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Reported Primary and Secondary Syphilis Cases in the United States: Implications for HIV Infection

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Abstract

Background: Recent increases in syphilis among men who have sex with men (MSM) are especially concerning, given the biologic and epidemiologic associations between syphilis and HIV infection. We sought to better describe the current epidemiology of primary and secondary (P&S) syphilis and the prevalence of HIV infection among reported P&S syphilis cases by demographic group, including sex of sex partner, in the United States in 2016.

Methods: We reviewed national P&S syphilis case report data from 2016, including available risk factor information such as sex of sex partner and HIV status. Data were extracted from the National Electronic Telecommunications System for Surveillance, the system through which Centers for Disease Control and Prevention receives notifiable sexually transmitted disease data from all 50 states and the District of Columbia. The proportion of cases with HIV coinfection was calculated using cases with known HIV status as the denominator.

Results: Of 27,814 P&S syphilis cases reported in 2016, 58.1% were among MSM, 13.9% were among men who have sex with women only, 11.0% were among women, and 16.9% were among men without data on sex of sex partners. Similar patterns were observed across geographic regions, race/ethnicity groups, and most age groups. Overall, 38.5% of reported P&S syphilis cases with known HIV status were coinfecting with HIV. The prevalence of HIV coinfection was highest among MSM (47.0%) compared with men who have sex with women only (10.7%) or women (4.1%). Among MSM with P&S syphilis, the prevalence of HIV coinfection was highest among black MSM, ranging from 33.8% among black MSM aged 15 to 19 years to 77.8% among black MSM aged 45 to 49 years.

Conclusions: These data underscore the epidemiologic linkages between syphilis and HIV, particularly among MSM. Primary and secondary syphilis may represent an opportunity to prevent HIV infection among persons who are HIV negative and identify and link to care persons living with HIV infection but not currently engaged in care.

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Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum* and can lead to serious neurologic and ophthalmologic complications if left untreated.^{1–3} In the United States, the national rate of reported primary and secondary (P&S) syphilis has risen dramatically over the last 15 years. After reaching an historic low in 2000 and 2001 (2.1 cases per 100,000 population), the national P&S syphilis rate more than tripled by 2016 (8.7 cases per 100,000 population).⁴ In 2016, there were 27,814 reported P&S syphilis cases in the United States, the highest number of cases reported in a single calendar year since 1993. These increases have largely been attributable to increases among men and, in particular, increases among gay, bisexual, and other men who have sex with men (collectively referred to as MSM),⁴ and estimated rates among MSM are much higher than rates among men who have sex with women only (MSW) or women.⁵ In 2015, the estimated P&S syphilis rate among MSM was 106 times the rate among MSW and 168 times the rate among women.⁵

These increases in syphilis are especially concerning given the biologic and epidemiologic associations between syphilis and HIV infection. Early syphilitic infection may facilitate transmission and acquisition of HIV infection.^{6–8} In addition, the populations disproportionately affected by HIV, including MSM and certain race/ethnicity groups, are similar to the populations at increased risk for syphilitic infection,⁹ and multiple reports have documented a high prevalence of HIV coinfection among men and MSM with P&S syphilis.^{4,10,11} Primary and secondary syphilis might be an indication of condomless sexual contact within sexual networks at high risk for HIV transmission. Therefore, a diagnosis of P&S syphilis might also represent an opportunity for public health and clinical intervention to (1) prevent HIV infection among those who are HIV negative and (2) identify and link to care those who are living with HIV infection but not currently engaged in care.

The Centers for Disease Control and Prevention (CDC) has previously reported national data on P&S syphilis among MSM, MSW, and women, as well as the proportion of cases coinfecting with HIV.⁴ The objectives of this analysis were to (1) better describe the distribution of reported P&S syphilis cases among MSM, MSW, and women by geographic region, race/ethnicity, and age group, and (2) describe the proportion of P&S syphilis cases coinfecting with HIV by demographic group and sex of sex partner.

