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Risk of HIV diagnosis following bacterial sexually transmitted infections in Tennessee, 2013–2017

Heather N. Grome, MD, MPH¹, Peter F. Rebeiro, PhD, MHS^{1,2}, Meredith Brantley, PhD, MPH³, Dyanne Herrera-Vasquez, PhD, MPH³, Samantha A. Mathieson, MPH³, April C. Pettit, MD, MPH^{1,2}

¹Division of Infectious Diseases, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA

²Division of Epidemiology, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA

³Division of HIV/STD/Viral Hepatitis, Tennessee Department of Health, Nashville, Tennessee, USA

Abstract

Background.—Data on associations between sexually transmitted infections (STIs) and incident HIV diagnoses beyond men who have sex with men (MSM) are lacking. Identifying STIs associated with greatest risk of incident HIV diagnosis could help better target HIV testing and prevention interventions.

Methods.—STI and HIV surveillance data from individuals 13 years in Tennessee from 1/2013–12/2017 were cross-matched. Individuals without diagnosed HIV, but with reportable STIs (chlamydia, gonorrhea, syphilis) were followed from first STI diagnosis until HIV diagnosis or end of study. Cox regression with time-varying STI exposure was used to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for subsequent HIV diagnosis; results were stratified by self-reported men who have sex with men (MSM).

Results.—We included 148,465 individuals without HIV (3,831 MSM; 144,634 non-MSM, including heterosexual men and women) diagnosed with reportable STIs; 473 had incident HIV diagnoses over 377,823 person-years (p-y) of follow-up (median 2.6 p-y). Controlling for demographic and behavioral factors, diagnoses of gonorrhea, early syphilis, late syphilis, and STI coinfection were independently associated with incident HIV diagnosis compared to chlamydia. Early syphilis was associated with highest HIV diagnosis risk overall (aHR 5.5, 95% CI: 3.5–5.8); this risk was higher for non-MSM (aHR 12.3, 95% CI: 6.8–22.3) versus MSM (aHR 2.9, 95% CI: 1.7–4.7).

Corresponding author: Heather N. Grome, MD, MPH, Division of Infectious Diseases, Vanderbilt University Medical Center, 1161 21st Avenue South, A2200-MCN, Nashville, TN 37232-2582, USA, heather.grome@vumc.org. Alternate corresponding author: April C. Pettit, MD, MPH, Division of Infectious Diseases, Vanderbilt University Medical Center, 1161 21st Avenue South, A2200-MCN, Nashville, TN 37232-2582, USA, Phone +1 (615) 343-0574, april.pettit@vumc.org.

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Conclusions.—While public health efforts often focus on MSM, non-MSM with STIs are also a subgroup at high risk of incident HIV diagnosis. Non-MSM and MSM with any STI, particularly syphilis, should be prioritized for HIV testing and prevention interventions.

Short Summary:

A population-based, Southern statewide observational cohort study found that syphilis was associated with the highest risk of incident HIV diagnosis overall as compared to chlamydia, regardless of self-reported sexual practices.

Keywords

Sexually transmitted infections; HIV; male-to-male sexual contact; Pre-exposure prophylaxis (PrEP)

Introduction

Rates of sexually transmitted infections (STIs) including chlamydia, gonorrhea and syphilis have shown a persistent increase in recent years, reaching an all-time high in the United States (US) in 2018 according to the Centers for Disease Control and Prevention.¹ The southern US, a region that includes the state of Tennessee (TN), has some of the highest rates of reportable STIs¹ and remains an area where the HIV epidemic is highly concentrated.² Integration of HIV and STI programming has been proposed as a method to help decrease disparities in HIV incidence between different demographic groups within communities of the South, and to further address HIV testing and prevention needs.

History of prior STI diagnosis is a risk factor for HIV acquisition,^{3,4} both as an indicator of condomless sex or membership in a sexual network in which STIs and HIV are present.^{5,6} Additionally, STIs biologically augment HIV infectivity and individual susceptibility to HIV infection.^{7,8} Abundant literature exists examining the associations between diagnosis of STIs and incident HIV among male subgroups with multiple anal sex partners,^{5,9,10} as men who have sex with men (MSM) are disproportionately affected by HIV and other STIs. Previous studies have shown that MSM without diagnosed HIV, but with rectal gonorrhea or syphilis are at increased risk of incident HIV infection,^{5,9–13} and recent work from two southern US states among women has also shown increased risk of HIV diagnosis among those diagnosed with syphilis or gonorrhea.^{14,15} However, data on associations between diagnosis of STIs and risk of subsequent HIV diagnosis in the same population of both men and women, regardless of sexual practices, from the southern US are limited.

