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High proportions of rectal and pharyngeal chlamydia and gonorrhea cases among cisgender men are missed using current CDC screening recommendations

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Abstract

Objectives. Pharyngeal and rectal *Chlamydia trachomatis* (CT) and *Neisseria gonorrhea* (NG) infections are often undiagnosed due to their asymptomatic nature. This study aims to determine: 1) the prevalence of CT/NG infections by anatomic site among cisgender men; 2) proportion of missed CT/NG rectal/pharyngeal infections if a) urogenital testing alone were performed or b) screening depended on self-reported behavior alone; and 3) predictive probability of self-reported behaviors for rectal CT/NG.

Methods. This cross-sectional study used electronic health records collected at a sexual health clinic in Los Angeles from November 18, 2018 until February 28, 2020. Included patients were: ≥ 18 years of age, cisgender men, who received CT/NG testing at least once during the study period. We calculated the proportion of missed pharyngeal/rectal CT/NG infections if only urogenital testing had been done and if testing were based only on self-reported anal sex. Separately, we ran logistic regressions for predictive probability of self-reported anal sex on CT/NG rectal infections.

Results. Overall, there were 13,476 unique patients with 26,579 visits. Prevalence of any extragenital CT/NG infection was 37.28%. Over 80% rectal/pharyngeal CT cases and over 65% rectal/pharyngeal NG cases would be missed if urogenital testing alone was performed. Likewise, over 35% rectal CT/NG cases would be missed had testing relied on self-reported sexual behaviors alone.

Conclusions. The proportion of missed rectal and pharyngeal CT/NG infections are high. Our data from a sexual health clinic lend support to three-site opt-out testing for cisgender men attending a sexual health/LGBTQ+ specialty clinic regardless of their sexual orientation or reported sexual behaviors.

Introduction

Chlamydia trachomatis (CT) and Neisseria gonorrhea (NG) are the most reported sexually transmitted infections (STIs) in the United States. In 2019, there were 1,808,703 reported cases of CT, a 2.8% increase compared to 2018, and 616,392 reported cases of NG, a 5.7% increase since 2018.[1] Because of stigma, access to culturally competent care, and inconsistent clinician adherence to screening guidelines, gay, bisexual, and other men who have sex with men (MSM) are disproportionally impacted by human immunodeficiency virus (HIV) and STIs, including extragenital (rectal and pharyngeal) CT/NG infections.[1-5] For instance, the prevalence of pharyngeal CT and NG has been shown to be 0-3.6% and 0.5-16.5% respectively, whereas rectal CT and NG has been estimated to be 2.1-23% and 0.2-24% respectively among MSM.[6] Moreover, rectal CT and NG are well-established risk factors for HIV infection which may be due to disruption of the mucosal tissue and increased inflammation.[3,6-11] The Centers of Disease Control and Prevention (CDC) recommends that sexually active MSM are screened annually for urogenital CT/NG if insertive sex is reported in the last 12 months, rectal CT/NG if receptive anal sex is reported in the last 12 months, and pharyngeal NG if receptive oral sex is reported in the last 12 months.[3,12] However, many pharyngeal and rectal CT and NG cases go undiagnosed and more importantly untreated because of their asymptomatic nature and lower screening rates.[2-6,13-16] Previous studies have demonstrated that screening for urogenital CT/NG alone among MSM may miss a substantial amount (14-85%) of CT/NG cases.[6,13,17-22] In other words, a negative urogenital test for CT/NG may miss positive CT/NG cases at the pharyngeal and rectal sites had urogenital testing alone been performed. Thus, pharyngeal and rectal CT/NG cases may only be detected by STI screening at those anatomic sites.[6,12,13,16-19]

Furthermore, screening recommendations are dependent on self-reported sexual behaviors which may be underreported.[23] Few studies have investigated the number of missed extragenital CT/NG cases relying on self-reported behaviors alone. A study from two health clinics in San Diego, California determined that 11% of CT/NG cases in a primary care clinic and 78% of CT/NG cases in a high resolution anoscopy (HRA) clinic would have been missed by self-reported behaviors alone.[23] The sensitivity of selfreported unprotected receptive anal intercourse at predicting a rectal STI infection was 86-100% in the primary care clinic and 12-35% in the HRA clinic. On the other hand, specificity was 30-33% in the primary care clinic and 82-86% in the HRA clinic. However, data for this study came from two clinics that were heterogenous from one another, only included men living with HIV, and only screened for STIs among individuals who reported certain sexual behaviors (i.e., self-reported number of sexual partners). In the Netherlands, a study of MSM and men who have sex with men and women (MSMW) attending a STI clinic showed that 51.8% of CT/NG cases and 40.0% CT/NG cases were missed when testing relied on symptoms (not including rectal symptoms) and self-reported sexual activity compared to universal testing of all anatomic sites (pharyngeal, urogenital, and rectal).[24] But, this study was not able to differentiate between receptive and insertive anal sex and may not be transportable to cisgender men in the United States.