METHODS

Primary and secondary syphilis case report data were extracted from the National Electronic Telecommunications System for Surveillance, the system through which CDC receives notifiable sexually transmitted disease (STD) data from all 50 states and the District of Columbia. Case report data are received as de-identified, line-listed data that include demographic information, such as sex, race/ethnicity, and age of reported cases. Case report data also include additional risk factor information, such as sex of sex partner and HIV status, for cases interviewed or investigated by the local public health department. This analysis focused on P&S syphilis because P&S syphilis represents the earliest stage of syphilitic infection, reflects symptomatic disease, and is an indicator of incident infection.¹² Also, because they represent recently acquired infections and are infectious, P&S syphilis cases are typically prioritized by STD control programs for case investigation and

interviews, and are therefore more likely to be reported with complete data on sex of sex partner and HIV status compared with later stages of syphilis.

For the purposes of this analysis, male cases were categorized as MSM if they reported having sex with any male partner in the last 12 months. Male cases were categorized as MSW if they reported having sex with only female partners in the last 12 months. The proportion of P&S syphilis cases with HIV coinfection was calculated using cases with known HIV status (either known to be living with HIV or known to be HIV negative) as the denominator and were examined by demographic group (race/ethnicity and age group) and by reported sex/sex of sex partner (MSM, MSW, and women). Reported HIV status was obtained based on self-report, the results of the most recent HIV test at the time of the case interview/investigation, or other records available to the health department.

RESULTS

In 2016, there were 27,814 reported cases of P&S syphilis in the United States (Table 1). Of these, 24,724 (88.9%) were male. Among male cases, 16,155 (65.3%) were MSM, 3880 (15.7%) were MSW, and 4689 (19.0%) were male cases without data on sex of sex partner. Overall, 58.1% of reported P&S syphilis cases in 2016 were among MSM, 13.9% were among MSW, and 11.0% were among women.

Similar patterns were observed across geographic regions, race/ethnicity groups, and most age groups. In every region, MSM accounted for most reported P&S syphilis cases (range, 56.9–60.7%), and female and MSW cases represented a much lower proportion of cases (range, 5.6–12.7% and 9.7–15.7%, respectively). When examined by race/ethnicity, MSM accounted for most reported P&S syphilis cases in every race/ethnicity group except for American Indian/Alaska Natives. The proportion of cases that were among MSM was highest among Native Hawaiian/other Pacific Islanders (70.8%), followed by Asians (69.6%), whites (62.1%), and those who identified as multirace (61.7%), and was lower among blacks (51.3%) and American Indian/Alaska Natives (45.8%). When examined by age group, MSM accounted for most reported cases in every age group except for those younger than 15 years.

In 2016, 21,193 (76.2%) reported cases of P&S syphilis were reported with known HIV status (Table 2). Among cases with known HIV status, 8154 (38.5%) were coinfecting with HIV. The proportion of cases with HIV coinfection was higher among male cases (42.5%) compared with female cases (4.1%). Among male cases with known sex of sex partner, the prevalence of HIV coinfection was higher among MSM (47.0%) than among MSW (10.7%). When examined by race/ethnicity group, the proportion of P&S syphilis cases with HIV coinfection was highest among those who identified as multirace (46.1%) and blacks (44.2%), and was lowest among American Indians/Alaska Natives (25.0%). When examined by region, the prevalence of HIV coinfection was lower among cases in the West (34.2%) than cases in the Northeast (45.9%), Midwest (41.3%), or South (38.2%).

