Repeat Syphilis Among Men Who Have Sex With Men in California, 2002–2006: Implications for Syphilis Elimination Efforts

Stephanie E. Cohen, MD, MPH, Rilene A. Chew Ng, MPH, Kenneth A. Katz, MD, MSc, MSCE, Kyle T. Bernstein, PhD, ScM, Michael C. Samuel, DrPH, Peter R. Kerndt, MD, MPH, and Gail Bolan, MD

Objectives. We examined rates of and risk factors for repeat syphilis infection among men who have sex with men (MSM) in California.

Methods. We analyzed 2002 to 2006 California syphilis surveillance system data.

Results. During the study period, a mean of 5.9% (range: 4.9%–7.1% per year) of MSM had a repeat primary or secondary (PS) syphilis infection within 2 years of an initial infection. There was no significant increase in the annual proportion of MSM with a repeat syphilis infection ($P = .42$). In a multivariable model, factors associated with repeat syphilis infection were HIV infection (odds ratio [OR] = 1.65; 95% confidence interval [CI] = 1.14, 2.37), Black race (OR = 1.84; 95% CI = 1.12, 3.04), and 10 or more recent sex partners (OR = 1.99; 95% CI = 1.12, 3.50).

Conclusions. Approximately 6% of MSM in California have a repeat PS syphilis infection within 2 years of an initial infection. HIV infection, Black race, and having multiple sex partners are associated with increased odds of repeat infection. Syphilis elimination efforts should include messages about the risk for repeat infection and the importance of follow-up testing. Public health attention to individuals repeatedly infected with syphilis may help reduce local disease burdens. (*Am J Public Health*. Published online ahead of print November 17, 2011: e1–e8. doi:10.2105/AJPH.2011.300383)

Syphilis incidence rates have risen dramatically in California over the past decade. After reaching a nadir of 687 cases in 2000, the number of early cases of syphilis (primary, secondary, and early latent) in California increased from 1802 (5.1 per 100 000 population) in 2002 to 3836 (10.2 per 100 000 population) in 2008.[1] Between 70% and 80% of syphilis cases in California occur among men who have sex with men (MSM), and in 2008, 57.2% of MSM with primary or secondary (PS) syphilis reported that they were infected with HIV.[1,2] Similar trends in syphilis infections have been reported throughout the United States and Europe.[3–6]

Syphilis causes significant morbidity, has long-term sequelae if untreated, and is associated with both HIV transmission and acquisition.[3,7–11] MSM who contract a repeat syphilis infection may disproportionately contribute to transmission of the disease.[12,13] Enhanced, focused public health interventions designed to address the needs of MSM with repeat syphilis may slow syphilis transmission and play an important role in elimination efforts. However, it is not known whether rates of repeat syphilis infection have increased with the rise in syphilis rates or which factors affect risk for repeat infection.

Several studies have identified HIV infection as a risk factor for repeat syphilis infection,[14–18] but it is unclear which factors mediate this association. The association may be confounded by common behavioral risk factors such as methamphetamine use and unprotected sexual activity. Previous studies of repeat syphilis infection have included primary, secondary, and early latent syphilis cases (hereafter referred to as early syphilis).[14–19] Including early latent syphilis cases in an analysis of repeat syphilis infection may introduce detection bias, in that HIV-infected MSM are screened frequently for syphilis (often in the setting of routine CD4 and HIV viral load monitoring) and therefore may be more likely than are HIV-uninfected MSM to have an early latent infection detected.[20,21]

Identifying risk factors for and delineating trends in repeat syphilis infection are important for the design and implementation of targeted syphilis prevention strategies. We performed a retrospective cohort analysis of syphilis cases during 2002 to 2006 among MSM in California to determine whether the annual proportion of MSM who contracted a repeat syphilis infection within the subsequent 2 years increased and to identify risk factors for repeat infection. To limit the impact of detection bias on the magnitude of the association between HIV and repeat syphilis infection, we limited our primary analysis to symptomatic (i.e., PS) syphilis cases at baseline and during follow-up.

METHODS

California regulations mandate that laboratories and health care providers report positive treponemal and nontreponemal syphilis tests and suspected syphilis cases, respectively, to the local health department.[22] Trained disease intervention specialists affiliated with the local health department attempt to interview and counsel all individuals with confirmed and suspected early syphilis. During these interviews, demographic, behavioral, and clinical information is obtained; prevention counseling is provided; partners are identified so that they can be notified and treated; and syphilis stage is determined (according to the criteria of the Centers for Disease Control and Prevention).[20]

In addition, the disease intervention specialist reviews the medical record and consults a statewide surveillance and case management database for the results of prior syphilis serological tests and treatment history. The final determination of syphilis stage is made after the complete case investigation. The data are recorded on a standardized form and merged to form a unified, statewide database.

