

Optimizing Coverage vs Frequency for Sexually Transmitted Infection Screening of Men Who Have Sex With Men

Kevin M. Weiss, ¹ Jeb S. Jones, ¹ Emeli J. Anderson, ¹ Thomas Gift, ² Harrell Chesson, ² Kyle Bernstein, ² Kimberly Workowski, ²³ Ashleigh Tuite, ⁴ Eli S. Rosenberg, ^{1,5} Patrick S. Sullivan, ^{1,6} and Samuel M. Jenness¹

¹Department of Epidemiology, Emory University, Atlanta, Georgia, USA, ²Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, ³Department of Medicine, Emory University, Atlanta, Georgia, USA, ⁴BlueDot Inc., Toronto, Ontario, Canada, ⁵Department of Epidemiology and Biostatistics, University at Albany, Albany, New York, USA, and ⁶Department of Global Health, Emory University, Atlanta, Georgia, USA

Background. The incidence of bacterial sexually transmitted infections (STIs) in men who have sex with men (MSM) has increased substantially despite availability of effective antibiotics. The US Centers for Disease Control and Prevention (CDC) recommends annual screening for all sexually active (SA) MSM and more frequent screening for high-risk (HR) MSM. The population-level benefits of improved coverage vs increased frequency of STI screening among SA vs HR MSM are unknown.

Methods. We used a network transmission model of gonorrhea (NG) and chlamydia (CT) among MSM to simulate the implementation of STI screening across different scenarios, starting with the CDC guidelines at current coverage levels. Counterfactual model scenarios varied screening coverage and frequency for SA MSM and HR MSM (MSM with multiple recent partners). We estimated infections averted and the number needed to screen to prevent 1 new infection.

Results. Compared with current recommendations, increasing the frequency of screening to biannually for all SA MSM and adding some HR screening could avert 72% of NG and 78% of CT infections over 10 years. Biannual screening of 30% of HR MSM at empirical coverage levels for annual SA screening could avert 76% of NG and 84% of CT infections. Other scenarios, including higher coverage among SA MSM and increasing frequency for HR MSM, averted fewer infections but did so at a lower number needed to screen.

Conclusions. The optimal screening scenarios in this model to reduce STI incidence among MSM included more frequent screening for all sexually active MSM and higher coverage of screening for HR men with multiple partners.

Keywords. mathematical model; men who have sex with men; screening; sexually transmitted infections.

The incidence of bacterial sexually transmitted infections (STIs) remains high and is increasing among men who have sex with men (MSM) in the United States [1]. Although syphilis is a major concern, *Neisseria gonorrheae* (NG; gonorrhea) and *Chlamydia trachomatis* (CT; chlamydia) are the 2 highestburden bacterial STIs for MSM [2–5]. These infections can be effectively diagnosed and treated at all sites of sexual exposure, but screening has focused on urogenital testing [6–8]. Asymptomatic infections, particularly rectal, that contribute to ongoing STI transmission are often missed unless detected through routine screening [9, 10]. The Centers for Disease Control and Prevention (CDC) STD Treatment Guidelines recommend annual NG and CT screening at all sites of sexual exposure for sexually active MSM [11]. Adherence to these guidelines is widely estimated to be poor [6, 12], but evaluation of current practice relative to these guidelines is challenging. Nationally representative data typically report the period prevalence of STI testing for any cause in the past year [8], whereas assessment of adherence to the guidelines requires data on routine screening in the absence of symptoms.

Despite uncertainty in current STI screening practice, a critical question is whether the recommendations are sufficient to reduce STI incidence below the persistence threshold, and, if not, where to focus additional screening efforts. Additional screening could be delivered through several targeting strategies, including increased coverage (proportion screened) or frequency (interval between routine screens). Mathematical models have evaluated the effects of increased screening coverage and frequency scenarios and highlighted the impact of frequent screening despite potential trade-offs with efficiency and cost [13, 14], although these have not always focused on comprehensive screening designs (all bacterial STIs).

Received 7 May 2019; editorial decision 6 September 2019; accepted 10 September 2019. Correspondence: K. M. Weiss, MPH, Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road, Atlanta, GA 30322 (kvnweiss@gmail.com).

Open Forum Infectious Diseases®

[©] The Author(s) 2019. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (http://creativecommons.org/licenses/ by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com D0I: 10.1093/ofid/ofz405

The CDC guidelines also recommend more frequent screening (every 3–6 months) for MSM "at increased risk," defined as persistent risk behaviors or having sex with multiple partners [11]. Because STI prevention resources are limited, designing an optimal screening strategy requires tradeoffs between population impact and intervention efficiency. Screening all sexually active MSM may greatly reduce overall STI incidence (population impact), but may be inefficient (require more tests per infection averted) compared with targeting a smaller group of high-risk MSM [15].

In this study, we used mathematical modeling to investigate the impact of targeted screening for NG and CT incidence among US MSM. By simulating different behavioral and clinical scenarios for the delivery of STI diagnostics to this target population, we compared alternative strategies varying coverage, frequency, and behavioral risk definitions for screening against a reference scenario of current recommendations and coverage levels. Our broader goal was to evaluate the performance of existing screening recommendations compared with strategies that may better address the recent resurgence in STI incidence in the United States.