The introduction and increasing availability of HIV pre-exposure prophylaxis (PrEP) for HIV prevention has escalated motivation for identifying populations at greatest risk for HIV infection. Current CDC guidelines recommend providers consider PrEP initiation in MSM and heterosexually active men and women with a bacterial STI diagnosed or reported within the last six months plus at least one other HIV risk factor.¹⁶ In this era of rising STI rates, identifying STIs associated with greatest risk of subsequent HIV could help better target effective HIV prevention efforts among individuals without HIV, particularly beyond existing HIV prevention programs currently targeted towards MSM. Our objective was to

use Tennessee Department of Health surveillance data to study incident HIV diagnosis following STI diagnoses among men and women, including individuals at least 13 years, regardless of their sexual practices.

Materials and Methods

Study Population and Follow-up

We conducted a population-based observational cohort study among individuals without diagnosed HIV at least 13 years of age, but with a diagnosis of chlamydia, gonorrhea, or syphilis reported to the Tennessee Department of Health (TDH) from January 2013–December 2017. We excluded people with prevalent HIV infection at the start of the observation period. Individuals were followed from date of first STI during the observation period until the date of HIV diagnosis or end of observation period (December 31, 2017). Recurrent STIs in the same individual were considered separately by apportioning follow-up time to the most recent prior STI. This study was approved by the Institutional Review Board at TDH and Vanderbilt University Medical Center.

Data Collection and Study Definitions

TDH currently maintains separate surveillance databases for STI and HIV data, both of which are reportable diagnoses by providers or laboratories. These groups provide information to TDH via a case report form or electronic laboratory reporting system. TDH's Sexually Transmitted Disease (STD) Prevention Program manages the STD case surveillance registry called the Patient Reporting Investigation Surveillance Manager (PRISM). PRISM contains positive STI laboratory results as well as demographic characteristics, behavioral risk factors, and STI treatment information. Similarly, the HIV Epidemiology and Surveillance Program manages the HIV case surveillance registry called the enhanced HIV/AIDS Reporting System (eHARS).¹⁷ Demographic information, vital status, HIV transmission risk factors, and HIV-related laboratory results are stored in eHARS. PRISM and eHARS were matched with the probabilistic matching Registry Plus Link Plus software, version 2.0 (Centers for Disease Control and Prevention, Atlanta, Georgia), using first and last names, date of birth, social security number, and sex. After review of the results, we identified a score above which all the proposed matches were true matches according to the suggested score cut-off from LinkPlus documentation. Approximately 14% of the total eHARS data was matched to individuals in PRISM and 2.6% of total PRISM data was matched to individuals in eHARS over the observation period; if the match score was 16.2 or greater the records were deemed to be generated from the same individual.

Outcome and Exposure

Our primary outcome was incident HIV diagnosis, with HIV diagnosis defined per CDC case definition.¹⁸ Only positive HIV test results are reportable, therefore individuals were considered HIV negative or unknown status unless otherwise reported. Our primary exposure of interest was STI pathogen, including syphilis (primary, secondary, early latent, late latent, or unknown/unrecorded duration), gonorrhea, or chlamydia defined per CDC case definitions.¹⁹ Syphilis diagnoses were further categorized by combining

primary, secondary and early latent diagnoses into an early syphilis category and late latent or unknown/unrecorded duration into a late syphilis category to match the general clinical approach to antimicrobial therapy.²⁰ Recurrent syphilis diagnoses were defined as recurrent symptoms or a sustained fourfold increase in nontreponemal test titer.¹⁹ Provider reports are included in the surveillance system and were used for syphilis staging. STI coinfection was defined as simultaneous diagnosis of at least 2 different STIs. Dates of STI and HIV diagnoses were defined as the dates of specimen result. For gonorrhea and chlamydia, the site of specimen was categorized as genitourinary (cervical, vaginal, urethral), oropharyngeal, rectal, other (synovial fluid, eye, blood), or not documented.