Outcome Variable

We used the statewide syphilis database to create a retrospective cohort of all cases of PS syphilis in California reported between January 1, 2002, and December 31, 2006. These data were used to create 2 analytic data sets, one to assess trends in repeat syphilis infections and one to assess factors associated with a repeat infection. For the trend analysis, we generated a single cohort for each year from 2002 to 2006 consisting of all reported cases of PS syphilis among MSM (5 cohorts in total) and identified MSM who had a repeat infection within the subsequent 2 years; thus, the follow-up period extended through December 31, 2008. For each cohort, we calculated the proportion of MSM who had at least 1 repeat PS syphilis infection within 2 years. A man with multiple syphilis infections over the 5-year period was included in the numerator for each cohort in which he had a repeat PS syphilis infection within the subsequent 2-year period.

In the analysis of risk factors for repeat syphilis infection, we generated a single cohort of all PS syphilis cases among MSM in California reported between January 1, 2004, and December 31, 2006, and identified individuals who had at least 1 repeat early (PS and early latent) syphilis infection within 2 years. This time frame was chosen because major improvements were made to the syphilis surveillance system in 2004, enhancing the quality and consistency of subsequent data on behavioral risk factors. For the risk factor analysis, only MSM who had been interviewed were included because there was no information on risk behaviors among those had not been interviewed. Among individuals with multiple repeat syphilis infections, we used the first syphilis infection and the first repeat syphilis infection within the study interval; thus, each individual was analyzed only once. Risk factor data were abstracted from the initial syphilis episode.

For both analyses, we used a score-based deterministic matching algorithm to identify repeat cases within the data set. The algorithm incorporated the following matching variables: exact or near match on first name and last name, exact date of birth, near match on date of birth (within 11 days, to allow for minor typographical errors), gender, race, and a combination variable that included the first 3 letters of the first name and the first 3 letters of the last name. Potential matches were assigned a score based on the variables that matched between the 2 records and the weight for each variable. The cutoff score used to define a match was based on extensive prior investigation of our matching algorithm. Records were manually reviewed after the automated match to increase match sensitivity and specificity. A matched case that occurred within 30 days of an initial case was considered a duplicate and was disregarded.

To test our hypothesis that including repeat early latent syphilis cases in the analysis would introduce a detection bias that would affect the association between HIV infection and repeat syphilis infection, we constructed 3 multivariable logistic regression models. For the primary analysis, the outcome was defined as repeat PS syphilis infection; MSM with a repeat early latent infection were excluded. For the second analysis, the outcome was defined as repeat early latent syphilis infection; MSM with a repeat PS syphilis infection were excluded. For the third analysis, the outcome was defined as repeat early syphilis infection; all repeat primary, secondary, and early latent infections were included. For each of the 3 analyses, we compared MSM with an initial PS syphilis infection who did and did not have a repeat infection within 2 years.

Explanatory Variables

We abstracted demographic (age, race/ethnicity, region of residence within California), clinical, and behavioral characteristics from the syphilis interview record obtained at the time of the initial syphilis infection. Regions were categorized as northern California, central California, bay area (excluding San Francisco), San Francisco city and county, southern California (excluding Los Angeles county), and Los Angeles county.[23] We determined HIV status (HIV infected, HIV uninfected, or HIV status unknown) via patient self-report at the time of the interview. Additional clinical factors obtained from the patient, provider, or surveillance database included history of syphilis infection, stage of syphilis at initial and repeat diagnosis, presence of neurosyphilis at initial or repeat diagnosis, and treatment regimen at initial infection.

Risk behaviors (self-reported at the time of the interview) included gender of sexual partners and number of sexual partners during the critical period (the interval during which the syphilis infection was most likely acquired: 3 months for primary syphilis and 6 months for secondary syphilis). MSM categorization was determined by a man's self-report of ever having had any male sex partners or by provider's documentation of sexual history. We also collected data on whether men had engaged in oral, anal insertive, anal receptive, or vaginal sex in the preceding 12 months and whether they had used a condom during their most recent vaginal or anal sex.

