomatis* and *Trichomonas vaginalis* using PCR-based nucleic acid amplification (Amplisens PCR Kits, Ecoli Ltd., Moscow, Russia, in compliance with quality guidelines by the Federal State Institution of Science, Central Research Institute of Epidemiology, Moscow) (15,16). Serum was tested for syphilis using the Venereal Disease Research Laboratory test (VDRL, Institute of Vaccines and Sera, St. Petersburg, Russia) and an enzyme-linked immunoassay (ELISA) that employs recombinant antigen to detect both IgM and IgG antibodies to *Treponema pallidum*. (Recombibest AntiPallidum, ZAO Vector-Best, Novosibirsk, Russia). Subjects were defined as having syphilis when both the ELISA and VDRL were positive and they had not been previously treated for syphilis. Participants with a positive VDRL and negative ELISA were considered false positives. None of the participants with a positive ELISA and no prior treatment had a negative VDRL.

Potential predictors—Potential predictors of STI were identified from the baseline assessment. Sociodemographic characteristics of interest included age, gender, and marital status. Potential health-related predictors included self-report of current antiretroviral (ARV) therapy or past history of STI, as well as the most recent CD4 count according to a medical record review. Sexual risk behaviors over the last three months were assessed, and included the number of sexual partners; the number of sexual encounters when a condom was not used; buying or selling sex for drugs or money; and, for men, any sexual activity with other men (MSM)(17). In addition, the assessment asked about the use of alcohol or drugs before or during sex in the last 30 days, a lifetime history of sexual victimization, and the propensity to seek out novel or risky sexual stimulation, using Kalichman's 11-item sexual sensation-seeking scale. This scale generates scores ranging from 1–4, with higher scores reflecting greater sensation-seeking (18). To assess potential alcohol-related predictors of STI, participants were asked about the quantity and frequency of alcohol consumption using a 30-day time-line follow-back (TLFB) (19). Heavy alcohol use was defined according to the NIAAA definition, described above (14). Alcohol dependence over the last year was evaluated using the Composite International Diagnostic Interview Short-Form (CIDI-SF)

(20). Drug-related variables included any use of heroin, prescription analgesics, marijuana, sedatives, tranquilizers, or stimulants (including amphetamines and cocaine) over the last year, drug dependence according to the CIDI-SF, and past history of injection drug use (IDU).

Data analysis

Descriptive statistics were used to characterize the study sample at baseline, both overall and by STI status. The frequency and proportion of STIs (i.e. testing positive by biological testing for any of four specific STIs), and of any history of STI by self-report were also described. To identify factors associated with testing positive for an STI, a series of logistic regression models were using the following manual, iterative model building approach. First, unadjusted logistic regression models for each factor of interest were fit. Factors with a p-value of less than 0.15 were then included together in a single multivariable model. In addition, covariates considered to be important potential confounders (i.e. gender, age, and marital status) were forced into the multivariable model. Factors in this multivariable model with a p-value greater than 0.15 were removed one at a time. Finally, factors not selected based on the initial unadjusted analyses were included one at a time in the current multivariable model to assess their importance in the presence of other variables. The continuous variables of age, sexual sensation seeking score and number of unprotected sexual encounters were included as tertiles. CD4 count was included as a dichotomous variable (>/= 350 cells/mm^3 vs < 350 cells/mm^3) as was the number of sexual partners (< 2 vs >/= 2), which is consistent both with the distribution of our data and the standard approach for measuring multiple partnering over fairly short time periods (21). To minimize the potential for collinearity, we assessed the correlation between all pairs of independent variables and verified that no pair of variables included in the same regression model was highly correlated (i.e., r>0.40). Due to a large number of missing values for CD4 cell count (30% of the sample), we used an indicator variable to create a category for missing values for this variable.

Secondary, exploratory analyses were also conducted to assess gender as a possible effect modifier. This analysis aimed to test the hypotheses that younger age may be a more important risk factor for STIs among women than men, and that the effects of certain behaviors on STI risk may also differ by gender (20). Potential interactions between gender and four factors hypothesized to have differential effects on STI risk among women and men (age, any alcohol use before or during sexual activity, sex trade involvement, and past year cocaine use) were evaluated.

All reported p-values were two-tailed, and a p-value of less than 0.05 was considered statistically significant. Analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC).

Results

As shown in Figure 1, 921 individuals were screened for eligibility. Of the 190 ineligible individuals, 110 did not meet the alcohol-related criteria and 134 did not meet the sex risk criteria. Seven hundred and two of the 731 eligible individuals (96%) agreed to participate. Among these, 682 had available STI results, and were included in the current analysis.

