Published in final edited form as:

J Acquir Immune Defic Syndr. 2015 October 01; 70(2): 179–185. doi:10.1097/QAI.0000000000000730.

Viral Loads Among HIV-Infected Persons Diagnosed With Primary and Secondary Syphilis in 4 US Cities: New York City, Philadelphia, PA, Washington, DC, and Phoenix, AZ

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Abstract

Background—Incident syphilis among HIV-infected persons indicates the ongoing behavioral risk for HIV transmission. Detectable viral loads (VLs) among coinfected cases may amplify this risk.

Methods—Primary and secondary cases reported during 2009–2010 from 4 US sites were crossmatched with local HIV surveillance registries to identify syphilis case-persons infected with HIV before or shortly after the syphilis diagnosis. We examined HIV VL and CD4 results collected within 6 months before or after syphilis diagnosis for the coinfected cases identified. Independent correlates of detectable VLs (≥200 copies/mL) were determined.

Results—We identified 1675 cases of incident primary or secondary syphilis among persons with HIV. Median age was 37 years; 99.5% were men, 41.1% were African American, 24.5% were Hispanics, and 79.9% of the HIV diagnoses were made at least 1 year before syphilis diagnosis. Among those coinfected, there were no VL results reported for 188 (11.2%); of the 1487 (88.8%) with reported VL results, 809 (54.4%) had a detectable VL (median, 25,101 copies/mL; range, 206–3,590,000 copies/mL). Detectable VLs independently correlated with syphilis diagnosed at younger age, at an sexually transmitted disease clinic, and closer in time to HIV diagnosis.

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The authors have no funding or conflicts of interest to disclose.

Conclusions—More than half of syphilis case-persons identified with HIV had a detectable VL collected within 6 months of the syphilis diagnosis. This suggests virologic and active behavioral risk for transmitting HIV.

Keywords

syphilis; HIV; viral load; STD/HIV coinfection; HIV transmission; men who have sex with men; HIV treatment

INTRODUCTION

Men who have sex with men (MSM) are disproportionately affected by both HIV and syphilis.[1–10] Genital ulcers (the hallmark of primary syphilis) are an anatomic risk factor for HIV acquisition and transmission to sex partners.[11] Incident bacterial sexually transmitted diseases (STDs) diagnosed among HIV-infected persons indicate unprotected sex and the potential for onward HIV transmission.[12–14] Reducing this augmented risk calls for a greater focus on HIV-infected persons with incident STDs, including linkage to and retention in HIV care,[15] effective antiretroviral therapy (ART),[15] routine STD screening,[16,17] timely partner services,[18] and behavioral counseling.[19,20]

HIV viral load (VL) is an indicator of HIV infectiousness.[21] Suppressing HIV VL in the blood, (ie, ART) can drastically reduce HIV transmission.[15,22] However, HIV VL increases with incident syphilis infection, irrespective of VL (or ART) before the syphilis infection.[23,24] Population-based data on VLs and transmission potential among persons coinfected with syphilis and HIV are limited, but this coinfected population is likely to transmit HIV. To assess the potential for forward HIV transmission among those infected with both HIV and syphilis, we examined VLs of HIV-infected persons diagnosed with primary and secondary syphilis in 2009 and 2010, in 4 diverse urban areas in the United States.

METHODS

Throughout the United States, health departments must be notified of syphilis diagnoses. Primary and secondary stage syphilis (henceforth referred to as “syphilis”) cases are entered into case registries maintained at the state and local health departments. HIV infection is also reportable throughout the United States. In addition to HIV diagnosis, many public health jurisdictions mandate the reporting of HIV VLs and CD4 counts.

Syphilis cases diagnosed and reported to 4 public health jurisdictions [New York City, Washington, DC, Philadelphia, PA, and Maricopa County (greater Phoenix area), AZ] from 2009 to 2010 were identified from STD surveillance registries. These cases were matched with the jurisdiction’s HIV registry to identify instances of coinfection using previously described methods.[25] Variables derived from the STD and HIV surveillance databases at each site included the following: gender, race/ethnicity, date of syphilis diagnosis, date of HIV diagnosis, stage of syphilis at diagnosis, age at syphilis diagnosis, age at HIV diagnosis, gender of sex partners, clinical setting in which syphilis was diagnosed (STD clinic or another type of clinical setting), and values and dates of VL and CD4 counts collected within 6 months before and after syphilis diagnosis. Using the dates of HIV and

syphilis diagnoses, we calculated the intervals between diagnoses. Matched data were deidentified and aggregated into a single database for analysis. CD4 counts and VL were considered a proxy for linkage to HIV care.[26] The data were collected from the existing surveillance data as part of routine public health surveillance activities and were deidentified before analysis. The analysis was considered a surveillance activity and did not involve human subjects.[27,28]