In addition, we analyzed information on homelessness, incarceration, exchange of money or drugs for sex, substance use (methamphetamine, cocaine, crack, heroin, nitrates or poppers), use of erectile dysfunction medications, and venues used to meet sex partners (bars or clubs, bathhouses, sex clubs, Internet, private parties, circuit parties) in the preceding 12 months. In the multivariable analyses, behavioral factors with missing data were treated as categorical variables with 3 possible values: yes, no, and unknown (missing or refused).

Statistical Analyses

The Cochrane–Armitage trend test was used to analyze yearly changes in the percentage of MSM with a repeat syphilis infection. We conducted univariable and multivariable analyses to compare demographic, clinical, and behavioral characteristics of interviewed MSM who did and did not have a repeat PS, early latent, or early syphilis infection within 2 years of an initial PS syphilis infection. We use the chi-square test or Fisher's exact test (when expected cell counts were small), with 2-tailed P values and 95% confidence intervals (CIs), to compare proportions.

We used univariable logistic regression in determining univariable odds ratios (ORs) and conducting likelihood ratio tests. We constructed a multivariable logistic regression model that included HIV status (identified as an independent risk factor for repeat syphilis infection in previous studies), potential confounders of the association between HIV infection and repeat syphilis infection (age, race, number of sex partners, substance use, and meeting venue), and variables that were significant in the univariable analysis (according to a likelihood ratio test) at the $P<.2$ level. Variables were sequentially removed from the

model, starting with those with the highest *P* value; confounders (identified a priori) and variables significant at the .05 level were retained during modeling. We used a likelihood ratio test that compared a model with and without interaction terms to assess interactions between variables. The significance level for interaction terms was set at $P<.2$. All *P* values were 2-tailed.

SAS version 9.1 (SAS Institute, Cary, NC) was used in the matching procedure to identify repeat syphilis cases; the procedure included blocking on key matching variables, use of the "complev" function to identify near matches on first name and last name, and use of PROC SQL to generate the matching score. We used Stata version 11.0 (Stata Corp LP, College Station, TX) to conduct all statistical analyses. Results from a study involving a subset of the data described here have been reported elsewhere.[15]

RESULTS

From 2002 to 2006, there were 5557 cases of PS syphilis among MSM in California. There was no significant increase during this period in the annual percentage of MSM who contracted a repeat PS syphilis infection within the subsequent 2 years (range=5.0% to 7.1%; $P=.43$; Figure 1). The median time to a repeat PS syphilis infection was 396 days (interquartile range[IQR]=259–543 days).

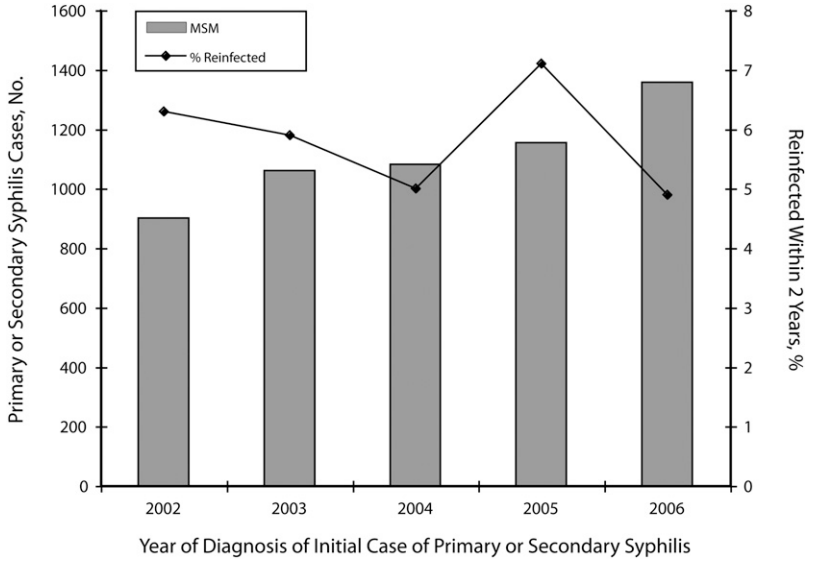
The analysis of risk factors for repeat syphilis infection was restricted to the 3396 MSM who had at least 1 PS syphilis infection reported in California between 2004 and 2006. We excluded from the risk factor analysis 396 (11.7%) men with PS syphilis who had not been interviewed, including 26 who had a repeat PS syphilis infection within 2 years. In addition, in our primary risk factor analysis, we excluded 138 MSM who had a repeat early latent syphilis infection. Of the remaining 2862 interviewed men with PS syphilis who were included in the risk factor analysis, 162 (5.7%) had a repeat PS syphilis infection within 2 years (Figure 2).