Demographic, health-related and behavioral characteristics of the study cohort are shown in Table 1. In general, the sample was young and 40% female, and, reflecting study eligibility criteria, had a high prevalence of heavy alcohol use and unprotected sex.

The prevalence of any STI among the 682 participants was 12.8% (95% CI 10.3, 15.3; Table 2). The prevalence appeared similar in women and men. Only 1.9% of all participants (n=13) had more than one STI. Chlamydia was diagnosed among 40 participants (5.8%); it was more prevalent among men than women (7.3% of men versus 3.6% of women). Trichomoniasis was also common with 37 participants (5.4%) testing positive; prevalence was 8.2% among women and 3.4% among men. Fourteen participants (2.0%) had gonorrhea and 13 (1.9%) met the case definition of untreated syphilis infection. About half of participants (47.7%) reported a past diagnosis of an STI, including syphilis, gonorrhea, chlamydia, trichomoniasis, genital warts, or herpes.

Bivariate analyses

. Based on the preliminary bivariate analyses, seven independent variables met criteria for entry into the initial multivariable model: The number of unprotected sexual encounters (OR 0.61, 95% CI 0.34, 1.10 for the middle vs. lowest tertile; OR 1.13, 95% CI 0.67, 1.91 for the highest vs. lowest tertile); buying or selling sex (OR 1.87, 95% CI 1.08, 3.24); any history of STI (OR 1.49, 95% CI 0.95, 2.34); MSM (OR 2.82, 95% CI 0.86, 9.20); using drugs or alcohol before sex (OR 1.50, 95% CI 0.95, 2.37); using alcohol before sex (OR 1.53, 95% CI 0.98, 2.41); and past year cocaine use (OR 1.92, 95% CI 1.01, 3.62). Using drugs *or* alcohol before sex was not included in the multivariable model due to its potential collinearity with using alcohol before sex, and past IDU was not included due to its potential collinearity with past-year heroin use. None of the other potential predictors described in the Methods section met criteria for inclusion in the multivariable model.

Final multivariable model

Using the model building approach outlined in the Methods, a final multivariable model was developed and is shown in Table 3. In this model, buying or selling sex was associated with a two-fold increased odds of having an STI (AOR 2.00, 95% CI 1.13, 3.55). No other factors were significantly associated with testing positive for an STI, though there were notable, non-significant increases in the odds of an STI among those reporting a past STI (AOR 1.46, 95% CI 0.91, 2.35) and among MSM compared to men reporting sex with women only (AOR 2.72, 95% CI 0.78, 9.49).

In secondary, exploratory analyses, there was no statistically significant interaction between gender and any of the following variables: Age, sex trade, cocaine use in the past year, or alcohol use before or during sexual activity.

Discussion

The prevalence of STIs in the HERMITAGE cohort of 682 HIV-infected heavy drinkers in Russia was 13%. This is comparable to what has been described in HIV-infected populations in other countries (12). Many in this group reported past IDU, which, consistent with the epidemiology of HIV in Russia, likely led to their HIV infection. However, sexual transmission of HIV is a growing concern in Russia (2), and the substantial prevalence of STIs in this sexually active cohort indicates a likely role for such infections in facilitating HIV transmission to others.

It is thus important to examine factors that may be associated with testing positive for an STI in this sub-group of HIV-infected Russians. In this study, the only variable that was significantly predictive of having an STI was buying or selling sex over the last three months, which doubled the odds of STI. The association between selling sex and STIs has been noted in many other studies, including several from Russia (23–25), where sex work is an important risk factor for HIV itself (24). However, there have been fewer data on the

association between sex trade involvement and STIs from HIV-infected cohorts, a group whose risk behaviors may be different from those without HIV (7,11). Also of note in the current study was the finding that despite the relationship between sex trade and STIs, there was no relationship between testing positive for an STI and either the number of sexual partners or the number of unprotected sexual encounters. Such a pattern has been observed in at least one other Russian study (25), suggesting that other, unmeasured sex risk factors (for example, being part of a particular sexual network with a high prevalence of STIs) may help account for STI risk among those who buy and sell sex in Russia.

Despite the small number (14, 3.4%) of men who reported having sex with other men (MSM), this variable nearly achieved statistical significance as a predictor of STI and had a large magnitude of association with an odds ratio of 2.72. Particularly given that the number of MSM may be an underestimate due to underreporting of stigmatized behavior in Russia (26), the finding may be clinically important.

