HIV Incidence Among Men Who Have Sex With Men After Diagnosis With Sexually Transmitted Infections

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Background: Men who have sex with men (MSM) are at high risk for acquiring HIV infection after diagnosis with other sexually transmitted infections (STIs). Identifying the STIs associated with the greatest risk of subsequent HIV infection could help target prevention interventions, particularly preexposure prophylaxis (PrEP).

Methods: Using matched HIV and STI surveillance data from Washington State from January 1, 2007, to June 30, 2013, we calculated the incidence of new HIV diagnoses after different STI diagnoses among MSM. Men entered observation at the time of their first STI diagnosis during the study period and exited at HIV diagnosis or June 30, 2013. Cox proportional hazards regression was used to conduct a global comparison of rates.

Results: From January 1, 2007, to June 30, 2013, 6577 HIV-negative MSM were diagnosed as having 10,080 bacterial STIs at 8371 unique time points and followed for 17,419 person-years. Two hundred eighty (4.3%) men were subsequently diagnosed as having HIV infection for an overall incidence of 1.6 per 100 person-years (95% confidence interval, 1.4–1.8). The estimated incidence of HIV diagnoses among all MSM in the state was 0.4 per 100 person-years. Men who have sex with men were at the greatest risk for HIV diagnosis after being diagnosed as having rectal gonorrhea (HIV incidence, 4.1 per 100 person-years), followed by early syphilis (2.8), urethral gonorrhea (1.6), rectal chlamydial infection (1.6), pharyngeal gonorrhea (1.1), late syphilis (1.0), and urethral chlamydial infection (0.6; $P < 0.0001$ overall).

Conclusions: Men who have sex with men diagnosed as having rectal gonorrhea and early syphilis were at the greatest risk for being diagnosed as having HIV infection after STI diagnosis. These men should be prioritized for more intensive prevention interventions, including PrEP.

Men who have sex with men (MSM) are disproportionately affected by HIV and other sexually transmitted infections (STIs). Being diagnosed as having an STI is among the most consistent and longstanding risk factors associated with HIV acquisition.[1–3] The elevated risk of HIV acquisition among MSM with bacterial STIs reflects some combination of increased susceptibility,[2–12] sustained risk behaviors, and sexual network factors. The advent of preexposure prophylaxis (PrEP) has created a new impetus for identifying the populations of MSM at greatest risk for HIV infection. Preexposure prophylaxis is efficacious[13] but expensive, and cost-effectiveness analyses have consistently found that it is only cost-effective when targeted to the highest-risk men.[14–18] Previous studies suggest that HIV-negative MSM diagnosed as having early syphilis, rectal gonorrhea, and rectal chlamydial infection may be at particularly high risk for subsequent HIV infection.[19–22] However, these studies did not estimate HIV incidence for all bacterial STIs by anatomic site or stage of infection, were limited to sexually transmitted disease (STD) clinics or study populations, did not estimate the proportion of all HIV infections among MSM occurring in men with a recent STI diagnosis, and measured only the incidence of HIV diagnosis rather than HIV infection. To identify MSM for prioritization of intensive HIV prevention interventions, including PrEP, we used matched HIV/STI surveillance data from Washington State to examine the incidence of new HIV diagnoses after STI diagnoses among MSM statewide and estimate the incidence of new infection among MSM diagnosed at an STD clinic and large community-based HIV/STI testing site. We used these findings to estimate the number of men who would need to receive PrEP to avert one HIV infection directly. Finally, based on a prior analysis among MSM in our STD clinic suggesting that substance use was associated with HIV risk even when controlling for STI diagnosis,[23] we assessed whether the risk of subsequent HIV diagnosis after STI diagnoses was modified by substance use.

