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MAJOR ARTICLE

Clinical Factors Associated With Accurate Presumptive Treatment of *Neisseria gonorrhoeae* Infections in Men Who Have Sex with Men and Transgender Women

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Background. *Neisseria gonorrhoeae* (*N. gonorrhoeae*) infections have increased among men who have sex with men and are high among transgender women. Presumptive treatment guidelines may lead to inaccurate treatments and possible antibiotic resistance. Using patient data from AIDS Healthcare Foundation sexually transmitted infection (STI) testing clinics in California and Florida, we identified clinical factors associated with accurate presumptive *N. gonorrhoeae* treatment.

Methods. Multivariable logistic regression analyses were conducted using patient visit data from 2013 to 2017. A sample of 42 050 patient encounters were analyzed. The primary outcome variable included accurate versus inaccurate presumptive treatment. Risk ratios were generated for particular symptoms, high-risk sexual behavior, and history of *N. gonorrhoeae*.

Results. Twelve percent (5051/42 050) of patients received presumptive *N. gonorrhoeae* treatment, and 46% (2329/5051) of presumptively treated patients tested positive for *N. gonorrhoeae* infection. Patients presenting with discharge or patients presenting with dysuria were more likely to receive accurate presumptive treatment.

Conclusions. Providers should continue to follow the Centers for Disease Control and Prevention guidelines and consider presumptive *N. gonorrhoeae* treatment based on specific symptoms. As the STI epidemic continues to rise in the United States, along with increased antibiotic resistance, it is imperative to accurately test, diagnose, and treat populations at risk for *N. gonorrhoeae* and other STIs.

Keywords. *Neisseria gonorrhoeae*; gonorrhea; men who have sex with men; presumptive treatment; sexually transmitted infections.

Neisseria gonorrhoeae (*N. gonorrhoeae*) infection is the second most common bacterial sexually transmitted infection (STI) in the United States, after *Chlamydia trachomatis*, contributes to serious health complications including epididymitis and increases the risk of human immunodeficiency virus (HIV) transmission particularly among gay, bisexual, and other men who have sex with men (collectively referred to as MSM) if left untreated [1,2].

The estimated *N. gonorrhoeae* case rate among MSM in the United States increased 375.5% between 2010 and 2018 [1]. Although trends are difficult to assess among transgender women due to lack of surveillance data inclusive of gender identity, recent studies demonstrate alarmingly high rates of *N. gonorrhoeae* infection among transgender women [3, 4]. The Centers for Disease Control and Prevention (CDC) guidelines recommend presumptive antibiotic treatment prior to a finalized laboratory result for patients with objective clinical evidence of *N. gonorrhoeae* infection, a known exposure, or those who are symptomatic and unlikely to follow up for treatment [5]. These guidelines are based on the fact that presumptive *N. gonorrhoeae* treatment reduces the need for a patient to return at a later date for treatment, hastens symptom resolution, and prevents further transmission [6]. Unfortunately, presumptive treatment faces growing concerns over antibiotic resistance. According to the CDC, more than half of all *N. gonorrhoeae* infections in 2018 were estimated to be resistant to at least one antibiotic [1]. Overtreating uninfected patients may promote antibiotic resistance [7].

It is well established that antibiotic resistance is a growing public health threat and that research and policies aimed at optimizing antibiotic treatment are needed [8]. This study aims to provide data on presumptive *N. gonorrhoeae* treatment practices by identifying clinical factors associated with accurate presumptive treatment of *N. gonorrhoeae* among MSM and

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Abbreviations: AHF, AIDS Healthcare Foundation; aRR, adjusted risk ratio; CA, California; CDC, The Centers for Disease Control and Prevention; CI, confidence interval; DAG, directional acyclic graph; FL, Florida; HIV, human immunodeficiency virus; IRB, Institutional Review Board; MSM, men who have sex with men; NAAT, nucleic acid amplification test; *N. gonorrhoeae*, *Neisseria gonorrhoeae*; STI, sexually transmitted infection.

