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Risk Factors for Acute and Early HIV Infection Among Men Who Have Sex With Men (MSM) in San Diego, 2008 to 2014

A Cohort Study

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Abstract: The objectives of this study were to identify risk factors associated with acute and early HIV infection (AEH) among men who have sex with men (MSM) undergoing community HIV testing and to compare demographics in those diagnosed with AEH with those diagnosed at chronic stage of HIV infection.

In this retrospective cohort study, we analyzed risk factors associated with AEH among 8925 unique MSM (including 200 with AEH [2.2%] and 219 [2.5%] with newly diagnosed chronic HIV infection) undergoing community-based, confidential AEH screening in San Diego, California.

The combination of condomless receptive anal intercourse (CRAI) plus ≥5 male partners, CRAI with an HIV-positive male, CRAI with a person who injects drugs, and prior syphilis diagnosis were significant predictors of AEH in the multivariable Cox regression model. Individuals reporting ≥1 of these 4 risk factors had a hazard ratio of 4.6 for AEH. MSM diagnosed with AEH differed in race ($P = 0.005$; more reported white race [$P = 0.001$], less black race [$P = 0.030$], trend toward less Native American race [$P = 0.061$]), when compared to those diagnosed with chronic HIV infection, while there was no difference observed regarding age.

We established a multivariate model for the predicting risk of AEH infection in a cohort of MSM undergoing community HIV screening, which could be potentially used to discern those in need of further HIV nucleic acid amplification testing for community screening programs that do not test routinely for AEH. In addition, we found that race differed between those diagnosed with AEH and those diagnosed at chronic stage of HIV infection underlining the need for interventions that reduce stigma and promote the uptake of HIV testing for black MSM.

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Abbreviations: Ab = antibody, AEH = acute and early HIV infection, CRAI = condomless receptive anal intercourse, HR = hazard ratio, MSM = men who have sex with men, NAT = nucleic acid amplification testing.

INTRODUCTION

Acute and early human immunodeficiency virus (HIV) infection (AEH) is associated with rapid immune destruction and significantly greater infectivity than during chronic infection, mainly due to transient levels of extremely high HIV-ribonucleic acid.[1,2] The detection of AEH is therefore critical to both prevention and treatment strategies.[3–5] Main deterrents of widespread use of AEH screening algorithms appear to be the elevated costs, which limit AEH testing in some settings to perceived high-risk populations, such as men who have sex with men (MSM).[6] MSM bear the greatest burden of HIV infection in California and the United States.[7–9] But while MSM represent a significant risk group, the risk of HIV infection within this population is not uniform. Studies have shown that MSM presenting to community HIV-screening programs may represent a subsegment of the MSM population at higher risk for the acquisition of HIV infection.[10–12]

The objectives of this study were to identify risk factors associated with AEH among MSM-undergoing community HIV testing and to compare demographics in those diagnosed with AEH with those diagnosed at chronic stage of HIV infection.

MATERIAL AND METHODS

In this retrospective observational cohort study, we analyzed risk behavior reported for the previous 12 months in individuals who enrolled in the voluntary ''Early Test'' HIV-screening program between April 2008 and July 2014. The ''Early Test'' is a community-based, confidential AEH screening program in San Diego, California that provides point-of-care rapid HIV serologic testing followed by reflex HIV nucleic acid amplification testing (NAT) in all antibody (Ab)-negative persons.[13,14] Males and female-to-male transsexual persons who reported sexual contact with one or more male partners during the previous 12 months were included in the analysis.

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AEH was characterized using previously published criteria for serologic and virologic test results.[15] In repeat testers, data reported at the most recent Early Test encounter were used. Eligible participants for the analysis of risk factors associated with AEH included MSM diagnosed with AEH (acute: HIV NAT+/Ab− and early: HIV Ab+/detuned HIV Ab c/w infection <70 days[16,17]) and those who were HIV uninfected.

In addition, we compared demographics and risk factors in those with AEH to those with newly diagnosed chronic HIV infection (ie, HIV Ab+/detuned not consistent with infection <70 days) to identify factors associated with delayed HIV diagnosis.