In general, HIV coinfection was more common in older age groups. Overall, the prevalence of coinfection increased from 11.9% among P&S syphilis cases aged 15 to 19 years to 53.8%

among cases aged 45 to 49 years; the prevalence among those aged at least 50 years was 48.5% (Table 2). Trends by age group were similar among MSM and MSW cases (Table 3). Among MSM, the proportion of P&S syphilis cases with HIV coinfection increased with increasing age from 18.5% among MSM cases aged 15 to 19 years to 63.0% among MSM cases aged 45 to 49 years but declined to 59.3% among MSM cases aged at least 50 years. Similarly, among MSW, the proportion of cases with HIV coinfection peaked in the age groups aged 45 to 49 years (16.1%). However, the prevalence of HIV coinfection was substantially higher among MSM cases in every age group compared with MSW cases. Among women, there were relatively few P&S syphilis cases with HIV coinfection in each age group (range, 0–17 cases). The proportion of female P&S syphilis cases with HIV coinfection was generally lower in each age group compared with MSM and MSW cases.

When P&S syphilis cases among MSM were examined by race/ethnicity and age group, different patterns were observed for black MSM, Hispanic MSM, and white MSM (Fig. 1). Among black MSM and Hispanic MSM, the highest number of P&S syphilis cases as well as the highest number of cases coinfecting with HIV occurred among those aged 25 to 29 years. Among white MSM, the highest number of P&S syphilis cases and highest number of cases coinfecting with HIV occurred among those aged at least 50 years. For each age group examined, including 15- to 19-year-olds, the prevalence of HIV coinfection was highest among black MSM P&S syphilis cases compared with Hispanic or white MSM cases. Among black MSM P&S syphilis cases with known HIV status, the proportion with HIV coinfection ranged from 33.8% among those aged 15 to 19 years to 77.8% among those aged 45 to 49 years. Among Hispanic MSM cases, the proportion with HIV coinfection ranged from 9.3% among those aged 15 to 19 years to 66.2% among those aged 45 to 44 years. Among white MSM cases, the proportion with HIV coinfection ranged from 7.3% among those aged 15 to 19 years to 61.9% among those aged 45 to 49 years.

DISCUSSION

In 2016, most reported P&S syphilis cases (58.1%) were among MSM compared with 13.9% of cases that were among MSW and 11.0% of cases that were among women (16.9% of cases were among men with unknown data on sex of sex partner). This analysis found similar distributions of cases among MSM, MSW, and women across demographic groups. Men who have sex with men accounted for a large plurality or most of reported cases in almost every race/ethnicity group (range, 45.8%–70.8%) and for most reported cases in every geographic region (range, 56.9%–60.7%) and every age group of a least 15 years (range, 51.2%–60.2%). This indicates that the current syphilis epidemic is largely an epidemic among MSM, regardless of geographic region or demographic group. Some demographic groups, such as the South, American Indians/Alaska Natives, blacks, and younger age groups, were observed to have relatively higher proportions of cases among women and MSW compared with other demographic groups, reflecting a relatively greater role of heterosexual transmission in these demographic groups. However, cases among MSM outnumbered cases among heterosexuals (MSW and women combined) in every demographic group except for those younger than 15 years.

This analysis also found a high overall prevalence (38.5%) of HIV coinfection among reported P&S syphilis cases in the United States. This prevalence is largely driven by the high proportion (47.0%) of P&S syphilis cases among MSM who are coinfecting with HIV. However, the prevalence of HIV infection among MSM (10.7%) and female (4.1%) P&S syphilis cases was also substantially higher than the prevalence of HIV infection among adult and adolescent male and female individuals in the general population (0.6% and 0.2%, respectively).⁹ The proportion of cases coinfecting with HIV generally increased with increasing age, with the highest proportion observed among those aged 45 to 49 years and those aged at least 50 years. This pattern is similar to that observed in the general population⁹ and likely reflects a cohort effect as individuals infected with HIV survive into later life. Although high prevalences of HIV infection were observed among MSM P&S syphilis cases across age groups and race/ethnicity groups, prevalences were particularly high among black MSM, a population that has previously been shown to be disproportionately affected by HIV, syphilis, and other sexually transmitted infections.^{9,13,14}

These findings highlight that in 2016, a considerable proportion of syphilis transmission in the United States occurred among persons living with HIV, and especially among MSM living with HIV. National guidelines recommend that all sexually active persons with HIV infection be tested for curable STDs, including syphilis, at the initial HIV care visit and at least annually during the course of HIV care,^{15,16} but there is evidence that rates of testing are suboptimal. It is estimated that only 55% of sexually active HIV-infected adults were tested at least once for syphilis in the past 12 months.¹⁷ Our findings indicate that improved identification and treatment of syphilis among those infected with HIV will be critical for syphilis control efforts in the country, and they support the current national recommendations for screening and testing among sexually active persons living with HIV.