Several independent variables surprisingly did not appear to have strong associations with STIs, most notably age and gender. In many other studies, including some of HIV-infected cohorts, age under 25 and female gender have been found to be strongly associated with STI (7, 10, 24, 25, 27, 28, 29). The impact of both age and gender on overall STI rates in the current study could have been attenuated by the high risk behavior exhibited by both men and women who participated. In addition, given that some studies have shown particularly high rates of STIs among 15–19 year-olds (28), the fact that all participants were 18 and over may have lessened the particular effect of age as a predictor in this cohort. The expected effect of gender would also not be seen if the men in this study were involved in disproportionately high-risk sexual activity, such as MSM, that they underreported. In other words, if MSM (or another high-risk, potentially underreported behavior among men) was in reality more common than reflected in the data, residual confounding would prevent us from gauging the true impact of gender alone on STI risk in multivariable analysis.

Patterns of alcohol use and the number of unprotected sexual encounters were not significantly associated with having an STI. The study's selection criteria meant that all participants reported heavy drinking and at least one episode of unprotected sex over the last six months. In this context, it may be understandable that neither increasing severity of the alcohol-related problem nor an increasing number of unprotected sexual encounters over the last three months was associated with increased STI risk.

The study also found that neither users of particular drugs, nor those with drug dependence were more likely to have STIs, in contrast to findings from several past studies in both HIV-infected and uninfected populations in the U.S. in which drug use, particularly marijuana and stimulant use, were risk factors for STI) (7,11,30). This raised the possibility that drug use had a differential effect on STI risk among men compared to women, as was seen in a recent study from India in which alcohol was more strongly associated with condom non-use among men (perhaps because men had more control than women over the decision to use condoms) (22). A secondary analysis was conducted in the current study, to investigate whether a similar process could have occurred for drug use and STI risk in the HERMITAGE cohort. There was, however, no significant interaction term between gender and cocaine use or alcohol use before sex.

Future studies should investigate the prevalence of STIs in other groups of HIV-infected Russians. Should the current findings be replicated, the data may have implications for STI screening practices in Russia, where current guidelines (in contrast to those issued by the United States Center for Disease Control) (31) recommend HIV-infected patients be screened for syphilis alone. HIV-infected Russians typically receive this screening from

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their HIV providers, while public STI clinics are available for treatment of symptomatic STIs. Given that STIs are often asymptomatic, many cases likely go untreated with this approach. Our analysis suggests furthermore that screening for STIs only among HIV-infected patients who report certain behavioral risk factors may also be insufficient, since few factors predicted STI in the current cohort, and those factors that were associated with STI (sex trade and perhaps MSM) are stigmatized behaviors that patients may not consistently report to providers. Future research could thus help clarify whether screening all HIV-infected Russians is indeed the optimal strategy, as our data suggest it to be, and whether screening is needed for all four of these treatable STIs or a subset of them.

Our study has several limitations. Rectal specimens, as opposed to urine samples alone, could have provided a more complete assessment for gonorrhea, chlamydia and trichomoniasis. The lower prevalence of chlamydia among women compared to men additionally raises the possibility of reduced sensitivity of the urine assay among women. Unfortunately, the available peer-reviewed report on the performance characteristics of the Russian chlamydia assay lists a sensitivity for urine specimens (92.3%) that was determined from male specimens only; only cervical and vaginal specimens were examined from females (sensitivity 87.2%) and these were not possible to obtain in the context of HERMITAGE (16). Finally, cohort eligibility criteria limited our ability to discern a relationship between alcohol and STIs, or condom use and STIs, and may also limit the study's generalizability to other HIV-infected Russians. However, these behaviors appear to be common among HIV-infected people in Russia; of the 921 HIV-infected patients who were screened for the study, only 110 did not meet the alcohol criteria and 134 failed to meet the sex risk criteria.

In summary, sexually transmitted infections (gonorrhea, chlamydia, trichomoniasis and syphilis) were common among HIV-infected Russian drinkers who reported recent unprotected sex. Multivariable analyses identified only sex trade involvement as a significant predictor of STI. Future research should investigate the prevalence of these four common, treatable STIs in a broader sample of HIV-infected Russians, to determine whether routine screening for all of these STIs, rather than syphilis alone, in this population should be a component of HIV prevention efforts in Russia.