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transgender women in STI testing clinics in California and Florida, 2 states that reported the highest and fourth-highest number of *N. gonorrhoeae* cases in 2018, respectively [1].

METHODS

AIDS Healthcare Foundation (AHF) provides free walk-in STI testing, diagnosis, and treatment for MSM and other patients at its Wellness Centers. Using a cross-sectional study design, de-identified patient data from existing Wellness Center electronic medical records in California and Florida between 1 January 2013 and 31 December 2017 were analyzed. *N. gonorrhoeae* testing data were extracted from cisgender MSM and transgender women patients who self-report their gender and sexual identity. MSM and transgender women who received pharyngeal, rectal, and/or urine site-specific nucleic acid amplification tests (NAATs) for *N. gonorrhoeae* were included in the initial data set.

N. gonorrhoeae testing was ordered for 43 881 clinical encounters among MSM and transgender women during this time frame. In total, 1780 encounters were dropped due to lack of testing results or equivocal test results due to inadequate sample or lab error. Among those clinical encounters that involved *N. gonorrhoeae* testing, treatment data were extracted for individuals receiving intramuscular ceftriaxone and either oral azithromycin or oral doxycycline per 2010 and 2015

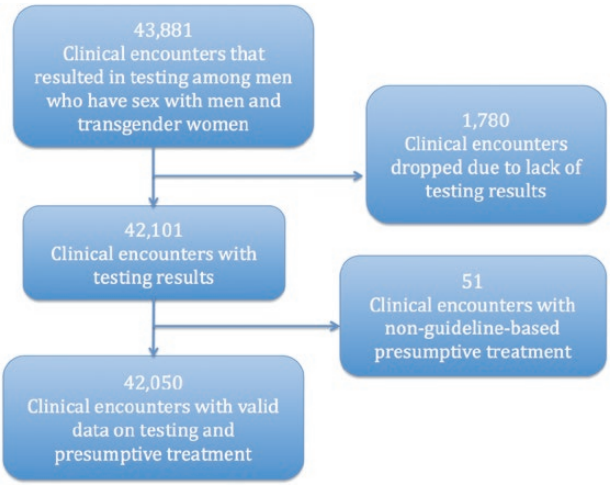

Figure 1. Patient encounters.