Covariates

We measured and adjusted for potential confounders and risk modifiers including age, gender, race/ethnicity, men who have sex with men (MSM) status, injection drug use history, TN region or metropolitan area, and year of study entry. Age was defined as age in years at the date of first reportable STI diagnosis during the observation period. Current gender was self-reported via interview at time of STI diagnosis and categorized as male, female, or unknown; transgender status was not recorded in state data during this observation period. Race/ethnicity was also self-reported and categorized as Black non-Hispanic, White non-Hispanic, Hispanic (any race), other non-Hispanic, or unknown. MSM status was collected by self-report; all women, men who did not report MSM, and those with unknown gender were considered non-MSM. Women were not considered separately due to low numbers of HIV events among this group. An individual was considered MSM if male-to-male sexual contact was documented at any time during the observation period. People who inject drugs (PWID) were defined as those with any self-reported injection drug use in the 12 months prior to STI diagnosis. TN area of residence was defined according to the location of residence at time of STI test and categorized into public health regions and metropolitan areas according to TDH.²¹ Due to small numbers within some regions, these were further combined into five groups including: Memphis/Shelby County, Nashville/Davidson County, West TN (West, Madison), Middle TN (Mid-Cumberland, South Central, Upper Cumberland) and East TN (East, Northeast, Southeast, Hamilton, Knox, Sullivan).

Statistical Analysis

Categorical variables are reported as frequency and proportion; continuous variables are reported as median and interquartile range (IQR). Missing data for gender and race/ethnicity was infrequent (<5%) and was therefore coded as unknown. Missing data for sexual behavior was also infrequent (<5%). This was coded as did not report MSM in the analysis.

Unadjusted and adjusted Cox proportional hazard regression models with time-varying STI exposure were used to estimate the adjusted hazard ratio (aHR) and 95% confidence interval (CI) for incident HIV diagnosis by STI type. For the time-varying analysis, follow-up time was apportioned according to the most recent prior STI diagnosis, including recurrent STIs, over the observation period. Adjusted models included age, gender, race/ethnicity, PWID status, health department region of STI test, and year of study entry. An interaction term for gender by MSM was significant and included in the model. Age and year of study entry were modeled using restricted cubic splines with 5 knots to relax linearity assumptions; 25

years and 2013 were used as reference values, respectively. Chlamydia was chosen as the reference group for the exposure, as it was the most frequent STI diagnosed in TN during each year of the observation period regardless of age group or gender.

Additional analyses stratified results by MSM status and an additional sensitivity analysis was conducted to determine results limited to females only. The proportionality assumption was tested by STI type using the scaled Schoenfeld residuals. Unadjusted incident HIV diagnosis rates were calculated by dividing the total number of new HIV diagnoses by the total person-time at risk. Rates of reported STIs were calculated by dividing number of new cases by TN state population during the year of interest.²² Analyses were conducted using STATA 15.0 (Stata Corp, College Station, TX).

Results

From January 2013–December 2017, 148,465 individuals without HIV were diagnosed with 206,892 reportable STIs in Tennessee. Overall, these individuals were followed for 377,823 person-years (p-y); median follow-up was 2.6 p-y (IQR 1.3–3.8). Females were followed for 242,026 p-y and individuals <18 for 40,794 p-y. Overall, the median age was 22 years (IQR 19–27) with 15,854 (10.7%) <18 years old; 37.4% were male, 48.6% were Black non-Hispanic, 2.6% self-reported MSM, and 0.4% were PWID among the total cohort. The combined East Regions contributed the highest number of individuals with reportable STIs (27.4%). Chlamydia was the most common STI at cohort entry (n=111,730, 75.3%), followed by gonorrhea (n=20,184, 13.6%). A majority of early (n=1,253, 78.6%) and late syphilis diagnoses (n=1,249, 64.7%) were among men; 46.8% and 21.4% of early and late syphilis diagnoses were among MSM, respectively (Table 1).