We calculated mean and median intervals between the dates of syphilis diagnosis and VL (or CD4) collection most proximal to syphilis diagnosis. Also, we estimated VL at the time of syphilis diagnosis using the closest VL collection date and value within 6 months before or after syphilis diagnosis. Bivariate correlates of having a detectable VL near the time of syphilis diagnosis were identified using χ^2 test with significance defined as $P \leq 0.05$. Bivariate correlates with a P value of <0.10 were included in a multivariate logistic regression model using a forward stepwise procedure.[29] All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

We defined HIV–syphilis coinfection as HIV infection diagnosed before or up to 30 days after syphilis diagnosis. Coinfections were further classified into 1 of 4 groups based on the timing of HIV diagnosis relative to syphilis diagnosis: (1) 30 days before to 30 days after syphilis diagnosis, (2) 31–90 days before syphilis diagnosis, (3) 91–365 days before syphilis diagnosis, and (4) >365 days before syphilis diagnosis (Fig. 1). For the final multivariate analysis, we compared HIV case-persons diagnosed with syphilis more than 1 year after the initial HIV diagnosis with those with syphilis diagnosed less than 1 year after HIV diagnosis.

HIV VL of ≤200 copies per milliliter was defined as undetectable.[26] For analytic purposes, we grouped VL values into 5 categories: (1) undetectable (≤200 copies/mL), (2) 201–1000 copies per milliliter, (3) 1001–10,000 copies per milliliter, (4) 10,001–100,000 copies per milliliter, and (5) >100,000 copies per milliliter, with mean and median values calculated.

RESULTS

During 2009–2010, a total of 3060 syphilis cases were reported to the 4 public health jurisdictions. Male-to-female syphilis case ratios were as follows: 18:1 overall; NYC, 23:1 (1928/83); Philadelphia, 8:1 (381/51); Washington, 22:1 (284/13), and Phoenix, 22:1 (306/14).

Overall, 54.7% (1675/3060) of syphilis case-persons (303 primary and 1372 secondary) from the 4 jurisdictions had a match in the HIV surveillance registries (indicating HIV coinfection) at the time of syphilis diagnosis. The percent of syphilis case-persons with a reported HIV diagnosis was high in each jurisdiction: NYC, 59.4% (1195/2011); Philadelphia, 44.0% (190/432); Maricopa County (Phoenix area), 51% (164/320); and Washington, 42% (126/297). Our analytic group comprised the 1675 syphilis and HIV coinfected cases. Most coinfected case-persons in our analysis—71.3% (1195/1675)—included a home address in NYC; 11.3% (190/1675) in Philadelphia; 9.8% (164/1675) in Maricopa County (Phoenix area); and 7.5% (126/1675) in Washington.

Seven of the coinfected case-persons were among women, 1 was transgender, and 1667 (99.5%) were among men. Of male case-persons, 85.3% (1422/1667) were self-reported MSM. The median age for all coinfected case-persons was 37 years (range, 17–70 years). Non-Hispanic blacks represented 41.1% (688/1675) of case-persons, Non-Hispanic whites represented 32.0% (536/1675) and Hispanics 24.5% (411/1675). The majority of syphilis diagnoses (86.9%, 1455/1675) were made in settings other than STD clinics (Table 1).

Most coinfected cases (79.9%, 1338/1675) were diagnosed with HIV more than 1 year before syphilis diagnosis; 7.4% (124/1675) were diagnosed within 91–365 days of syphilis diagnosis, 2.5% (41/1675) within 31–90 days, and 10.3% (172/1675) within 30 days before or 30 days after syphilis diagnosis (Fig. 1).

There was at least 1 VL collected within 6 months before or after syphilis diagnosis for 88.8% (1487/1675) of coinfected cases: 384 of these (25.8%) had VL collected before the syphilis diagnosis, 637 (42.8%) at the same time as syphilis diagnosis (±2 days), and 466 (31.3%) at least 2 days after the syphilis diagnosis. Median intervals between syphilis diagnosis and most proximal VL collection date ranged from 7 to 20 days for each of the 4 HIV/syphilis diagnosis intervals (Table 2).