Furthermore, these findings demonstrate that a diagnosis of P&S syphilis represents a clinical and public health opportunity to identify undiagnosed HIV infections, to link persons living with diagnosed HIV to HIV care and treatment services, and also to potentially prevent future HIV infection among those who are HIV negative. Given that the prevalence of HIV infection among those diagnosed with P&S syphilis is substantially higher than the prevalence among the general population, and given that P&S syphilis is a likely marker of condomless sexual activity within a sexual network with a high prevalence of HIV infection, all persons with uncertain HIV status who are diagnosed as having P&S syphilis should be screened for HIV infection. The CDC recommends that this screening should be routine, regardless of whether the patient reports any additional specific behavioral risks for HIV infection.¹⁶

For persons with P&S syphilis who are newly diagnosed as having HIV, or who had been previously diagnosed as having HIV but are not currently engaged in HIV care and treatment, a diagnosis of P&S syphilis is an opportunity for the health care and public health systems to identify these individuals and ensure that they are linked to appropriate services. Early detection of HIV infection and viral suppression through effective treatment with antiretroviral therapy are associated with improved life expectancy for persons living with HIV as well as decreased risk of transmitting HIV to others.^{18,19} As a result, antiretroviral therapy is recommended for all HIV-infected individuals, regardless of symptoms or CD4

count.²⁰ However, it is estimated that approximately 14% of the 1.2 million persons living with HIV have not been diagnosed and are not aware of their status, and that 60% are not engaged in HIV medical care.²¹ Because the diagnosis and treatment of P&S syphilis might bring individuals who are not otherwise engaged in care in contact with the health system, clinical providers and public health programs should take advantage of this opportunity to identify and link to care those who are living with diagnosed HIV.

For persons with P&S syphilis who are currently HIV negative, a diagnosis of P&S syphilis represents a potential opportunity to prevent future HIV infection. A diagnosis of P&S syphilis can indicate recent or current sexual exposures that place an individual at increased risk for both syphilitic and HIV infection, and is likely a marker for future risk. Among men with syphilis, studies in New York City and Florida have found high rates of subsequent HIV infection after the syphilis diagnosis (annual incidence of 3.6% and 2.3%, respectively).^{22,23} Annual incidence was even higher (5.6%) among MSM after a diagnosis of syphilis.²² Taken together, these data indicate that persons diagnosed as having syphilis should be evaluated for ongoing risk of HIV infection and, if appropriate, targeted for HIV prevention services and considered possible candidates for preexposure prophylaxis (PrEP). The use of PrEP (combination emtricitabine and tenofovir as a single pill taken daily) has been shown to be safe and effectively prevents HIV infection among MSM and among heterosexual men and women.^{24,25} National guidelines recommend that PrEP be considered for people who are HIV negative and at substantial risk for HIV infection, including MSM diagnosed as having an STD in the past 6 months and heterosexual men and women who do not regularly use condoms during sex with partners of unknown HIV status who are at substantial risk for HIV infection.^{26,27} Therefore, a P&S syphilis diagnosis in an HIV-negative MSM, as well as HIV-negative MSW and women assessed to be at high risk, can be a key opportunity to offer and initiate PrEP.