There were 3,831 MSM without diagnosed HIV, but with 6,818 reportable STIs over 8,938 p-y of follow-up (median follow-up 2.3 p-y; IQR 0.3–3.5) and 144,634 non-MSM without diagnosed HIV, but with 200,074 reportable STIs over 369,609 p-y of follow-up (median 2.6 p-y follow-up; IQR 1.3–3.8). STI frequencies rose over time from 35,962 in 2013 (586.5 cases per 100,000 population) to 47,590 total cases in 2017 (716.5 cases per 100,000 population) (Figure 1). Among chlamydia diagnoses, 56,286 (40.9%) were genitourinary (GU) specimens, 776 (0.6%) were oropharyngeal specimens, 259 (0.2%) were rectal specimens, 19,728 (14.4%) were documented from another site and the remaining 43.9% had no site documented. Among gonorrhea diagnoses, 11,505 (42.5%) were GU, 832 (3.1%) were oropharyngeal, 388 (1.4%) were rectal, and 6,711 (24.5%) were recorded from another site with the remainder 38.9% not documented.

Overall, 473 (0.32%) were diagnosed with HIV following an STI diagnosis (12.5 diagnoses per 10,000 p-y). Reported HIV diagnoses following STI diagnoses increased from 42 in 2013 (0.6 per 100,000 population) to 283 in 2017 (4.2 per 100,000 population). Among those who were not diagnosed with HIV following STI diagnosis during the observation period, median age at cohort entry was 22 years (IQR 19–27), with 37.2% male, 48.5% Black non-Hispanic, 2.4% MSM and 0.4% PWID (Table 2). In comparison, among those with an HIV diagnosis following STI diagnosis during the observation period, the median age at cohort entry was 24 years (IQR 20–30), with 89.0% male, 69.3% Black non-

Hispanic, 46.9% MSM, and 2.5% PWID. The Memphis/Shelby County public health region contributed the highest number of individuals with incident HIV diagnosis following STI diagnosis (Table 2). Among individuals <18 years diagnosed with incident HIV diagnoses (n=14, 3.0% of total HIV diagnoses), a majority were male (n=10, 71%). Among self-reported MSM, 222 (5.8%) had incident HIV diagnosis following STI diagnosis (25.01 per 1,000 p-y) and among non-MSM, 251 (0.2%) had incident HIV diagnosis following STI diagnosis (36.6 per 1,000 p-y).

Time-varying Exposure Analysis

When the exposures were treated as time-varying and time at risk apportioned separately by STI, individuals with chlamydia were followed for the greatest amount of time (287,474.3 p-y), followed by those with gonorrhea (49,281.3 p-y) and any coinfection (34,496.9 p-y). All reportable STIs were independently associated with an increased hazard of incident HIV diagnosis compared to chlamydia. The adjusted hazard of incident HIV diagnosis was greatest for those diagnosed with early syphilis (aHR=5.5, 95% CI: 3.8–7.9) and late syphilis (aHR=5.0, 95% CI: 3.3–7.5) as compared to those diagnosed with chlamydia (Table 3). In addition to each of the STIs, PWID status was independently associated with a greater hazard of incident HIV diagnosis (aHR=4.0, 95% CI: 2.2–7.5) as compared to no reported use. Individuals of White non-Hispanic race had a lower hazard of incident HIV diagnosis (aHR=0.6, 95% CI: 0.5–0.7) as compared to those of Black non-Hispanic race and there was no significant difference in risk of incident HIV diagnosis among age groups.

When analyses were stratified by self-identified sexual risk behavior, non-MSM (including heterosexual men and women) showed the greatest hazard of incident HIV diagnosis following diagnosis of early syphilis (incidence=10.3 per 1000 p-y; aHR=12.3, 95% CI: 6.8–22.3) and late syphilis (incidence=6.1 per 1000 p-y; aHR=9.9, 95% CI: 5.6–17.2), and all STIs were associated with a significantly greater hazard of incident HIV diagnosis compared to chlamydia diagnoses. MSM had the greatest hazard of incident HIV diagnosis following a diagnosis of early syphilis (incidence=50.2 per 1000 p-y; aHR=2.9, 95% CI: 1.7–4.7), and all STIs were associated with significantly greater hazard of incident HIV diagnosis compared to chlamydia (Table 4). Among females, incidence of HIV diagnosis was highest among those diagnosed with early syphilis, but no STI was independently associated with a greater hazard of incident HIV diagnosis compared to chlamydia.