Of the 1487 cases with a reported VL collected within 6 months of syphilis diagnosis, 54.4% (809) were detectable VLs. The median VL value of those with detectable values was 25,101 copies per milliliter (range, 206–3,590,000 copies/mL). There was no reported VL collected within 6 months of syphilis diagnosis for 11.2% (188/1675) of case-persons. However, 52.7% (99/188) of these cases did have a VL reported between 6 months to 1 year before or after syphilis diagnoses. Of these, 67.7% (67/99) had detectable VLs.

Detectable VLs among coinfected cases were most common among case-persons aged 17–24 years (81.9%, 145/177), followed by those aged 25–34 years (64.5%, 289/448) and 35–44 years (49.2%, 259/526). Among race/ethnicity groups, the American Indian/Asian/Pacific Islander group had the highest proportion of cases with a detectable VL (62.5%, 20/32) followed by non-Hispanic blacks (59.1%, 353/597), Hispanics (53.2%, 202/380), and non-Hispanic whites (49.1%, 233/475). Of the 7 female cases, 6 (85.7%) had undetectable VLs collected within 6 months of their syphilis diagnoses. Detectable VLs were more common among cases diagnosed with syphilis at STD clinics (69.1%, 114/165) as compared with persons diagnosed in other clinical settings (52.6%, 695/1322) ($P = 0.02$) and among persons diagnosed with HIV within 30 days of syphilis diagnosis (98.0%, 146/149) as compared with persons diagnosed with HIV 31–90 days (87.2%, 34/39), 91–365 days (77.8%, 84/108), and more than 365 days (45.8%, 545/1191) before syphilis diagnosis (Table 3).

In multivariate analysis adjusting for study site, age at syphilis diagnosis, race/ethnicity, type of diagnosing facility, and timing of syphilis diagnosis relative to HIV diagnosis, variables significantly associated with having detectable VLs collected within 6 months of syphilis diagnosis were as follows: being in any age group <45 years, syphilis diagnosis made in an STD clinic setting, and HIV diagnosis made less than 365 days before syphilis diagnosis (Table 3). The odds of detectable VL increased with proximity of syphilis to HIV diagnoses

as follows: HIV diagnosis 91–365 days before syphilis diagnosis [odds ratio (OR), 3.5; 95% confidence interval (CI): 2.1 to 5.7], HIV diagnosis 31–90 days before syphilis diagnosis (OR, 6.6; 95% CI: 2.5 to 17.6), and HIV diagnosis 30 days before or 30 days after syphilis diagnosis (OR, 44.4; 95% CI: 14.0 to 141.3). In multivariate analysis adjusting for age, race/ethnicity, syphilis stage, and study site, case-persons diagnosed in STD clinics were more likely to be diagnosed with HIV within 30 days of syphilis diagnosis as compared with case-persons diagnosed in other clinical settings (23% versus 8%) (adjusted OR, 3.2; 95% CI: 2.0 to 4.9; $P < 0.0001$).

CD4 counts were reported within 6 months of syphilis diagnosis for 1406 coinfected cases (83.9%); median CD4 count was 432 cells per cubic millimeter (range, 10–1888 cells/mm^3). Among all coinfected cases, 96.7% (1619/1675) had at least 1 VL or CD4 count collected within 1 year before or after syphilis diagnosis, suggesting that these coinfected cases were connected to HIV care. Among the 89 cases with no reported VL collected within 1 year before or after syphilis diagnosis, 37.1% (33/89) had a CD4 count collected during that time.

DISCUSSION

To our knowledge, this is the first reported use of multisite population-based STD and HIV surveillance data to gauge HIV infectiousness among syphilis and HIV coinfected persons near the time of syphilis diagnosis. Crossmatching STD and HIV databases revealed that 55% of case-persons with syphilis had HIV coinfection and 48% of coinfected case-persons had detectable HIV VLs. Among case-persons with detectable VL, the median VL value was high (25,101 copies/mL). The superposition of syphilis infection on preexisting HIV suggests ongoing sexual risk and thus potential for onward transmission of HIV. The extent of HIV coinfection among syphilis cases suggests that the time of syphilis diagnosis is an important moment to evaluate for HIV infection (if current status unknown), relink to HIV care as needed for syphilis patients with preexisting HIV infection, and emphasize adherence to effective ART. Behavioral risk (eg, unprotected sex) combined with a lack of viral suppression pose considerable risk of HIV transmission around the time of syphilis diagnosis.[8,9,12,15,22]