This current study aims to expand on previous literature to address the following: 1) identify the prevalence of CT/NG cases by anatomic site among cisgender MSM, MSMW, and men who have sex with women (MSW); 2) assess the proportion of missed CT/NG rectal and pharyngeal cases if urogenital testing alone were performed; 3) assess the proportion of missed CT/NG rectal cases had screening depended on self-reported behavior alone; and 4) estimate the predictive probability (sensitivity, specificity, and area under the curve (AUC)) of self-reported behaviors for rectal CT/NG.

Methods

Study Design

This cross-sectional study was conducted using electronic health records collected at the Sexual Health Education and Prevention Program (SHEP) at the Los Angeles LGBT Center ("the Center"), a Federally Qualified Health Center. The SHEP sees approximately 13,000 unique patients annually in one of two sites: the Hollywood neighborhood of Los Angeles, California and in West Hollywood, California for HIV/STI testing and treatment, sexual health counseling, and post-exposure prophylaxis (PEP)/pre-exposure prophylaxis (PrEP) services for HIV prevention.

Data for this study were collected from November 18, 2018 until February 28, 2020. Patients were included in the study if they were 18 years of age or older, cisgender men, and received a chlamydia or gonorrhea screening at least once during the study period. Some patients had more than one testing visit during the study period.

Data Collection

All patients receiving HIV/STI testing complete clinic registration (demographics) and an online self-administered sexual health risk assessment prior to their appointment. Patients report on last sexual partner(s) demographics, sexual health behaviors in the last three months, and type of reported sex (insertive anal sex, receptive anal sex, and vaginal sex). Patients who have had an HIV/STI testing visit within six months of their last visit receive an abbreviated risk assessment that includes questions on the patient's last sexual encounter only.

CT/NG Testing – or – Laboratory Testing

All patients who receive HIV/STI testing are offered three-site (urogenital, pharyngeal, and rectal)

CT/NG testing regardless of their gender or self-reported sexual behaviors. However, pharyngeal CT testing is only routinely ordered for PrEP or PEP visits, and not for routine STI testing since the CDC recommends against such testing.[3] Providers collect pharyngeal swabs and patients self-collect urine and rectal swabs, respectively. All specimens undergo nucleic acid amplification tests using the APTIMA

Combo 2 Assay (Hologic Gen-Probe, San Diego, CA); detailed laboratory methods for CT/NG diagnosis have been previously described.[25] A positive CT/NG case is deemed as such if the patient receives a positive result for CT/NG at the urogenital, pharyngeal, and/or rectal sites.

Ethics

This study was approved by the Los Angeles County Department of Public Health Institutional Review Board (Project Number: 2020-07-884).

Variable Definitions

The primary predictor for this study is self-reported receptive anal sex with last partner. Patients were asked "Did you have receptive anal sex (bottom) including toys and any body parts with your last sexual partner" with answer choices yes with a barrier (condom, dam, gloves), yes without a barrier (condom, dam, gloves), no, I don't have this type of sex, and declined. We deemed receptive anal sex with last partner if patients stated yes with or without a barrier and no if they reported no, don't have this type of sex, or declined.

We categorized patients as MSM, MSMW, and MSW based on self-reported gender of their sexual partner(s) in the last year. All groups were mutually exclusive. We chose not to differentiate between cisgender and transgender partners because of how the CDC recommends sexual health questions ("What is the gender(s) of your partner(s)?").[3]

Statistical Analyses

We used frequency and continuous distributions as appropriate to describe patient demographics, sexual behaviors, and the prevalence of CT/NG positive cases among the total population and stratified by partner type (MSM, MSMW, and MSW).

We calculated potentially missed pharyngeal/rectal CT/NG cases among those who received urogenital testing overall and by partner type. Furthermore, we calculated potentially missed rectal CT/NG cases if CT/NG screening had relied on self-reported anal sex alone in the total population and by partner type. We used total testing visits to capture the overall prevalence of missed CT/NG cases over the study period had each pharyngeal/rectal test relied on urogenital or self-reported anal sex.