Demographic, behavioral, and clinical characteristics of MSM included in the primary analysis are shown in Table 1. Overall, the median age of MSM in this analysis was 38 years (IQR=31–43 years). The median age of men without a repeat infection was 38 years as well (IQR=31–43 years), and the median age of men with a repeat infection was 36.5 years (IQR=30–42 years). Most cases were reported in southern California, including Los Angeles county (65.9%), or San Francisco city and county (19.5%). The majority of the patients were White (55.2%), followed by Latino (27.7%), Black (9.1%), and Asian (4.9%).

Data on HIV status were available for 2598 (90.8%) MSM; 1508 (52.7%) of these men were HIV infected. The median number of sexual partners was 3 (IQR=1–6), and 467 (16.5%) men reported having 10 or more sexual partners during the critical period. Of the 1987 men who provided data on their condom use practices (69.4% of the MSM included in the analysis), 700 (35.2%) reported having used a condom during their most recent anal intercourse.

MSM who had a repeat PS syphilis infection within 2 years were more likely than those who did not to have had 10 or more sex partners during the critical period (25.0% vs 16.0%; $P<.01$), to have had anonymous sex partners in the preceding 12 months (69.8% vs 59.8%; $P<.05$), to have used methamphetamines in the preceding 12 months (27.8% vs 19.4%; $P<.05$), to be HIV infected (65.4% vs 51.9%; $P<.01$), and to be Black (13.6% vs 8.8%; $P<.05$; Table 1). Black MSM were more likely than were White MSM to have a repeat syphilis infection, despite being less likely to report having 10 or more sex partners during the critical period (11.9% vs 19.2%; $P<.01$). Black MSM were also more likely than were Latino MSM to have a repeat infection. Other demographic, clinical, and behavioral factors, including age, history of syphilis, treatment regimen, presence of neurosyphilis at the time of the initial syphilis infection, use of a condom during most recent intercourse, and exchange of money or drugs for sex in the preceding 12 months, were not significantly associated with the odds of repeat infection in univariable analyses.

In multivariable analyses, factors associated with repeat PS syphilis infection were HIV infection (adjusted odds ratio [AOR]=1.65; 95% CI=1.14, 2.37), Black race (reference category=White race; AOR=1.84; 95% CI=1.12, 3.04), and 10 or more sexual partners during the critical period (reference category=1 partner; AOR=1.98; 95% CI=1.12, 3.50; Table 1). Black race was also significantly associated with repeat infection in a model in which Latino race was the referent category (AOR=1.78; 95% CI=1.03, 3.06). There were no significant interactions between HIV status, race, and number of sex partners.



Note. $P=.43$ for Cochrane–Armitage test of trend for annual proportion of MSM with a repeat primary or secondary syphilis infection within 2 years.

FIGURE 1—Number of cases of primary or secondary syphilis among men who have sex with men (MSM) and annual proportion of MSM with a repeat PS syphilis infection within 2 years: California, 2002–2006.

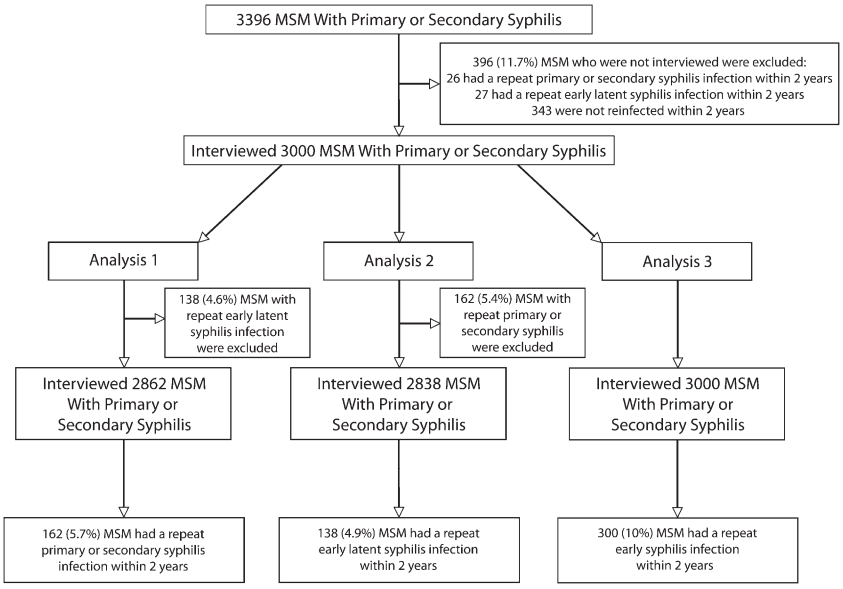


FIGURE 2—Flow sheet of men who have sex with men (MSM) who were excluded from the risk factor analysis.