For statistical analysis SPSS 21 (SPSS Inc., Chicago, IL) was used. Analyses were performed using Chi-Squared and Mann–Whitney *U* tests. Univariate and multivariate Cox proportional hazards regression analysis was conducted for risk factors (such as sexually transmitted infections) and risk behavior variables associated with high AEH prevalence rates (above 4%) in the current and/or previous studies (selected on the basis of epidemiological evidence [12,18–21]). For the Cox regression model, AEH diagnosis was used as outcome, time of follow-up (beginning of study period to last eligible test) as time, and hazard ratios (HR) including 95% confidence intervals were displayed. In the first step, univariate analyses were performed, and variables with $P < 0.20$ were included in the multivariable model. Variables in the final model were selected with a forward stepwise procedure.

The University of California, San Diego Human Research Protections Program approved the study protocol, consent and all study-related procedures. All study participants provided voluntary, written informed consent before any study procedures were undertaken.

RESULTS

A large population (n = 14,612 unique clients) underwent HIV screening using the ''Early Test'' between April 2008 and July 2014, including 8935 (61%) individual MSM (with 17,333 voluntary HIV tests). Overall, 419 of 8935 MSM (4.69 %) were newly diagnosed with HIV infection; 219 (2.45%) with chronic HIV infection and 200 (2.24%) with AEH (125/200 [63%] at their first ''Early Test'', 75/200 [37%] at a repeat visit).

Predictors of Acute and Early HIV Infection

Table 1 provides the prevalence of risk behaviors reported for the 12 months prior to the most recent test and demographics for the study population, as well as AEH prevalence per risk behavior. Individuals with AEH were significantly younger (median 30 years interquartile range [IQR 25–40] vs 33 years [IQR 27–43], $P = 0.001$) and reported significantly more male sex partners (median 10 [IQR 5–20] vs 5 [IQR 3–10], $P < 0.001$) than those with negative test results. Condomless receptive anal intercourse (CRAI) was associated with a significantly higher rate of being diagnosed with AEH (3.7% vs 2.2%, $P < 0.001$), as was reporting 5 or more male sexual partners in the prior 12 months (3.1% vs 2.2%, $P < 0.001$). When the number of male sexual partners was combined with CRAI, a dose response relationship between risk and proportion of AEH diagnoses was observed (CRAI and 3 male partners was 4.2%, CRAI and 5 male partners 4.7%, and CRAI and 10 partners was 5.5%, all $P < 0.001$).

Univariate and multivariate Cox regression models of risk factor and behaviors were performed (variables included in the model are listed in Table 2). The combination of CRAI and 5 or more male partners was the strongest predictor of AEH, followed by CRAI with an HIV-positive male, reported syphilis diagnosis within last 12 months, and CRAI with a person who injects drugs. Individuals reporting at least 1 of the 4 risk behaviors of the multivariable Cox regression model (n = 2971 with 139 AEH) had an HR of 4.612 (95% confidence interval 3.382–6.289; $P < 0.001$) for AEH. AEH prevalence rates increased in those that reported higher numbers of risk behaviors of the final model, as shown in Table 2.

AEH Diagnoses Versus Chronic HIV Diagnoses

MSM diagnosed with AEH differed in race ($P = 0.005$; more reported white race [$P = 0.001$], less black race [$P = 0.030$], and trend toward less Native American race [$P = 0.061$]), when compared to those diagnosed with chronic HIV infection, while there was no difference observed regarding age. Those with AEH also reported more male partners ($P < 0.001$) and CRAI ($P = 0.023$) than those with newly diagnosed chronic HIV infection. No differences were found for drug use (with the exception of gamma hydroxybutyrate) and sexually transmitted infections (chlamydia, syphilis, and gonorrhea) (Table 1). Overall, 12/22 (55%) black MSM with chronic HIV diagnoses reported at least 1 of the 4 risk behaviors of the multivariable Cox regression model, which was similar to MSM reporting white race (54/99 [55%]).

DISCUSSION

We conducted a study on risk factors for incident HIV infection and generated a profile for AEH risk among MSM that undergo community-based HIV screening. These data showed a HR of 4.6 for AEH in individuals reporting at least 1 of the 4 risk behaviors of the final model. We also found that a higher proportion of white MSM were diagnosed with AEH, while a higher proportion of black MSM were diagnosed with chronic HIV infection.