Finally, we conducted bivariate and adjusted logistic regressions to determine how well self-reported sexual behaviors alone predicted CT/NG rectal infections. We evaluated sensitivity, specificity, and AUC for CT and NG separately. Adjusted logistic regression models controlled for age and partner type.

Models used each unique patient's most recent testing visit.

All analyses were conducted using SAS software Version 9.4 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Overall, there were 13,476 unique patients in our sample who contributed 26,579 visits over the study period. The mean age overall was 33.58 (standard deviation 9.74) years. Most patients identified as gay (69.81%), bisexual (11.37%), or heterosexual (9.97%), with differences among MSM, MSW, and MSMW. Receptive anal sex with their last partner was reported by 34.31% of patients in all visits (**Table 1**).

Table 1 - Frequency distribution of demographics, sexual behaviors, and chlamydia/gonorrhea infection by site and partner type among cisgender men at community-based STI clinic in Los Angeles, November 2018 - February 2020 (N= 26,579 total visits)

	Overall n (%)	MSM n (%)	MSW n (%)	MSMW n (%)
Demographics				
Age, years, Mean (SD)	33.58 (9.74)	33.88 (10.03)	32.50 (8.81)	32.30 (9.80)
Sexual orientation				
Homosexual/Gay	9,407 (69.81)	7,511 (83.94)	4 (0.29)	49 (10.40)
Bisexual	1,532 (11.37)	836 (9.34)	110 (7.87)	264 (56.05)
Heterosexual	1,344 (9.97)	43 (0.48)	1,064 (76.16)	50 (10.62)
Pansexual/Queer	164 (1.22)	70 (0.78)	14 (1.00)	31 (6.58)
Homosexual/Gay Bisexual Heterosexual	1,532 (11.37) 1,344 (9.97)	836 (9.34) 43 (0.48)	110 (7.87) 1,064 (76.16)	264 (56.05) 50 (10.62)

Other	244 (1.81)	121 (1.35)	33 (2.36)	29 (6.16)
Unknown	787 (5.83)	367 (4.10)	172 (12.31)	48 (10.19)
Total Unique Patients	13,476 (100.0)	8,948 (100.0)	1,397 (100.0)	471 (100.0)
Sexual Behaviors				
Reported anal sex with last				
partner				
Yes	9,120 (34.31)	8,491 (48.46)	133 (7.08)	301 (34.96)
No	11,405 (42.91)	8,440 (48.17)	1,726 (91.86)	539 (62.60)
Unknown	6,054 (22.78)	590 (3.37)	20 (1.06)	21 (2.44)
Total Visits	26,579 (100.0)	17,521 (100.0)	1,879 (100.0)	861 (100.0)
Chlamydia	n/N (%) ^a	n/N (%) ^a	n/N (%) ^a	n/N (%) ^a
Urogenital Positive	714/25,435 (2.81)	413/16,742 (2.47)	95/1,817 (5.23)	31/822 (3.77)
Rectal Positive	1,974/24,723 (7.98)	1,316/16,424 (8.01)	71/1,598 (4.44)	54/798 (6.77)
Pharyngeal Positive	58/8,046 (0.72)	26/3,776 (0.69)	1/107 (0.93)	1/167 (0.60)
Any Chlamydia Positive ^b	2,441/9,562 (25.53)	1,585/4,969 (31.90)	122/205 (59.51)	77/226 (34.07)
Gonorrhea				
Urogenital Positive	692/25,425 (2.72)	514/16,737 (3.07)	28/1,814 (1.54)	25/821 (3.05)
Rectal Positive	1,664/24,660 (6.75)	1,130/16,385 (6.90)	37/1,589 (2.33)	56/794 (7.05)
Pharyngeal Positive	1,431/25,437 (5.63)	949/16,729 (5.67)	22/1,806 (1.22)	49/827 (5.93)
Any Gonorrhea Positive	2,605/24,360 (10.69)	1,744/16,189 (10.77)	56/1,574 (3.56)	82/787 (10.42)
Any Extragenital ^c				
Positive	4,041/10,840 (37.28)	2,680/5,941 (45.11)	118/201 (58.71)	117/258 (45.35)

Abbreviations. STI= sexually transmitted infection; MSM= Men who have sex with men; MSW= Men who have sex with women; MSMW= Men who have sex with men and women; SD= Standard Deviation

Note, the overall sample includes all cisgender men regardless of partner type and is therefore larger than the summation of MSM, MSMW, and MSW.