Adjusted odds ratios of repeat syphilis for HIV-infected MSM relative to HIV-uninfected MSM were 3.45 (95% CI=2.19, 5.44) when the repeat infection was early latent syphilis and 1.65 (95% CI=1.14, 2.37) when the repeat infection was PS syphilis (Table 2). The odds ratios and corresponding *P* values for repeat syphilis infection associated with having 10 or more sex partners compared with a single partner were virtually the same regardless of whether repeat early latent syphilis cases were included in the outcome case definition; however, the association between Black race and repeat syphilis infection was not statistically significant in the analysis that included repeat early latent syphilis cases only or in the analysis that included all early (PS and early latent) syphilis cases (Table 2).

DISCUSSION

Despite increasing rates of early syphilis in California between 2002 and 2006, the annual proportion of MSM with a repeat PS syphilis infection within 2 years of an initial PS syphilis infection did not change. This finding suggests that the syphilis epidemic in California is continuing to extend to previously uninfected individuals and highlights the importance of ongoing primary syphilis prevention efforts. At the same time, the presence of a group of MSM who are infected with syphilis multiple times, similar in proportion but expanding in absolute numbers, may be contributing to ongoing syphilis transmission and to unsuccessful elimination efforts to date.

In our analysis, 5.7% of MSM had a repeat PS syphilis infection during 2004 to 2006, and an additional 4.9% had a repeat early latent syphilis infection. These findings are consistent with other reports of repeat syphilis infections. For example, a San Francisco study showed that 6.7% of MSM with early syphilis in 2001 and 2002 had a repeat early syphilis infection within 1 year.[14] In a Chicago study, 10.1% of MSM diagnosed with early syphilis during 2000 to 2005 had a repeat early syphilis infection,[18] whereas in a Florida study, 7.5% of MSM diagnosed with any stage of syphilis between 2000 and 2008 had a repeat infection.[17]

Comparisons of rates of repeat syphilis infection across studies are limited by different study populations (all individuals or only MSM), different case definitions (early syphilis or only PS), and different time frames for repeat infection (within 1 year, within 2 years, or ever). A standardized approach to the analysis of repeat syphilis infection would facilitate cross-study comparisons. Although consistent methodologies have not been used across studies, all published studies of which we are aware have revealed that a small but potentially important proportion of patients with reported syphilis cases will have a repeat infection.

After controlling for behavioral risk factors and limiting our analysis to symptomatic syphilis infections, we found that HIV-infected MSM were more likely than were HIV-uninfected MSM to have a repeat PS syphilis infection. Several possible factors may explain this result. Serosorting (selective unprotected sex with partners of the same serostatus) has been used by MSM as a harm reduction strategy to decrease the risk of HIV transmission and acquisition.[24–26] A higher baseline prevalence of syphilis within a sexual network of HIV-infected MSM who are serosorting could partially explain the association between HIV and repeat syphilis infections. However, because we did not have sufficient data on the HIV serostatus and condom use practices of sex partners, we could not directly assess the role of serosorting in the risk for repeat syphilis infection. An alternative hypothesis is that immunosuppression secondary to HIV infection could lead to an increased biological susceptibility to syphilis acquisition or transmission.[27]

We found that the adjusted odds ratio of repeat syphilis among HIV-infected MSM relative to HIV-uninfected MSM increased when early latent syphilis cases were included in the outcome case definition. Although we cannot statistically assess the significance of this difference, the trend suggests that the magnitude of the association between HIV and repeat syphilis infection depends on the stage of syphilis at repeat infection.

Because HIV-infected MSM are screened more frequently for syphilis and are significantly more likely than are HIV-uninfected MSM to have a repeat syphilis test after an initial infection,[20,28,29] they may be more likely either to have a true early latent syphilis infection detected or, in the event of fluctuating syphilis titers or treatment failure, to be misclassified as having a new early latent syphilis infection.[30–32] If some of the association between HIV infection and repeat syphilis infection is caused by more intensive screening for syphilis among HIV-infected MSM than among HIV-uninfected MSM, we may be underestimating the incidence of repeat syphilis

TABLE 1—Risk Factors for Repeat Primary or Secondary Syphilis Infection Among Men Who Have Sex With Men: California, 2004–2006