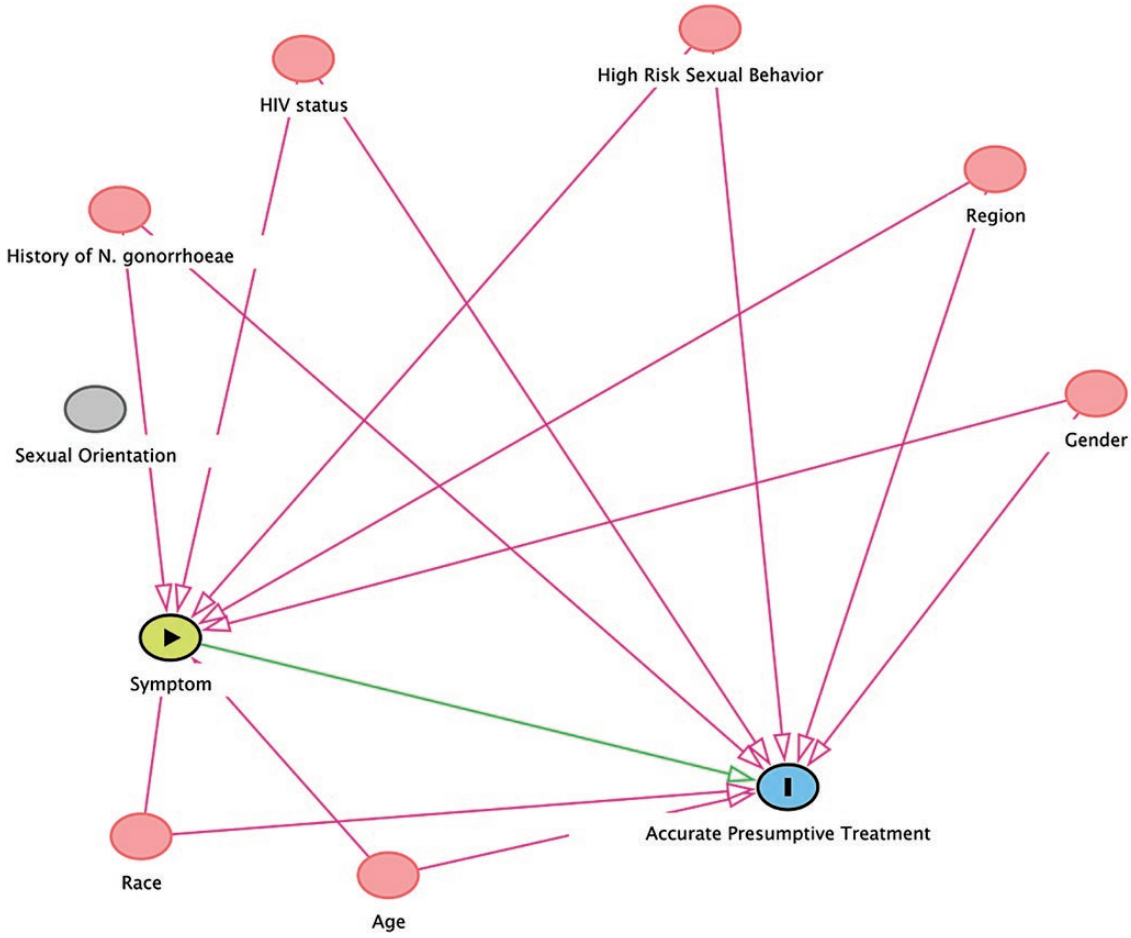

Figure 2. Covariates for multivariable logistic regression model: symptom. Abbreviation: HIV, human immunodeficiency virus.

CDC guidelines [5, 9]. Clinical encounters that included non-guideline-based presumptive treatment with ceftriaxone alone (36 clinic encounters) or ceftriaxone, azithromycin, and doxycycline (15 clinical encounters) were dropped from the data set. A total of 42 050 patient encounters were analyzed (Figure 1).

The outcome of interest was accurate presumptive *N. gonorrhoeae* treatment. This was defined as clinical encounters that involved same-day *N. gonorrhoeae* testing and CDC guideline-based presumptive *N. gonorrhoeae* treatment plus a positive *N. gonorrhoeae* laboratory test result. In order to create this outcome variable, an initial presumptive treatment variable was created. Presumptive treatment was defined as clinical encounters that involved CDC guideline-based treatment on the same day of *N. gonorrhoeae* testing. Laboratory testing for *N. gonorrhoeae* typically takes at least 24 hours to result into the electronic medical records database; therefore, same-day treatment was assumed to be presumptive because there was not enough time for results to be confirmed. Presumptive treatment was coded as a binary variable where 0 = no same day treatment and 1 = same day (and therefore presumptive) treatment. Next, a test result variable was created and coded as a binary variable where 0 = negative *N. gonorrhoeae* test result and 1 = positive *N. gonorrhoeae* test result. These variables were then multiplied to create the outcome variable, accurate presumptive treatment: 1 = same day presumptive treatment and positive *N. gonorrhoeae* test result; 0 = any other combination that does not result in same day (presumptive) treatment and positive *N. gonorrhoeae* test result. In other words, 0 represents all other outcomes that are not defined as accurate presumptive treatment.

Therefore, accurate presumptive treatment occurred among patients who received a positive *N. gonorrhoeae* test result on any laboratory sample (urine, pharyngeal swab, and/or rectal swab) collected on the same day of presumptive treatment. For example, if patients were treated for *N. gonorrhoeae* on the same day of sample collection and received a positive *N. gonorrhoeae* laboratory result the following day, then they were categorized as accurate presumptive *N. gonorrhoeae* treatment.