Among the HIV and syphilis coinfected case-persons included in our analysis, the majority were male, belonged to a racial/ethnic minority group, and were diagnosed with HIV before being diagnosed with syphilis. Similar to previously reported findings, detectable VLs were more likely to be observed among young men and those with more recent HIV diagnoses.[26,30] Detectable VLs were also more likely to be reported among case-persons diagnosed with syphilis at an STD clinic. These findings highlight the role of STD clinics in diagnosing HIV infection and providing safety net testing and partner referral services. STD diagnoses present important opportunities for connecting or reconnecting HIV-infected persons to HIV care. Addressing behavioral risk reduction and also linkage and engagement with HIV care should be prioritized as part of routine public health case investigation of HIV cases coinfected with other STDs in addition to managing sex partners' exposure to both syphilis and HIV, which could include referral for preexposure prophylaxis among partners who are HIV negative.[18,31]

VL and CD4 count data collected as part of HIV surveillance are used as surrogate markers for connection to and engagement in HIV care.[28,32,33] Nationally, HIV-infected patients with incomplete engagement in HIV care represent the largest proportion of HIV-infected individuals with detectable VL.[34] Approximately half (46%) of this population had an undetectable VL (≤200 copies/mL) collected within 6 months before or after syphilis diagnosis. This proportion is considerably higher than recent national estimates (24%)[35,36] and indicates the connection to HIV care and suppressive treatment for this subset, although this varied across the jurisdictions we included. Overall, 97% of case-persons had a VL or a CD4 count collected within 1 year before or after syphilis diagnosis, demonstrating linkage to HIV care.[35] High levels of connection to HIV primary care were further supported by the finding of nearly 43% of cases having VL collection dates that coincided with syphilis diagnosis dates, which suggests that these patients may have been diagnosed with syphilis in an HIV care setting. HIV care providers can and should incorporate prevention activities and messages into the routine care of HIV patients, including expedited suppressive HIV treatment and also counseling to reduce transmission risk[19,20,36] and routine screening for other STDs,[17] services that can be augmented with standard protocols and clinical reminders.[37–39]

There are limitations to our analysis. Our assumption that VL collected within 6 months of syphilis diagnosis is a reasonable proxy for actual values at the time of syphilis diagnosis could have been incorrect; however, when we looked closely at these intervals, we found that more than half of case-persons in each HIV diagnosis category had a VL collected within 1 month of syphilis diagnosis, and therefore, these VLs were likely to approximate actual values at time of syphilis diagnosis. It is possible that undetectable VL and low CD4 values were missing for some records in the data sets used for this analysis, as reporting of undetectable VL is not mandated in Arizona and incomplete reporting of HIV laboratory data has been described in NYC, where all VL and CD4 values are required to be reported.[32] However, only 5% of cases in this sample had missing VL within 1 year of syphilis diagnosis, so any overestimate of persons not linked to HIV care is likely to be small. VLs may have been performed as part of a diagnostic workup for HIV and may not reflect connection to HIV care. We did not have access to information on sexual practices (such as serosorting) for our analysis, nor did we have information on the use of and adherence to antiretroviral medications. Fluctuations in plasma VL and the lack of correlation between plasma VL and VL at exposed anatomic sites[40–42] limit the validity of using plasma VL alone to estimate transmission risk. Increases in plasma VL can occur as a result of syphilis coinfection[23,24]; thus, VL in this analysis may be higher than values among HIV-infected persons without syphilis. Data were not available to characterize a more specific clinical setting of syphilis diagnosis. The contribution of specific sexual behaviors in influencing transmission risk could not be evaluated. Syphilis can be transmitted during oral sex,[43] a practice that confers a minimal risk for HIV transmission[44]; therefore, all syphilis infections may not have resulted from unprotected insertive or receptive anal intercourse. Finally, in 2012, the Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents were updated to include a recommendation for ART for all HIV-infected individuals.[45] VLs of cases included in this analysis, reported in 2009–2010, would not have been affected by this expanded treatment recommendation.