By using multivariate modeling, we have created a set of risk factors associated with diagnosis of AEH in MSM undergoing HIV screening (Table 2). Although most previous HIV-risk models have focused on newly diagnosed chronic infection,[10,22–24] this represents one of the biggest studies to date to focus on incident HIV infection.[1,18,25] Although each of the 4 risk behaviors of our final model has been described previously to be associated with HIV infection individually (combination CRAI and 5 or more male partners,[18,26,27] CRAI with an HIV-positive male,[23,28–30] CRAI with a person who injects drugs,[28,31,32] and self-reported syphilis infection during the last 12 months),[33,34] these risk factors have not been described together in a multivariate model. By focusing only on AEH and investigating all of these factors together, we were able to generate a profile for AEH risk among MSM undergoing field-based screening, with an HR of 4.6 for AEH in individuals reporting at least 1 of the 4 risk behaviors.

In contrast to previous studies,[1,18,25] methamphetamine and other noninjection drug use, injection drug use, and injection drug use with shared needles did not remain significant predictors of AEH in our final model. Other studies have reported that methamphetamine and other stimulant drugs seem to be a driver for sexual-risk behavior, and even dose-response associations between number and frequency of substance use and high-risk sexual behaviors among HIV-negative MSM have been described.[35,36] However, usage rates of for example methamphetamine, nitrites, or gamma hydroxybutyrate differ depending on geographic location.[37–39] In addition, methamphetamine use has

TABLE 1. Risk Behavior and Demographics Reported for the 12 Months Prior to Diagnosis/Last HIV Test in MSM With Acute/Early HIV as Compared to Those With Negative HIV Test Results and Those With Newly Diagnosed Chronic HIV

	Prevalence of Risk Behavior, Demographic Characteristics Among Individuals With and Without HIV				
Risk-Factor/Risk Behavior and Demographics	**Individuals With Negative HIV Test Result(s) (n = 8516)***	**Individuals With Acute/ Early HIV Infection (n = 200)***	***P* Value†**	**Individuals With Newly Diagnosed Chronic HIV Infection (n = 219)***	***P* Value† When Compared to Acute/ Early HIV Infection**
Number of male partners (median, IQR)	5 (3–10)	10 (5–20)	<0.001	5 (3–10)	<0.001
10 or more male partners	2799/8508 (32.9%)	110 (55.0%)	<0.001	77 (35.2%)	<0.001
Intercourse with females	785/8503 (9.2%)	12 (6.0%)	n.s.	19/217 (8.8%)	n.s.
CIAI with male	5173/8434 (61.3%)	153 (76.5%)	<0.001	145/216 (67.1%)	0.045
CRAI	4205/8438 (49.8%)	163 (81.5%)	<0.001	156/218 (71.6%)	0.023
CRAI and 5 or more male partners	2618/8435 (31.0%)	130 (65.0%)	<0.001	86/218 (39.4%)	<0.001
CRAI and 10 or more male partners	1569/8435 (18.6%)	92 (44.5%)	<0.001	56/218 (25.7%)	<0.001
CRAI with HIV positive	411/8096 (5.1%)	35/170 (20.6%)	<0.001	35/181 (19.3%)	n.s.
CRAI with PWID‡	104/8347 (1.2%)	12/191 (6.3%)	<0.001	10/208 (4.8%)	n.s.
CRAI with sex worker	36/8337 (0.4%)	3/192 (1.6%)	0.022	2/212 (0.9%)	n.s.
Worked as sex worker	128/6317 (2.0%)	11/136 (8.1%)	<0.001	8/135 (5.9%)	n.s.
Chlamydia	352 (4.1%)	14 (7%)	0.046	13 (5.9%)	n.s.
Syphilis	152 (1.8%)	15 (7.5%)	<0.001	9 (4.1%)	n.s.
Gonorrhoea	507 (6.0%)	23 (11.5%)	0.001	19 (8.7%)	n.s.
Other STI§	168 (2.0%)	9 (4.5%)	0.012	8 (3.7%)	n.s.
Methamphetamine, not injected	564 (6.6%)	37 (18.5%)	<0.001	41 (18.7%)	n.s.
Ecstasy, not injected	863 (10.1%)	36 (18.0%)	<0.001	36 (16.4%)	n.s.
GHB, not injected	420 (4.9%)	29 (14.5%)	<0.001	16 (7.3%)	0.027
Nitrites, inhaled	1128 (13.2%)	32 (16.0%)	n.s.	36 (16.4%)	n.s.
Cocaine, not injected	810 (9.5%)	30 (15.0%)	0.009	22 (10.0%)	n.s.
IDU‡	108 (1.3%)	6 (3.0%)	0.047	8 (3.7%)	n.s.
IDU with shared needles‡	71/8483 (0.8%)	6 (3.0%)	0.008	4 (1.8%)	n.s.
Demographic data					
Age (years; median, IQR)	33 (27–43)	30 (25–40)	<0.001	31 (26–41)	n.s.
Male	8497 (99.8%)	200 (100%)	n.s.	218 (99.5%)	n.s.
Female–male TSX	19 (0.2%)	–	n.s.	1 (0.5%)	n.s.
Hispanic ethnicity	2264/8283 (27.3%)	64/194 (33.0%)	n.s.	89/216 (41.2%)	n.s.
Race	–	–	n.s.	–	0.005
White	5422/8005 (67.7%)	137/194 (70.6%)	n.s.	114/202 (56.4%)	0.001
Black	428/8005 (5.3%)	10/194 (5.2%)	n.s.	24/202 (11.9%)	0.030
Asian	577/8005 (7.2%)	11/194(5.7%)	n.s.	8/202 (4.0%)	n.s.
Pacific Islander	185/8005 (2.3%)	4/194 (2.1%)	n.s.	6/202 (3.0%)	n.s.
Native American	47/8005 (0.6%)	0	n.s.	5/202 (2.5%)	n.s.
Other	1346/8005 (16.8%)	32/194 (16.5%)	n.s.	44/202 (21.8%)	n.s.