Correlates thought to be associated with accurate presumptive treatment were identified in an a priori manner via literature review and clinician judgement. Correlates included specific *N. gonorrhoeae* symptoms (eg, discharge, urogenital

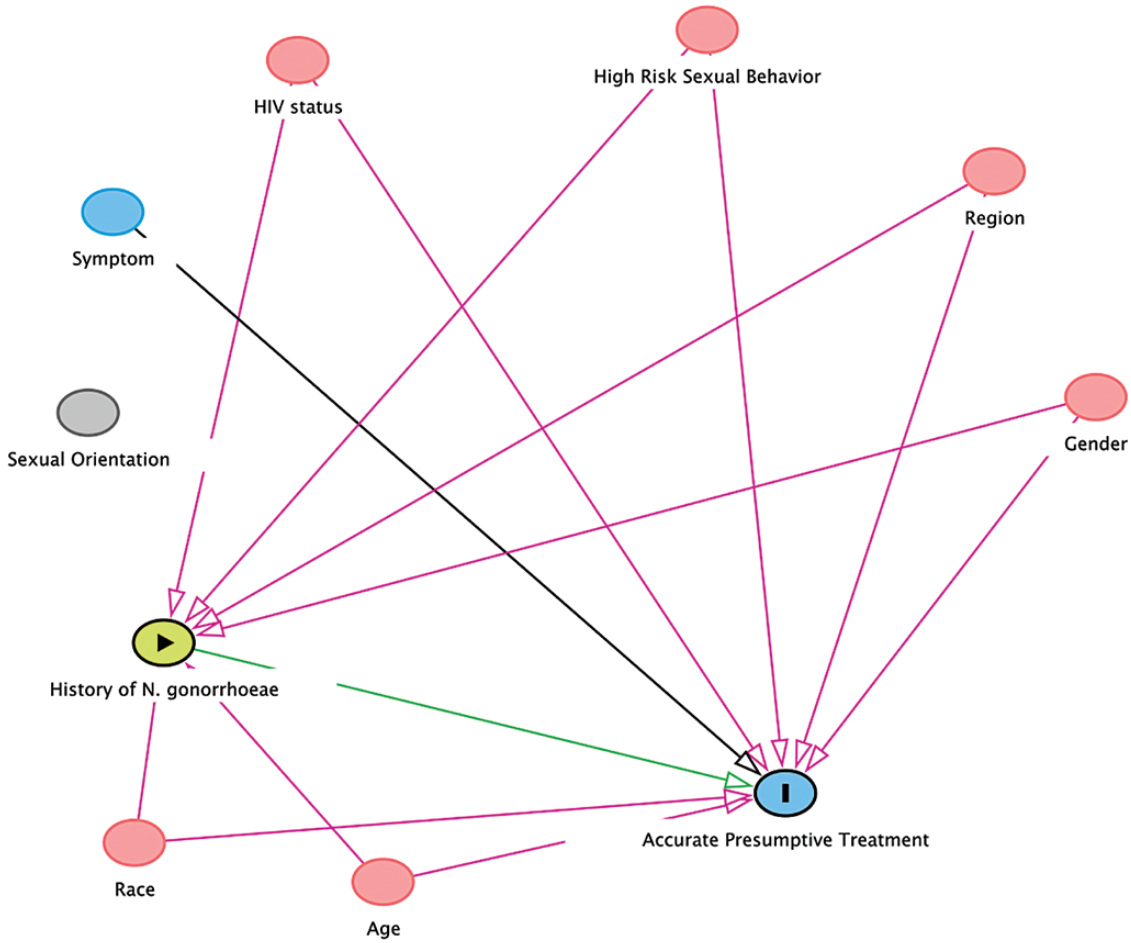

Figure 3. Covariates for multivariable logistic regression model: history of *N. gonorrhoeae*. Abbreviation: HIV, human immunodeficiency virus.

inflammation, dysuria, and acute pharyngitis), as well as high-risk sexual behavior and history of *N. gonorrhoeae* infection.