Characteristic	Overall (n = 2862), No. (%)	Repeat Infection (n = 162), No. (%)	No Repeat Infection (n = 2700), No. (%)	Crude OR (95% CI)	AOR (95% CI)
Region[a]					
Los Angeles county (Ref)	991 (34.6)	62 (38.3)	929 (34.3)	1.00	1.00
San Francisco city and county	557 (19.5)	41 (25.3)	516 (19.1)	1.19 (0.79, 1.79)	1.24 (0.63, 2.43)
Bay area	312 (10.9)	11 (6.8)	301 (11.2)	0.55 (0.28, 1.05)	0.57 (0.25, 1.29)
Northern	75 (2.6)	2 (1.2)	73 (2.7)	0.41 (0.10, 1.71)	0.23 (0.03, 1.79)
Southern	894 (31.2)	46 (28.4)	848 (31.4)	0.81 (0.55, 1.20)	0.82 (0.43, 1.55)
Race/ethnicity					
White (Ref)	1580 (55.2)	84 (51.9)	1496 (55.4)	1.00	1.00
Black	260 (9.1)	22 (13.6)	238 (8.8)	1.67 (1.03, 2.72)	1.84 (1.12, 3.04)
Latino	794 (27.7)	42 (25.9)	752 (27.9)	1.01 (0.69, 1.48)	1.07 (0.72, 1.58)
Asian	141 (4.9)	11 (6.8)	130 (4.8)	1.53 (0.80, 2.94)	1.62 (0.83, 3.17)
Other	87 (3.0)	3 (1.9)	84 (3.1)	0.82 (0.19, 3.45)	0.98 (0.23, 4.19)
History of syphilis	318 (11.1)	24 (14.8)	294 (10.9)	1.38 (0.88, 2.16)	
Syphilis stage					
Primary	836 (29.2)	41 (25.3)	795 (29.4)	0.81 (0.56, 1.17)	
Secondary (Ref)	2026 (70.8)	121 (74.7)	1905 (70.6)	1.00	
HIV status					
HIV negative (Ref)	1090 (38.1)	45 (27.8)	1045 (38.7)	1.00	1.00
HIV positive	1508 (52.7)	106 (65.4)	1402 (51.9)	1.76 (1.23, 2.51)	1.65 (1.14, 2.37)
Status unknown	264 (9.2)	11 (6.8)	253 (9.4)	1.01 (0.51, 1.98)	1.18 (0.59, 2.37)
No. of sex partners[b]					
0	224 (7.9)	11 (6.9)	213 (8.0)	1.32 (0.63, 2.76)	1.05 (0.49, 2.26)
1 (Ref)	583 (20.6)	22 (13.8)	561 (21.0)	1.00	1.00
2–4	1130 (40.0)	61 (38.1)	1069 (40.1)	1.46 (0.88, 2.39)	1.45 (0.87, 2.41)
5–9	424 (15.0)	26 (16.3)	398 (14.9)	1.67 (0.93, 2.98)	1.58 (0.87, 2.89)
≥10	467 (16.5)	40 (25.0)	427 (16.0)	2.39 (1.40, 4.08)	1.98 (1.12, 3.50)
Condom used at most recent intercourse					
No (Ref)	1287 (45.0)	67 (41.4)	1220 (45.2)	1.00	
Yes	700 (24.5)	34 (20.1)	666 (24.7)	0.93 (0.61, 1.42)	
Unknown/data missing	875 (30.6)	61 (37.7)	814 (30.1)	1.36 (0.95, 1.96)	
Anonymous sex partners in past 12 mo					
No (Ref)	907 (31.7)	40 (24.7)	867 (32.1)	1.00	
Yes	1727 (60.3)	113 (69.8)	1614 (59.8)	1.52 (1.05, 2.20)	
Unknown/data missing	228 (8.0)	9 (5.6)	219 (8.1)	0.89 (0.43, 1.86)	
Sexual practices in past 12 mo					
No anal sex	130 (4.5)	3 (1.9)	127 (4.7)	0.34 (0.11, 1.09)	
Only insertive anal sex	186 (6.5)	11 (6.8)	175 (6.5)	0.91 (0.48, 1.71)	
Only receptive anal sex	146 (5.1)	10 (6.2)	136 (5.0)	1.06 (0.54, 2.07)	
Insertive and receptive anal sex (Ref)	1788 (62.5)	116 (71.6)	1672 (61.9)	1.00	
Unknown/data missing	612 (21.4)	22 (13.6)	590 (21.9)	0.54 (0.34, 0.86)	
Use of Internet as meeting venue in past 12 mo					
No (Ref)	1537 (53.7)	85 (52.5)	1452 (53.8)	1.00	
Yes	944 (33.0)	61 (37.7)	883 (32.7)	1.18 (0.84, 1.66)	
Unknown/data missing	381 (13.3)	16 (9.9)	365 (13.5)	0.75 (0.43, 1.29)	

