HIV Incidence Among Men Diagnosed With Early Syphilis in Atlanta, San Francisco, and Los Angeles, 2004 to 2005

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Background: Syphilis outbreaks among men who have sex with men (MSM) in the United States have raised concerns about increased HIV transmission in this population. We sought to estimate HIV incidence among men diagnosed with primary or secondary (P&S) syphilis in sexually transmitted disease (STD) clinics in Atlanta, San Francisco, and Los Angeles.

Methods: We analyzed deidentified sociodemographic information from routine syphilis surveillance databases and matching remnant sera from consecutive male patients with P&S syphilis who were tested for syphilis at 3 public health laboratories during January 2004 through January 2006. Deidentified sera positive for *Treponema pallidum* by particle agglutination were screened for HIV-1 antibodies by enzyme immunoassay (EIA). Specimens that were confirmed HIV-positive by Western blot analysis were then tested for recent HIV infection using the less sensitive (LS) HIV-1 Vironostika EIA and BED HIV-specific IgG/total IgG assay.

Results: Of 357 men with P&S syphilis (98 in Atlanta, 151 in San Francisco, and 108 in Los Angeles), 32% had primary syphilis and 85% were MSM (12% no MSM risk and 3% no information). The median age was 36 years; 40% were white, 31% black, 20% Hispanic, and 8% other. Among men with P&S syphilis, 160 (45%) were HIV-positive, of whom 8 were classified as having acquired recent HIV infection by the LS-Vironostika EIA (all confirmed by BED) and had no history of antiretroviral use or HIV-positive results >6 months earlier. Seven of the 8 men with recent HIV infection were MSM. The estimated HIV incidence was 9.5% per year (95% confidence interval [CI]: 2.9 to 16.0) among all men and 10.5% per year (95% CI: 2.7 to 18.3) among MSM.

Conclusions: We found high HIV incidence among a high-risk population of US men diagnosed with P&S syphilis in STD clinics in Atlanta, San Francisco, and Los Angeles. Intensive integrated HIV/STD prevention programs are needed for this population.

Key Words: BED, HIV incidence, men who have sex with men, serologic testing algorithm for recent HIV seroconversion, syphilis

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Since 1998, outbreaks of syphilis among men who have sex with men (MSM) have been documented in numerous US cities[1–6] and internationally[7–10] and have raised concerns about increased HIV transmission in this population. Approximately 50% to 60% of newly identified primary and secondary (P&S) syphilis infections among MSM in these cities are among persons already known to be HIV-infected.[1–5] Syphilis infection facilitates acquisition and transmission of HIV infection,[11–15] and possible increases in sexual risk behavior accompanying the outbreaks of syphilis[16,17] may also contribute to sustained or increasing HIV incidence among MSM.

Preliminary studies using the sensitive/less sensitive (LS) enzyme immunoassay (EIA) testing strategy (also known as the serologic testing algorithm for recent HIV seroconversion [STARHS])[18] have documented high HIV incidence in men diagnosed with early syphilis. Among 74 men who were diagnosed with P&S syphilis at the San Francisco municipal sexually transmitted disease (STD) clinic during 2002 to 2003 and who accepted confidential HIV testing, estimated HIV incidence was 13.9% per year (95% confidence interval [CI]: 0.3 to 27.5).[19] A study of anonymous sera from 212 men with early syphilis diagnosed in STD clinics and other public sites in Los Angeles County during 2002 to 2004 estimated HIV incidence at 17.0% per year (95% CI: 12.0 to 22.0).[20] These 2 studies provide relatively imprecise estimates of incidence, and their validity may be affected, respectively, by potential volunteer bias and by misclassification of incident HIV cases because of limited HIV testing history information. However, these preliminary findings suggest frequent HIV transmission in

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The findings and conclusions from this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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proximity to syphilis acquisition (before, after, or concurrently) in MSM diagnosed with syphilis. These serologic studies are also corroborated by the findings that a substantial proportion of recently and acutely HIV-infected persons have genital ulcer disease or other STDs and are identified at the STD clinics.[21]

The objective of this study was to estimate HIV incidence in a large systematic sample of men diagnosed with P&S syphilis in select STD clinics in 3 major US cities during 2004 to 2005 to inform HIV/STD prevention and disease control programs for this at-risk population.