CIAI = condomless insertive anal intercourse, CRAI = condomless receptive anal intercourse, GHB = gamma hydroxybutyrate, IDU = injection drug use, IQR = interquartile range, MSM = men who have sex with men, n.s. = not significant, PWID = person who injects drugs, STI = sexual transmitted infection, TSX = transsexual.

* Data available from all individuals, otherwise denominator depicted.

† Calculated using Chi-square or Mann–Whitney *U* test.

‡ All MSM fulfilling reporting ''IDU with shared needles'' were included in the IDU group as well. 41/116 MSM that reported CRAI with a PWID did also report IDU, and 37/41 MSM who reported CRAI with a PWID and IDU did also report shared needles.

§ Genital herpes, genital warts, and others.

TABLE 2. Univariate and Multivariate Cox Regression Model of Risk Factors and Risk Behaviors Associated With Acute/Early HIV Infection (vs Negative Test Result) in MSM

	Univariate Cox Regression Analysis			Multivariable Cox Regression Analysis		
Risk Factor/Risk Behavior (Within 12 Months Prior to Test)	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Number of male partners	1.005	1.003–1.006	<0.001			n.s.
CRAI and 5 or more male partners	3.998	2.99–5.347	<0.001	2.823	2.032–3.923	<0.001
CRAI with HIV positive	3.977	2.742–5.769	<0.001	2.081	1.353–3.202	0.001
CRAI with PWID	4.058	2.262–7.281	<0.001	2.113	1.121–3.984	0.021
CRAI with sexworker	3.799	1.213–11.893	0.022			n.s.
STI Chlamydia infection	1.743	1.012–3.001	0.045			n.s.
STI Syphilis	4.673	2.76–7.911	<0.001	3.131	1.722–5.690	<0.001
STI Gonococcal infection	1.979	1.282–3.056	0.002			n.s.
Methamphtamine, not injected	3.662	2.562–5.235	<0.001			n.s.
Nitrites, inhaled	0.966	0.662–1.41	0.857			n.i.
Ecstasy, not injected	1.996	1.391–2.864	<0.001			n.s.
GHB, not injected	3.668	2.473–5.44	<0.001			n.s.
IDU shared needles	3.534	1.567–7.969	0.002			n.s.