MATERIALS AND METHODS

Data Sources

We used matched HIV/STI surveillance data from Washington State from January 1, 2007, to June 30, 2013. STI surveillance and partner services data are routinely matched with HIV surveillance data from the Enhanced HIV/AIDS Reporting System (eHARS) through a 2-step process. First, an automated probabilistic matching algorithm of all persons in the STI surveillance system and all individuals in eHARS based on legal and alias names, date of birth, and sex is run weekly. Second, Washington State Department of Health staff conduct a monthly manual review of STI cases not matched to eHARS but with an indication of HIV infection in STI surveillance or partner services data.

Population

HIV-negative MSM or MSM with unknown status diagnosed as having syphilis of known stage or urethral, rectal, or pharyngeal gonorrhea or chlamydial infection were included in this analysis (98% of reported infections). Men who reported sex with men in the last year during partner services interviews, whose provider indicated male sex partners on the case report, or who were diagnosed as having rectal gonorrhea or chlamydial infection were defined as MSM. (Medical providers in Washington State are legally required to complete a case report form for each person they diagnose as having syphilis, gonorrhea, or chlamydial infection. This form includes gender of sex partners, which was available for 79% of all bacterial STI cases in men during the study period.) To include only HIV-negative MSM and MSM with unknown status, men whose HIV diagnosis date in eHARS preceded the date of their first STI diagnosis during the study period or who were diagnosed as having HIV infection or reported a prior HIV diagnosis at the time of their first STI diagnosis during this period were excluded.

Analyses

Incidence of HIV Diagnosis by STI Type. We calculated incidences of HIV diagnosis after STI diagnosis defined by pathogen and anatomic site or stage of infection (STI type) by dividing the total number of new HIV diagnoses within a given STI stratum by the total time at risk within that stratum (see later for a description of how we defined these strata). We conducted a global comparison of incidences using Cox proportional hazards regression including all STI types as a time-varying covariate. The time scale for the Cox model was calendar time. Men entered observation on the date of their first STI diagnosis during the study period and exited either on the date of HIV diagnosis from eHARS or June 30, 2013 (administrative censoring). Before the analyses, we created a hierarchy of STI types by calculating the incidence of HIV diagnosis after STI diagnosis separately for each type and ranking them in descending order as follows: rectal gonorrhea, early syphilis (primary, secondary, and early latent), rectal chlamydial infection, urethral gonorrhea, late syphilis, pharyngeal gonorrhea, urethral chlamydial infection, and pharyngeal chlamydial infection. Because interventions would be targeted based on an individual's highest-risk STI, MSM diagnosed as having concurrent infections or infections at 1 or more sites were assigned the higher-risk STI for that time point, and men with multiple infections over time could move up, but not down, the STI hierarchy. In a parallel analysis, we examined the incidence of HIV diagnosis after coinfections with the 3 highest-risk STI types by incorporating them into the hierarchy as follows: rectal gonorrhea and early syphilis, rectal chlamydial infection and early syphilis, and rectal gonorrhea and rectal chlamydial infection.

Incidence of HIV Diagnosis by Substance Use. Partner services staff elicit substance use (methamphetamine, inhaled nitrites, and erectile dysfunction [ED] drugs) in the year before STI diagnosis during interviews. We calculated the incidence of HIV diagnosis after STI diagnosis by substance use by dividing the total number of new HIV diagnoses within a given substance use stratum, by the total time at risk within that stratum. We compared incidences using Cox proportional hazards regression with substance use and STI types as time-varying covariates. The time scale for the Cox model was calendar time. Men entered observation on the date of their first STI diagnosis during the study period at which substance use was ascertained and exited on their HIV diagnosis date or June 30, 2013. Men diagnosed as having multiple STIs over time could be recategorized from nonusers to users of substances, but not from users to nonusers.