MATERIALS AND METHODS

Overview

This survey was done as part of the public health response to syphilis outbreaks among urban MSM across the United States.[6] We examined remnant syphilis serum specimens and associated surveillance data from men, primarily MSM, diagnosed with P&S syphilis in select STD clinics in Atlanta, San Francisco, and Los Angeles. In Los Angeles, cases of male patients with early latent (EL) syphilis from the same clinic sites were also included. Remnant sera were obtained from the public health laboratories that served these STD clinics in each city. We aimed originally to estimate HIV incidence in approximately 100 men from each of the 8 US cities with the highest estimated syphilis morbidity among MSM in 2002 (Atlanta, Chicago, San Francisco, Los Angeles, New York City, Ft. Lauderdale, Miami, and Houston).[5,6,22] However, because of logistic barriers (including the inability to identify or secure participation from dedicated laboratories that performed testing for a large number of syphilis cases and that could reserve and release deidentified remnant blood specimens), only the 3 aforementioned cities participated.

Procedures

We evaluated deidentified epidemiologic data and remnant sera from male patients with P&S syphilis (and with EL syphilis in Los Angeles) initially screened for syphilis by the public health department laboratories affiliated with the participating STD clinics in Fulton and Dekalb Counties in Atlanta (September 2004 to January 2006), in San Francisco (January 2004 to March 2005), and in Los Angeles County (January 2004 to May 2005). Positive reactions from sera on a nontreponemal test (eg, rapid plasma reagin [RPR], venereal disease research laboratory [VDRL]) and a confirmatory treponemal test (eg, *Treponema pallidum* particle agglutination assay [TP-PA]) were required for definitive diagnosis of syphilis infection and for inclusion in this study. Syphilis infection was staged by the staff at each local health department by standardized criteria[23] as primary syphilis (characterized by a painless chancre or ulcer at the site of inoculation appearing, on average, 21 days [range: 14 to 90 days] after infection), secondary syphilis (characterized by skin rash, mucocutaneous lesions, and lymphadenopathy typically appearing 6 to 8 weeks after primary chancre), and EL syphilis (a stage lacking clinical manifestations and within 1 year of infection, as evidenced in the previous year by a negative serologic test result, symptoms or signs of primary or secondary syphilis, or contact with a sex partner with early stage syphilis). Staff at each local health department abstracted limited information for syphilis cases from the existing routine and enhanced[24] syphilis and STD surveillance databases and case report forms. Data collected included age, race/ethnicity, behavioral risk factor information (sex with a male partner in the past 12 months), expanded HIV testing history (especially date of first HIV-positive test result, if applicable and known), and antiretroviral (ARV) use history (if applicable and known). After verifying the completeness and consistency of the data, the health department staff removed all personally identifying information from serum specimens and the corresponding epidemiologic data and assigned each patient a nonidentifying code. The linkage between patient names and codes was then destroyed. The epidemiologic data were transferred to the Centers for Disease Control and Prevention (CDC) for centralized entry and management. The remnant sera were shipped to the New York State Diagnostic HIV Laboratory (Albany, NY) for all further testing.

The survey did not involve any additional data collection or contact with patients and did not constitute human subjects research in accordance with the human research guidelines of the US Department of Health and Human Services. We examined HIV incidence in preexisting deidentified sera to minimize the likelihood of the bias that has been shown to occur in studies of volunteers.[25–28] Consistent with current standards of care,[29] participating STD clinics offered routine voluntary HIV antibody testing to all persons with syphilis. Therefore, all persons whose serum specimens were included in this survey had the opportunity to learn their HIV infection status through usual voluntary testing and counseling practices at the participating STD clinics.