This analysis identified syphilis infection superimposed on preexisting HIV, indicating sexual risk for HIV transmission. Detectable VL was common in these patients with syphilis and suggests the potential for onward HIV transmission near the time of syphilis diagnosis. In addition, these results demonstrate how integrated surveillance registries for STDs and HIV can provide insight into trends in coinfection,[25] the timing of one disease event relative to the other, which population-based subgroups are the most likely to be infectious for HIV using VL, and connection to HIV care among coinfected cases. More than a decade has now passed since the resurgence of syphilis began among MSM.[46] What was once an epidemic among men between the age 35 and 39 years, now encompasses younger male populations, with highest rates among those aged 20–24 years along with accompanying high rates of HIV coinfection.[7,47] Syphilis diagnosis may be a sentinel event for HIV transmission and acquisition. These intersecting epidemics offer the opportunity to optimize the use of surveillance data to integrate prevention efforts and target resources to populations at high risk for HIV acquisition and transmission.[48]

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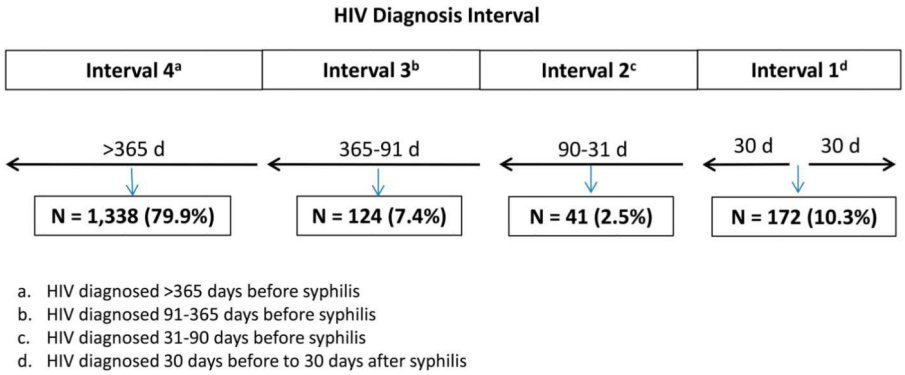

FIGURE 1.

Timing of HIV diagnosis relative to syphilis diagnosis among coinfected cases in 4 US jurisdictions, 2009–2010 (n = 1675).

TABLE 1.

Demographics and Selected Clinical Characteristics Among Persons Coinfected With HIV and Primary and Secondary Syphilis in New York City, Philadelphia, Washington Dc, and Phoenix, 2009–2010

Variable	Number (%)
Population	1675
Study site	
New York City, NY	1195 (71.3)
Philadelphia, PA	190 (11.3)
Maricopa County (Phoenix area)	164 (9.8)
Washington, DC	126 (7.5)
Gender	
Male	1667 (99.5)
Female	7 (0.4)
Transgender (male to female)	1 (0.06)
Sexual behavior	
MSM	1422 (84.9)
Men who have sex with women	228 (13.6)
Women who have sex with men	7 (0.04)
Unknown	18 (1.0)
Age, yrs	
17–24	209 (12.5)
25–34	514 (30.7)
35–44	577 (34.5)
45–54	319 (19.0)
55+	56 (3.3)
Race	
White non-Hispanic	536 (32.0)
African American non-Hispanic	688 (41.1)
Hispanic	411 (24.5)
American Indian/Alaska native non-Hispanic	8 (0.5)
Asian non-Hispanic	29 (1.7)
Other/unknown non-Hispanic	3 (0.2)
Clinical site of primary and secondary syphilis diagnosis	
STD clinic	220 (13.1)
Non-STD clinic	1455 (86.9)
Syphilis stage at diagnosis	
Primary	303 (18.1)
Secondary	1372 (81.9)
HIV diagnosis (relative to syphilis diagnosis)	
Interval 1: HIV 30 d before to 30 d after syphilis diagnosis	172 (10.3)
Interval 2: HIV 31–90 d before syphilis diagnosis	41 (2.5)
Interval 3: HIV 91–365 d before syphilis diagnosis	124 (7.4)

Variable	Number (%)
Interval 4: HIV >365 d before syphilis diagnosis	1338 (79.9)
VL (collected nearest to and within 6 mo of syphilis diagnosis)	
Undetectable (≤200 copies/mL)	678 (40.5)
Detectable (>200 copies/mL)	809 (48.2)
Mean (copies/mL)	82,754
Median (copies/mL)	25,101
Range (copies/mL)	206–3,590,000
Unavailable	188 (11.2)
VL categories *	
≤200 copies/mL	678 (45.6)
201–1000 copies/mL	97 (6.5)
1001–10,000 copies/mL	182 (12.2)
10,001–100,000 copies/mL	357 (24.0)
>100,000 copies/mL	173 (11.6)
CD4 count (collected nearest to, and within 6 mo of syphilis diagnosis) (n = 1406)	
Available	1406 (83.9)
Mean (cells/mm^3)	453
Median (cells/mm^3)	432
Range (cells/mm^3)	10–1888
Unavailable	269 (16.1)

* VL collection nearest to syphilis diagnosis and within 180 days of syphilis diagnosis for those with available values (n = 1487).

