Treatment of Chlamydia and Gonorrhea in Primary Care and Its Patient-Level Variation: An American Family Cohort Study

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ABSTRACT

PURPOSE Chlamydia and gonorrhea are the 2 most common bacterial sexually transmitted infections in the United States. Nonadherence to the Centers for Disease Control and Prevention treatment guidelines remains a concern. We examined how well chlamydia and gonorrhea treatment in primary care settings adhered to guidelines.

METHODS We used electronic health records from the PRIME registry to identify patients with diagnosis codes or positive test results for chlamydia and/or gonorrhea from 2018 to 2022. Outcomes were the first dates of antibiotic administered within 30 days after a positive test result for the infection. Descriptive statistics were calculated for patient sociodemographic characteristics. We used a multivariate parametric accelerated failure time analysis with shared frailty modeling to assess associations between these characteristics and time to treatment.

RESULTS We identified 6,678 cases of chlamydia confirmed by a positive test and 2,206 cases of gonorrhea confirmed by a positive test; 75.3% and 69.6% of these cases, respectively, were treated. Females, individuals aged 10-29 years, suburban dwellers, and patients with chlamydia-gonorrhea coinfection had higher treatment rates than comparator groups. Chlamydia was infrequently treated with the recommended antibiotic, doxycycline (14.0% of cases), and gonorrhea was infrequently treated with the recommended antibiotic, ceftriaxone (38.7% of cases). Time to treatment of chlamydia was longer for patients aged 50-59 years (time ratio relative to those aged 20-29 years = 1.61; 95% CI, 1.12-2.30) and for non-Hispanic Black patients (time ratio relative to White patients = 1.17; 95% CI, 1.04-1.33).

CONCLUSIONS Guideline adherence remains suboptimal for chlamydia and gonorrhea treatment across primary care practices. Efforts are needed to develop interventions to improve quality of care for these sexually transmitted infections.

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INTRODUCTION

Chlamydia and gonorrhea are the 2 bacterial sexually transmitted infections (STIs) most commonly reported by the Centers for Disease Control and Prevention (CDC) in the United States.[1] From 2009 to 2022, the annual incidence of chlamydia increased by 22% (from 405.3 to 495 per 100,000 patients) and that of gonorrhea increased by 98% (from 98.1 to 194.4 per 100,000), resulting in 1,649,716 chlamydia cases, and 648,056 gonorrhea cases in 2022.[2] Because of the high prevalence of these and other STIs in the United States, considerable public health resources are committed to STI-related care.[3]

Untreated chlamydia and gonorrhea can result in severe long-term health consequences[4-6] and substantial economic burden.[7] Although the CDC has provided comprehensive clinical guidance for health care professionals,[8] adherence to these guidelines remains a concern. Patients require prompt treatment after a confirmed diagnosis. The recommended regimen for chlamydia infections among adults and adolescents is 100 mg of doxycycline orally twice a day, for 7 days. For uncomplicated gonorrhea infections, the recommended treatment is 500 mg of ceftriaxone administered intramuscularly in a single dose. Alternative regimens may be used in patients with allergies or when the recommended treatment is not available.[8]

Although some studies have indicated high treatment rates using the recommended regimens,[9,10] others based on administrative claims have found low rates.[11] A plethora of studies have focused on aspects of guideline nonadherence, such as delayed treatment or use of nonrecommended treatment regimens across clinical

settings.[10,12-20] Some have attributed this lack of adherence to limited access to health care, patient allergies, supply and staff shortages, practice location, and clinician type.[10,12-18,21] Gaps in clinicians' knowledge and education have also been cited as potential reasons for guideline nonadherence.[19,20]

STI screening, diagnosis, and treatment have been increasingly performed in the primary care setting in recent years.[22-24] As primary care represents a substantial part of the care network in the United States, it is crucial to examine diagnosis, testing, and treatment patterns in this setting. Although efforts have been made to increase screening rates[25] and improve the quality of care,[23,26] studies in primary care examining the timeliness of treatment following STI diagnosis—especially large-scale analyses using electronic health records (EHRs)—are scarce.

Given that primary care is the health care system's frontline in the United States and that primary care practices and their populations are highly diverse, we hypothesized that significant variability in adherence to treatment guidelines would exist for patients with chlamydia and gonorrhea, and that some of these discrepancies might be driven by social determinants of health. Accordingly, our study had 2 aims. First, we sought to quantify the overall treatment rate for these STIs and adherence to treatment guidelines. Second, among patients with chlamydia or gonorrhea, we endeavored to examine the relevance of social determinants of health and their potential impact on treatment selection.

METHODS

Data Source

The PRIME registry is a clinical data repository capturing data from more than 2,000 primary care clinicians across the United States (Supplemental Appendix).[27,28] All registry data are stored in the American Family Cohort database, including detailed demographics, diagnosis codes, procedures, laboratory test results, medication records (including prescriptions), and free-text clinical notes. This study was approved by the Stanford Institutional Review Board (IRB no. 61956).