Laboratory Methods

Local laboratories were asked to store 0.5 mL of remnant sera from all eligible male patients with syphilis frozen at $\leq -20°C$. Deidentified TP-PA–positive sera were then shipped in batches on dry ice overnight to the New York State Diagnostic HIV Laboratory. Here, the sera were screened for HIV-1 antibodies by EIA, using the first-generation Vironostika HIV-1 Microelisa System (bioMérieux, Durham, NC; September 2004 to June 2006) or the second-generation Genetic Systems rLAV EIA (Bio-Rad Laboratories, Redmond, WA; from July 2006 to August 2006). EIA-positive specimens confirmed HIV-positive by Western blot (WB) analysis (Bio-Rad Laboratories) were then tested using the LS HIV-1 Vironostika EIA (bioMérieux) and the immunoglobulin G-capture BED–EIA (BED; Calypte Biomedical Corporation, Lake Oswego, OR).[30] Specimens that tested reactive with the standard EIA and nonreactive with the LS-Vironostika (standardized optical density [SOD] cutoff <1.00) were classified as recent HIV infection (mean seroconversion period of 170 days, 95% CI: 145 to 200). Likewise, specimens that tested reactive with the standard EIA and nonreactive with the BED (normalized optical density [OD-n] cutoff <0.80) were classified as recent HIV infection (mean seroconversion period of 155 days, 95% CI: 139 to 186). In addition,

HIV-negative specimens were screened for HIV-1 RNA using a pooled protocol with a branched DNA (bDNA) test (Versant HIV-1 RNA 3.0 assay; Bayer Diagnostics, Tarrytown, NY) to identify persons with acute HIV infection who have not yet developed HIV antibodies.[21,31–33] Finally, EIA-positive specimens that had indeterminate WB results were tested using the Multispot HIV-1/HIV-2 EIA Rapid Test (Bio-Rad Laboratories).

Statistical Methods

To compare HIV incidence estimates by LS-Vironostika and BED directly, we used the mean seroconversion period of 155 days in all incidence calculations. We first calculated the proportion of recently HIV-infected persons as the number of recently HIV-infected persons divided by the number of uninfected persons plus half of recently HIV-infected persons (to represent the risk group in the midst of the year, assuming that persons seroconvert at a steady rate throughout the year). This estimate represents the incidence during the mean seroconversion period. HIV incidence was annualized by multiplying the proportion of recently HIV-infected persons by the correction factor of (365.25/155) × 100. Upper and lower 95% CIs were constructed by multiplying HIV incidence by 1.96 (a 97.5% quantile of the normal distribution) divided by the square root of the number of recently HIV-infected persons and by adding or subtracting this value from the HIV incidence estimate.[34] In addition to estimating crude HIV incidence by this method, we corrected incidence estimates[18,30] by excluding data from men who tested as recently HIV-infected by LS-Vironostika or BED but who also had a history (documented or by self-report) of an HIV-positive test result >6 months before their initial syphilis screening or who were using ARVs within 6 months before their initial syphilis screening. For the Los Angeles site, we compared the characteristics of EL syphilis cases and P&S syphilis cases using Wilcoxon rank sum and χ^2 tests. All analyses were done using SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

The syphilis cases were identified through public STD clinics in Dekalb and Fulton Counties in Atlanta; the City Clinic, the municipal STD clinic in San Francisco; and public STD clinics (59% of cases) and private providers (41% of cases) in Los Angeles County. We analyzed specimens from 457 men (median age = 35 years) with early syphilis (357 P&S and 100 EL) of diverse race/ethnicity (37% white, 30% black, and 25% Hispanic) who were primarily men who had sex with men in the past 12 months (80%) (Table 1). The men with P&S syphilis in Atlanta were mostly black (77%), whereas in San Francisco, they were mostly white (57%), and in Los Angeles, they were predominantly white (37%) and Hispanic (35%). In Los Angeles, the men with EL syphilis were similar to those with P&S syphilis with respect to age (P = 0.87) but were somewhat more likely to be nonwhite (P = 0.10) and somewhat less likely to have recorded behavioral risk factor information (P = 0.14).