Comparison With the General Population of MSM. For comparison, we estimated the incidence of HIV diagnosis among sexually active HIV-negative MSM in Washington State during the study period. We used the number of new HIV diagnoses among MSM in eHARS as the numerator and 3.9% of men age 15 years and older from Washington State census estimates (based on US Centers for Disease Control and Prevention estimate of proportion of men who have had sex with men in the past 5 years[24]) minus the number of MSM known to be living with HIV from eHARS as the denominator. Because HIV risk in Washington is concentrated among MSM younger than 65 years, we also compared the incidence of HIV diagnosis after STI diagnosis among MSM aged 15 to 64 years (99.5% of STI cases; 99% of HIV diagnoses among MSM with STIs) to the incidence among sexually active HIV-negative MSM in Washington State aged 15 to 64 years (99.6% of HIV cases among MSM).

Number Needed to Treat (NNT) and Population-Level Impact. We calculated the NNT with PrEP for 1 year to prevent one HIV infection among PrEP recipients as follows: $1 \div$ (HIV incidence $\times$ PrEP effectiveness)[25]. To address differences in PrEP effectiveness due to adherence, we used 3 efficacy estimates from iPrEx: the overall estimate of 44% reduction in HIV acquisition, the estimate among MSM reporting at least 90% adherence of 73%, and the estimate among MSM with detectable blood levels of emtricitabine, tenofovir, or their metabolites of 92%.[13]

To provide an upper bound for the potential direct population-level impact of a prevention intervention targeted toward MSM diagnosed as having bacterial STIs, we calculated the proportion of HIV cases reported among MSM in the last 2 years of the study period who had been diagnosed as having an STI in the 2 years before HIV diagnosis.

Sensitivity Analyses

The primary analysis has the potential to underestimate the true HIV incidence and overestimate NNTs because men who were not tested for HIV infection at the time of STI diagnosis may have been misclassified as uninfected, passive follow-up may fail to identify new HIV infections, and incidence of HIV diagnosis is sensitive to the lag between HIV acquisition and diagnosis. To address these limitations, we conducted an analysis among STI cases diagnosed at 2 publicly funded HIV/STI testing programs (Public Health–Seattle & King County STD Clinic and Gay City), unless partner services data indicated that cases were not HIV tested at STI diagnosis. At these sites, near-universal HIV testing at STI diagnosis reduced misclassification of persons at study entry, and frequent HIV testing should diminish the influence of passive follow-up and the lag between HIV acquisition and diagnosis. In addition, we calculated an incidence of HIV infection (rather than diagnosis) by estimating the infection date as the midpoint between the last negative and first positive HIV test results from surveillance or partner services data. Men entered observation on the date of their first STI diagnosis at these sites during the study period and exited on the date of HIV infection or June 30, 2013.

Analyses were conducted using SAS 9.3 (SAS Institutes, Cary, NC) and Stata 11.0 (Stata Corp, College Station, TX). These analyses were conducted as part of public health program activities and not considered human subjects research.

RESULTS

From January 2006 to June 2013, 10,080 bacterial STIs were reported among 6577 HIV-negative MSM or MSM with unknown status in Washington State at 8371 unique time points. These men were followed up for a total of 17,419 person-years

(median, 2.4 years; interquartile range, 1.1–4.0 years), and 280 (4.3%) were diagnosed as having HIV infection during follow-up for an overall incidence of 1.61 diagnoses per 100 person-years (95% confidence interval [CI], 1.43–1.81), 4 times greater than the estimated incidence of diagnoses among all HIV-negative MSM statewide (0.41 per 100 person-years). Restricted to MSM aged 15 to 64 years, incidence of HIV diagnosis was 1.60 per 100 person-years among men after STI diagnoses, more than 3-fold higher than the 0.48 per 100 person-years among all HIV-negative MSM. Sociodemographic characteristics at each individual's initial reported STI during the study period and HIV testing history are presented in Table 1.