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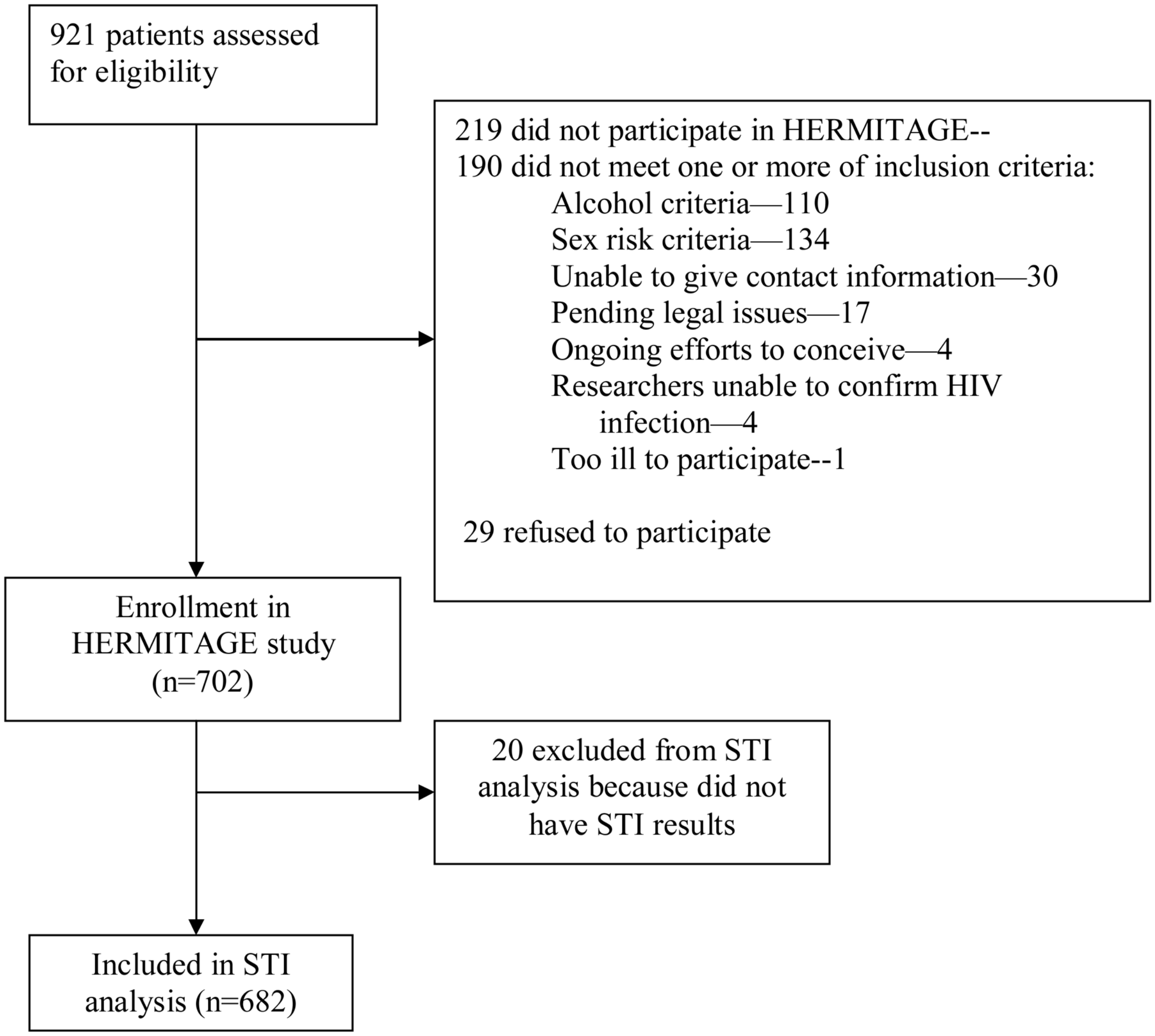

Figure 1.
Enrollment of participants in the HERMITAGE study and inclusion in the current analysis of STI data

Table 1

Baseline characteristics of HIV-infected heavy drinkers with recent unprotected sex in St. Petersburg

