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## Repeat Syphilis Among HIV-Infected Men in Florida and Louisiana 2000–2018: Implications for Screening Recommendations

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### Abstract

Syphilis rates have continued to rise in the United States. Florida and Louisiana consistently report high numbers of cases. We evaluated rates of reinfection to see if frequent rescreening might lead to earlier treatment and prevent infections. All syphilis records of all stages for males and females aged 15–70 years from the Florida and Louisiana Departments of Health surveillance databases 2000–2018 were evaluated. The first episode of syphilis during this period was considered the initial diagnosis for each person. Demographics of cases and repeaters (individuals reported with two or more cases of syphilis) were examined. Percentages of syphilis cases from repeaters by year were calculated as were percentages from HIV+ males. During 2000–2018, 124,827 syphilis cases were reported from 107,405 individuals: 73,811 (68.7%) males; 33,594 (31.3%) females. There were 12,545 individuals (repeaters) with two or more syphilis diagnoses ( $n = 17,422$  cases; range, 2–10). From 2010 to 2018, repeaters accounted for steadily increasing percentage of all syphilis reported: 2010 (11%), 2013 (16%), 2015 (20%), and 2018 (26%). Among HIV+ male cases the percentage from repeaters also increased: 2010 (28%), 2013 (35%), 2015 (42%), and 2018 (50%). In 2018, 19% of all cases ( $n = 2,455$ ) were from HIV+ males who had a previous syphilis diagnosis. Among HIV+ males diagnosed with syphilis in 2015, 34% had a repeat syphilis diagnosis within 3 years. Most syphilis diagnosed in Florida and Louisiana was among persons infected for the first time. However, some subgroups could possibly benefit from more frequent screening. Males living with HIV who had a prior syphilis diagnosis were at very high risk of repeat infection.

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Author Disclosure Statement

The authors have no conflicts of interest to disclose.

## Keywords

syphilis; reinfection; screening; men

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## Introduction

Three previous syphilis epidemics in the United States (1975, 1982, and 1990) peaked within 5–6 years, but the current epidemic is still increasing after 20 years.<sup>1</sup> Rates have risen steadily, after reaching its nadir of 2.1 per 100,000 population of infectious syphilis in 2000, which were the lowest recorded rates since syphilis surveillance started in 1941.<sup>2–4</sup> The highest rates in 2000 were in the South and accounted for 62% of cases. Then rates of primary and secondary syphilis started increasing among men who have sex with men (MSM) many who were infected with HIV.<sup>2–7</sup> This increase followed the release and subsequent uptake of highly effective antiretrovirals to treat HIV.<sup>7,8</sup>

In 2016, the United States Preventive Services Task Force (USPSTF) issued guidance on screening for syphilis.<sup>9</sup> The Task Force rendered a Grade A (its highest designation) recommendation for screening for syphilis in nonpregnant adults and adolescents. Specifically, the USPSTF recommends screening for syphilis in persons who are at *increased risk* for infection. The Grade A designation indicates: “there is high certainty that the net benefit is substantial,” the USPSTF recommends the service, and in practice it should be offered or provided. During discussions of the evidence for its recommendation MSM living with HIV were determined to be the highest-risk group. The possibility of screening every 3 months was mentioned but it was not included in the formal recommendation. The recommendation suggested that clinicians should make the decision about screening based on community prevalence.

Several studies examining the influence of syphilis reinfections were published in the first decade of this epidemic finding that reinfections had a moderate but rising effect on syphilis rates.<sup>4,10</sup> These studies were conducted in an earlier phase of the epidemic and covered short time periods of 3–8 years. We examined all syphilis records from two states that consistently report high syphilis morbidity, Florida and Louisiana, to explore the influence of reinfections on rates for the past 18 years.