METHODS

Overview

This study extends our mathematical modeling research exploring HIV/STI transmission dynamics and prevention interventions among US MSM [16, 17] using the *EpiModel* platform [18], which uses temporal exponential random graph models to simulate STIs over dynamic sexual partnership networks [19]. This model represents the underlying network and intrahost and interhost epidemiology of HIV, NG, and CT (Appendix). Extensions to the model included the structure, parameterization, and analysis methods for an interval-based screening framework for all STIs, complementing HIV and site-specific NG and CT infection model codes [17].

STI Transmission and Recovery

We simulated dynamic sexual networks of MSM defined by main, casual, and 1-time sexual partnerships (Appendix). Many behavioral model parameters were drawn from sexual network data collected from Atlanta MSM [2, 3]. Factors influencing partnership formation and dissolution included partnership type, partner age, sexual role (receptive, insertive, or versatile), and number of current ongoing partners. Constant hazards of relationship dissolution reflected median durations of main and casual partnerships. We simulated anal intercourse (AI) within partnerships, with rates varying by partnership type, role, and disclosure of HIV status. Base transmission rates per partnership reflected sexual frequency, role, and condom use.

Transmission of NG, CT, and HIV was simulated across this partnership network. MSM could recover from STIs through natural clearance or through antibiotic treatment. STI transmission was directional and site-specific during AI (eg, insertive AI with a partner infected with rectal CT was necessary to acquire urethral CT), and STI acquisition likelihood was modified by condom use and sexual role. Men could be infected at either or both urethral or rectal sites with either or both NG and CT.

Uncertainty in parameter estimates for site- and diseasespecific transmission risks, HIV acquisition relative risks given prevalent STI infection, and STI clinical encounters were addressed using Bayesian inferential methods [20]. We defined prior probability distributions and fit simulations to empirical estimates of NG and CT incidence to define posterior parameter distributions.

STI Symptoms, Screening, and Diagnosis

Symptomatic status for new NG and CT infections varied by site of infection [9], with a lower probability of symptoms for rectal infections. Exhibiting symptoms increased the probability of testing and treatment compared with asymptomatic infection. For men with dual-site concurrent infections (eg, rectal and urethral NG), treatment of infection at 1 anatomical site resulted in effective treatment at both sites. Men presenting with symptoms were tested for NG and CT at that anatomical site.

STI screening was modeled following current CDC recommendations, which indicate sexually active MSM for annual screening at sites of sexual contact and more frequent screening if at "increased risk" [11]. In the model, any sexual activity in the year before risk assessment (sexually active [SA]) indicated a man for annual screening at his anatomical sites of sexual activity. MSM with multiple recent partners (>1 partner in prior 6 months) were considered "high risk" (HR) and indicated for biannual screening. Screening indications were dynamic and assessed at each time step. Based on stochastically changing sexual behaviors, men could move between screening trajectories or have no indications due to no recent sexual activity. We made the simplifying assumption that screening tests were 100% sensitive and specific, and all diagnosed men were treated. We explored imperfect adherence to assigned screening strategies (Supplementary Tables 13 and 14) to evaluate suboptimal test sensitivity, lower adherence to CDC recommendations, and failure to treat.

Our first set of scenarios varied screening intervals of both SA and HR groups, keeping the 6-month behavioral assessment fixed. We also varied thresholds for the number of partners characterizing MSM as "high risk." A secondary analysis varied 2 parameters: SA screening coverage and HR screening coverage, or the proportion of MSM indicated for a screening trajectory who started that regimen. SA screening coverage was modeled continuously from empirical values to a 40% proportional increase across all STIs. HR screening coverage was modeled continuously from 0% to 100%. As more men became eligible to screen (increased denominator), more men could be assigned to screen (increased numerator) to maintain the specified screening coverage value. MSM assigned to a trajectory continued to screen at that frequency until their dynamic behaviors stopped indicating them for that trajectory. MSM indicated for, but not assigned to, an HR screening trajectory could still be assigned to screen annually.

The level of asymptomatic screening in the reference model was calibrated to a background level of interval-based screening based on estimates of the period prevalence of STI testing. Empirical data from National HIV Behavioral Surveillance (NHBS) estimated that 45.8% of HIV-uninfected MSM were tested for either NG or CT in the prior year, compared with 64.1% (NG) and 62.8% (CT) of HIV-positive MSM [21]. These data sources do not separate symptoms-based testing and routine, asymptomatic screening. Model-calibrated values reflect a mixture of symptoms-based testing and asymptomatic screening, with the observed split similar to other empirical data, where <10% of testing events were symptoms-driven [22]. Reference models assumed only annual screening (0% HR coverage), given the lack of nationally representative data on screening frequency; a recent analysis suggested minimal associations of risk behavior and screening interval, where HIVnegative MSM screened, on average, less than annually [22].

Simulation and Analysis

Equilibrium NG and CT prevalence and incidence, preintervention and allowing for recent STI incidence trends, were

established in an open population of 10 000 MSM through model calibration to the best available pooled estimates of NG (4.2/100 person-years [PY]) and CT (6.6/100 PY) incidence drawn from a meta-analysis of non-PrEP-using MSM [23], which were similar to pooled NG (3.4/100 PY) and CT (5.6/100 PY) incidence estimates from the study population [2]. Primary model outcomes included NG and CT incidence per 100 person-years at risk, calculated across the final simulation year, percentage of infections averted (PIA) over 10 years compared with the reference model, and the number of screening tests needed to prevent 1 new infection (number needed to screen [NNS]), reflecting incremental screening divided by the number of infections averted. Counterfactual model scenarios were simulated 250 times over a 10-year intervention time horizon. We summarized model outcomes by their medians and interquartile ranges across these simulations to account for model stochasticity.