The symptom variables were extracted via key-word searches of clinician notes and/or ICD-9/10 codes. Discharge was defined as penile or anal discharge. Urogenital inflammation was defined as penile inflammation, urethritis, rectal inflammation, or proctitis. Dysuria was defined as dysuria or as burning, pain, or discomfort with urination. High-risk sexual behavior was defined as condomless anal sex within the last 12 months based on patient self-report. History of *N. gonorrhoeae* was defined as any prior history of *N. gonorrhoeae* infection based on patient self-report. All clinical encounters at AHF Wellness Centers included standardized questions regarding high-risk sexual behavior and history of *N. gonorrhoeae*.

Bivariate analysis was performed to determine unadjusted risk ratios (RRs) with the outcome variable. Correlates were further examined in multivariable logistic regression models. Covariates for multivariable logistic regression models were determined in an *a priori* manner based on literature review and directional acyclic graphing (Figures 2–4). All multivariable analyses adjusted for covariates: age, race, gender, and HIV status. Based on the current literature, each of the above-mentioned covariates is associated with *N. gonorrhoeae* infection and high-risk sexual behavior [1, 10–19]. Therefore, we ascertained that these covariates would influence the correlate variables (symptoms, history of *N. gonorrhoeae,* and high-risk sexual behavior) as well as the primary outcome variable (accurate presumptive treatment) and must be controlled for as potential confounders. Additionally, all multivariable analyses adjusted for region (California vs Florida). It was assumed in an a priori manner that there would be regional differences in *N. gonorrhoeae* rates, high-risk sexual behavior, and presumptive treatment practices. History of *N. gonorrhoeae* and high-risk sexual behavior variables were also controlled for in each respective model where the respective variables were not the primary correlate of interest. All statistical models were generated in accordance with directional acyclic graphing models (Figures 2–4). The assumptions of multivariable logistic regression were verified for each adjusted model. Hosmer-Lemeshow's test was used to determine goodness of fit. Multi-collinearity was assessed by computing tolerance and the Variance Inflation Factor statistic.