## Methods

Syphilis is a notifiable condition in all US states.<sup>11</sup> Positive syphilis tests are reported by laboratories and syphilis diagnoses are reported by clinicians. The individual’s name, test results, and demographic information including the ordering provider are required for reporting. These reports are entered into statewide surveillance registries. Surveillance personnel compare reported test results with previous test results and treatment information to see if the test suggests a new infection. Personnel also cross match their HIV/AIDS registries with their sexually transmitted disease surveillance registries to determine if individuals are co-infected. After the record search, if the test result is suspected to be a new case, surveillance personnel contact the provider to gather information on signs and symptoms, diagnosis, treatment, demographics, and how to locate the potential case. Then

disease investigation specialists contact the individual for interview. New information on diagnosis, stage, and treatment are recorded in the registry.

We conducted a retrospective cohort study of all syphilis records, all stages (early, nonprimary nonsecondary, and unknown duration or late) for males and females aged 15–70 years from January 1, 2000 to December 31, 2018. Demographics of cases and repeaters (individuals reported with two or more cases of syphilis), including age, race/ethnicity, gender, and HIV status were examined. We did not have access to a sexual orientation variable, which was incomplete in the early years of the study. Time to second infection and number of subsequent infections were assessed for repeaters. We calculated the percentages of syphilis cases that were from repeaters each year as well as percentages of cases from people living with HIV (PLWH). We also assessed the likelihood of reinfection within 3 years for persons with an initial diagnosis of syphilis in 2015.

All data management and statistical analyses were conducted using Statistical Analysis Software (version 9.4 for Windows; SAS Institute Inc., Cary, NC).<sup>12</sup> The figures were created using R (version 4.0.4) in R Studio (version 1.4.1103) using the “ggplot2” package.<sup>13–15</sup>

Centers for Disease Control and Prevention (CDC) did not have access to personal identifiers. This was an evaluation of routinely collected public health program data and, therefore, received a nonresearch determination by the CDC. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy: 45 C.F.R. part 46 102(1)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

## Results

From 2000 to 2018, 124,827 syphilis cases were reported to the states of Florida and Louisiana from men and women between the ages of 15 and 70. These cases were diagnosed from 107,405 individuals: 73,811 (68.7%) males and 33,594 (31.3%) females (Table 1). Florida contributed 90,279 (72.3%) of the cases; from 75,706 (70.5%) individuals. There were 94,860 (88.3%) persons with a single episode of syphilis reported and 12,545 (11.7%) from individuals with two or more syphilis diagnoses reported (repeaters). Diagnoses among persons who had a previous diagnosis accounted for 17,422 (14%) of all cases (this case count does not include their initial diagnosis). Including their initial diagnosis, repeaters accounted for 29,967 (24%) of all cases reported. Individuals had up to 10 total infections. Mean time to reported second infection was 3.6 years (median = 2.6 years). Over time, repeaters accounted for a steadily increasing percentage of all syphilis reported: 11% in 2011, 16% in 2013, 20% in 2015, and 26% by 2018 (Fig. 1).

Repeat infection was more common among men with syphilis (14.9%) compared with women (4.6%). Repeaters accounted for a higher percentage of all infections: for Hispanics (16.0%) and non-Hispanic Whites (Whites) (14.2%), than non-Hispanic Blacks (Blacks) (8.9%). The likelihood of repeat infection was remarkably consistent across all age categories until it decreased for persons >50 years. Repeat syphilis was much more likely

among HIV-positive persons with syphilis (27.8%) compared with HIV-negative persons with syphilis (6.8%).

There were 1,544 women with repeat infections that accounted for 12.3% of all repeaters and 1685 (9.7%) of all repeat episodes reported (range, 2–5 cases). These repeat infections among women represent 1.3% of all cases. Mean time to second infection was 3.5 years (median = 2.3 years). From 2010 to 2018, female repeaters accounted for a slowly increasing percentage of all syphilis reported: 2010 (5.1%), 2013 (5.9%), 2016 (6.8%), and reached (10.3%) in 2018. For syphilis among females living with HIV, cases from repeaters also increased: 2010 (13%), 2014 (16%), 2016 (21%), and 2018 (25%) (Data not shown).