RESULTS

Table 1 shows the final-year incidence of NG and CT, PIA, and NNS relative to the reference model across varied screening intervals and partner number thresholds. Across all scenarios in this table, baseline coverage levels of SA screening were assumed, in addition to 5% coverage of HR screening. We first

Table 1. NG and CT Incidence Rates Over the Final Simulation Year, PIA, and NNS, by Screening Interval of SA and HR Screening Indications, and High-Risk Screening Partner Cutoff Among MSM in the United States

		NG			СТ	
Model Scenario	Incidence (IQR)	PIA (IQR)	NNS (IQR)	Incidence (IQR)	PIA (IQR)	NNS (IQR)
Reference model (baseline SA coverage)	4.50 (2.58 to 6.45)		_	6.58 (5.41 to 7.67)	_	_
SA screening interval (baseline SA covera	age + 5% high-risk c	overage)				
6 mo (182 d)	0.00 (0.00 to 0.28)	0.72 (0.60 to 0.81)	29.4 (21.4 to 46.8)	0.04 (0.00 to 0.12)	0.78 (0.75 to 0.81)	18.9 (16.5 to 21.0)
9 mo (273 d)	0.63 (0.08 to 1.32)	0.56 (0.39 to 0.69)	24.0 (15.5 to 38.3)	0.31 (0.16 to 0.56)	0.68 (0.63 to 0.72)	14.3 (12.3 to 16.9)
12 mo (364 d)	1.20 (0.43 to 2.14)	0.45 (0.16 to 0.61)	16.9 (10.6 to 29.9)	0.85 (0.60 to 1.26)	0.57 (0.50 to 0.63)	12.2 (10.0 to 14.8)
15 mo (448 d)	1.87 (0.80 to 3.43)	0.33 (0.06 to 0.53)	12.6 (7.3 to 28.5)	1.77 (1.32 to 2.40)	0.45 (0.35 to 0.53)	11.5 (8.7 to 15.7)
18 mo (539 d)	2.49 (1.27 to 4.13)	0.25 (-0.06 to 0.46)	8.8 (-8.6 to 19.0)	2.50 (1.84 to 3.27)	0.36 (0.26 to 0.45)	9.9 (7.3 to 14.3)
HR screening interval (baseline SA cover	age + 5% high-risk d	coverage)				
1 mo (28 d)	0.42 (0.03 to 1.16)	0.59 (0.40 to 0.69)	30.5 (20.5 to 54.6)	0.38 (0.17 to 0.62)	0.67 (0.61 to 0.71)	19.6 (16.7 to 23.1)
3 mo (91 d)	0.86 (0.25 to 1.58)	0.52 (0.33 to 0.67)	21.7 (14.1 to 36.7)	0.58 (0.34 to 0.94)	0.62 (0.55 to 0.66)	14.3 (11.7 to 17.2)
6 mo (182 d)	1.20 (0.43 to 2.14)	0.45 (0.16 to 0.61)	16.9 (10.6 to 29.9)	0.85 (0.60 to 1.26)	0.57 (0.50 to 0.63)	12.2 (10.0 to 14.8)
9 mo (273 d)	1.62 (0.72 to 3.14)	0.35 (0.02 to 0.54)	14.1 (6.6 to 25.6)	1.27 (0.85 to 1.69)	0.51 (0.43 to 0.60)	11.6 (9.3 to 15.2)
12 mo (364 d)	2.52 (1.01 to 4.15)	0.25 (-0.02 to 0.49)	10.9 (-7.4 to 25.5)	2.05 (1.53 to 2.71)	0.41 (0.32 to 0.51)	10.4 (7.9 to 14.3)
HR screening 6-mo partner threshold (ba	seline SA coverage	+ 5% high-risk covera	age)			
>1 partners	1.20 (0.43 to 2.14)	0.45 (0.16 to 0.61)	16.9 (10.6 to 29.9)	0.85 (0.60 to 1.26)	0.57 (0.50 to 0.63)	12.2 (10.0 to 14.8)
>2 partners	1.32 (0.44 to 2.44)	0.41 (0.14 to 0.59)	19.6 (11.5 to 37.3)	0.76 (0.46 to 1.11)	0.59 (0.52 to 0.65)	12.7 (10.6 to 15.5)
>3 partners	1.40 (0.56 to 2.78)	0.39 (0.07 to 0.59)	14.1 (7.5 to 26.2)	1.08 (0.72 to 1.57)	0.53 (0.45 to 0.59)	11.4 (9.5 to 14.6)
>4 partners	1.97 (0.98 to 3.26)	0.32 (0.05 to 0.50)	12.1 (5.8 to 26.1)	1.87 (1.37 to 2.51)	0.44 (0.35 to 0.51)	9.9 (8.3 to 13.7)
>5 partners	2.82 (1.62 to 4.60)	0.20 (-0.11 to 0.43)	6.8 (-11.0 to 15.0)	3.12 (2.41 to 3.81)	0.32 (0.21 to 0.42)	9.1 (6.1 to 13.7)

Incidence rates reflect an average of the incidence rate in the 10th year of the 10-year model simulation period. Interquartile range (25% to 75% percentile) of the simulation outcomes is the incidence expressed per 100 person-years at risk. Prevalence is expressed as a proportion of all persons. Infected PY accounts for the person-time contributed by all individuals infected with any STI. Baseline screening coverage in HIV-uninfected MSM: gonorrhea: 44%, chlamydia: 44%. Baseline screening coverage in HIV-infected MSM: gonorrhea: 61%, chlamydia: 61%. Baseline SA screening interval: 12 months (364 days). Baseline HR screening interval: 6 months (182 days).