The overall prevalence of WB-confirmed HIV infection among all men (P&S and EL cases) was 41%, and among those with P&S syphilis, it was 45% (Table 2). The prevalence ranged from 63% among P&S syphilis cases in Atlanta to 27% among EL syphilis cases in Los Angeles. Among men known to be MSM, the overall HIV prevalence was 47%; it was the highest (70%) among MSM in Atlanta.

Of 187 HIV-positive men with WB-confirmed infection, 114 (61%) had a history of an HIV-positive test result >6 months before their initial syphilis screening or of using ARVs within 6 months before their initial syphilis screening. Among 127 (68%) HIV-positive men who had ARV use information available, 55 (43%) had taken ARVs. Only 19 (10%) of the 187 men had no reported history for HIV status or ARV use.

Based solely on laboratory assay results, 38 men had evidence of recent HIV infection by BED or LS-Vironostika (28 men by LS-Vironostika results alone, 31 men by BED results alone, and 21 men by concordant BED and LS-Vironostika results). From among the 38 men, we excluded

TABLE 1. Characteristics of Men Newly Diagnosed With Early Syphilis in STD Clinics in Atlanta, San Francisco, and Los Angeles, 2004 to 2005

	Atlanta P&S (n = 98)	San Francisco P&S (n = 151)	Los Angeles P&S (n = 108)	Los Angeles EL (n = 100)	Total (N = 457)
Age, y, median (Q1 to Q3)	31 (24 to 39)	39 (32 to 43)	33 (25 to 39)	33 (24 to 41)	35 (27 to 41)
Race/ethnicity, n (%)					
White	18 (18)	86 (57)	40 (37)	23 (23)	167 (37)
Black	75 (77)	13 (9)	22 (20)	27 (27)	137 (30)
Hispanic	3 (3)	32 (21)	38 (35)	42 (42)	115 (25)
Asian/Pacific Islander	1 (1)	17 (11)	4 (4)	2 (2)	24 (5)
Other	0 (0)	3 (2)	2 (2)	2 (2)	7 (2)
Unknown	1 (1)	0 (0)	2 (2)	4 (4)	7 (2)
MSM (12 mo), n (%)					
Yes	84 (86)	143 (95)	78 (72)	60 (60)	365 (80)
No	14 (14)	8 (5)	19 (18)	22 (22)	63 (14)
Unknown	0	0	11 (10)	18 (18)	29 (6)
Primary syphilis, n (%)	19 (19)	64 (42)	32 (30)	N/A	115 (32)

Q indicates quartitle.

TABLE 2. HIV Incidence Estimated by LS-Vironostika and BED Among Men Newly Diagnosed With Early Syphilis in STD Clinics in Atlanta, San Francisco, and Los Angeles, 2004 to 2005

Category	Total	No. HIV$^+$	HIV Prevalence (%)	No. HIV$^-$	No. Recent HIV$^+$	HIV Incidence (95% CI)
All male syphilis cases						
Atlanta P&S	96*	60	63	36	2	12.7 (0.0 to 30.4)
San Francisco P&S	151	65	43	86	3	8.1 (0.0 to 17.2)
Los Angeles P&S	108	35	32	73	3	9.5 (0.0 to 20.2)
Los Angeles EL	100	27	27	73	3	9.5 (0.0 to 20.2)
All P&S	355	160	45	195	8	9.5 (2.9 to 16.0)
All P&S and EL	455	187	41	268	11	9.5 (3.9 to 15.1)
MSM syphilis cases						
Atlanta P&S	82	57	70	25	1	9.2 (0.0 to 27.4)
San Francisco P&S	143	64	45	79	3	8.8 (0.0 to 18.7)
Los Angeles P&S	78	29	37	49	3	14.0 (0.0 to 29.8)
Los Angeles EL	60	21	35	39	3	17.5 (0.0 to 37.2)
All P&S	303	150	50	153	7	10.5 (2.7 to 18.3)
All P&S and EL	363	171	47	192	10	12.0 (4.5 to 19.4)