The data presented in this report are subject to certain caveats and limitations. This analysis was based on surveillance data, and owing to underascertainment and underreporting, the number of reported cases in surveillance data likely underestimates the true burden of P&S syphilis in the country. In addition, a substantial proportion of cases were reported with incomplete data on HIV status and sex of sex partner. For this reason, one of the main analyses of this report, calculating the proportion of P&S syphilis cases with HIV coinfection, was limited to the 76% of cases with known HIV status. Given that 24% of reported P&S syphilis cases had unknown HIV status or were missing data on HIV status, it is possible that the true proportion coinfecting with HIV differs from those reported. However, even if all cases with unknown HIV status were considered HIV negative and included in the denominator, the prevalence of HIV infection among P&S syphilis cases would still be substantially higher than that in the general population (data not shown). Similarly, our analysis of the distribution of cases by sex and sex of sex partner is limited by incomplete information on sex of sex partner; 19% of male cases were reported without data on sex of sex partners, and misclassification of cases is possible if men were reluctant to report male sex partners.

This report underscores that, across geographic regions and demographic groups, the current syphilis epidemic is largely an epidemic among MSM. This report also highlights the

epidemiologic link between syphilis and HIV. The recent increases in syphilis in the United States, combined with the high prevalence of HIV coinfection among reported P&S syphilis cases, particularly among MSM, have implications for both syphilis control and HIV prevention programs. All sexually active persons living with HIV should be tested for syphilis at least annually, and all persons diagnosed as having P&S syphilis should be tested for HIV if they are not already known to be living with diagnosed HIV. A diagnosis of P&S syphilis represents an important opportunity to identify undiagnosed HIV infections, link persons living with diagnosed HIV to HIV care and treatment services, and potentially prevent future HIV infection among those who are HIV negative through PrEP and other preventive services.

Conflict of Interest and Sources of Funding:

None declared.

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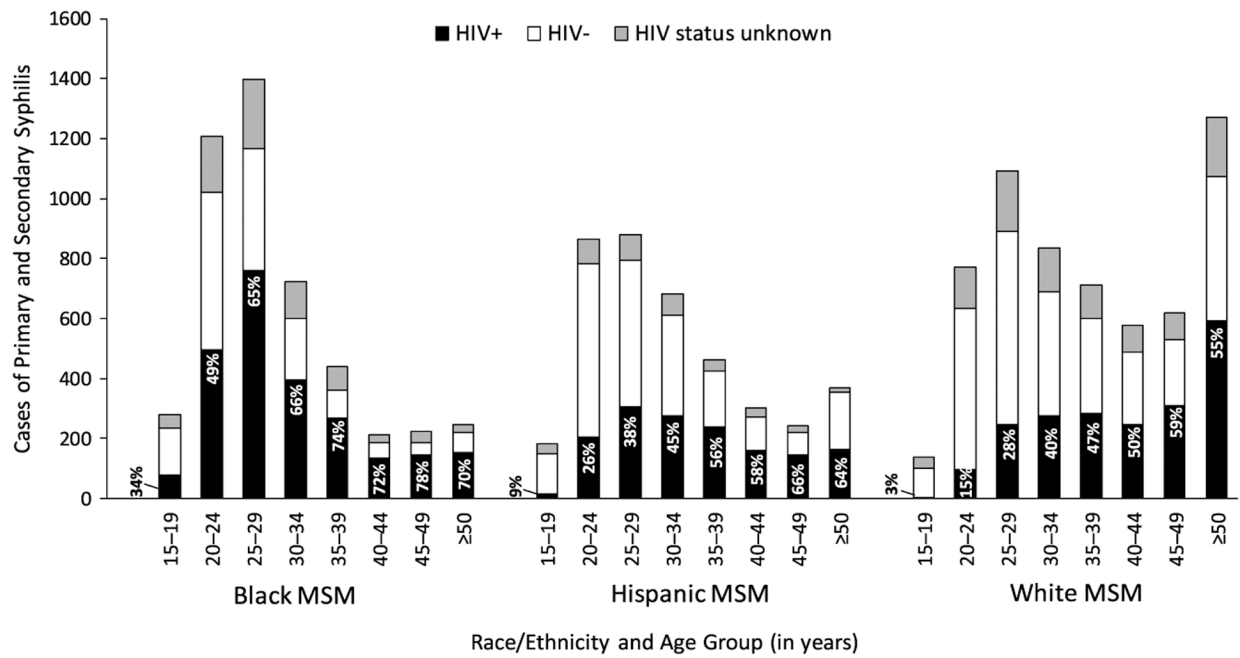


Figure 1.