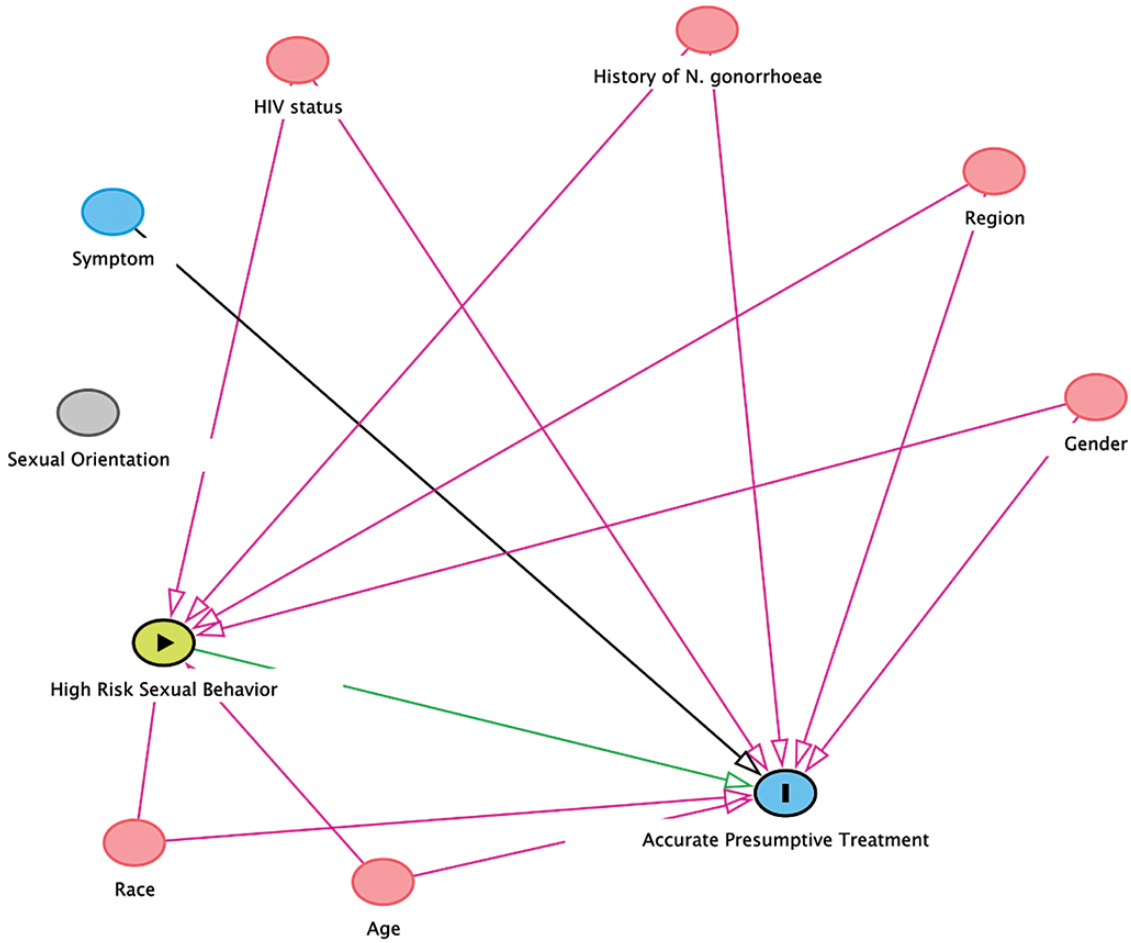

Figure 4. Covariates for multivariable logistic regression model: high-risk sexual behavior. Abbreviation: HIV, human immunodeficiency virus.

Table 1. Demographic and Risk Behavior Characteristics of Patients Seeking *N. gonorrhoeae* Testing at AIDS Healthcare Foundation Wellness Centers in California and Florida—2013–2017 (N = 42 050)

Variable	n	%
Age group (Years)		
18–24	13 584	32.3
25–29	4780	11.4
30–34	6965	16.6
35–39	9817	23.4
40+	6904	16.4
Gender		
Male	41 894	99.6
Transgender male to female	156	0.4
Sexual orientation		
Gay male	35 242	83.8
Bisexual	6334	15.1
Other	474	1.1
Race		
White	30 624	72.8
Black	6979	16.6
Asian or Asian American	2067	4.9
Native American, Alaska Native, or American Indian	119	0.3
Native Hawaiian or Pacific Islander	106	0.3
Other	2155	5.1
Region		
California	15 288	36.4
Florida	26 762	63.6
Presumptive treatment year		
2013	3041	7.2
2014	6879	16.4
2015	10 201	24.3
2016	10 750	25.6
2017	11 179	26.6
HIV status		
Negative	32 809	78.0
Positive	4845	11.5
Unknown	4396	10.5
Sexual behavior		
No condomless anal sex in the past 12 months	23 704	56.4
Condomless anal sex in the past 12 months	18 346	43.6
History of prior NG infection		
No	37 039	88.1
Yes	5011	11.9
Discharge		
Not present	35 313	84.0
Present	6737	16.0
Urogenital Inflammation		
Not present	37 684	89.6
Present	4366	10.4
Dysuria		
Not present	36 211	86.1
Present	5839	13.9
Acute Pharyngitis		
Not present	36 421	86.6
Present	5629	13.4

Abbreviations: HIV, human immunodeficiency virus; NG, *N. gonorrhoeae.*

Multivariable logistic regression was used to generate adjusted risk ratios to test the association between correlates (presence of symptoms, history of *N. gonorrhoeae*, and sexual behavior) and accurate presumptive *N. gonorrhoeae* treatment. Adjusted risk ratios (aRRs) are presented with 95% confidence intervals (CIs) and considers $P < .05$ as statistically significant. All analyses were performed using Stata v.14.2 (Stata Corp, College Station, Texas).