When considering any chlamydia or gonorrhea diagnosis by specimen source, all individuals with rectal chlamydia or gonorrhea had a significantly greater hazard of incident HIV diagnosis (aHR=4.5, 95% CI: 2.7–7.6) as compared to those with genitourinary (GU) sources, followed by those with a diagnosis of chlamydia or gonorrhea from an oral source (aHR=3.2, 95% CI: 1.9–5.5) (Table 5). Among those diagnosed with only chlamydia or only gonorrhea, rectal source of infection was again associated with the greatest hazard of incident HIV compared to GU sources of infection (aHR=7.6, 95% CI: 3.3–17.6 and aHR 3.1, 95% CI: 1.86–6.1, respectively). Among the total cohort, there were 52 individuals who were diagnosed with 2 different STIs at different documented sites on the same date. Separately, there were 8,548 individuals with 2 different STIs at the same documented site on the same date.

Discussion

We estimated the risk of HIV diagnosis after a reported STI diagnosis among all individuals in TN from 2013–2017 using statewide public health surveillance data. Among all individuals diagnosed with reportable STIs over this 5-year observation period, risk of incident HIV diagnosis differed by STI type. All STIs (gonorrhea, early syphilis, late syphilis, and any STI coinfection) were independently associated with increased risk of incident HIV diagnosis in the overall cohort compared to chlamydia, with greatest risk following a diagnosis of syphilis.

When stratified by self-reported non-MSM (including heterosexual men and women) versus MSM status, non-MSM notably displayed a remarkable 12-fold increased risk of incident HIV diagnosis following diagnosis of early syphilis and a 9-fold increased risk of HIV diagnosis following diagnosis of late syphilis compared to non-MSM with chlamydia. Several influential studies have assessed the risk of HIV associated with STI diagnosis among males including heterosexual males in the US,^{5,13,23,24} showing high HIV incidence among male non-MSM diagnosed with primary or secondary syphilis as compared to no STI. These prior studies have focused on non-MSM from populations in metropolitan areas such as Baltimore and New York City. Our study supports their findings, and helps further quantify risk of incident HIV diagnosis when compared to other STIs in the southern US among a broader population including women and adolescents.

Our results also support previous studies showing a history of rectal chlamydia and/or gonorrhea to be significantly associated with subsequent HIV infection among MSM. Prior published data has found a direct correlation between the incidence of rectal chlamydia²⁵ or gonorrhea and incident HIV among MSM not on PrEP,^{11,26–30} and noteworthy work by Mullick *et al*¹² suggests that a rectal gonorrhea and incident HIV correlation could help predict high-risk sexual behavior in PrEP trials. Our results show that compared to genitourinary diagnoses, those with rectal chlamydia and/or gonorrhea had significantly greater risk of incident HIV diagnosis in the overall cohort including heterosexual men and women. We also observed that oral chlamydia and/or gonorrhea diagnoses also had elevated risk compared to genitourinary diagnoses, though we hypothesized this finding may be partially due to these individuals also having rectal swabs completed at the same visit. These findings may help expand understanding of the STI and HIV correlation and add to prediction tools for HIV diagnoses without limitation to MSM subgroups.

This study also demonstrates the value of using statewide surveillance data to guide HIV testing and prevention strategies as well as advance health policy. We observed 3% of all those with incident HIV diagnoses following an STI diagnosis to be in individuals <18 years (crude incidence rate of 0.34 per 1,000 p-y among this population). This outcome reinforces the need to maintain HIV testing and PrEP access in younger populations and supports consideration of providers in TN offering PrEP without parental consent when medically appropriate.

These results may also help influence our current statewide PrEP guidelines and further inform prevention tactics. Current public health emphasis and CDC guidelines recommend

offering PrEP to MSM at risk of sexual HIV acquisition,¹⁶ though short appointment times and provider discomfort often result in a limited sexual history and patients frequently do not disclose same-sex behaviors in areas of the southern US where stigma remains. Our study reinforces emphasis on offering PrEP to all individuals at time of STI diagnosis with history of bacterial STI in the southern US regardless of reported sexual practices. It also adds to our understanding of HIV risk among the Tennessee population and may help prioritize limited resources, as not all STIs among different cohorts convey the same HIV risk.