Number of Reported Risk Factors/Risk Behaviors of the Multivariable Model	**Acute or Early HIV Infection Prevalence Rates % (Absolute Numbers)**
0	1.1% (61/5745)*
1	3.9% (101/2558)†
2	7.9% (27/340)
≥3	15.1% (11/73)

CI = confidence interval, CRAI = condomless receptive anal intercourse, GHB = gamma hydroxybutyrate, IDU = injection drug use, MSM = men who have sex with men, n.i. = not included due to $P > 0.200$ in univariate analysis, n.s. = not significant, PWID = person who injects drugs, STI = sexually transmitted infection.

* A total of 314 of those 5745 (5.5%; 5 with AEH and 309 without) had missing data for 1 or more of the 4 risk behaviors.

† A total of 236 of those 2558 (9.2%; 29 with AEH and 207 without) reported 1 of the 4 risk behaviors but had missing data for 1 or more of the remaining 3 risk behaviors.

recently been decreasing in many settings while sexual-risk behaviors are steadily increasing.[39,40]

Whereas condomless anal intercourse or CRAI alone have been described as predictors of HIV infection in prior studies,[22–24] we found that CRAI alone was associated only with slightly increased AEH risk, whereas the combination of CRAI and number of male partners may be a more useful predictor of AEH. Results going into the same direction were reported by Ostrow et al[18] who found that the risk of seroconversion increased linearly with the number of CRAI sex partners.

We also found that the proportion of individuals reporting white race was higher among AEH diagnoses as compared to chronic HIV diagnoses, while the opposite was true for those reporting black race. This is further evidence of the marked racial disparities found throughout the care continuum of HIV in the United States.[41] In particular, infrequent HIV testing, undiagnosed infection, and late diagnosis are common among black MSM in the United States.[42] Our results indicate additional measures (eg, promotion of AEH testing) for black MSM are needed in order to increase testing and achieve earlier HIV diagnoses. In contrast to previous studies,[43,44] we did not find differences in age between those diagnosed with AEH and those with chronic HIV.

Our study has several limitations including its single-center and retrospective design. Additionally, we cannot completely rule out that subjects reported risk behaviors more openly with time and repeat testing, which may have impacted results of our multivariable model.

In conclusion, we established a multivariate model for predicting risk of AEH infection in a cohort of MSM undergoing community HIV screening, which could be potentially used to discern those in need of further HIV NAT testing for community screening programs that do not test routinely for AEH. In addition, we found that race differed between those diagnosed with AEH and those diagnosed at chronic stage of HIV infection underlining the need for interventions that reduce stigma and promote the uptake of HIV testing for black MSM.