Primary and secondary syphilis cases among black, Hispanic, and white gay, bisexual, and other men who have sex with men (MSM) by age group and HIV status, United States, 2016. Note: Percent shown was calculated based on cases with known HIV status as the denominator.

TABLE 1.
Reported P&S Syphilis Cases by Demographic Group and Sex of Sex Partner, United States, 2016

	MSM, n (%)	MSW, n (%)	Men Without Data on Sex Partners, n (%)	Women, n (%)	Unknown Sex, n (%)	Total, n (%)
All cases	16,155 (58.1)	3880 (13.9)	4689 (16.9)	3049 (11.0)	41 (0.1)	27,814 (100.0)
Region						
West	5085 (58.7)	1226 (14.1)	1328 (15.3)	1027 (11.9)	4 (0.1)	8670 (100.0)
Midwest	2334 (60.7)	524 (13.6)	586 (15.2)	398 (10.4)	2 (0.1)	3844 (100.0)
South	6155 (56.9)	1697 (15.7)	1585 (14.6)	1374 (12.7)	13 (0.1)	10,824 (100.0)
Northeast	2581 (57.7)	433 (9.7)	1190 (26.6)	250 (5.6)	22 (0.5)	4476 (100.0)
Sex [*]						
Male	16,155 (65.3)	3880 (15.7)	4689 (19.0)	-	-	24,724 (100.0)
Female	-	-	-	3049 (100.0)	-	3049 (100.0)
Race/Ethnicity [†]						
American Indian/Alaska Native	87 (45.8)	34 (17.9)	24 (12.6)	45 (23.7)	0 (0)	190 (100.0)
Asian	469 (69.6)	69 (10.2)	94 (14.0)	40 (5.9)	2 (0.3)	674 (100.0)
Black	4730 (51.3)	1673 (18.1)	1484 (16.1)	1313 (14.2)	22 (0.2)	9222 (100.0)
Hispanic	3880 (62.7)	828 (13.4)	939 (15.2)	538 (8.7)	7 (0.1)	6192 (100.0)
Native Hawaiian/other Pacific Islander	51 (70.8)	4 (5.6)	10 (13.9)	7 (9.7)	0 (0)	72 (100.0)
White	6016 (62.1)	1074 (11.1)	1651 (17.0)	943 (9.7)	4 (<0.1)	9688 (100.0)
Multirace	250 (61.7)	32 (7.9)	80 (19.8)	41 (10.1)	2 (0.5)	405 (100.0)
Age, y [‡]						
<15	2 (10.5)	2 (10.5)	3 (15.8)	12 (63.2)	0 (0)	19 (100.0)
15–19	664 (51.2)	178 (13.7)	115 (8.9)	340 (26.2)	1 (0.1)	1298 (100.0)
20–24	3120 (60.3)	629 (12.2)	669 (12.9)	744 (14.4)	10 (0.2)	5172 (100.0)
25–29	3721 (60.2)	815 (13.2)	1002 (16.2)	624 (10.1)	15 (0.2)	6177 (100.0)
30–34	2500 (58.4)	599 (14.0)	707 (16.5)	464 (10.9)	8 (0.2)	4278 (100.0)
35–39	1767 (58.1)	456 (15.0)	506 (16.6)	311 (10.2)	3 (0.1)	3043 (100.0)
40–44	1220 (57.0)	293 (13.7)	431 (20.1)	193 (9.0)	3 (0.1)	2140 (100.0)
45–19	1198 (56.4)	284 (13.4)	488 (23.0)	152 (7.2)	1 (<0.1)	2123 (100.0)
50	1961 (55.6)	623 (17.7)	743 (21.1)	199 (5.6)	0 (0)	3526 (100.0)

^{*} Does not include 41 cases with unknown sex.