The incidence and cumulative hazard of HIV diagnosis after STI diagnosis by STI type are presented in Table 2A and Figure 1, respectively. Men who have sex with men were at the greatest risk for acquiring HIV after diagnosis with rectal gonorrhea (incidence, 4.1 per 100 person-years), followed by early syphilis (2.8), urethral gonorrhea (1.6), rectal chlamydial infection (1.6), pharyngeal gonorrhea (1.1), late syphilis (1.0), and urethral chlamydial infection (0.6; $P < 0.0001$ overall). Consequently, the NNT with PrEP was lowest for rectal gonorrhea and early syphilis (Table 2A; Fig. 2A). If PrEP reduces the risk of acquiring HIV by 44%, 55 and 80 MSM diagnosed as having rectal gonorrhea and early syphilis, respectively, would need to be treated with PrEP for 1 year to prevent 1 new infection among PrEP recipients. Using the highest estimate of PrEP efficacy (92% risk reduction), 26 and 38 MSM with rectal gonorrhea and early syphilis would need to be treated.

Men were concurrently diagnosed as having more than 1 bacterial pathogen at 810 time points (9.7% of 8371), including 24 early syphilis–rectal gonorrhea, 29 early syphilis–rectal chlamydia,

TABLE 1. Characteristics of 6577 HIV-Negative MSM Diagnosed as Having Bacterial STIs From January 2007 to June 2013 in Washington State

Characteristics at Initial STI Diagnosis During Study Period and HIV Testing History	Median or No.	IQR or %
Age, y	28	23–37
Race/Ethnicity		
White	3966	60%
Hispanic/Latino (any race)	969	15%
Black	575	9%
Asian/Pacific Islander	394	6%
Native American/Alaska Native	65	1%
Multiple race	143	2%
Unknown	420	6%
King County residence	4202	64%
HIV testing status*		
Tested HIV negative at the time of or after initial STI diagnosis	3371	51%
Tested HIV negative before initial STI diagnosis or at unknown time	865	13%
Reported no prior HIV test	237	4%
No HIV testing history available	2105	32%
Years of follow-up	2.4	1.1–4.0
HIV diagnosis during follow-up	280	4.3%
Tested HIV negative at the time of or after initial STI diagnosis and before HIV diagnosis†	221	79%

*Based on self-reported HIV testing history from STI partner services interviews.

†Based on self-reported HIV testing history or medical record review from HIV surveillance, HIV partner services, or STI partner services.

IQR indicates interquartile range.

and 251 rectal gonorrhea–rectal chlamydia coinfections. The incidences of HIV diagnosis after these coinfections were the greatest we observed: 11.8, 10.8, and 5.9 per 100 person-years, respectively.

Table 2B and Figure 2B describe the HIV incidence and NNTs from the sensitivity analysis conducted among STI cases from publicly funded testing programs and estimating the incidence of HIV infection. Overall, HIV incidence after STI diagnosis was 2.48 per 100 person-years, a 54% increase from 1.61 in the primary analysis. The absolute difference between estimated incidence of diagnosis and infection was small for gonococcal infections regardless of anatomic site and urethral chlamydial infection, but higher for early and latent syphilis and rectal chlamydial infection. Despite these differences, MSM continued to be at greatest risk for acquiring HIV after diagnosis with rectal gonorrhea (incidence, 4.4 per 100 person-years) and early syphilis (3.7).

From July 2011 to June 2013, 736 MSM were diagnosed as having HIV infection in Washington State, of whom 104 (14%) had a history of bacterial STI in the 2 years before HIV diagnosis, including 47 (6.4%) with a history of early syphilis or rectal gonorrhea (Fig. 3).

Among 3715 men (56% of total) for whom information regarding substance use was available from at least 1 STI diagnosis, 306 (8.2%) reported using methamphetamine, 632 (17%) inhaled nitrites, and 401 (11%) ED medications in the year before STI diagnosis. In bivariable analyses, men who reported using each of these substances experienced greater incidences of HIV diagnosis after STI diagnosis than did men who denied using these substances (methamphetamine, 5.09 vs. 1.65 per 100 person-years; inhaled nitrites, 4.40 vs. 1.53; ED drugs, 3.91 vs. 1.71; $P < 0.001$ for all). In multivariable analyses including all 3 substances and STI type, methamphetamine and inhaled nitrite use remained significantly associated with incidence of HIV diagnosis (adjusted hazard ratios, 1.92 [95% CI, 1.29–2.84] and 2.2 [1.6–3.1], respectively; $P < 0.001$ for both).