TABLE 2.

Days Between Syphilis Diagnosis and HIV VL Collection by HIV Diagnosis Interval (n = 1487 Persons)

HIV Diagnosis Interval (Relative to Syphilis Diagnosis)	No. Persons	Available VL (%)	Days Between Syphilis Diagnosis and HIV VL Collection		
			Mean*	Median	Range
Interval 1: HIV 30 d before to 30 d after syphilis diagnosis	172	149 (86.6)	24.5	9	0–170
Interval 2: HIV 31–90 d before syphilis diagnosis	41	39 (95.1)	25.9	20	0–137
Interval 3: HIV 91–365 d before syphilis diagnosis	124	108 (87.1)	24.6	8.5	0–167
Interval 4: HIV >365 d before syphilis diagnosis	1338	1191 (89.0)	27.1	7.0	0–182
Total	1675	1487 (88.8)	26.6	8.0	0–182

*Mean, median, range reflect absolute value of days elapsed from syphilis diagnosis to VL collection.

TABLE 3.

Correlates of a Detectable VL Among Men Coinfected With HIV and Primary and Secondary Syphilis, 4 Sites, 2009–2010

Variable	n*	Detectable VL (%)†	Mean VL (Range), Copies/mL	Adjusted OR (95% CI)‡	*P*
Total	1487	809 (54.4)	82,753 (206–3,590,000)	—	—
Study site					
New York City, NY	1135	611 (53.8)	73,949 (206–750,005)	1.1 (0.8 to 1.7)	0.4
Philadelphia, PA	142	82 (57.8)	95,897 (214–1,233,698)	Ref	—
Maricopa County, AZ (Phoenix)	97	62 (63.9)	150,937 (220–3,590,000)	1.4 (0.8 to 2.6)	0.1
Washington, DC	113	54 (47.8)	84,133 (270–927,090)	0.8 (0.4 to 1.3)	0.07
Age§					
17–24	177	145 (81.9)	63,051 (214–627,283)	5.9 (3.7 to 9.7)	<0.001
25–34	448	289 (64.5)	90,454 (219–1,233,698)	2.9 (2.1 to 4.0)	0.04
35–44	526	259 (49.2)	85,988 (206–3,590,000)	1.7 (1.3 to 2.3)	0.002
45+	336	116 (34.5)	80,973 (209–577,067)	Ref	—
Race/ethnicity					
White	475	233 (49.1)	1,152,212 (209–3,590,000)	Ref	
Hispanic	380	202 (53.2)	74,568 (222–1,233,698)	1.0 (0.7 to 1.3)	0.9
African American	597	353 (59.1)	69,078 (206–750,005)	1.1 (0.8 to 1.5)	0.6
Asian, PI, American Indian, Other	32	20 (62.5)	32,762 (220–124,485)	1.0 (0.4 to 2.2)	0.9
Unknown	3	1 (33.3)	763 (763)	0.7 (0.1 to 7.8)	0.8
Site of diagnosis					
STD clinic	165	114 (69.1)	56,971 (254–520,000)	1.7 (1.1 to 2.5)	0.01
Non-STD clinic	1322	695 (52.6)	86,983 (206–3,590,000)	Ref	—
Syphilis stage					
Primary	263	130 (49.4)	55,399 (220–927,090)	0.7 (0.6 to 1.0)	0.06
Secondary	1224	679 (55.5)	87,991 (206–3,590,000)	Ref	—
HIV diagnosis interval (relative to syphilis diagnosis)‖					
HIV ≤365 d before syphilis diagnosis	296	264 (89.2)	108,599 (214–3,590,000)	7.7 (5.2 to 11.5)	<0.001
HIV more than 365 d before syphilis diagnosis	1191	545 (45.8)	70,233 (206–1,233,698)	Ref	—

*Persons with a VL collected within 180 days of syphilis diagnosis.

[†]Detectable VL defined as >200 copies per milliliter.

[‡]Comparison of having a detectable versus undetectable VL within 180 days of syphilis diagnosis adjusting for study site, age group, race/ethnicity, site of syphilis diagnosis, syphilis stage, and HIV diagnosis interval.

[§]Because of sample size, age groups 45–54 and 55+ were combined for the multivariate model.

[‖]HIV diagnosis intervals less than 365 days were combined into one variable for this multivariate model.

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2019 September 18.