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CT/NG Prevalence

Across all visits, there were 714 cases of urogenital CT (2.81%), 1,974 cases of rectal CT (7.98%), and 58 cases of pharyngeal CT (0.72%). For NG, there were 692 urogenital infections (2.72%), 1,664 rectal infections (6.75%), and 1,431 pharyngeal infections (5.63%). There were 4,041 extragenital CT/NG infections (37.28%). Finally, prevalence of any extragenital infection was 45.11% for MSM, 45.35% for MSMW, and 58.71% for MSW. However, it should be noted that the denominators for any chlamydia

^aMay not add to 100% because patient was missing an STI test;

^bPharyngeal CT not performed for all patients/visits. Missing data for this test drives the denominator for "Any Chlamydia Positive" to be smaller than that of other CT testing (i.e., urogenital and rectal)

^cAny Extragenital has a smaller denominator because pharyngeal CT was not performed for all patients/visits. Missing data for this test drives the denominator for "Any Extragenital" to be smaller than those of other CT/NG testing.

positive and any extragenital infection is smaller because pharyngeal CT testing was not performed for all patients/visits. (**Table 1**).

Urogenital Testing

For CT, 86.11% of rectal infections (n=1,667/1,936) and 89.66% of pharyngeal infections (n=52/58) had a negative urogenital test. Likewise, 67.46% of rectal NG (n=1,103/1,635) and 83.55% pharyngeal NG (n=1,173/1,404) infections had negative urogenital tests. Of 3,961 positive extragenital infections, 78.41% (n=3,106) cases had a negative urogenital test.

When categorized by partner type, 88.08% (n=1,138/1,292 cases) of rectal CT among MSM, 36.23% (n=25/69 cases) of rectal CT among MSW, and 84.62% (n=44/52 cases) of rectal CT among MSMW would have been missed had testing relied on urogenital alone. Similarly, a large proportion of rectal NG would have also been missed had testing relied on urogenital alone which accounted for 63.82% (n=709/1,111 cases) of cases among MSM, 38.89% (n=14/36 cases) among MSW, and 60.00% (n=33/55 cases) among MSMW. A higher proportion of pharyngeal NG cases would have been missed by urogenital testing alone of which, 81.51% (n=758/930 cases) would have been among MSM, 72.73% (n=16/22 cases) among MSW, and 76.60% (n=36/47 cases) among MSMW (Table 2).

Table 2 - Proportion of missed extragenital chlamydia and gonorrhea overall and by partner type had testing relied on positive urogenital screenings and self-reported anal sex among total visits (N=26,579 total visits)

	Overall	MSM	MSW	MSMW
	n/N (%)	n/N (%) ^a	n/N (%) ^a	n/N (%) ^a
Rectal Chlamydia				
Proportion missed by Urogenital Testing ^c	1,667/1,936 (86.11)	1,138/1,292 (88.08)	25/69 (36.23)	44/52 (84.62)
Proportion missed by reported anal sex				
with last partner ^d	537/1,441 (37.27)	402/1,256 (32.01)	64/71 (90.14)	26/51 (50.98)
Pharyngeal Chlamydia				
Proportion missed by Urogenital Testing ^c	52/58 (89.66)	24/26 (92.31)	b	b
Rectal Gonorrhea				
Proportion missed by Urogenital Testing ^c	1,103/1,635 (67.46)	709/1,111 (63.82)	14/36 (38.89)	33/55 (60.00)
Proportion missed by reported anal sex				
with last partner ^d	542/1,234 (43.92)	438/1,085 (40.37)	35/37 (94.59)	24/51 (47.06)
Pharyngeal Gonorrhea				
Proportion missed by Urogenital Testing ^c	1,173/1,404 (83.55)	758/930 (81.51)	16/22 (72.73)	36/47 (76.60)

Any extragenital

Proportion missed by Urogenital Testing^c 3,106/3,961 (78.41) 2,034/2,628 (77.40) 46/115 (40.00) 83/112 (74.11)

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Self-reported Anal Receptive Sex

If testing relied on self-reported anal sex with last partner, 537 cases of rectal CT (37.27%) and 542 cases of rectal NG (43.92%) would have been missed because the patient did not report anal sex with a last partner. Reliance on self-reported anal sex with last partner would have led to 32.01% (n=402 cases) of missed rectal CT cases among MSM, 90.14% (n=64 cases) among MSW, and 50.98% (n=26 cases) among MSMW. Likewise, reliance on self-reported anal sex with last partner would have led to 40.37% (n=438 cases) of missed rectal NG cases among MSM, 94.59% (n=35 cases) among MSW, and 47.06% (n=24 cases) among MSMW (Table 2).