Study Population

We identified all patients having a primary care visit from January 1, 2018 to December 31, 2022 with an *International Classification of Diseases, 10th Revision, Clinical Modification* (ICD-10-CM) code for chlamydia or gonorrhea diagnosis and/or a code for a positive test confirming chlamydia or gonorrhea (Supplemental Table 1 and Supplemental Table 2).

For main analyses, we used a stringent definition for incident cases of the index STI, requiring that the visit have a positive test confirming chlamydia or gonorrhea, without any diagnoses or positive tests within the 30 days before the visit. Cases with a diagnosis or positive test in the preceding 30 days were excluded because they were considered prevalent cases rather than incident cases.

We classified patients as having coinfection if they had a positive confirmatory test for the index STI (chlamydia or gonorrhea) plus a diagnosis or positive test for the other STI on the same visit date.

Outcome/Treatment Definition

We identified chlamydia and gonorrhea treatments in the PRIME registry medication tables by antibiotic names, as detailed in Supplemental Table 3. We ascertained administration or prescription of treatment in the 30-day period after the date of the positive test result.

The co-primary outcomes for chlamydia treatment were the first treatment date, defined as the first date on which the antibiotic was administered (or the prescription date if the administration date was not available) and the antibiotic(s) administered in the 30-day follow-up period. The antibiotics assessed were doxycycline, azithromycin, levofloxacin, amoxicillin, and erythromycin. The secondary outcome for chlamydia treatment was the time to administration of doxycycline, the CDC-recommended treatment,[8] during the follow-up period.

The co–primary outcomes for gonorrhea treatment were the time to first treatment and the antibiotic(s) administered in the 30-day follow-up period. We assessed treatment with the antibiotics ceftriaxone, ceftizoxime, cefoxitin, cefotaxime, cefixime, gentamycin, gemifloxacin, spectinomycin, and azithromycin, and/or use of the Current Procedural Terminology/Healthcare Common Procedure Coding System code of J0696 representing treatment via injection.

We also ascertained combinations of antibiotics used for treatment during the follow-up period for each index STI.

Social Determinants of Health

We obtained patient gender, age group at the time of the index visit (split into 10-year increments, starting at 10-19 years of age and extending up to ≥80 years of age), race and ethnicity, residence, social deprivation index, and presence of coinfection. Race and ethnicity groups were categorized into Asian, Hispanic, non-Hispanic Black, non-Hispanic White, and a composite group of other, unknown, or missing. Postal zip codes were sorted into 3 categories: urban (>60% of the population lives in an urban area); suburban (40%-60% live in urban or rural areas, meaning approximately equal distribution); or rural (>60% lives in a rural area). Social deprivation was measured using a county-level social deprivation index, a composite measure of area-level deprivation based on 7 demographic characteristics collected by the American Community Survey; possible values range from 1 to 100, with higher values indicating greater socioeconomic deprivation.[29,30]

Statistical Analysis

We calculated descriptive statistics for categorical sociodemographic variables. We compared values between groups with nonparametric Wilcoxon tests for continuous variables and χ^2 tests for categorical variables.

To evaluate the impact of patient and other characteristics on first antibiotic prescribed in the 30-day follow-up period, we implemented multivariate parametric accelerated failure time (AFT) shared frailty models. This modeling approach was chosen to estimate adjusted time ratios (aTRs) for patient sociodemographics and other salient characteristics. As patients could have had multiple episodes of STIs during the study period, we used a shared frailty model that accounts for the clustering of episodes for each patient within a primary care practice. The likelihood ratio test was used to compare the shared frailty effect between an AFT model with and without accounting for episode clustering. We considered multiple candidate distribution models, including Weibull, log-logistic, Gaussian, and Gamma. The Akaike information criterion was used to select the most appropriate model, and the Weibull distribution was ultimately chosen for the final model fit because of its minimized fit statistic.

The primary models were fitted against patients who had a positive test for the STI, while a sensitivity analysis was conducted that fit identical models against patients who had only a diagnosis of chlamydia or gonorrhea without a positive test for confirmation (Supplemental Table 4).

We performed all data management and descriptive analyses using a combination of SAS version 9.4 (SAS Institute) and structured query language in a cloud platform (Google Cloud Computing). All multivariate models were performed using Stata version 17 (StataCorp). All statistical testing was conducted at the .05 significance level.

RESULTS

Patient Characteristics

The sociodemographic characteristics of the patient populations with a positive test for chlamydia or gonorrhea are shown in Table 1. For both STIs, patients were predominantly female, younger, and urban dwellers. Only 19.5% of the patients testing positive for chlamydia had a gonorrhea coinfection, but 57.9% of patients testing positive for gonorrhea had a chlamydia coinfection.