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REFERENCES

1. Hightow-Weidman LB, Golin CE, Green K, et al. Identifying people with acute HIV infection: demographic features, risk factors, and use of health care among individuals with AHI in North Carolina. *AIDS Behav.* 2009;13:1075–1083.
2. Oxenius A, Price DA, Easterbrook PJ, et al. Early highly active antiretroviral therapy for acute HIV-1 infection preserves immune function of CD8+ and CD4+ T lymphocytes. *Proc Natl Acad Sci U S A.* 2000;97:3382–3387.
3. Cohen MS, Gay CL, Busch MP, et al. The detection of acute HIV infection. *J Infect Dis.* 2010;202(Suppl 2):S270–S277.
4. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365:493–505.
5. Khanna AS, Goodreau SM, Gorbach PM, et al. Modeling the impact of post-diagnosis behavior change on HIV prevalence in Southern California men who have sex with men (MSM). *AIDS Behav.* 2014;18:1523–1531.
6. Kelly JA, Morin SF, Remien RH, et al. Lessons learned about behavioral science and acute/early HIV infection. The NIMH Multisite Acute HIV Infection Study: V. *AIDS Behav.* 2009;13:1068–1074.
7. Fisher HH, Habarta N, Hardnett F, et al. Characteristics of first-time and repeat HIV tests among men who have sex with men who test at CDC-supported sites, 2007. *AIDS Educ Prev.* 2011;23:17–29.
8. Xia Q, Nonoyama A, Molitor F, et al. Recent decline in the incidence of human immunodeficiency virus infection among California men who have sex with men. *Am J Epidemiol.* 2011;174:203–210.
9. Xia Q, Osmond DH, Tholandi M, et al. HIV prevalence and sexual risk behaviors among men who have sex with men: results from a statewide population-based survey in California. *J Acquir Immune Defic Syndr.* 2006;41:238–245.
10. Koblin BA, Husnik MJ, Colfax G, et al. Risk factors for HIV infection among men who have sex with men. *AIDS.* 2006;20:731–739.
11. MacKellar DA, Valleroy LA, Secura GM, et al. Repeat HIV testing, risk behaviors, and HIV seroconversion among young men who have sex with men: a call to monitor and improve the practice of prevention. *J Acquir Immune Defic Syndr.* 2002;29:76–85.
12. Menza TW, Hughes JP, Celum CL, et al. Prediction of HIV acquisition among men who have sex with men. *Sex Transm Dis.* 2009;36:547–555.
13. Morris SR, Little SJ, Cunningham T, et al. Evaluation of an HIV nucleic acid testing program with automated Internet and voicemail systems to deliver results. *Ann Intern Med.* 2010;152:778–785.
14. Hoenigl M, Weibel N, Mehta SR, et al. Development and validation of the San Diego Early Test (SDET) Score to predict acute and early HIV infection risk in men who have sex with men. *Clin Infect Dis.* 2015Apr 22. pii: civ335. [Epub ahead of print].
15. Le T, Wright EJ, Smith DM, et al. Enhanced CD4+ T-cell recovery with earlier HIV-1 antiretroviral therapy. *N Engl J Med.* 2013;368:218–230.
16. Hare CB, Pappalardo BL, Busch MP, et al. Seroreversion in subjects receiving antiretroviral therapy during acute/early HIV infection. *Clin Infect Dis.* 2006;42:700–708.
17. Hurt CB, McCoy SI, Kuruc J, et al. Transmitted antiretroviral drug resistance among acute and recent HIV infections in North Carolina from 1998 to 2007. *Antivir Ther.* 2009;14:673–678.
18. Ostrow DG, Plankey MW, Cox C, et al. Specific sex drug combinations contribute to the majority of recent HIV seroconversions among MSM in the MACS. *J Acquir Immune Defic Syndr.* 2009;51:349–355.
19. Shoptaw S, Reback CJ. Associations between methamphetamine use and HIV among men who have sex with men: a model for guiding public policy. *J Urban Health.* 2006;83:1151–1157.
20. Shoptaw S, Weiss RE, Munjas B, et al. Homonegativity, substance use, sexual risk behaviors, and HIV status in poor and ethnic men who have sex with men in Los Angeles. *J Urban Health.* 2009;86(Suppl 1):77–92.
21. Drumright LN, Gorbach PM, Little SJ, et al. Associations between substance use, erectile dysfunction medication and recent HIV infection among men who have sex with men. *AIDS Behav.* 2009;13:328–336.
22. Bruce D, Harper GW, Suleta K, et al. Sexual risk behavior and risk reduction beliefs among HIV-positive young men who have sex with men. *AIDS Behav.* 2013;17:1515–1523.
23. Drabkin AS, Sikkema KJ, Wilson PA, et al. Risk patterns preceding diagnosis among newly HIV-diagnosed men who have sex with men in New York City. *AIDS Patient Care STDS.* 2013;27:333–341.