Characteristic	N (%), total (n=682)	N (%), any STI (n=87)	N (%), no STI (n=595)
Demographics			
Male	408 (60.0)	48 (55.2)	360 (60.5)
Mean age (range, std)	30.0 (18–57, 5.2)	29.6 (21–44, 5.0)	30.1 (18–57, 5.2)
College/university educated	391 (57.3)	49 (56.3)	342 (57.4)
Currently married or cohabitating	244 (35.8)	30 (34.5)	214 (36.0)
Employed	498 (73.0)	57 (65.5)	399 (67.0)
Ever incarcerated	260 (38.1)	26 (29.9)	234 (39.3)
Health characteristics			
CD4>/=350 cells/mm^3 (n=479)[1]	249 (52.0)	28 (43.1)	221 (53.4)
Currently on ARV therapy	117 (17.2)	11 (12.6)	106 (17.8)
Sexual risk behaviors[2]			
Two or more partners	181 (26.5)	25 (28.7)	156 (30.1)
Inconsistent condom use[3]	518 (76.2)	66 (75.9)	452 (76.2))
Number unprotected sexual encounters (median, IQR)	5 (1 – 18)	5 (1 – 26)	5 (1 – 17)
MSM[4]	14 (3.4)	4 (4.6)	10 (1.7)
Bought or sold sex for drugs or money	102 (15.0)	20 (23.0)	82 (13.8)
Drugs/alcohol before sex, past 30d	339 (49.9)	51 (58.6)	288 (48.6)
Substances used before/during sex, past 30d:			
Alcohol	281 (41.4)	44 (50.6)	237 (40.0)
Heroin	149 (21.9)	17 (19.5)	132 (22.3)
Stimulants	40 (5.9)	8 (9.2)	32 (5.4)
Cannabis	35 (5.2)	3 (3.5)	32 (5.4)
Sexual sensation-seeking score (tertiles):			
1 – 1.750	236 (34.7)	31 (36.1)	205 (34.5)
1.875 – 2.375	223 (32.8)	27 (31.4)	196 (32.9)
2.50 – 4.0	222 (32.6)	28 (32.6)	194 (32.6)
Any history of sexual victimization	231 (33.9)	31 (35.6)	200 (33.6)
Alcohol and drug use			
Heavy drinking, last 30 days	554 (81.2)	72 (82.8)	482 (81.0)
Ever injected drugs	566 (83.0)	70 (80.5)	496 (83.4)
Alcohol dependence, last year	434 (63.6)	57 (65.5)	377 (63.4)
Drug use in last year:			
Sedative or tranquilizer	256 (37.6)	38 (43.7)	218 (36.7)
Amphetamines or stimulants	213 (31.3)	27 (31.0)	186 (31.3)
Analgesics or Rx painkillers	227 (33.3)	30 (34.5)	197 (33.1)
Inhalants	15 (2.2)	3 (3.5)	12 (2.0)
Marijuana	319 (46.8)	38 (43.7)	281 (47.2)
Cocaine, crack or free base	68 (10.0)	14 (16.1)	54 (9.1)
LSD/other hallucinogens	53 (7.8)	7 (8.14)	46 (7.7)

Characteristic	N (%), total (n=682)	N (%), any STI (n=87)	N (%), no STI (n=595)
Heroin	432 (63.4)	51 (58.6)	381 (64.1)
Drug dependence, last year	425 (62.3)	50 (57.5)	375 (63.0)

[1] CD4 count was available for 479 participants, of whom 28 had STI and 221 did not have STI. Percentages shown use 479, 65 and 414 as the denominators.

[2] All items refer to behaviors over the last three months, except where noted

[3] At least one episode of sex without a condom in the last three months

[4] Men who reported any sex with men. Percentages in this row reflect the proportion among men only.

Table 2

Prevalence of sexually transmitted infections (STI)

	N (%) among total (n=682) 95% CI
Tested positive for any STI[1]	87 (12.8) (10.3 – 15.3)
Specific STIs: (n=682)	
Gonorrhea	14 (2.0) (1.0 – 3.4)
Chlamydia	40 (5.8) (4.0 – 7.5)
Trichomoniasis	37 (5.4) (3.6 – 7.0)
Syphilis	13 (1.9) (1.0 – 3.2)
Tested positive for more than one STI	13 (1.9) (1.0–3.2)
Self report of lifetime STI	334 (47.7) (44.0 – 51.4)

[1]Gonorrhea, chlamydia, trichomoniasis or syphilis

Table 3

Characteristics associated with STI in the final multivariable model

Characteristic	Adjusted odds ratio (95% confidence interval)	P-value
Age		
18–27	Referent	0.78
28–31	0.95 (0.54, 1.67)	
32–57	0.84 (0.47, 1.50)	
Gender		
Male	0.88 (0.54, 1.43)[1]	0.60
Marital status		
Married or living with partner	0.92 (0.54, 1.43)	0.76
Number of unprotected sexual encounters[2] (tertiles)		
1–2	1.00	0.10
3–14	0.59 (0.32, 1.09)	
15–483	1.12 (0.64, 1.94)	
Bought or sold sex over last 3 mos	2.00 (1.13, 3.55)	0.02
Past history of STI	1.46 (0.91, 2.35)	0.12
Men who have sex with men	2.72 (0.78, 9.49) [3]	0.12

[1]OR represents comparison of men who report sex with women only vs. women

[2]Over the past three months

[3]OR is comparison of men who report any sex with men vs. men who report sex with women only, over the last three months.