The crude sensitivity of self-reported anal sex with last partner for rectal CT was 60% with a specificity of 58%. Self-reported anal sex with last partner was associated with 2 times the odds of rectal CT in all three models with the AUC largest in the model adjusting for partner type and age (AUC=0.61). The crude sensitivity of self-reported anal sex with last partner for rectal NG was 59% with a specificity of 51%. Self-reported anal sex with last partner was associated with 1.3-1.4 times the odds of rectal NG in all three models, with the AUC highest in model 3 (0.60) adjusting for partner type and age (**Table 3**).

Table 3 - Prediction modeling of rectal chlamydia or gonorrhea given self-reported anal sex with last sexual partner among cisgender men at community-based STI clinic in Los Angeles, November 2018 - February 2020 (N=13,476)

=0=0 (11 10, 170)	,			
	n	Estimate	95% CI	AUC
	9,94			
Chlamydia	4			

^aMay not add to 100% because of missing urogenital, reported sexual behaviors, or extragenital screening

^bOnly 1 case noted for this sample

The denominator included all positive pharyngeal/rectal CT/NG cases and the numerator included pharyngeal/rectal CT/NG cases given their urogenital screening

^dThe denominator included all rectal CT/NG positive cases and the numerator included rectal CT/NG cases given the patient's self-reported anal sex behavior (as currently recommended by the CDC).

Sensitivity		0.60	(0.59, 0.61)	
Specificity		0.58	(0.54, 0.62)	
	9,94			
Model 1	4	2.09	(1.78, 2.46)	0.59
	9,45			
Model 2	6	2.05	(1.72, 2.44)	0.60
	9,45			
Model 3	6	1.98	(1.67, 2.36)	0.61
	9,91			
Gonorrhea	3			
Sensitivity		0.59	(0.58, 0.60)	
Specificity		0.51	(0.47, 0.55)	
	9,91			
Model 1	3	1.49	(1.26, 1.75)	0.55
	9,42			
Model 2	7	1.33	(1.12, 1.58)	0.57
	9,42			
Model 3	7	1.27	(1.06, 1.51)	0.60

Abbreviations. STI= sexually transmitted infection; CI= Confidence Interval; AUC= Area Under the Curve

Model 1: Crude model of self-reported anal sex with last partner on rectal Chlamydia/Gonorrhea respectively

Model 2: Model of self-reported anal sex with last partner on rectal Chlamydia/Gonorrhea respectively, adjusting for partner type

Model 3: Model of self-reported anal sex with last partner on rectal Chlamydia/Gonorrhea respectively, adjusting for partner type and age

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Discussion

In this study of CT/NG testing in over 13,000 predominantly MSM patients at an STI clinic in Los Angeles, we determined that over 80% of rectal and pharyngeal CT cases and over 65% of rectal and pharyngeal NG cases would be missed if urogenital testing alone was performed. Likewise, over 35% of rectal CT and NG cases would be missed had testing relied on self-reported sexual behaviors alone with different proportions of missed cases by partner type. Finally, the sensitivity and specificity of self-reported anal sex with last partner is poor for both CT/NG rectal infections. Even after adjusting for other

variables, the predictive probability of self-reported receptive anal sex on rectal CT/NG infections remained low (AUC 60-61%). Our findings support previous studies' findings on missed extragenital CT/ NG cases had testing relied on urogenital testing and expand the literature on missed rectal CT/NG cases had testing relied on self-reported anal sex. Furthermore, this study builds upon this work with a few key strengths: 1) patients received testing regardless of their gender, reported sexual orientation, or reported sexual behaviors; 2) the study population is large; 3) there is broader generalization than previous studies. This study highlights the need for three-site testing, especially in high-prevalence settings, regardless of urogenital STI results, self-reported sexual behaviors, sexual orientation, or sexual partner type. This conclusion is three-fold. First, urogenital CT/NG infections are typically symptomatic whereas, extragenital CT/NG cases are typically asymptomatic.[2,4-6,12,13,15-19] Thus, reliance on urogenital testing alone may lead to a large proportion of missed extragenital cases as seen in this study and as reported previously in the literature. [6,13,17-22] Second, social desirability bias may cause underreporting of sexual behaviors especially among MSW and MSMW thus leading to missed CT/NG pharyngeal and rectal infections.[23] Currently, the CDC recommends testing of rectal and pharyngeal sites only if the patient has reported anal or oral sex, respectively, in the last 12 months.[3,12] However, the findings from this study show that 37% of rectal CT and 44% of rectal NG would be missed by following the CDC recommendations, a finding similar to previous reports. [23,24] Third, testing has primarily focused on MSM alone as current recommendations state that MSM should be screened annually.[3,12] This study showed that those who are MSW or MSMW have a prevalence of 59% and 45% for any extragenital CT/NG, respectively. Likewise, 36-38% of rectal CT/NG and 73% of pharyngeal NG would be missed among MSW had testing relied on urogenital screening alone and 85% of rectal CT, 60% of rectal NG, and 77% of pharyngeal NG would be missed among MSMW. Simulation studies also support three-site CT/NG testing among MSM populations. For instance, a simulation study found that targeting rectal and pharyngeal sites for CT/NG screening has the greatest