Continued

TABLE 1—*Continued*

Use of bathhouse or sex club as meeting venue in past 12 mo					
No (Ref)	1355 (47.3)	66 (40.7)	1289 (47.7)	1.00	
Yes	510 (17.8)	36 (22.2)	474 (17.6)	1.48 (0.98, 2.26)	
Unknown/data missing	997 (34.8)	60 (37.0)	937 (34.7)	1.25 (0.87, 1.80)	
Methamphetamine use in past 12 mo					
No (Ref)	1217 (45.5)	59 (36.4)	1158 (42.9)	1.00	1.00
Yes	569 (19.9)	45 (27.8)	524 (19.4)	1.69 (1.13, 2.52)	1.30 (0.85, 1.99)
Unknown/data missing	1076 (37.6)	58 (35.8)	1018 (37.7)	1.11 (0.77, 1.62)	0.79 (0.48, 1.29)
Erectile dysfunction medication use in past 12 mo					
No (Ref)	1522 (53.2)	84 (51.9)	1438 (53.3)	1.00	
Yes	264 (9.2)	20 (12.4)	244 (9.0)	1.40 (0.85, 2.32)	
Unknown/data missing	1076 (37.6)	58 (35.8)	1018 (37.7)	0.98 (0.69, 1.38)	

Note. AOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio. Percentages may not sum to 100% because of rounding.
[a]Excludes 33 cases from central California for which there were no repeat infections.
[b]Number of partners during preceding 3 months for primary syphilis and preceding 6 months for secondary syphilis; excludes 34 cases with missing data.

infection in the latter group. This finding highlights the importance of improving follow-up serological testing after an early syphilis infection for all MSM, regardless of their HIV status.

In this study, Black MSM were more likely than were White MSM to have a repeat PS syphilis infection. Previous studies have shown that Black MSM have a higher incidence of sexually transmitted diseases (STDs) and HIV than do White MSM despite a lower prevalence of self-reported sexual risk behaviors.[33] The reasons for this apparent discrepancy are unclear; possible explanations include differences in structural-level factors (e.g., socioeconomic status and access to care) and network-level factors (e.g., network size and interconnectedness).[34] Black MSM are more likely to report same-race sexual partnering,[35,36] which can lead to more tightly connected sexual networks, fostering the spread of STDs.[37] Several studies have shown that Black MSM are more likely than are White MSM to report serodiscordant unprotected anal intercourse.[26,38,39]

The extent to which the association between Black race and repeat syphilis infection reflects differences in sexual network structure, serosorting practices, or other factors warrants further study. Assessing how these factors intersect to affect risk in other racial/ethnic groups, including Latinos and Asians, is also important. The association between Black race and risk of repeat syphilis infection was not significant in the 2 analyses that included repeat early latent syphilis cases. This finding may reflect differences in access to care and STD screening and detection between Black and White MSM, in that White MSM may be more likely than are Black MSM to be screened for syphilis when they are asymptomatic and thus may be more likely to have an early latent syphilis infection detected.[40,41]

TABLE 2—Factors Associated With Risk of Repeat Syphilis Infection Among Men Who Have Sex With Men (MSM) in Multivariable Analyses, by Stage of Syphilis at Repeat Diagnosis: California, 2004–2006

Stage at Repeat Diagnosis	HIV, AOR (95% CI)	Black Race, AOR (95% CI)	≥10 Sex Partners, AOR (95% CI)
Primary or secondary[a] (n = 162[b])	1.65 (1.14, 2.37)	1.84 (1.12, 3.04)	1.98 (1.12, 3.50)
Primary, secondary or early latent[c] (n = 300[b])	2.27 (1.70, 3.02)	1.39 (0.92, 2.10)	1.99 (1.30, 3.05)
Early latent[d] (n = 138[b])	3.45 (2.19, 5.44)	0.88 (0.45, 1.71)	1.98 (1.08, 3.64)

Note. AOR = adjusted odds ratio; CI = confidence interval. Odds ratios were adjusted for region, race, HIV status, number of sex partners, and methamphetamine use.
[a]Baseline group: 2862 interviewed MSM with an initial primary or secondary syphilis infection who did not have a repeat early latent syphilis infection.
[b]Number of MSM reinfected within 2 years.
[c]Baseline group: 3000 interviewed MSM with an initial primary or secondary syphilis infection.
[d]Baseline group: 2838 interviewed MSM with an initial primary or secondary syphilis infection who did not have a repeat primary or secondary syphilis infection.