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Does not include 1059 cases with unknown race/ethnicity or 312 cases with “other” race/ethnicity.

Does not include 38 cases with unknown age.

MSM indicates men who have sex with men; MSW, men who have sex with women only; P&S, primary and secondary.

TABLE 2.

Proportion of Reported P&S Syphilis Cases Coinfected With HIV, United States, 2016

	Total P&S Syphilis Cases	Cases With Known HIV Status	HIV+ Cases (%) [*]
All cases	27,814	21,193	8154 (38.5)
Sex [†]			
Male	24,724	18,936	8048 (42.5)
MSM	16,155	13,727	6457 (47.0)
MSW	3880	3002	320 (10.7)
Female	3049	2230	92 (4.1)
Race/Ethnicity [‡]			
American Indian/ Alaska Native	190	136	34 (25.0)
Asian	674	536	184 (34.3)
Black	9222	7022	3100 (44.2)
Hispanic	6192	5108	1874 (36.7)
Native Hawaiian/Other	72	59	17 (28.8)
Pacific Islander			
White	9688	7207	2538 (35.2)
Multirace	405	295	136 (46.1)
Age, y [§]			
<15	19	13	0 (0)
15–19	1298	987	117 (11.9)
20–24	5172	4029	1006 (25.0)
25–29	6177	4718	1727 (36.6)
30–34	4278	3229	1310 (40.6)
35–39	3043	2338	1071 (45.8)
40–44	2140	1612	769 (47.7)
45–49	2123	1589	855 (53.8)
50	3526	2676	1298 (48.5)
Region			
West	8670	6685	2283 (34.2)
Midwest	3844	2998	1238 (41.3)
South	10,824	8396	3204 (38.2)
Northeast	4476	3114	1429 (45.9)

^{*} Percent calculated based on cases with known HIV status as the denominator.

[†] Does not include 41 cases with unknown sex; 4689 male cases did not have data on sex of sex partner.

[‡] Does not include 1059 cases with unknown race/ethnicity or 312 cases with “other” race/ethnicity.

[§] Does not include 38 cases with unknown age.

MSM indicates men who have sex with men; MSW, men who have sex with women only; P&S, primary and secondary.

TABLE 3.

Proportion of Reported P&S Syphilis Cases Coinfected With HIV, by Sex/Sex of Sex Partner and Age Group, United States, 2016

Age, y	Total P&S Syphilis Cases	Cases With Known HIV Status	HIV+ Cases (%) [*]
MSM			
<15	2	2	0 (0)
15–19	664	540	100 (18.5)
20–24	3120	2669	859 (32.2)
25–29	3721	3132	1401 (44.7)
30–34	2500	2116	1027 (48.5)
35–39	1767	1514	840 (55.5)
40–44	1220	1050	588 (56.0)
45–9	1198	1020	529 (63.0)
50	1961	1683	998 (59.3)
MSW			
<15	2	1	0 (0)
15–19	178	141	7 (5.0)
20–24	629	495	28 (5.7)
25–29	815	638	53 (8.3)
30–34	599	447	52 (11.6)
35–39	456	346	47 (13.6)
40–44	293	217	30 (13.8)
45–19	284	223	36 (16.1)
50	623	493	67 (13.6)
Women			
<15	12	8	0 (0)
15–19	340	250	2 (0.8)
20–24	744	567	14 (2.5)
25–29	624	476	14 (2.9)
30–34	464	321	17 (5.3)
35–39	311	220	16 (7.3)
40–44	193	133	8 (6.0)
45–49	152	114	7 (6.1)
50	199	141	14 (9.9)

* Percent calculated based on cases with known HIV status as the denominator.

MSM indicates men who have sex with men; MSW, men who have sex with women only; P&S, primary and secondary.