impact on reducing missed cases for individuals who are already receiving STI testing.[14] Another simulation study showed that multi-site testing for NG among MSM may be more cost-effective than traditional testing that relies on urogenital screening alone.[26] If three-site testing is not feasible, it has been recommended that it is most effective to at least provide rectal CT/NG screening.[14,22]

Moreover, extragenital CT/NG testing may also help with HIV treatment, HIV prevention, and prevention of STI infections. First, rectal CT/NG increases the risk of HIV infection so testing of this site helps combat the HIV epidemic.[3,6-10] Jones et al., estimated that about 10% of HIV infections may be attributable to CT/NG infections. In other words, 10% of HIV infections may be prevented given sufficient STI control.[11] Second, extragenital testing may help identify more individuals who are eligible for PrEP.[3,4,6] Previous studies and guidelines in the United States and Australia, have demonstrated that STI infections, or history of STIs, among MSM are strong criteria for PrEP indication. Thus, three-site extragenital testing may capture infections that would have otherwise been missed and in turn can help identify those who are eligible and may highly benefit from PrEP.[4,27-29] Finally, untreated extragenital CT/NG infections may be a reservoir for subsequent CT/NG infections. In a recent study, it was shown that most of the urogenital NG cases in the sample were likely due to NG infection in the rectum or pharynx of the case's partner.[30] Routine extragenital CT/NG testing would lead to identification and treatment of these cases, reducing transmission of subsequent STI infections to partners.

Limitations

There are limitations that must be considered. First, data come from medical records and there may still be underreporting of sexual behaviors and sexual partners because of stigma and social desirability bias despite clients receiving care at an LGBTQ+ specialty clinic.[23] Second, the prevalence of CT/NG may not be generalizable to all cisgender men as data are coming from an STI specialty clinic in Los Angeles,

California. Therefore, the prevalence of CT/NG cases may be higher among MSM, MSW, and MSMW than the general population. Third, we did not have data on symptoms at the rectal or pharyngeal sites. Those reporting symptoms would be more likely to receive site-specific testing at clinics where extragenital testing is available and would not be missed. However, most rectal/pharyngeal infections are asymptomatic and would likely be missed if extragenital testing is not performed.[2,3,6,13-16] Moreover, we did not have data on reported oral sex behaviors and could not identify missed cases of pharyngeal CT/NG based on these reported behaviors alone. Finally, we used rectal anal sex with last partner as a proxy for reported anal sex in the last 12 months. The noted CT/NG infection may have occurred before this point leading to mismeasurement of reported anal sex. However, sexual health screening at other health clinics may be similar.

Conclusion

Current CDC guidelines for extragenital CT/NG testing are recommended for "at risk groups," such as MSM; however, self-reported data such as sexual risk behaviors and gender of sexual partner(s) may miss a large proportion of extragenital CT/NG cases. Our data support three-site testing for cisgender men attending a sexual health clinic, LGBTQ+ specialty clinic, or other health clinic with a high prevalence of STIs regardless of their sexual orientation or reported sexual behaviors while allowing patients to opt out of any site testing. This recommendation offers two different improvements for CT/NG testing. First, it helps minimize social desirability bias among patients; there may be stigma or discrimination that patients face given different sexual histories. By providing three-site testing regardless of the patient's reported behavior, social stigma may be minimized while providing optimal care. Second, three-site testing has been shown in simulation studies to be cost-effective. Three-site testing allows for better capture and treatment of all CT/NG cases, especially those that are asymptomatic such as rectal and pharyngeal CT/NG infections. Future research should further investigate the cost-effectiveness/cost-benefit analysis

of three-site extragenital testing and the utility of relying on self-reported oral sex behaviors for pharyngeal testing.

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Author Contributions

RDA: conception, design, analysis and interpretation of data, drafting, and critically revising manuscript, final approval. NJC: conception, design, interpretation of data, drafting, and critically revising manuscript. PCA: interpretation of data and critically revising manuscript. JTJ: critically revising manuscript. RKB: critically revising manuscript.