*Two men in Atlanta who had HIV-positive EIA screening test results but insufficient serum for WB confirmation were excluded from the analyses.

from HIV incidence calculations 25 who had been HIV-positive for >6 months before their syphilis screening (23 had been HIV-positive for ≥1 year and 18 had a history of ARV use) and an additional 2 men who had uncertain dates of HIV-positive test results but had a history of ARV use. Thus, we identified 11 men who had evidence of recent HIV infection by BED and LS-Vironostika (100% concordance of results for the 2 assays) and who had no contradictory history of HIV testing or ARV use. Ten of the 11 men were MSM. Among all early syphilis cases, the corrected HIV incidence estimates were 9.5% per year (95% CI: 3.9 to 15.1) for all men and 12.0% per year (95% CI: 4.5 to 19.4) for MSM. Among P&S syphilis cases, the estimates were 9.5% per year (95% CI: 2.9 to 16.0) for all men and 10.5% per year (95% CI: 2.7 to 18.3) for MSM.

Without exclusion based on HIV testing and ARV use history, uncorrected HIV incidence estimates for all men with early syphilis were 25.8% per year (95% CI: 16.7 to 34.8) by BED only and 17.8% (95% CI: 10.2 to 25.4) if based on concordant BED and LS-Vironostika results.

In stratified analyses, the estimated HIV incidence was 14.1% per year (95% CI: 2.8 to 25.5) among men <30 years old (n = 151), 8.0% per year (95% CI: 0.0 to 17.0) among men 30 to 39 years old (n = 161), and 5.4% per year (95% CI: 0.0 to 12.9) among men ≥40 years old. The estimated HIV incidence was 14.3% per year (95% CI: 2.9 to 25.7) among white men, 6.5% per year (95% CI: 0.0 to 15.4) among black men, and 6.0% (95% CI: 0.0 to 14.2) among Hispanic men.

HIV-1 RNA Results

In San Francisco and Los Angeles, none of the HIV-seronegative specimens had HIV RNA present. In Atlanta, of 34 specimens that were HIV-seronegative by EIA (Vironostika or rLAV) on initial screening, 6 (18%) were found to have HIV RNA present. Of these 6 specimens, 4 were nonreactive by rLAV EIA but weakly reactive by Vironostika EIA; all 4 specimens were of insufficient quantity for WB testing or confirmatory testing by another HIV RNA assay. Of these 4 men, 3 had HIV-negative results by self-report within the past 2 to 6 months and the remaining man had an indeterminate WB test result 2 months after his initial syphilis test.* The discrepant Vironostika and rLAV EIA results, together with the self-reported recent HIV-negative results, suggest that these 4 patients may have been undergoing HIV seroconversion at the time of their initial syphilis test. The additional 2 patients had nonreactive Vironostika EIA results and insufficient serum for rLAV EIA or WB testing. One of these 2 men had a negative HIV test result by self-report 2 years previously, and the other had no HIV testing history. These 2 men might represent cases of acute HIV infection, but their definitive classification would have required confirmatory HIV RNA and serologic testing of follow-up blood specimens, which were not available. None of these 6 specimens were included in BED or LS-Vironostika testing, because these assays require initial confirmation of HIV infection by WB testing.