This study has several limitations inherent with use of surveillance system data. First, it is likely that because the surveillance system was unable to capture people lost to follow-up with respect to diagnosis of HIV, such as by moving out of TN after diagnosis of an STI or those who stopped receiving medical care altogether, it may lead to an overestimation of outcome-free time at risk. In addition, for both STI and HIV diagnoses, the diagnosis date indicated in the surveillance system does not represent date of true infection but the date of positive diagnostic test. This documentation may have resulted in an underestimation of true numbers of STIs due to individuals with clinical diagnoses who did not undergo confirmatory testing. While this likely biases our results towards the null, we were still able to see striking risk differences despite this potential underestimation of incident HIV diagnosis. Additionally, PrEP data was not collected until the end of the observation period by state surveillance systems, and therefore could not be considered in our analysis. While PrEP uptake was minimal in TN during this time, inability to account for it is a limitation of this analysis. Additionally, information pertaining to risk factors for STI or HIV diagnosis was obtained by self-report, and inaccuracies due to limited self-reporting are probable. This may be especially true for self-report of sexual behavior, which seems likely due to the low proportion of MSM listed in the STI surveillance system and the existing stigma that remains present in the Southern US. While the analysis may be under-reporting MSM, it does not change the emphasis that persons with STIs should be offered HIV testing and prevention interventions at time of STI diagnosis. It is also possible that MSM and women had an increase in STI testing due to self-determination of risk or increase in symptomatic disease, which may lead to screening bias. Additionally, diagnosis depends on testing and testing may be more frequent in some groups compared to others. Finally, because these data represent only those individuals living in TN, results may not be generalizable to elsewhere in the country.

In conclusion, we found that all individuals diagnosed with any reportable STI in Tennessee (particularly early and late syphilis) were at high risk for future HIV diagnosis when compared to chlamydia diagnosis regardless of self-reported sexual practices. This analysis may provide guidance for providers in identifying individuals at risk of HIV diagnosis through awareness of which STIs have greatest risk of subsequent HIV diagnosis; this may be especially useful in high-volume clinical settings in which a detailed HIV risk history assessment may not be easily obtained or in which resources are limited. These individuals might also be better targeted by public health agencies for specific HIV testing and prevention outreach. While these results show the benefits of using surveillance data to guide prevention strategies, further research is needed to better understand the relationships

between specific STI diagnoses and the subsequent timing of HIV diagnosis among broad populations.

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Figure 1:

Rate of reported cases of Chlamydia, Gonorrhea and Syphilis (all stages) in Tennessee (TN) by calendar year of STI diagnosis during the observation period, 2013–2017. Pearson's χ^2 test statistic used to compare STI frequencies among all three groups.

Demographic characteristics at cohort entry of 148,465 HIV-negative individuals diagnosed with a reportable sexually transmitted infection in Tennessee from 1/1/2013–12/31/2017 overall and by cohort entry STI diagnosis.

Table 1.