Abbreviations: CT, chlamydia; HR, high-risk; IQR, interquartile range; MSM, men who have sex with men; NG, gonnorhea; NNS, number of STI screening tests required to prevent 1 new STI infection; PIA, percentage of infections averted; SA, sexually active; STI, sexually transmitted infection.

examined the effect of screening frequency among all sexually active MSM, finding that more frequent screening would result in lower projected NG and CT incidence, a higher PIA, and higher NNS values. Screening sexually active MSM biannually, rather than annually, at current (empirical) coverage levels was predicted to reduce the number of incident NG and incident CT infections by 72% and 78%, respectively, over a 10-year interval. As the SA screening interval became longer, incidence increased. We then examined the effect of differing screening frequencies for high-risk MSM, finding that, at 5% HR coverage, more frequent screening of high-risk MSM averted more infections and increased the number treated per infected person-year (Supplementary Table 15). Across all screening frequency scenarios, PIA values for CT incidence exceeded PIA values for NG.

We evaluated different risk thresholds for MSM to be considered high risk. Analyses of the partner threshold for HR screening (Table 1 and Figure 1) demonstrated that more restrictive thresholds (increasing the number of recent partners needed to be considered HR) reduced the PIA for NG (45% vs 20% for 1 vs 5 partners) and CT (57% vs 32% for 1 vs 5 partners) but were more efficient (lower NNS) (Supplementary Table 15). In Figure 1, increased coverage (moving horizontally left to right at a fixed partner threshold) averted more NG and CT infections as more MSM were screened semiannually. Increasing the partner threshold at a fixed coverage level (moving vertically) generally lowered the PIA.

Increased coverage for both HR and SA screening trajectories was associated with decreased STI incidence and increased PIA, with more infections averted when scaling up HR (biannual) screening compared with scaling up SA (annual) screening (Table 2). Over the 10-year time horizon, a 20% increase in screening coverage of the SA group was observed to avert 17% of NG and 26% of CT infections, whereas increasing HR screening coverage to 30%, with fixed SA coverage, was predicted to avert 76% of NG and 84% of CT infections. With increasing SA and HR coverage, the number treated per infected PY (Appendix) and NNS both increased, with greater NNS values observed when scaling high-risk coverage (40% HR coverage: NNS = 41.4 for NG and 26.4 for CT).

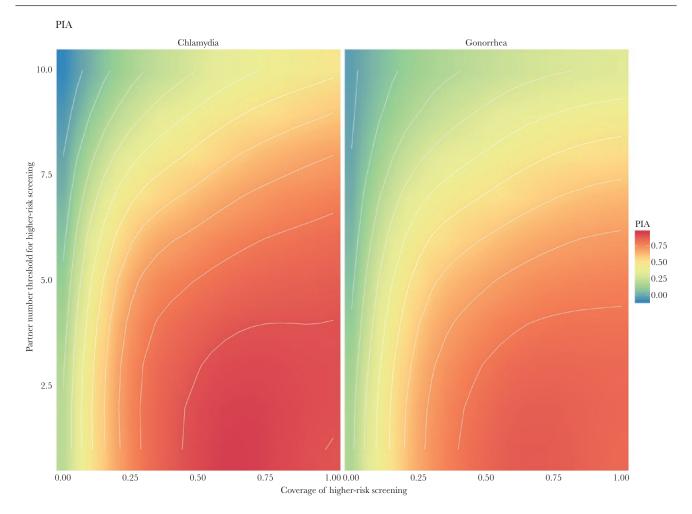


Figure 1. Percentage of total infections averted across absolute values of the number of partners in the prior 6 months (partner number threshold) required for high-risk screening and the percent coverage of among men meeting indications for high-risk screening (coverage of high-risk screening). Abbreviation: PIA, percentage of total infections averted.