DISCUSSION

In Washington State, MSM diagnosed as having any bacterial STI experienced 3- to 4-fold greater incidence of HIV diagnosis after their STI than did MSM overall, with the greatest risks observed among MSM diagnosed as having rectal gonorrhea and early syphilis or reporting methamphetamine or inhaled nitrite use. However, only 1 in every 7 MSM newly diagnosed as having HIV infection had been diagnosed as having a bacterial STI in the 2 years before HIV diagnosis, and only 6.4% had a recent history of rectal gonorrhea or syphilis. These results suggest that targeting HIV prevention interventions to MSM diagnosed as having STIs, specifically rectal gonorrhea and early syphilis and methamphetamine or inhaled nitrite users, has the potential to reach very high risk men but will only directly affect a relatively small subset of MSM who will ultimately acquire HIV infection. These findings highlight the potential value of using specific STIs to target resource-intensive interventions such as PrEP, but suggest how such a highly targeted approach might have limited direct population-level impact.

This population-based study supports conclusions from previous studies in clinical and research settings that MSM with rectal infections and early syphilis are at extremely high risk for subsequently acquiring HIV, although our absolute risk estimates are lower than those previously reported.[19–22] Similar to a study in New York City STD clinics,[19] we observed higher HIV incidence after rectal gonorrhea than rectal chlamydia diagnosis, but HIV incidence in both groups was greater in New York City than in Washington State (7.1 vs. 4.1 per 100 person-years for rectal gonorrhea; 5.9 vs. 1.6 for rectal chlamydial infection). In iPrEx,[21]

TABLE 2. HIV Incidence After STIs by Infection Type and Associated NNT With PrEP to Prevent 1 HIV Infection

					NNT With PrEP by Estimate of Efficacy†		
Panel A: Primary Analysis—Incidence of HIV Diagnosis Among MSM With STIs in Washington State							
	Total No. STIs	No. STIs Based on Order*	Subsequent HIV Diagnoses	Incidence of HIV Diagnosis Per 100 Person-Years (95% CI)	44%	73%	92%
Overall	10,080	7064	280	1.61 (1.43–1.81)	141	85	68
Rectal GC	985	871	79	4.13 (3.31–5.15)	55	33	26
Early syphilis	771	675	51	2.83 (2.15–3.72)	80	48	38
Rectal CT	1480	939	29	1.59 (1.10–2.29)	143	86	68
Urethral GC	2087	1537	66	1.63 (1.28–2.07)	140	84	67
Late syphilis	188	155	4	1.04 (0.39–2.78)	218	131	104
Pharyngeal GC	1205	528	11	1.08 (0.60–1.95)	210	127	100
Urethral CT	3124	2283	39	0.62 (0.45–0.84)	369	222	176
Pharyngeal CT	240	76	1	1.08 (0.15–7.65)	211	127	101

Panel B: Sensitivity Analysis—Incidence of HIV Infection Among MSM Diagnosed as Having STIs at Publicly Funded HIV/STI Testing Programs

				NNT With PrEP by Estimate of Efficacy†		
	No. STIs Based on Order*	Subsequent HIV Diagnoses	Incidence of HIV Infection‡ Per 100 Person-Years (95% CI)	44%	73%	92%
Overall	2223	135	2.48 (2.10–2.94)	92	55	44
Rectal GC	541	54	4.36 (3.34–5.70)	52	31	25
Early syphilis	204	19	3.74 (2.38–5.86)	61	37	29
Rectal CT	515	27	2.31 (1.59–3.37)	98	59	47
Urethral GC	303	17	1.99 (1.24–3.21)	114	69	55
Late syphilis	39	3	3.06 (0.99–9.49)	74	45	36
Pharyngeal GC	290	8	1.26 (0.63–2.51)	181	109	86
Urethral CT	298	7	0.77 (3.69–1.62)	293	177	140
Pharyngeal CT	33	0	0	N/A	N/A	N/A

*STI types are presented in hierarchical order based on prior analyses identifying descending incidence of HIV diagnosis. Men diagnosed as having concurrent infections or infections at more than 1 site were assigned the higher order STI for that time point. Repeat infections of the same type were not included in this count.