Characteristic	Cohort Entry Diagnosis											
	Overall		Chlamydia		Gonorrhea		Early Syphilis		Late Syphilis		Coinfection	
	n	%	n	%	n	%	n	%	n	%	n	%
Age, years^a												
Median 22												
(IQR 19,27)												
13–17	15,854	10.7	12,407	11.1	1,224	6.1	24	1.5	17	0.9	2,182	16.8
18–24	79,188	53.3	63,075	56.4	8,155	40.4	455	28.5	318	16.5	7,185	55.2
25–29	27,176	18.3	20,194	18.1	4,392	21.8	329	20.6	289	15.0	1,972	15.1
30–34	12,281	8.3	8,422	7.5	2,587	12.8	208	13.0	229	11.9	835	6.4
35–40	6,257	4.2	3,935	3.5	1,557	7.7	155	9.7	219	11.4	391	3.0
40–44	3,232	2.2	1,851	1.7	859	4.3	121	7.6	205	10.6	196	1.5
45	4,477	3.0	1,846	1.7	1,410	7.0	303	19.0	653	33.8	265	2.0
Gender												
Male	55,483	37.4	35,679	68.1	11,277	55.9	1,253	78.6	1,249	64.7	6,025	46.3
Female	92,970	62.6	76,045	31.9	8,905	44.1	342	21.4	680	35.2	6,998	53.7
Unknown	12	0.0	6	0.0	2	0.0	0	0.0	1	0.1	3	0.0
Race/Ethnicity												
Black non-Hispanic	72,146	48.6	48,774	43.7	12,127	60.1	929	58.2	1,190	61.7	9,126	70.1
White non-Hispanic	61,658	41.5	50,818	45.5	6,606	32.7	577	36.2	532	27.6	3,125	24.0
Hispanic ^b	6,202	4.2	5,282	4.7	462	2.3	65	4.1	132	6.8	261	2.0
Other	2,248	1.5	1,824	1.6	243	1.2	15	0.9	45	2.3	121	0.9
Unknown	6,211	4.2	5,032	4.5	746	3.7	9	0.6	31	1.6	393	3.0
MSM												
Yes	3,831	2.6	875	0.8	1,165	5.8	747	46.8	413	21.4	631	4.8
No ^c	144,634	97.4	110,855	99.2	19,019	94.2	848	53.2	1,517	78.6	12,395	95.2

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted infection; MSM, men who have sex with men; PWID, people who inject drugs; TN, Tennessee.

^bHispanic of any race.

c Includes both heterosexual men and women.

Table 2:

Demographic characteristics at cohort entry of 148,465 HIV-negative individuals diagnosed with a reportable sexually transmitted infection in Tennessee from 1/1/2013–12/31/2017 shown by outcome of incident HIV diagnosis during study period.

Characteristic	Remained HIV-Negative n=147,992		Incident HIV Diagnosis n=473	
	n	%	n	%
Age, years ^a				
13–17	15,840	10.7	14	3.0
18–24	78,947	53.4	241	51.0
25–29	27,078	18.3	98	20.7
30–34	12,234	8.3	47	9.9
35–40	6,230	4.2	27	5.7
40–44	3,214	2.2	18	3.8
45	4,449	3.0	28	5.9
Gender				
Male	55,062	37.2	421	89.0
Female	92,918	62.8	52	10.7
Unknown	12	0.0	0	0.0
Race/Ethnicity				
Black non-Hispanic	71,818	48.5	328	69.3
White non-Hispanic	61,525	41.6	133	28.1
Hispanic ^b	6,190	4.2	12	2.5
Other	2,248	1.5	0	0.0
Unknown	6,211	4.3	0	0.0
MSM				
Yes	3,609	2.4	222	46.9
No ^c	144,383	97.6	251	53.1
PWID				
Yes	612	0.4	12	2.5
No	147,380	99.6	461	97.5
TN Regions and Metropolitan Areas				
Memphis/Shelby County	37,535	25.4	161	34.0
Nashville/Davidson County	20,588	13.9	108	22.8
West TN	14,845	10.0	40	8.5
Middle TN	34,483	23.3	64	13.5
East TN	40,541	27.4	100	21.1

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted Infection; MSM, men who have sex with men; PWID, people who inject drugs; TN, Tennessee.

^aAge is age at time of cohort entry STI diagnosis.

^bHispanic of any race.

^cIncludes both heterosexual men and women

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Table 3.

Adjusted hazard ratios and 95% confidence intervals for incident HIV-infection by STI type.