		DN			CT	
Model Scenario	Incidence (IQR)	PIA (IQR)	NNS (IQR)	Incidence (IQR)	PIA (IQR)	NNS (IQR)
Reference model (baseline SA coverage)	4.50 (2.58 to 6.45)	I	I	6.58 (5.41 to 7.67)	I	I
SA screening coverage (0% HR coverage)	ge)					
10% increase	3.31 (2.04 to 5.42)	0.13 (-0.33 to 0.40)	1.9 (-3.7 to 4.4)	4.90 (4.09 to 5.85)	0.15 (0.00 to 0.27)	3.7 (0.5 to 7.0)
20% increase	3.07 (1.73 to 4.68)	0.17 (-0.13 to 0.40)	5.0 (-7.8 to 9.9)	3.51 (2.79 to 4.38)	0.26 (0.13 to 0.38)	6.9 (4.2 to 12.2)
30% increase	2.39 (1.30 to 4.07)	0.25 (-0.08 to 0.50)	7.2 (-8.6 to 15.4)	2.50 (1.94 to 3.22)	0.37 (0.25 to 0.48)	8.2 (5.9 to 13.1)
40% increase	2.08 (0.99 to 3.53)	0.30 (0.01 to 0.53)	9.9 (4.1 to 22.5)	1.79 (1.32 to 2.43)	0.45 (0.37 to 0.53)	8.9 (7.3 to 12.1)
HR screening coverage (baseline SA coverage)						
10%	0.51 (0.03 to 1.20)	0.59 (0.41 to 0.71)	25.1 (17.6 to 42.3)	0.24 (0.09 to 0.42)	0.71 (0.65 to 0.75)	15.6 (13.6 to 18.3)
20%	0.01 (0.00 to 0.32)	0.71 (0.58 to 0.79)	35.5 (24.7 to 53.0)	0.00 (0.00 to 0.06)	0.81 (0.78 to 0.84)	20.6 (17.8 to 23.2)
30%	0.00 (0.00 to 0.10)	0.76 (0.67 to 0.83)	38.8 (28.8 to 59.9)	0.00 (0.00 to 0.00)	0.84 (0.82 to 0.87)	23.8 (20.6 to 26.4)
40%	0.00 (0.00 to 0.00)	0.80 (0.72 to 0.86)	41.4 (31.5 to 59.6)	0.00 (0.00 to 0.00)	0.87 (0.84 to 0.88)	26.4 (23.2 to 28.9)

In Figure 2, we display the interaction between screening coverage and screening frequency, with different x-axis values for screening intervals for the top 2 plots and the bottom 2 plots. For SA screening for both CT (top left) and NG (top right), increased frequency (moving right to left at a fixed coverage level) averted more infections than varying coverage (moving vertically) at a fixed frequency. For HR screening for CT (bottom left) and NG (bottom right), increased frequency had a limited impact below 10% coverage, and increasing coverage averted more infections. Reductions in NG and CT incidence required moderate HR coverage levels and increased with increasing screening frequency.

DISCUSSION

Abbreviations: CT, chlamydia; HR, high-risk; IQR, interquartile range; MSM, men who have sex with men; NG, gonnorhea; NNS, number of STI screening tests required to prevent 1 new STI infection; PIA, percentage of infections averted; SA, sexually

sexually transmitted infection.

active; STI,

Routine chlamydia and gonorrhea screening, implemented consistent with recommendations in the CDC's STD Treatment Guidelines but with increased coverage and frequency, was projected to halt or reverse recent rising STI incidence trends among US MSM. Overall, our model suggests that three-quarters of NG and CT infections expected among MSM over the next decade could be averted if (1) sexually active MSM were screened, on average, twice annually at all anatomic sites of exposure, even without increasing observed coverage values; or (2) 30% of MSM with multiple recent partners (>1 partner in the prior 6 months) were screened biannually. More frequent screening for sexually active MSM (~90% of the model population) and scaling up targeted screening for men with multiple recent partners (~60% of the model population) were the most effective strategies for reducing infections but were less efficient.

Screening and treatment are the foundation of STI control, but selecting screening strategies that maximize both prevention benefits and efficiency is complex. Routine screening can identify asymptomatic STIs that often remain undiagnosed, contribute to ongoing STI transmission, and increase risk of HIV acquisition and transmission [24]. Routine STI screening among MSM remains suboptimal, particularly at extragenital (pharynx and rectum) sites, where STIs are frequently asymptomatic [6-9, 12]. A recent venue-based study estimated that 1 in 8 MSM had prevalent extragenital NG or CT infection and one-third reported not having been tested for STIs in the past 12 months, suggesting that high-risk MSM were not being screened per CDC recommendations [10]. Behavioral risk is estimated to have little impact on STI screening frequency, with the screening rate increasing only 1.4% per additional anal sex partner in 1 national study [22]. The sensitivity of our current model to screening frequency provides further evidence that high-risk MSM are not screening frequently.

A key strength of our study is the representation of act-level individual and partnership behavioral dynamics, including role positioning (receptive, insertive, and versatile) and site-specific

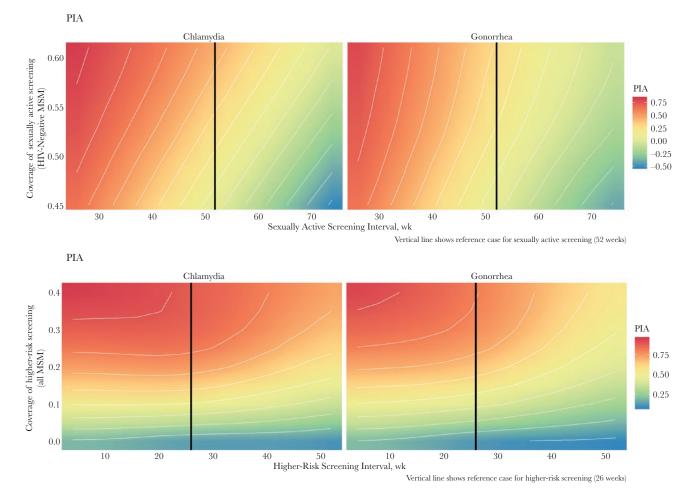


Figure 2. Percentage of total infections averted across absolute values of percent coverage of screening among sexually active men and the associated screening interval in weeks (top left and top right) and the PIA across absolute values of percent coverage of screening among high-risk men and the associated screening interval in weeks (bottom left and bottom right). Abbreviations: MSM, men who have sex with men; PIA, percentage of total infections averted.