This study was deemed as non-humans subject research by the Boston University Institutional Review Board and therefore was considered as IRB exempt.

RESULTS

A total of N = 42 050 patient encounters resulted in *N. gonorrhoeae* testing. The vast majority of these encounters (n = 41 894; 99.6%) involved cis-gender men (Table 1). Twelve percent (n = 5051) received presumptive *N. gonorrhoeae* treatment. Among the 5051 patient encounters that led to presumptive treatment for *N. gonorrhoeae*, 46.1% (n = 2329) tested positive for *N. gonorrhoeae* infection and therefore received accurate presumptive treatment. Among the 53.9% (n = 2722) of patient encounters that resulted in inaccurate presumptive *N. gonorrhoeae* treatment, 14.8% (n = 404) received a positive *Chlamydia trachomatis* result.

Among the symptom correlate models, only discharge and dysuria were significantly associated with accurate presumptive treatment. Patients presenting to AHF Wellness Centers with discharge were 4.5 times more likely to receive accurate presumptive treatment compared to patients not presenting with discharge (aRR: 4.51; 95% CI: 4.12–4.88), and patients presenting with dysuria were 2.5 times more likely to receive accurate presumptive treatment compared to patients presenting without dysuria (aRR: 2.52; 95% CI: 2.31–2.75). Conversely, patients presenting with acute pharyngitis were 1.3 times less likely to receive accurate presumptive treatment compared with patients presenting without acute pharyngitis (aRR: .67; 95% CI: .58–.76) (Table 2).

Additionally, individuals with a history of *N. gonorrhoeae* infection were 1.7 times more likely to receive accurate presumptive treatment compared to individuals without a prior history (aRR: 1.71; 95% CI: 1.55–1.88). Finally, individuals who had engaged in high-risk sexual behavior prior to their visit to AHF Wellness Centers were 1.2 times more likely to receive accurate presumptive treatment compared to individuals who did not report engaging in high-risk sexual behavior (aRR: 1.20; 95% CI: 1.11–1.30) (Table 3).

There was no statistically significant difference in accurate presumptive treatment rates between cis-gender MSM and transgender women.

DISCUSSION

This study includes *N. gonorrhoeae* testing and treatment data from AHF Wellness Centers that provide standardized, free, and walk-in STI testing services in California and Florida. Nearly half

Table 2. Symptoms Associated With Accurate Presumptive *N. gonorrhoeae* Treatment Among Patients Seeking *N. gonorrhoeae* Testing at AIDS Healthcare Foundation Wellness Centers in California and Florida—2013–2017

Correlate	RR	(95% CI)	aRR	(95% CI)
Discharge (present vs not)	4.91	(4.54, 5.30)	4.51[a]	(4.12, 4.88)[a]
Urogenital inflammation (present vs not)	1.06	(.94, 1.21)	0.97[a]	(.85, 1.10)[a]
Dysuria (present vs not)	2.71	(2.49, 2.95)	2.52[a]	(2.31, 2.75)[a]
Acute pharyngitis (present vs not)	0.73	(.64, .84)	0.67[a]	(.58, .76)[a]

Abbreviations: aRR, adjusted risk ratio; CI, confidence interval; RR, risk ratio.
[a]Adjusted for age, race, gender, region, high-risk sexual behavior, history of *N. gonorrhoeae*, and human immunodeficiency virus (HIV) status.