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Conflicts of Interests

The authors of this manuscript do not have any conflicts of interest, actual or potential, to disclose.

References

- 1. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2019. Atlanta: U.S. Department of Health and Human Services; 2021.
- 2. Johnson Jones ML, Chapin-Bardales J, Bizune D, et al. Extragenital Chlamydia and Gonorrhea Among Community Venue-Attending Men Who Have Sex with Men Five Cities, United States, 2017. MMWR Morb Mortal Wkly Rep 2019;68(14):321-25. doi: 10.15585/mmwr.mm6814a1 [published Online First: 2019/04/12]
- 3. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep 2021;70(4):1-187. doi: 10.15585/mmwr.rr7004a1 [published Online First: 2021/07/23]

- 4. Dombrowski JC. Chlamydia and Gonorrhea. *Ann Intern Med* 2021 doi: 10.7326/AITC202110190 [published Online First: 2021/10/12]
- 5. Kirkcaldy RD, Weston E, Segurado AC, et al. Epidemiology of gonorrhoea: a global perspective. *Sex Health* 2019;16(5):401-11. doi: 10.1071/SH19061 [published Online First: 2019/09/11]
- 6. Chan PA, Robinette A, Montgomery M, et al. Extragenital Infections Caused by Chlamydia trachomatis and Neisseria gonorrhoeae: A Review of the Literature. *Infect Dis Obstet Gynecol* 2016;2016:5758387. doi: 10.1155/2016/5758387 [published Online First: 2016/07/02]
- 7. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet* 1998;351 Suppl 3:5-7. doi: 10.1016/s0140-6736(98)90002-2 [published Online First: 1998/07/04]
- 8. Pathela P, Braunstein SL, Blank S, et al. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. *Clin Infect Dis* 2013;57(8):1203-9. doi: 10.1093/cid/cit437 [published Online First: 2013/06/27]
- 9. Weinstock H, Workowski KA. Pharyngeal gonorrhea: an important reservoir of infection? *Clin Infect Dis* 2009;49(12):1798-800. doi: 10.1086/648428 [published Online First: 2009/11/17]
- 10. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect 1999;75(1):3-17. doi: 10.1136/sti.75.1.3 [published Online First: 1999/08/17]
- 11. Jones J, Weiss K, Mermin J, et al. Proportion of Incident Human Immunodeficiency Virus Cases Among Men Who Have Sex With Men Attributable to Gonorrhea and Chlamydia: A Modeling Analysis. Sex Transm Dis 2019;46(6):357-63. doi: 10.1097/OLQ.000000000000980 [published Online First: 2019/05/17]
- 12. Barrow RY AF, Bolan GA, Workowski KA. Recommendations for Providing Quality Sexually Transmitted Diseases Clinical Services, 2020. MMWR Recomm Rep 2020;68((No. RR-5)):1–20.
- 13. Lutz AR. Screening for Asymptomatic Extragenital Gonorrhea and Chlamydia in Men Who Have Sex with Men: Significance, Recommendations, and Options for Overcoming Barriers to Testing. *LGBT Health* 2015;2(1):27-34. doi: 10.1089/lgbt.2014.0056 [published Online First: 2016/01/21]
- 14. Earnest R, Ronn MM, Bellerose M, et al. Population-level Benefits of Extragenital Gonorrhea Screening Among Men Who Have Sex With Men: An Exploratory Modeling Analysis. Sex Transm Dis 2020;47(7):484-90. doi: 10.1097/OLQ.00000000001189 [published Online First: 2020/05/02]
- 15. Unemo M, Shafer WM. Antimicrobial resistance in Neisseria gonorrhoeae in the 21st century: past, evolution, and future. *Clin Microbiol Rev* 2014;27(3):587-613. doi: 10.1128/CMR.00010-14 [published Online First: 2014/07/02]
- 16. Annan NT, Sullivan AK, Nori A, et al. Rectal chlamydia--a reservoir of undiagnosed infection in men who have sex with men. Sex Transm Infect 2009;85(3):176-9. doi: 10.1136/sti.2008.031773 [published Online First: 2009/01/30]
- 17. Patton ME, Kidd S, Llata E, et al. Extragenital gonorrhea and chlamydia testing and infection among men who have sex with men--STD Surveillance Network, United States, 2010-2012. *Clin Infect Dis* 2014;58(11):1564-70. doi: 10.1093/cid/ciu184 [published Online First: 2014/03/22]