NG and CT infection, along with natural differences in the symptomology of NG/CT infections by site of exposure [9]. Rectal screening among MSM is highly efficient [25], particularly among younger MSM, because prevalent rectal infections are more likely to be asymptomatic and missed by symptoms-based testing. Our analysis supports the benefit of screening patients for STIs at rectal and urogenital sites of exposure based on simple risk assessments during clinic visits. The CDC recommends screening MSM at all anatomical sites of exposure, consistent with research demonstrating the benefits of extragenital screening [25], and we plan on modeling site-specific screening strategies, including the unique transmission dynamics of pharyngeal infections, to further evaluate this recommendation.

Increased screening frequency may identify many asymptomatic infections missed with longer screening intervals [26, 27]. Even at high coverage levels, more frequent screening for all sexually active MSM could reduce the duration of the infectious period. NG (25 weeks) and CT (44 weeks) were modeled as relatively short-duration infections in the absence of clinical intervention, consistent with previous modeling approaches [28, 29], with a return to susceptibility after natural disease clearance. Screening intervals greater than the average length of the infectious period could yield reduced benefits because of natural clearance. Accordingly, we observed a greater effect of screening interventions on longer-duration CT infection, compared with NG. The optimal screening frequency should reflect the natural history of NG and CT infection.

Increased screening coverage of sexually active MSM or even just a high-risk subset of MSM led to STI incidence declines in the model. Scaling coverage to 30% in the high-risk subset, assuming relatively high levels of annual screening, yielded greater reductions in STI incidence than scaling among all sexually active MSM, with PIA (>75%) and NNS (NG: 39; CT: 24) values comparable to those for scenarios evaluating biannual screening of SA MSM. This demonstrates the value of targeted screening compared with population-level screening, similar to findings surrounding the importance of focusing on a core group for prevention of disease transmission [30]. In the model, as infections decreased, fewer than 10% of testing events were symptoms-driven, consistent with empirical data from MSM [22]. It is important to note that previous analyses have shown that if there were an influx of new STI cases into the MSM population, potentially imported from other areas or from bridging with heterosexual populations, reduced screening levels could lead to a rebound in infections [15].

Efforts to increase screening frequency for all sexually active MSM or coverage among high-risk MSM would require patients to visit clinics or providers more regularly, even in absence of other medical needs. This increased frequency of visits might exceed system capacity, as providers already report lower screening priority for gonorrhea and chlamydia [15, 26]. A flexible strategy that includes other methods of STI screening, including home-based self-collection of specimen or pharmacy-based screening, could expand service provision while reducing provider burden and costs and deserves expanded research among MSM [31]. Primary care physicians with established MSM patients might be better placed to screen the same men more frequently and send regular screening reminders, whereas other locations and organizations, such as health departments and community-based organizations and clinics, may be better placed to handle increased screening of men. Achieving these increased screening rates may also be possible if integrated within other health care programs requiring ongoing clinical monitoring, such as HIV PrEP [17]. However, given these barriers to implementing STI screening as idealized in the CDC recommendations, achieving the reductions observed in the model may be difficult. Supplementary analyses (Supplementary Tables 13 and 14) further demonstrated that imperfect adherence to recommendations could result in increased incidence.

Although a key component of the CDC guidelines is the differential screening strategy for high-risk men, the optimal behavioral indications differentiating high-risk men from lowrisk men are uncertain. High extragenital NG and CT prevalence among community-sampled MSM suggests that the general population of sexually active MSM, not just high-risk MSM attending STD clinics, might be at elevated risk for STI acquisition [10]. Previous studies have explored the importance of targeted STI screening, as financial resources limit the ability to screen the entire population [15, 28, 32]. Increasing the partner threshold for more frequent screening with fixed coverage above 3 partners lessened the detection and treatment of asymptomatic cases, resulting in a reduced population-level PIA as the size of the higher-frequency screening group decreased. Increasing the partner threshold to >2 from >1 may reduce the number of tests, conserving financial resources while maintaining similar efficacy (PIA) and efficiency (NNS).

A reliance on patient-reported partner number for risk assessment may highlight gaps in accurate sexual history-taking that can result from factors such as reluctance to discuss sexual behavior and low provider awareness of screening recommendations for extragenital sites [33, 34]. The CDC's provider guidelines for sexual history-taking, meant to foster open dialogue and build patient-provider trust, recommend asking patients about the number and gender of sexual partners, sites of sexual activity, and condom usage [35]. Other definitions of behavioral risk, beyond recent partner number, may more efficiently address the significant proportion of incident STIs in the model contributed by MSM with few recent partners. The CDC's clinical provider guidelines for PrEP may provide an alternative framework for behavioral indications, particularly given the quarterly recommendations for STI screening for PrEP users [36]. Given the suboptimal uptake of STI testing among MSM and in other populations, the projected effects in this model, given faultless implementation, could exceed the real-world effects of screening programs [37, 38].