(46.1%) of presumptively treated patients in this analysis were accurately treated for *N. gonorrhoeae*. In a similar study of patients in Los Angeles County, California, nearly one-third of patients presumptively treated for N. *gonorrhoeae* were accurately treated [20]. Based on the aRRs, patients with reported discharge or dysuria were more likely to be accurately presumptively treated for *N. gonorrhoeae* compared to presumptively treated patients who did not report these symptoms.

This study had several key limitations. The CDC recommends that individuals with a known exposure or contacts of persons with *N. gonorrhoeae* presenting for evaluation are presumptively treated. In this analysis the electronic medical records database did not include contact exposure from patients seeking testing. Second, patient symptom data were entered manually by clinical staff into the electronic medical records database using open-ended notes, which can lead to data entry errors. Third, symptoms may have been caused by other bacterial or viral agents not tested at AHF Wellness Centers, such as *Mycoplasma genitalium*. Furthermore, presumptive treatment cases were defined as cases that included *N. gonorrhoeae* testing and *N. gonorrhoeae* treatment during the same visit (prior to a diagnostic test result); it is possible that some patients received presumptive treatment and did not follow-through with laboratory testing due to unreported reasons.

Finally, given that this study is based on clinic data in metropolitan areas in California and Florida, there may limitations in generalizability to other parts of the United States, particularly rural areas and parts of the country where stigma towards gender identity and sexual orientation may prevent high-risk individuals from seeking STI clinic services. However, clinics that specifically cater its STI services toward MSM and transgender women may be able to adjust its presumptive treatment guidelines based on the findings of this large study.

Ultimately, the greatest hindrance in accurate treatment for *N. gonorrhoeae* and other STIs is the length of time from test to diagnosis. Although rapid point-of-care testing is the next evolution in STI testing technology, there is only one instrument currently approved by the Food and Drug Administration that can offer point-of-care *N. gonorrhoeae* urine test results in 30 minutes [21]. Alternatively, setting up in-house, certified laboratories to run STI specimens same-day using current STI testing technology may be too cost-prohibitive for STI clinics. Until STI clinics can provide rapid, point-of-care test results similar to HIV antibody testing, providers will continue to rely on patient-reported symptoms, exam findings, and clinical judgement regarding presumptive treatment.

Therefore, the results of this study suggest the need to improve presumptive *N. gonorrhoeae* treatment where same-day diagnoses are not available. Providers should continue to follow CDC guidelines and consider presumptive *N. gonorrhoeae* treatment based on specific symptoms. However, additional research is needed to better elucidate how presumptive treatment practices may affect antibiotic resistance, especially as the CDC suggests few antibiotic options remain for *N. gonorrhoeae* that are highly effective and well studied [1]. As the STI epidemic continues to rise in the United States, along with increased antibiotic resistance for *N. gonorrhoeae*, it is imperative to accurately test, diagnose, and treat patients at risk for *N. gonorrhoeae* and other STIs.

Notes

Acknowledgments. The authors acknowledge Michael Hancock, Senior Database Developer at AIDS Healthcare Foundation, for extracting the data.

Table 3. Clinical Correlates Associated With Accurate Presumptive *N. gonorrhoeae* Treatment Patients Seeking *N. gonorrhoeae* Testing at AIDS Healthcare Foundation Wellness Centers in California and Florida—2013–2017 (N = 42 050)

Clinical Correlate	RR	(95% CI)	aRR	(95% CI)
History of Gonorrhea (yes vs. no)	1.82	(1.66, 2.02)	1.71[b]	(1.55, 1.88)[b]
High-risk sexual behavior (yes vs. no)	1.25	(1.15, 1.35)	1.20[c]	(1.11, 1.30)[c]

Abbreviations: aRR, adjusted risk ratio; CI, confidence interval; RR, risk ratio.
[b]Adjusted for age, race, gender, region, high-risk sexual behavior and human immunodeficiency virus (HIV) status.
[c]Adjusted for age, race, gender, region, history of *N. gonorrhoeae* and HIV status.

Potential conflicts of interest. The 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.

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