The 11,001 male repeaters accounted for 87.7% of all repeaters and 15,737 (90.3%) of all repeat episodes (range of 2–10 infections). Mean time to second infection for these men was 3.7 years (median = 2.6 years). Male repeaters accounted for an increasing percentage of syphilis cases reported over time: 2010 (14%), 2013 (19%), 2015 (24%), and in 2018 (30%). For syphilis among males living with HIV, the percentage of cases from repeaters also increased: 2010 (28%), 2013 (35%), 2015 (42%), and 2018 (50%) (Fig. 2). In 2018, 19% of all cases were from 2,455 HIV+ males that had a previous syphilis diagnosis.

We conducted a subset analysis looking at individuals infected in 2015 to see how many became reinfected by 2018. Among the individuals diagnosed with syphilis in 2015, 18% became reinfected within 3 years; for males, 21% became re-infected; for HIV+ males, 34% had a repeat syphilis diagnosis within 3 years; for women, 5% became reinfected by 2018 and 8% of HIV+ women were reinfected within the 3 years.

## Discussion

Syphilis reinfections are not new or recent phenomena. But our study indicates over an extended period of years in this latest epidemic that the proportion of reinfections have dramatically increased. We found 26% of all infections in 2018 were reinfections. And for HIV+ men, 50% of all infections in 2018 were reinfections. This suggests that frequent rescreening of persons after the diagnosis of syphilis would lead to earlier diagnosis and might help decrease transmission. When we tested this with persons diagnosed in 2015, we found 18% were reinfected within 3 years, and for HIV+ men 34% were reinfected within 3 years. Women's risk of repeat syphilis was lower than males (5% within 3 years of 2015). In a previous study of syphilis reinfections in Florida between 2000 and 2008, 2.5% of all syphilis diagnoses were from repeaters.<sup>4</sup> Other studies of repeaters have reported varying time periods covering different years making direct comparisons difficult. They reported reinfection rates of between 2.5% and 17.6%.<sup>4,10,16–19</sup>

In 2000, the current syphilis outbreak coincided with the uptake of antiretroviral therapy for the treatment of HIV.<sup>7</sup> Researchers have also investigated the influence of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) in MSM for the prevention of HIV and reported on the subsequent increase in sexually transmitted infections (STIs).<sup>20–24</sup> PrEP and PEP arrived in a time of electronic applications (APPS) to meet sexual partners, possible change in sexual behaviors of less condom use and increase in condomless anal intercourse

(CAI).<sup>23,24</sup> One comprehensive study of CAI, partnership type and shared biomedical disclosure (PrEP use), found that as both partners were using PrEP CAI increased compared with one partner using PrEP or no partners disclosing PrEP use.<sup>23</sup> This association was not found in partnerships of non-PrEP using MSM. The authors concluded that as “PrEP matching” increases in MSM the practice could contribute to disproportionate STI risk.<sup>23</sup>

A study among PLWH in military personnel between 2014 and 2017 found that 18.9% of participants who completed a year of follow-up acquired an STI.<sup>25</sup> More than a quarter (27.2%) of the infections reported were syphilis. A study of PLWH reported from a Kaiser Mid-Atlantic, a large nonprofit health maintenance organization (HMO), called for more quality of care measures (QMs) beyond viral suppression to improve process metrics with ultimate goal of improving outcome metrics.<sup>26</sup> The military and HMO studies of PLWH/PWH illustrate even with people knowledgeable of STI risk and access to quality health care is not sufficient. Broader quality of care measures (QMs) and a holistic health approach may eventually lead to better outcomes.<sup>26</sup> Currently, the USPSTF recommends screening people at high risk, we have quantified groups and subgroups at extremely high risk.<sup>9</sup> As syphilis continues to rise, more frequent screening of men with a past history of syphilis and in particular more screening of HIV+ men with a past history of syphilis may be warranted to attempt to better control this latest epidemic that has been with us approaching 20 years. Further research to quantify the optimal time between screenings should be pursued for the most at risk groups.