Limitations

Few data exist on the frequency of asymptomatic screening for STIs, which was a parameter in our model during calibration. Estimates of the period prevalence of testing for STIs in a time frame were accessible [6, 21], but further data to differentiate between symptoms-based testing and asymptomatic screening for STIs among MSM are needed. The model proportions of MSM tested or screened in the prior year matched empirical estimates from NHBS (Appendix), but those estimates do not differentiate screening rates by risk group or symptomatic status. Second, this current model does not include syphilis, which is the third most common bacterial STI for MSM. Despite the much lower incidence rates of syphilis compared with NG and CT among MSM [2-5], syphilis incidence is increasing [1]. Future models will work toward integrating syphilis into our modeling platform. Third, this study modeled only anal intercourse (no pharyngeal STIs) between MSM due to limited data on oral exposures. Fourth, despite comparability to broader national data [39], network and sexual behavior parameters sourced from urban Atlanta MSM studies may not generalize to other populations of lower HIV/STI incidence. Pooled NG and CT incidence values used for model calibration were broadly similar to the incidence observed in the study population. Finally, we did not incorporate antibiotic resistance for NG into this model; ineffective treatment could sustain transmission despite regular STI screening [40].

CONCLUSIONS

Targeting high-risk MSM based on a behavioral indication, multiple recent sexual partners, can effectively identify, test, and treat asymptomatic or untreated STIs at all sites of sexual exposure that would otherwise contribute to ongoing transmission. Although increased screening may have associated time and financial costs, these upfront increased costs to the provider and health care system could lead to reductions in costs over time due to lowered costs for STI treatment and case investigation. Implementing the guidelines as recommended can reduce infections, although barriers could prevent projected reductions from being achieved, but focusing on more frequent routine screening of all sexually active MSM and increased coverage of screening of high-risk MSM at all anatomic sites of sexual activity would provide the maximal reduction in STI burden.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowlegment

The authors would like to thank the members of the scientific and public health advisory group of the Coalition for Applied Modeling for Prevention project for their input on this study, and specifically those members who reviewed a previous version of this manuscript: Mary Anne Chiasson, Gregory Felzien, Jane Kelly, Susan Blank.

Financial support. This work was supported by the Centers for Disease Control and Prevention (grant number: U38 PS004646), the National Institutes of Health (grant number: R21 MH112449; grant number: R01 AI138783), and the Center for AIDS Research at Emory University (grant number: P30 AI050409).

Disclaimer. The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the US National Institutes of Health or the US Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. K.M.W., J.S.J., E.S.R., and S.M.J. conceived of and designed the analysis. T.G., H.C., K.B., K.W., and A.T. provided expertise and feedback. K.M.W. and S.M.J. performed the analysis and wrote the paper. All authors reviewed and approved the final draft.

Data availability. All data and software codes necessary to simulate these models and run these analyses are stored on GitHub at http://github. com/statnet/EpiModelHIV (branch is stitestguidelines) and http://github. com/EpiModel/stitestguidelines.

References

- Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2017. Atlanta, GA: Centers for Disease Control and Prevention 2018. Available at: https://www.cdc.gov/nchhstp/newsroom/2018/2017-STDsurveillance-report.html
- Kelley CF, Vaughan AS, Luisi N, et al. The effect of high rates of bacterial sexually transmitted infections on HIV incidence in a cohort of black and white men who have sex with men in Atlanta, Georgia. AIDS Res Hum Retroviruses 2015; 31:587–92.
- 3. Hernández-Romieu AC, Sullivan PS, Rothenberg R, et al. Heterogeneity of HIV prevalence among the sexual networks of black and white men who have sex with men in Atlanta: illuminating a mechanism for increased HIV risk for young black men who have sex with men. Sex Transm Dis 2015; 42:505–12.
- de Voux A, Kidd S, Grey JA, et al. State-specific rates of primary and secondary syphilis among men who have sex with men - United States, 2015. MMWR Morb Mortal Wkly Rep 2017; 66:349–54.
- Stenger MR, Pathela P, Anschuetz G, et al. Increases in the rate of neisseria gonorrhoeae among gay, bisexual and other men who have sex with men—findings from the Sexually Transmitted Disease Surveillance Network 2010-2015. Sex Transm Dis 2017; 44:393–7.
- 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; 58:1564–70.