- 18. Abara WE, Llata EL, Schumacher C, et al. Extragenital Gonorrhea and Chlamydia Positivity and the Potential for Missed Extragenital Gonorrhea With Concurrent Urethral Chlamydia Among Men Who Have Sex With Men Attending Sexually Transmitted Disease Clinics-Sexually Transmitted Disease Surveillance Network, 2015-2019. Sex Transm Dis 2020;47(6):361-68. doi: 10.1097/OLQ.000000000001170 [published Online First: 2020/05/16]
- 19. Anschuetz GL, Paulukonis E, Powers R, et al. Extragenital Screening in Men Who Have Sex With Men Diagnoses More Chlamydia and Gonorrhea Cases Than Urine Testing Alone. *Sex Transm Dis* 2016;43(5):299-301. doi: 10.1097/OLQ.000000000000435 [published Online First: 2016/04/23]
- 20. Jenkins WD, Nessa LL, Clark T. Cross-sectional study of pharyngeal and genital chlamydia and gonorrhoea infections in emergency department patients. *Sex Transm Infect* 2014;90(3):246-9. doi: 10.1136/sextrans-2013-051358 [published Online First: 2013/12/25]
- 21. Koedijk FD, van Bergen JE, Dukers-Muijrers NH, et al. The value of testing multiple anatomic sites for gonorrhoea and chlamydia in sexually transmitted infection centres in the Netherlands, 2006-2010. *Int J STD AIDS* 2012;23(9):626-31. doi: 10.1258/ijsa.2012.011378 [published Online First: 2012/10/04]
- 22. Hiransuthikul A, Sungsing T, Jantarapakde J, et al. Correlations of chlamydia and gonorrhoea among pharyngeal, rectal and urethral sites among Thai men who have sex with men: multicentre community-led test and treat cohort in Thailand. *BMJ Open* 2019;9(6):e028162. doi: 10.1136/bmjopen-2018-028162 [published Online First: 2019/06/30]
- 23. Cachay ER, Sitapati A, Caperna J, et al. Denial of risk behavior does not exclude asymptomatic anorectal sexually transmitted infection in HIV-infected men. *PLoS One* 2009;4(12):e8504. doi: 10.1371/journal.pone.0008504 [published Online First: 2009/12/31]
- 24. van Liere GA, Hoebe CJ, Niekamp AM, et al. Standard symptom- and sexual history-based testing misses anorectal Chlamydia trachomatis and neisseria gonorrhoeae infections in swingers and men who have sex with men. Sex Transm Dis 2013;40(4):285-9. doi: 10.1097/OLQ.0b013e31828098f8 [published Online First: 2013/03/15]
- 25. Shover CL, DeVost MA, Beymer MR, et al. Using Sexual Orientation and Gender Identity to Monitor Disparities in HIV, Sexually Transmitted Infections, and Viral Hepatitis. *Am J Public Health* 2018;108(S4):S277-S83. doi: 10.2105/AJPH.2018.304751 [published Online First: 2018/11/02]
- 26. Earnest R, Ronn MM, Bellerose M, et al. Modeling the Cost-Effectiveness of Express Multi-Site Gonorrhea Screening among Men Who Have Sex with Men in the United States. *Sex Transm Dis* 2021 doi: 10.1097/OLQ.000000000001467 [published Online First: 2021/05/17]
- 27. Cornelisse VJ, Fairley CK, Stoove M, et al. Evaluation of Preexposure (PrEP) Eligibility Criteria, Using Sexually Transmissible Infections as Markers of Human Immunodeficiency Virus (HIV) Risk at Enrollment in PrEPX, a Large Australian HIV PrEP Trial. *Clin Infect Dis* 2018;67(12):1847-52. doi: 10.1093/cid/ciy370 [published Online First: 2018/05/10]
- 28. Kasaie P, Berry SA, Shah MS, et al. Impact of Providing Preexposure Prophylaxis for Human Immunodeficiency Virus at Clinics for Sexually Transmitted Infections in Baltimore City: An Agent-based Model. Sex Transm Dis

- 2018;45(12):791-97. doi: 10.1097/OLQ.000000000000882 [published Online First: 2018/06/27]
- 29. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2014 clinical practice guideline. Atlanta, GA: Department of Health and Human Services., 2014.
- 30. Cornelisse VJ, Zhang L, Law M, et al. Concordance of gonorrhoea of the rectum, pharynx and urethra in same-sex male partnerships attending a sexual health service in Melbourne, Australia. *BMC Infect Dis* 2018;18(1):95. doi: 10.1186/s12879-018-3003-2 [published Online First: 2018/03/01]