Indeterminate Western Blot Results

In San Francisco (n = 151), among the specimens reactive by EIA (n = 81), 65 had positive WB results, 5 had indeterminate results, and 11 had negative results. Of the 16 persons with negative or indeterminate WB test results, none had a history of HIV-positive results and all had negative results on further testing with the Multispot HIV-1/HIV-2 EIA Rapid Test, suggesting that these persons were not undergoing HIV seroconversion. Fifteen of these specimens were part of the first 106 specimens from San Francisco, which had been heat treated at 56°C for 30 minutes as part of VDRL testing procedures at the local laboratory. This large number of unconfirmed apparently false-positive Vironostika EIA results

*The local health department staff abstracted epidemiologic data for syphilis cases at least 1 month after their initial syphilis test to allow time for definitive confirmation of P&S syphilis infections and for case interview. The staff members were asked to abstract HIV results preceding the initial syphilis test; however, occasionally, HIV results performed after the initial syphilis test were available and abstracted. In all instances, data abstraction was completed and sera with associated data were deidentified before specimens were shipped to the centralized laboratory for further testing.

may be related to serum processing and/or possible contamination, although HIV incidence estimates in San Francisco were similar for heat-treated and non–heat-treated sera (data not shown). In Los Angeles and Atlanta, only 1 and 2 specimens, respectively, were EIA reactive and WB-negative and none were WB indeterminate.

DISCUSSION

In this population of consecutive men diagnosed with early syphilis in STD clinics in Atlanta, San Francisco, and Los Angeles, we found a high incidence of HIV infection during 2004 to 2005: HIV incidence was estimated at 9.5% per year (95% CI: 3.9 to 15.1) among all men, and at 12.0% per year (95% CI: 4.5 to 19.4) among MSM. HIV incidence estimates were similar in the analyses limited to P&S syphilis cases. Using the results of the BED and LS-Vironostika without additional contextual information substantially overestimated HIV incidence in this population which had a high prevalence (41% overall) of HIV infection. Exclusions based on history of HIV testing and ARV use reduced the number of men classified as having recent HIV infection by both assays from 21 to 11 and reduced estimated HIV incidence by almost 2-fold.

Our findings of high HIV prevalence corroborate the results from syphilis outbreak investigations, surveillance data, and research studies since 1998, which indicate that syphilis transmission in the United States is concentrated among MSM, many of whom are HIV-infected and engage in unsafe sex behaviors.[1–5,35,36] In these sexual networks, HIV-uninfected men acquiring syphilis are simultaneously at a high risk of HIV acquisition for multiple reasons. First, recent syphilis infection is not only an established indicator of unsafe sex behaviors but facilitates HIV acquisition because syphilitic ulcers disrupt epithelial and mucosal barriers and local inflammation may lead to recruitment of CD4 target cells to the site of ulceration.[15] Second, these HIV-uninfected men are sexually active within the networks of MSM with syphilis, a population that we and others have found to have a high HIV prevalence; thus, their probability of encountering an HIV-infected sex partner is increased. Third, their dually infected male partners are likely at higher risk of transmitting HIV not only because syphilitic ulcers in an HIV-infected partner may aid the passage of HIV to the HIV-uninfected partner but because the HIV-infected partner's viral load may be elevated in early syphilis infection.[13,14,37]

The high rates of HIV infection among men diagnosed with syphilis in this and prior studies[19,20] have raised concerns that current syphilis epidemics may fuel increases in HIV incidence among all MSM in the United States. A review of existing epidemiologic and behavioral data in 2005, however, found that the absolute contribution of syphilis epidemics to HIV incidence among urban MSM in the United States seemed limited,[16] because almost half of urban MSM with early syphilis were already HIV-infected and because the estimated number of syphilis cases among MSM in these cities was small compared with the likely far greater number of MSM at risk for HIV infection.