- Flagg EW, Weinstock HS, Frazier EL, et al. Bacterial sexually transmitted infections among HIV-infected patients in the United States: estimates from the medical monitoring project. Sex Transm Dis 2015; 42:171–9.
- An Q, Wejnert C, Bernstein K, Paz-Bailey G. Syphilis screening and diagnosis among men who have sex with men, 2008–2014, 20 U.S. cities. JAIDS J Acquir Immune Defic Syndr 2017; 75:S363–9.
- 9. Kent CK, Chaw JK, Wong W, et al. Prevalence of rectal, urethral, and pharyngeal chlamydia and gonorrhea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. Clin Infect Dis **2005**; 41:67–74.
- Johnson Jones ML, Chapin-Bardales J, Bizune D, et al; National HIV Behavioral Surveillance Sexually Transmitted Infection Study Group. 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; 68:321–5.
- Centers for Disease Control and Prevention. 2015 STD treatment guidelines. MMWR Recomm Reports 2015; 64.
- Gunn RA, O'Brien CJ, Lee MA, Gilchick RA. Gonorrhea screening among men who have sex with men: value of multiple anatomic site testing, San Diego, California, 1997-2003. Sex Transm Dis 2008; 35:845–8.
- Tuite AR, Fisman DN, Mishra S. Screen more or screen more often? Using mathematical models to inform syphilis control strategies. BMC Public Health 2013; 13:606. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3699384/
- Gray RT, Hoare A, Prestage GP, et al. Frequent testing of highly sexually active gay men is required to control syphilis. Sex Transm Dis 2010; 37:298–305.
- Tuite AR, Shaw S, Reimer JN, et al. Can enhanced screening of men with a history of prior syphilis infection stem the epidemic in men who have sex with men? A mathematical modelling study. Sex Transm Infect 2018; 94:105–10.
- Jenness SM, Goodreau SM, Rosenberg E, et al. Impact of the Centers for Disease Control's HIV preexposure prophylaxis guidelines for men who have sex with men in the United States. J Infect Dis 2016; 214:1800–7.
- Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of gonorrhea and chlamydia following human immunodeficiency virus preexposure prophylaxis among men who have sex with men: a modeling study. Clin Infect Dis 2017; 65:712–8.
- Jenness S, Goodreau SM, Morris M. EpiModel: an R package for mathematical modeling of infectious disease over networks. J Stat Softw 2018; 84:1–47.
- Krivitsky PN, Handcock MS. A separable model for dynamic networks. J R Stat Soc Series B Stat Methodol 2014; 76:29–46.
- Toni T, Welch D, Strelkowa N, et al. Approximate Bayesian computation scheme for parameter inference and model selection in dynamical systems. J R Soc Interface 2009; 6:187–202.
- Hoots BE, Torrone EA, Bernstein KT, Paz-Bailey G; NHBS Study Group. Selfreported chlamydia and gonorrhea testing and diagnosis among men who have sex with men 20 U.S. cities, 2011 and 2014. Sex Transm Dis. 2014; 45:469-475.
- 22. Jenness SM, Weiss KM, Prasad P, et al. Bacterial sexually transmitted infection screening rates by symptomatic status among men who have sex with men in the United States: a hierarchical Bayesian analysis. Sex Transm Dis 2019; 46:25–30.
- Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. AIDS 2016; 30:2251–2.
- Barbee LA, Khosropour CM, Dombrowksi JC, Golden MR. New human immunodeficiency virus diagnosis independently associated with rectal gonorrhea and chlamydia in men who have sex with men. Sex Transm Dis 2017; 44:385–9.
- Tuddenham S, Ghanem KG, Gebo KA, et al. Gonorrhoea and chlamydia in persons with HIV: number needed to screen. Sex Transm Infect 2019; 95:322–7.
- Cantor AG, Pappas M, Daeges M, Nelson HD. Screening for syphilis: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA 2016; 315:2328–37.
- Cohen SE, Vittinghoff E, Philip SS, et al. Quarterly STI screening optimizes STI detection among PrEP users in the demo project. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 2016. Boston, MA: CROI, 22-25 February 2016.
- Chesson HW, Bernstein KT, Gift TL, et al. The cost-effectiveness of screening men who have sex with men for rectal chlamydial and gonococcal infection to prevent HIV infection. Sex Transm Dis 2013; 40:366–71.
- Turner K, Adams E, Grant A, et al. Costs and cost effectiveness of different strategies for chlamydia screening and partner notification: an economic and mathematical modelling study. BMJ 2011; 342:c7250.
- Hethcote HW, Yorke JA. Gonorrhea transmission dynamics and control. In: Levin S, ed. Lecture Notes in Biomathematics. Vol 56. New York: Springer-Verlag Berlin Heidelberg; 1984: 32-48. Available at: https://link.springer.com/content/ pdf/10.1007%2F978-3-662-07544-9.pdf
- Habel MA, Scheinmann R, Verdesoto E, et al. Exploring pharmacy and homebased sexually transmissible infection testing. Sex Health 2015; 12:472–9.

- Chesson HW, Kidd S, Bernstein KT, et al. The cost-effectiveness of syphilis screening among men who have sex with men: an exploratory modeling analysis. Sex Transm Dis 2016; 43:429–32.
- Schroder KE, Carey MP, Vanable PA. Methodological challenges in research on sexual risk behavior: II. Accuracy of self-reports. Ann Behav Med 2003; 26:104–23.
- Virgolino A, Roxo L, Alarcão V. Facilitators and barriers in sexual history taking. In: IsHak WW, ed. The Textbook of Clinical Sexual Medicine. Cham: Springer International Publishing; 2017:53–78.
- Centers for Disease Control and Prevention. A Guide to Taking a Sexual History. Atlanta: Centers for Disease Control and Prevention 2011. Available at: https:// npin.cdc.gov/publication/guide-taking-sexual-history
- Centers for Disease Control and Prevention, Service UPH. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2017 Update: A Clinical Practice Guideline. Atlanta: Centers for Disease Control and Prevention; 2018.
- Althaus CL, Turner KM, Schmid BV, et al. Transmission of *Chlamydia* trachomatis through sexual partnerships: a comparison between three individual-based models and empirical data. J R Soc Interface 2012; 9: 136–46.
- Smid J, Althaus CL, Low N. Discrepancies between observed data and predictions from mathematical modelling of the impact of screening interventions on *Chlamydia trachomatis* prevalence. Sci Rep 2019; 9:7547.
- Wejnert C, Le B, Rose CE, et al. HIV infection and awareness among men who have sex with men—20 cities, United States, 2008 and 2011. Sullivan PS, ed. PLoS One 2013; 8:e76878.
- Unemo M, Del Rio C, Shafer WM. Antimicrobial resistance expressed by *Neisseria gonorrhoeae*: a major global public health problem in the 21st century. Microbiol Spectr 2016; 4. Available at: https://www.asmscience.org/content/ journal/microbiolspec/10.1128/microbiolspec.EI10-0009-2015