†This represents an estimate of the number of HIV-negative MSM with each infection that would need to be treated with PrEP for 1 year to prevent 1 HIV infection among PrEP recipients based on 3 estimates of PrEP effectiveness from iPrEx[17]: overall (44%), with at least 90% adherence (73%), and with detectable blood levels of PrEP drug (92%).

‡The date of HIV infection was estimated as the midpoint between the last negative and first positive HIV test results from HIV surveillance, HIV partner services, or STI partner services data.

GC indicates gonorrhea; CT, chlamydial infection' N/A, not applicable.

which was conducted primarily in South America, MSM experienced an HIV incidence of 8.0 per 100 person-years after syphilis diagnosis, more than twice the 2.8 per 100 person-years observed among MSM in Washington State. Variations in absolute risk across studies may reflect differences in HIV incidence among MSM in these geographic areas, differences in risk in the study populations (i.e., population-based vs. STD clinic clients or study participants), or, in the case of iPrEx, greater ascertainment of infection through active follow-up.

The relationship between HIV and STI acquisition is complex and multidirectional. Some evidence suggests that genital tract inflammation caused by bacterial STIs increases the risk of HIV transmission by increasing HIV shedding by HIV-infected partners and causing breaches in the genital tract epithelium and recruitment of targets cells to this area in HIV-susceptible partners.[2–12] However, these biological mechanisms require the pathogen to be present at the time of HIV exposure. Rather, our findings are likely a result of the association between different STI and subsequent behaviors and sexual network factors that result in exposure to HIV. Rectal infections are direct markers of condomless receptive anal sex, which is associated with a greater risk of HIV acquisition than oral or insertive anal sex,[26–28] and because the syphilis epidemic in the United States and other developed countries is concentrated among MSM living with HIV,[29] early syphilis may be a marker of condomless sex within sexual networks including high-risk MSM living with HIV. It is also possible that men at higher risk for acquiring HIV are more likely to seek STI screening in general, in clinical settings where extragenital testing is available, or are more likely to recognize or seek care in response to symptoms. Exploring the reasons that STI diagnoses predict future HIV acquisition may help identify additional targets for prevention interventions.