## **SYPHILIS REINFECTION**

Other researchers have developed innovative approaches to combat the increasing syphilis rates and other STIs in MSM.<sup>27–30</sup> They have assessed the feasibility and conducted pilot trials of chemoprophylaxis to prevent syphilis and other STIs. Their focus has been on core groups and the ongoing use of doxycycline prophylaxis to prevent incidence and the associated transmission. Our findings support concentrating these efforts on HIV-infected men who have had syphilis in the past.

Our study has some limitations. Some infections may remain undiagnosed. We included cases diagnosed in Florida and Louisiana reported to the State Departments of Health from 2000 to 2018, so the first episode of syphilis during this period was considered the initial diagnosis although some likely had a prior diagnosis before 2000. Likewise, persons diagnosed late in the study period (e.g., 2018) would not have had the opportunity to repeat. There may have been in and out migration of people from the states influencing whether all syphilis cases were diagnosed and reported. We did not have complete sexual orientation data. PLWH may get screened more often for syphilis as they have more opportunities to be screened due to monitoring of their HIV treatment.

This study has strengths as well. To our knowledge this is the longest study of syphilis reinfection (18 years). The study includes data from the beginning of the ongoing long epidemic. We were able to examine syphilis records from two states, which strengthen that the results were not an anomaly seen in only one state.

There has been a steady and dramatic increase in the proportion of new syphilis cases that are in persons who have had syphilis in the past. In 2018, 26% of all infections and 50% of infections among HIV+ men are contributed by persons with past syphilis. Frequent screening of this small number of individuals could identify infections early and might reduce onward transmission.