24. Drumright LN, Little SJ, Strathdee SA, et al. Unprotected anal intercourse and substance use among men who have sex with men with recent HIV infection. *J Acquir Immune Defic Syndr.* 2006;43:344–350.
25. Carrel M, Eron JJ Jr, Emch M, et al. Spatial epidemiology of recently acquired HIV infections across rural and urban areas of North Carolina. *PLoS One.* 2014;9:e88512.
26. Schwarcz S, Scheer S, McFarland W, et al. Prevalence of HIV infection and predictors of high-transmission sexual risk behaviors among men who have sex with men. *Am J Public Health.* 2007;97:1067–1075.
27. Plankey MW, Ostrow DG, Stall R, et al. The relationship between methamphetamine and popper use and risk of HIV seroconversion in the multicenter AIDS cohort study. *J Acquir Immune Defic Syndr.* 2007;45:85–92.
28. Haukoos JS, Lyons MS, Lindsell CJ, et al. Derivation and validation of the Denver Human Immunodeficiency Virus (HIV) risk score for targeted HIV screening. *Am J Epidemiol.* 2012;175:838–846.
29. Buchbinder SP, Vittinghoff E, Heagerty PJ, et al. Sexual risk, nitrite inhalant use, and lack of circumcision associated with HIV seroconversion in men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2005;39:82–89.
30. Scott HM, Vittinghoff E, Irvin R, et al. Age, race/ethnicity, and behavioral risk factors associated with per contact risk of HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2014;65:115–121.
31. Fernyak SE, Page-Shafer K, Kellogg TA, et al. Risk behaviors and HIV incidence among repeat testers at publicly funded HIV testing sites in San Francisco. *J Acquir Immune Defic Syndr.* 2002;31:63–70.
32. Chen YH, McFarland W, Raymond HF. Risk behaviors for HIV in sexual partnerships of San Francisco injection drug users. *AIDS Care.* 2014;26:554–558.
33. Zetola NM, Bernstein KT, Wong E, et al. Exploring the relationship between sexually transmitted diseases and HIV acquisition by using different study designs. *J Acquir Immune Defic Syndr.* 2009;50:546–551.
34. Ferrer L, Furegato M, Foschia JP, et al. Undiagnosed HIV infection in a population of MSM from six European cities: results from the Sialon project. *Eur J Public Health.* 2015;25:494–500.
35. Santos GM, Coffin PO, Das M, et al. Dose-response associations between number and frequency of substance use and high-risk sexual behaviors among HIV-negative substance-using men who have sex with men (SUMSM) in San Francisco. *J Acquir Immune Defic Syndr.* 2013;63:540–544.
36. Ghanem A, Little SJ, Drumright L, et al. High-risk behaviors associated with injection drug use among recently HIV-infected men who have sex with men in San Diego, CA. *AIDS Behav.* 2011;15:1561–1569.
37. Marsolek MR, White NC, Litovitz TL. Inhalant abuse: monitoring trends by using poison control data, 1993-2008. *Pediatrics.* 2010;125:906–913.
38. Johnston LD, O'Malley PM, Bachman JG, et al. Monitoring the Future national results on drug use: 2012 Overview, Key Findings on Adolescent Drug Use Ann Arbor: Institute for Social Research, The University of Michigan; 2013.
39. Raymond H F, Chen Y H, Ick T, et al. A new trend in the HIV epidemic among men who have sex with men, San Francisco, 2004–2011. *J Acquir Immune Defic Syndr.* 2013;62:584–589.
40. Centers for Disease Control and Prevention (CDC). HIV testing and risk behaviors among gay, bisexual, and other men who have sex with men - United States. *MMWR Morb Mortal Wkly Rep.* 2013;62:958–962.
41. Rosenberg ES, Millett GA, Sullivan PS, et al. Understanding the HIV disparities between black and white men who have sex with men in the USA using the HIV care continuum: a modeling study. *Lancet HIV.* 2014;1:e112–e118.
42. Mannheimer SB, Wang L, Wilton L, et al. Infrequent HIV testing and late HIV diagnosis are common among a cohort of black men who have sex with men in 6 US cities. *J Acquir Immune Defic Syndr.* 2014;67:438–445.
43. Iwuji CC, Churchill D, Gilleece Y, et al. Older HIV-infected individuals present late and have a higher mortality: Brighton, UK cohort study. *BMC Public Health.* 2013;13:3972458-13-397.
44. Trepka MJ, Fennie KP, Sheehan DM, et al. Late HIV diagnosis: Differences by rural/urban residence, Florida, 2007∗–∗2011. *AIDS Patient Care STDS.* 2014;28:188–197.