FIGURE 1. Cumulative hazard of HIV diagnosis following bacterial STIs (STI) GC = gonorrhea. CT = chlamydial infection.
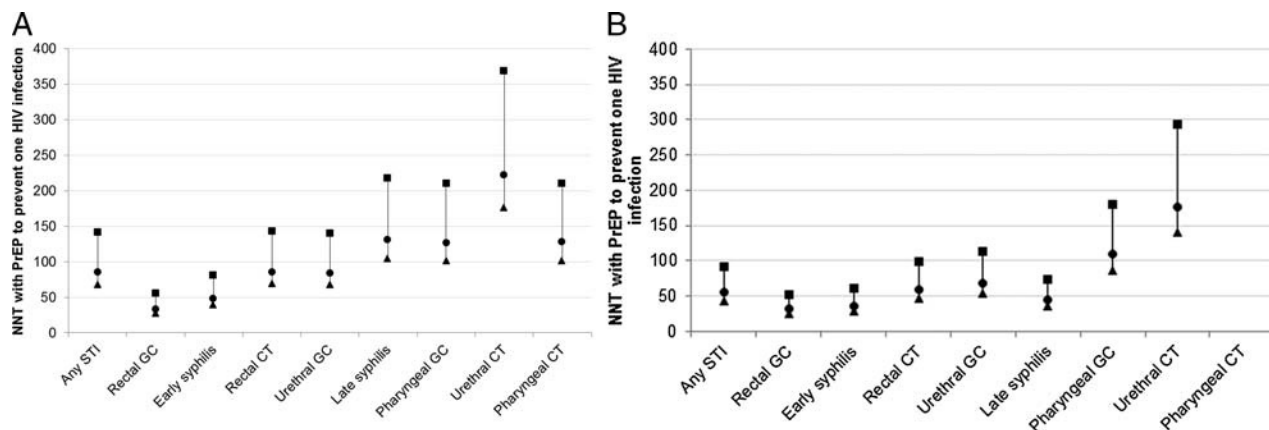
FIGURE 2. NNT with HIV PrEP to directly prevent 1 new HIV infection by STI type. A, Primary analysis—estimated from incidence of HIV diagnosis in Washington State. B, Sensitivity analysis—estimated from incidence of HIV infection among MSM diagnosed at publicly funded HIV/STI testing programs This figure presents estimates of the number of HIV-negative MSM with each infection that would need to be treated with PrEP for 1 year to prevent 1 HIV infection among PrEP recipients (NNT) based on 3 estimates of PrEP effectiveness from iPrex13: overall (44%; ■), with at least 90% adherence (73%; ●), and with detectable blood levels of PrEP drug (92%; ▲). A, NNTs estimated from the incidence of HIV diagnosis after STI diagnoses among all MSM in Washington State (primary analysis). B, Estimates from the incidence of HIV infection among MSM diagnosed at publicly funded HIV/STI testing programs (sensitivity analysis). The date of HIV infection was estimated as the midpoint between the last negative and first positive HIV test results from HIV surveillance, HIV partner services, or STI partner services data. GC indicates gonorrhea; CT, chlamydial infection.

Preexposure prophylaxis implementation is resource-intensive, and several cost-effectiveness analyses have found that despite its potential impact on HIV incidence, providing PrEP to general populations of MSM in the United States and Australia is probably not cost-effective at current medication costs.[14–17,30] Prioritizing subpopulations of MSM with higher HIV incidence, however, may be cost-effective in some situations.[14–18] With that in mind, we designed our analysis to identify populations at high risk for HIV infection for PrEP prioritization and assess the potential population-level effects of such an approach. Numbers Needed to Treat can be used to compare the effectiveness of targeting interventions to subpopulations with different levels of risk, intervention adherence, and other factors. Similar to an analysis from iPrEx,[31] relatively few MSM diagnosed as having syphilis would need to be treated with PrEP to prevent one new HIV infection among PrEP recipients, but the proportion of HIV infections occurring in men with a prior syphilis diagnosis was small. In iPrEx, condomless receptive anal sex with a partner of any HIV status was associated with a similar NNT but a much larger population attributable fraction, suggesting that offering PrEP to all men reporting condomless receptive anal sex would have a larger population-level impact than offering it to MSM with rectal gonorrhea or early syphilis alone at a similar cost per case directly averted. Our study does not directly address the relative benefits of targeting MSM with syphilis or rectal gonorrhea versus all MSM who engage in condomless receptive anal sex. However, in a prior analysis among MSM attending an STD clinic, we found that condomless receptive anal sex was not associated with HIV incidence when adjusting for diagnosis with a bacterial STI and methamphetamine or inhaled nitrite use in the prior year,[23] suggesting that NNTs may be substantially higher in a group defined solely by condomless receptive anal sex and not stronger risk factors. Neither the iPrEx study population (primarily South American MSM) nor MSM in Washington State are likely to provide accurate estimates of HIV risk for prioritizing PrEP among MSM in other settings. Preexposure prophylaxis targeting criteria should be context-specific and may not be appropriate in settings where HIV risk in the general population of MSM is extremely high. Regardless, offering PrEP to MSM diagnosed as having higher-risk STIs may help increase the cost-effectiveness of PrEP programs.