## Funding Information

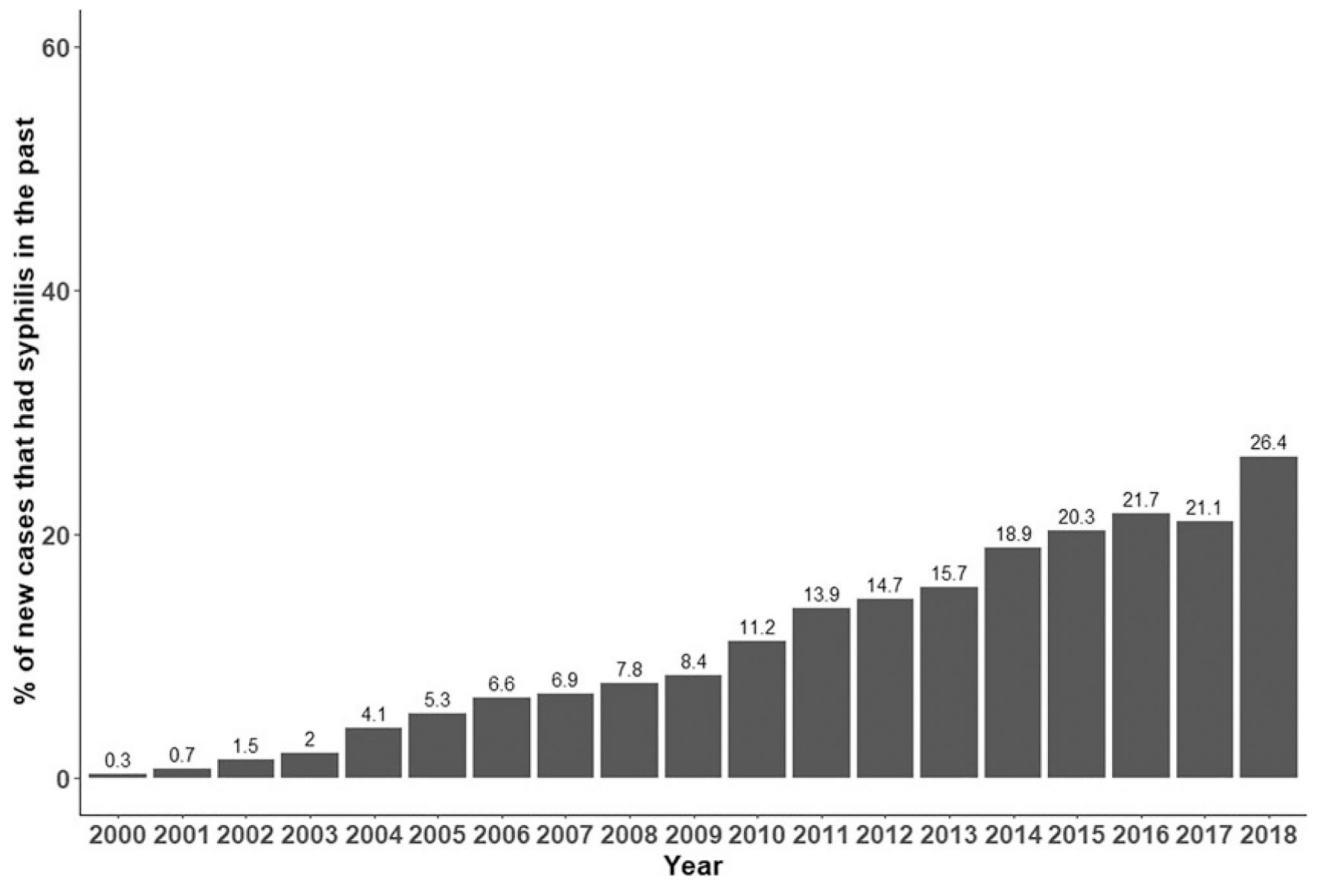
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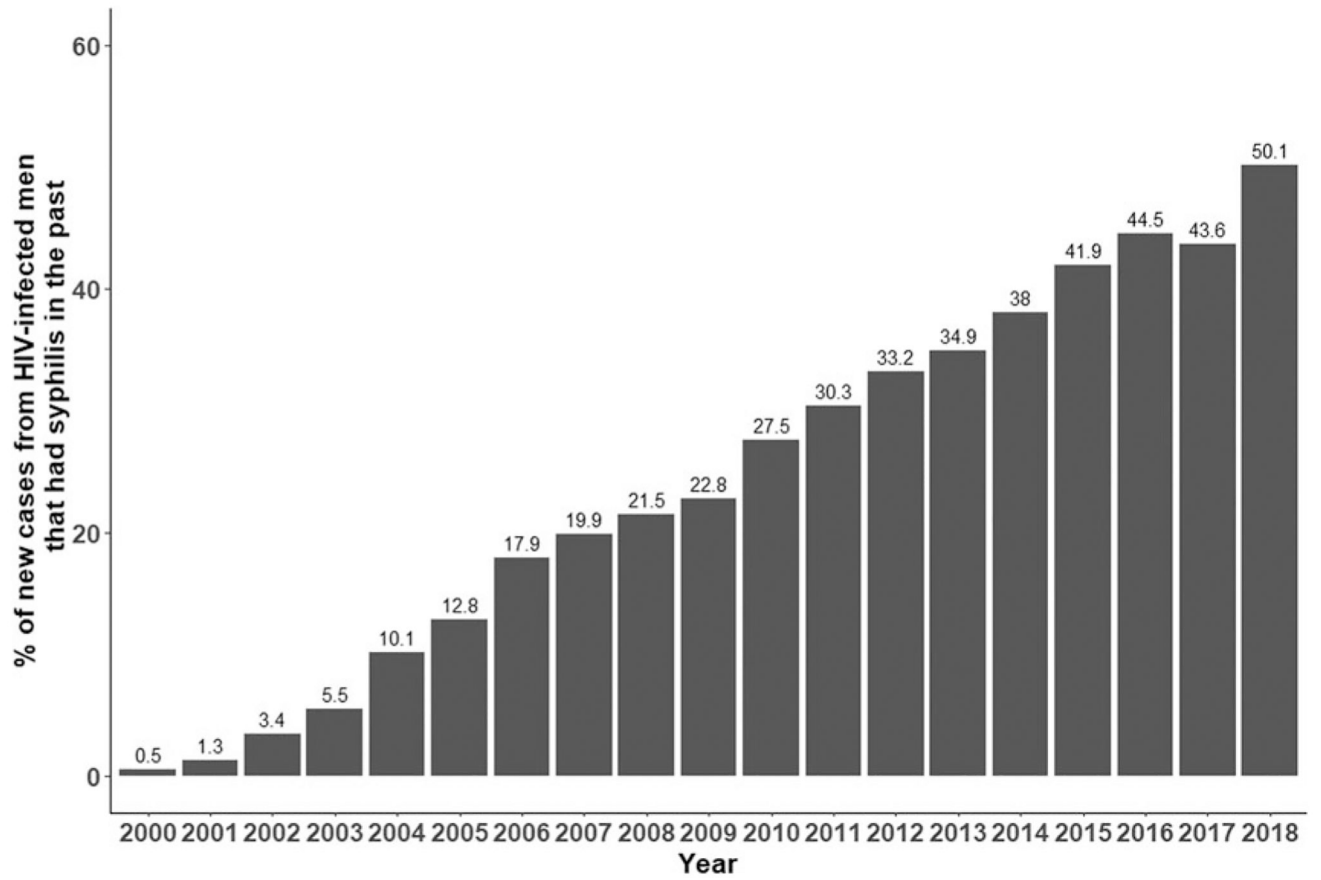