Characteristic n=148,465; HIV events=473	HIV Incidence Rate ^a	Adjusted Hazard Ratio ^b	
	per 1000 p-y	aHR	95% CI
STI Diagnosis			
Chlamydia	0.5	Ref.	Ref.
Gonorrhea	4.8	4.5	3.5 – 5.8
Early Syphilis	28.4	5.5	3.8 – 7.9
Late Syphilis	11.5	5.0	3.3 – 7.5
Coinfection	5.1	3.3	2.4 – 4.4
Age, years^c			
20	1.8	1.1	0.8 – 1.4
25	2.2	Ref.	Ref.
30	1.5	1.0	0.8 – 1.2
40	3.3	1.0	0.8 – 1.2
50	4.6	0.9	0.6 – 1.3
Gender			
Female	0.3	\$	\$
Male	4.7	\$	\$
Race/Ethnicity			
Black non-Hispanic	2.7	Ref.	Ref.
White non-Hispanic	1.2	0.6	0.5 – 0.7
Hispanic ^d	1.0	0.5	0.3 – 0.9
Other	0	0.0	—
Unknown	0	0.0	—
MSM Status			
No ^e	0.9	\$	\$
Yes	41.7	\$	\$
PWID			
No	1.9	Ref.	Ref.
Yes	11.7	4.0	2.2 – 7.5
TN Regions and Metropolitan Areas			
Memphis/Shelby County	2.5	Ref.	Ref.
Nashville/Davidson County	3.3	1.0	0.8 – 1.3
West TN	1.5	0.7	0.5 – 1.0
Middle TN	1.1	0.5	0.4 – 0.7
East TN	1.4	0.6	0.4 – 0.7

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted Infection; aHR, adjusted hazard ratio; CI, confidence interval; Ref, reference category; MSM, men who have sex with men; PWID, people who inject drugs; TN, Tennessee.

^aUnadjusted/crude HIV incidence rate by variable.

^b Adjusted for all variables included in the table, in addition to calendar year of study entry.

^c Age is age at time of first STI diagnosis during the study period. Age was modeled using restricted cubic splines with 5 knots to relax linearity assumptions; 25 years was used as reference value.

^d Hispanic of any race.

^e Includes both heterosexual men and women.

Bold estimates have $p < 0.05$.

[§] An interaction term was used for gender by MSM status in adjusted analysis.

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Table 4.

Adjusted hazard ratios and 95% confidence intervals for incident HIV-infection by STI type, stratified by self-reported MSM status.

STI Diagnosis	Non-MSM ^a			MSM		
	n=144,652; HIV events=253			n=3,813; HIV events=220		
	HIV Incidence Rate ^b			HIV Incidence Rate ^b		
	per 1000 p-y	aHR	95% CI	per 1000 p-y	aHR	95% CI
Chlamydia	0.4	Ref.	Ref.	22.5	Ref.	Ref.
Gonorrhea	2.8	5.5	4.1 – 7.4	37.0	2.1	1.3 – 3.3
Early Syphilis	10.3	12.3	6.8 – 22.3	50.2	2.9	1.7 – 4.7
Late Syphilis	6.1	9.9	5.6 – 17.2	35.1	2.2	1.2 – 4.1
Coinfection	1.9	2.8	1.9 – 4.2	72.4	2.3	1.4 – 3.8

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted Infection; aHR, adjusted hazard ratio; CI, confidence interval; Ref, reference category; p-y, person-years; MSM, men who have sex with men.

^a non-MSM includes both heterosexual men and women.

^b Unadjusted/crude HIV incidence rate.

Bold estimates have p <0.05.

Table 5.

Adjusted hazard ratios and 95% confidence intervals for incident HIV-infection by STI type, stratified by specimen source for Chlamydia or Gonorrhea diagnoses.

Specimen Source	Chlamydia or Gonorrhea n=132,351; HIV events=278		Chlamydia Only n=114,243; HIV events=112		Gonorrhea Only n=24,289; HIV events=166	
	aHR	95% CI	aHR	95% CI	aHR	95% CI
Genitourinary	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Oral	3.2	1.9 – 5.5	3.9	1.3 – 11.6	2.4	1.3 – 4.4
Rectal	4.5	2.7 – 7.6	7.6	3.3 – 17.6	3.1	1.6 – 6.1
Other	1.2	0.8 – 1.9	0.7	0.3 – 1.7	1.6	0.9 – 2.9
Not Documented	1.5	1.1 – 2.0	1.3	0.8 – 2.0	1.7	1.2 – 2.5

Adjusted for age at cohort entry, self-reported MSM status, race/ethnicity, history of injection drug use, Tennessee region/metropolitan area, year of study entry.

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted Infection; aHR, adjusted hazard ratio; CI, confidence interval; Ref, reference category; p-y, person-years; MSM, men who have sex with men.

Bold estimates have p <0.05.