This study has several limitations. First, without being able to measure the true date of HIV infection, the primary analysis relied on the date of the first positive test result. This approach likely led us to underestimate the true incidence of HIV infection after STI diagnosis for several reasons: the lag between HIV acquisition and diagnosis, failure to identify infections in men who did not test during follow-up, and underascertainment of infections in men who migrated out of the area. Our approach may also have misclassified HIV-infected MSM who tested HIV negative during acute infection or did not test at the time of their initial STI diagnosis, potentially leading to an overestimate of the true HIV incidence in the population. To partially address these limitations, we undertook an analysis restricted to MSM diagnosed as having STIs in large publicly funded testing programs and estimated time of HIV infection based on patients' HIV testing history. Numbers Needed to Treat were somewhat lower in this analysis, suggesting that relying on HIV diagnosis as a surrogate for HIV infection led us to overestimate NNTs in our main analysis. Some of this variation, however, may reflect differences between persons seen in an STD clinic or community-based program and the general
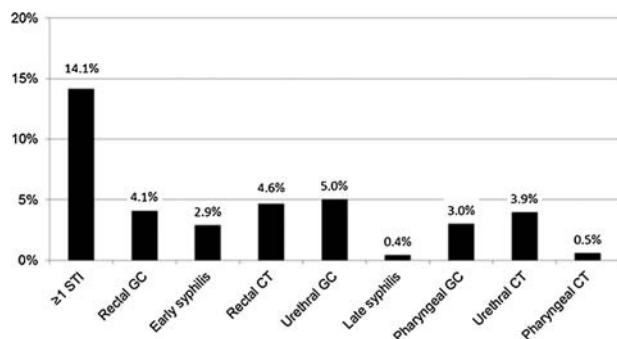

FIGURE 3. Percent of 736 MSM newly diagnosed as having HIV infection from July 2011 to June 2013 with a reported STI diagnosis in the 2 years before HIV diagnosis GC indicates gonorrhea; CT, chlamydial infection.

population. In addition, many bacterial STIs in MSM are asymptomatic, and it is possible that the elevated rate of HIV diagnoses we observed overall and following specific STI types reflects a pattern of more frequent testing in men with these STIs rather than a true elevation of HIV risk. Although we cannot completely exclude this possibility, that some asymptomatic STIs (e.g., urethral chlamydial infection and pharyngeal gonorrhea) were associated with a relatively low risk of subsequent HIV acquisition argues against the idea that our findings are simply a result of ascertainment bias. Moreover, from a public health perspective, our findings clearly identify groups at high risk for HIV acquisition that could benefit from PrEP. Missing data regarding substance use may affect estimates of the association with subsequent HIV diagnosis and limited our ability to calculate the potential population-level effects of such prioritization. Furthermore, our NNTs were limited to the direct effects of PrEP on individuals taking the medications and did not take into account potential infections averted among partners and sexual networks. Last, the utility of PrEP efficacy estimates from iPrEx for calculating NNTs may be affected by differences in behavior and adherence between MSM in Washington State and the study population due to differential knowledge regarding PrEP effectiveness, access to intensive risk reduction or adherence counseling, or frequency and intensity of HIV exposures.

In conclusion, we found that MSM with rectal gonorrhea and syphilis and MSM with STIs who use methamphetamine or inhaled nitrites were at very high risk for future HIV infection. Gonorrhea and syphilis are reportable throughout the United States, and insofar as gonococcal infections are reportable with data on anatomic site of infection, the population with these infections is readily defined and could be targeted by public health agencies for specific prevention outreach, particularly promoting frequent HIV/STI testing and PrEP. At a minimum, clinicians should discuss PrEP as an HIV prevention option with MSM with rectal gonorrhea or early syphilis, or who report methamphetamine or inhaled nitrite use concurrent with any STI diagnosis.

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