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**FIG. 1.**  
Among all new cases of syphilis, the percent that had syphilis in the past.





**FIG. 2.** For new cases of syphilis among HIV-infected men, the percent that had syphilis in the past.

**Table 1.**  
Demographics of All Persons with Single Episodes and Repeat Episodes of Syphilis

	All syphilis		Single episode		Repeaters		Repeat risk <sup>a</sup> %
	N = 107,405	% <sup>b</sup>	N = 94,860	% <sup>b</sup>	N = 12,545	% <sup>b</sup>	
Site							
Florida	75,706	70.5	65,531	69.1	10,175	81.1	13.4
Louisiana	31,699	29.5	29,329	30.9	2370	18.9	7.5
Gender							
Male	73,811	68.7	62,810	66.2	11,001	87.7	14.9
Female	33,594	31.3	32,050	33.8	1544	12.3	4.6
Race/ethnicity							
White	23,479	21.9	20,139	21.2	3340	26.6	14.2
Black	49,519	46.1	45,088	47.5	4431	35.3	8.9
Hispanic	19,929	18.6	16,750	17.7	3179	25.4	16.0
Asian, Indian, PI	733	0.7	645	0.7	85	0.7	11.6
Other/unknown	13,745	12.8	12,235	12.9	1510	12.4	11.0
Age, years <sup>c</sup>							
15–19	7013	6.5	6161	6.5	852	6.8	12.1
20–29	35,863	33.4	31,527	33.2	4336	34.6	12.1
30–39	27,794	25.9	24,307	25.6	3487	27.8	12.5
40–49	21,635	20.1	18,908	19.9	2727	21.7	12.6
50–70	15,100	14.1	13,597	14.7	1143	9.1	7.6
HIV status							
Negative	82,507	76.8	76,877	81.0	5630	44.9	6.8
Positive	24,898	23.2	17,983	19.0	6915	55.1	27.8

<sup>a</sup>Repeat risk is a row percent calculated: Repeaters#/All Syphilis# × 100. All other percents are for columns.

<sup>b</sup>All percent columns may not sum to 100 due to rounding.

<sup>c</sup>Age for “All Syphilis” and “Single Episode” is age at first diagnosis on or after January 1, 2000. Age for “Repeaters” is age at time of the second diagnosis. PI, Pacific Islander.