Limitations

This study involved several limitations. Negative serological tests for syphilis are not reportable to the state, and we did not have complete records of follow-up syphilis tests for treated patients; thus, it was not possible to assess directly the impact of screening on detection of repeat syphilis infections. Limiting the analysis to PS syphilis infection did not completely eliminate this source of bias because HIV-infected MSM might be more likely than are HIV-uninfected MSM to have access to primary and urgent care, allowing for more timely detection of symptomatic (i.e., PS) syphilis infection.

In addition, we were not able to identify individuals with a repeat syphilis infection who moved outside of California during the follow-up period or who provided a different name or birth date at one or several diagnoses of syphilis. Although lack of sensitivity in matching syphilis cases to subsequent cases in the follow-up period would lead to underestimation of the number of repeat infections, we would not expect the sensitivity of the match to change

over the study interval or to be different across the demographic, clinical, or behavioral risk factors we examined.

We restricted the analysis to interviewed MSM; 396 (11.7%) MSM with PS syphilis who were not interviewed were excluded. Although MSM with PS syphilis who could not be contacted for an interview or refused to be interviewed did not differ with respect to age or race from those who were interviewed (data not shown), they could have differed in terms of behavioral risk factors. Thus, our findings may not be generalizable to individuals with PS syphilis who are not interviewed by a disease intervention specialist. We did not have information on rate of new partner acquisition, interval between sex partners, partners' risk behaviors, or network-level factors (e.g., network size, interconnectedness, or concurrency), all of which have been shown to affect risk for STDs.[42–44] In addition, because no follow-up data were available for men who did not have a repeat syphilis infection, we were unable to assess dynamic changes in risk behaviors between the initial and repeat infection that may have influenced risk for repeat infection.

Conclusions

Despite these limitations, this study provides a comprehensive review of repeat syphilis infection across the state of California. Our data suggest that behavioral and network-level factors are important determinants of risk for repeat syphilis infection among MSM. Improving follow-up after the first syphilis infection for both HIV-uninfected and HIV-infected MSM, particularly those with high numbers of sex partners, and improving access and linkage to STD screening and treatment among Black MSM may help reduce rates of syphilis.[45] Syphilis elimination efforts and other public health interventions targeting MSM should include messages about the risk for repeat syphilis infection, the importance of follow-up syphilis testing, and the need to modify risk behaviors to prevent future infections. ■

About the Authors

Stephanie E. Cohen is with the Center for AIDS Prevention Studies, San Francisco, CA, and the STD Control Branch, California Department of Public Health, Richmond. Rilene A. Chew Ng, Michael C. Samuel, and Gail Bolan are with the STD Control Branch, California Department of Public Health. Kenneth A. Katz is with the HIV, STD, and Hepatitis Branch, Public Health Services, Health and Human Services Agency, County of San Diego, San Diego, CA. Kyle T. Bernstein is with STD Prevention and Control Services, San Francisco Department of Public Health, San Francisco, CA. Peter R. Kerndt is with the STD Program, Los Angeles County Department of Public Health, Los Angeles, CA.

Correspondence should be sent to Stephanie E. Cohen, MD, MPH, San Francisco City Clinic, 356 7th St, San Francisco, CA 94103 (e-mail: stephanie.cohen@sfdph.org). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints/Eprints" link.

This article was accepted July 18, 2011.

Contributors

S.E. Cohen designed the study, conducted the analysis, prepared the initial draft, contributed to revisions of the article, and prepared the final version of the article. R.A. Chew Ng and M.C. Samuel assisted with the statistical analysis and preparation of the article. K.A. Katz, K.T. Bernstein, and P.R. Kerndt assisted with data collection, interpretation of results, and preparation of the article. G. Bolan assisted with the study design, interpretation of results, and preparation of the article.

Acknowledgments

This study was supported in part by grant 1H25PS001379-01 (Gail Bolan) from the Centers for Disease Control and Prevention (Comprehensive STD Prevention Systems) and by grant T32 MH-19105-21 from the National Institute of Mental Health.

This work was previously presented in poster form at the 18th Conference on Retroviruses and Opportunistic Infections, Boston, MA, February 2011.

Human Participant Protection

No protocol approval was needed for this study because routine surveillance data collected for public health purposes were used.

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