Our findings should be interpreted in light of the following caveats and limitations. First, we studied men diagnosed with early syphilis in select STD clinics in Atlanta, San Francisco, and Los Angeles, which were served by 3 public health laboratories. Our findings may not reflect HIV incidence in other populations of men with early syphilis or in those seen and tested by private health care providers using private laboratories. Second, the period of collection of remnant sera varied by city, and it is unknown whether HIV incidence has been stable among men with syphilis over that period. Third, a small proportion of remnant sera were of insufficient quantity for all required HIV testing, the processing and freezing of sera were not standardized (some sera may have been left at room temperature for several hours during syphilis testing), and two thirds of specimens from San Francisco were subjected to heat treatment for VDRL testing. Such handling of specimens could lead to HIV RNA degradation and reduce the likelihood of detecting acute HIV infection, if present. Fourth, we analyzed preexisting routinely collected syphilis surveillance and case management data. Although HIV testing and/or ARV use history was available for most men, this information was incomplete or missing for some men. Fifth, some initial studies have found that BED and LS-Vironostika assays misclassify as recently HIV-infected 5% to 6% of ARV-naive persons known to have seroconverted >12 months earlier,[38–40] but our findings suggest that rates of misclassification may be greater in other populations, particularly those receiving ARVs. Although we attempted to correct for this misclassification by exclusion of cases with contradictory HIV testing and ARV use history, we cannot rule out the possibility that our results may still overestimate HIV incidence. We cannot determine which cases were truly incident HIV infections, because this was a cross-sectional deidentified survey and not a prospective seroconverter cohort.

Finally, we do not have comparative HIV incidence data for men without syphilis from the same STD clinic sites to examine the relative influence of syphilis infection versus sexual behavior on risk of HIV acquisition in this population. Although leftover sera may be available from other men testing for STDs in these clinics, analogous information on sexual risk behavior and history of HIV testing as obtained during syphilis case interviews is not always collected with the same level of detail for men without STDs. Given that HIV incidence rates in other populations of MSM in recent years have been estimated at 3% to 4% per year[12,16,19,33,45] and that syphilis infection has been shown to increase the risk of HIV acquisition by 2- to 3-fold,[15] our finding of ~10% HIV incidence among MSM with syphilis is consistent with the existing data.

A key strength of this survey was the design, which minimized the potential for selection bias and underestimation of HIV prevalence and incidence, a demonstrated shortcoming in studies using volunteers.[27,28] In addition, we had access to HIV testing and ARV use history data, which were more complete than data in some prior smaller cross-sectional studies[20] and were essential for correcting the inflated BED and LS-Vironostika HIV incidence estimates in this population with a high HIV prevalence.

Our findings indicate that intensive and integrated HIV/STD testing, care, and prevention services are needed for men diagnosed with syphilis. Persons recently diagnosed with

syphilis are not only at an increased risk of HIV infection but, if already HIV-infected, may be at particularly high risk of transmitting HIV to their sexual partners, because HIV viral load may be elevated in the presence of syphilis and other STDs[14,37,41] and is particularly high in acute and recent HIV infection.[42,43] The CDC recommends that all patients seeking treatment for STDs, including syphilis, should be screened routinely for HIV during each visit for a new complaint.[44] In addition, persons who have multiple sex partners or have received a recent diagnosis of an STD should be provided with or referred to HIV/STD risk reduction counseling and testing services and offered assistance with partner counseling and referral services.[29,44] HIV-negative men diagnosed with syphilis should have follow-up visits at 3 and 6 months for verification of their response to syphilis treatment, repeat HIV antibody testing, risk reduction education, and linkage to HIV care in the event of HIV seroconversion.

Our findings support existing recommendations and the importance of focusing prevention and case management efforts on men, particularly MSM, diagnosed with syphilis and their sexual partners to reduce onward HIV transmission. These findings also argue for continued monitoring of HIV incidence in sentinel populations of men diagnosed with syphilis and other populations at high risk of infection with HIV and other STDs by using HIV incidence assays and appropriate adjustments for exclusion of false recent infections. Further evaluation of pooled protocols for HIV RNA screening of HIV-seronegative persons diagnosed with STDs or seen in STD clinics[32,45] is also warranted.

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