Treatment Rates

We determined that 5,028 (75.3%) of 6,678 episodes of chlamydia with a positive test and 1,535 (69.6%) of 2,206 episodes of gonorrhea with a positive test were treated within 30 days of the positive test result (Table 2). Throughout the study period, there were a mean 1.12 infections per patient (SD = 0.39 for chlamydia and 0.43 for gonorrhea).

Women who tested positive for the STIs had a substantially higher treatment rate than men (chlamydia: 78.4% vs 67.2%; gonorrhea: 78.9% vs 51.4%). Non-Hispanic White patients had the highest 30-day treatment rates for chlamydia and gonorrhea, at 76.8% and 73.5%, respectively. Similarly, the age groups 10-19 years and 20-29 years saw the highest treatment rates for both STIs. Chlamydia treatment rates for patients aged 10-19 years and 20-29 years were 76.7% and 76%, respectively, while gonorrhea treatment rates for those age groups were 76.4% and 70.7%, respectively. Patients with gonorrhea having chlamydia coinfection had a higher treatment rate than those without coinfection (76.4% vs 60.1%). Those whose zip codes were classified as suburban had the highest observed treatment rates for both STIs.

Treatments Received

The antibiotic(s) received as treatment during the 30-day follow-up period, treatment rates at various time points after a positive test, and times to treatment among those treated are shown in Table 2. For both chlamydia and gonorrhea, a similar proportion of those treated first received antibiotics in the initial week after the positive test: 85.2% and 84.4%, respectively. Notably, 945 (18.8%) of the chlamydia cases and 275 (17.9%) of the gonorrhea cases received same-day treatment after their positive test.

For all treated chlamydia episodes, only 645 (12.8%) received doxycycline alone as treatment and 702 (14.0%) received doxycycline overall (either alone or with another antibiotic). Even though doxycycline was the CDC's recommended treatment for chlamydia in 2021,[7] the majority of treatment regimens (4,220, or 83.9%) consisted of azithromycin alone.

Similarly, for gonorrhea, azithromycin alone represented the largest proportion of all treatment regimens: a total of 914 (59.5%). Azithromycin was commonly prescribed with ceftriaxone, representing 390 (25.4%) of all gonorrhea treatment regimens. Although ceftriaxone is currently the recommended treatment for gonorrhea,[8] it was prescribed alone in only 13.2% of cases; it was more often combined with other antibiotics, but even so, merely 38.7% of cases received any ceftriaxone (either alone or with another antibiotic).

Time to Treatment

For chlamydia cases, age group, race, gender, and coinfection were significantly associated with time to treatment (Table 3). Particularly noteworthy was that non-Hispanic Black patients and those with other, unknown, and/or missing race/ethnicity had longer times to treatment than non-Hispanic White patients, with aTRs of 1.17 (95% CI, 1.04-1.33) and 1.36 (1.20-1.55), respectively. Contextualizing this in terms of incremental days to treatment, assuming the median time to first treatment was 3 days for the reference group as an arbitrary reference time to treatment (Table 2), that time would be 0.52 days and 1.09 days longer, respectively, for non-Hispanic Black individuals and individuals with other, unknown, and/or missing race/ethnicity to receive treatment relative to non-Hispanic White peers. The time to treatment of chlamydia was longer for patients aged 50-59 years than for those aged 20-29 years (aTR = 1.61; 95% CI, 1.12-2.30). It was approximately 1.14 days shorter for females than for males (aTR = 0.62; 95% CI, 0.55-0.70).

For gonorrhea cases, urban dwellers had a longer time to treatment than suburban peers (aTR = 1.25; 95% CI,

1.02-1.53), and females had a shorter time to treatment than males (aTR = 0.38; 95% CI, 0.29-0.48) (Table 3). These differences would translate to an increase of 0.74 days above the median time for urban patients, assuming suburban patients were treated at the median time, and a decrease of 1.87 days from the median for female patients.

DISCUSSION

This study assessed adherence to CDC recommendations for chlamydia and gonorrhea treatment in a large convenience sample representing the US primary care population from 2018 to 2022. Analysis of data from this large registry showed 75.3% of chlamydia cases and 69.6% of the gonorrhea cases were treated within 30 days after a positive confirmatory test. We also found that for both STIs, more than 80% of the cases that were treated received the treatment within 7 days. Generally, females, individuals aged 10-29 years, suburban residents, and patients with coinfections saw higher treatment rates compared with other groups. Treatment with guideline-recommended antibiotics was uncommon: only 14.0% of chlamydia cases were treated with doxycycline and only 38.7% of gonorrhea cases were treated with ceftriaxone. A time-to-treatment analysis revealed that, for both STIs, males

Table 1. Baseline Characteristics of Patients With Chlamydia or Gonorrhea in Primary Care, Overall and by Treatment Status (2018-2022)

	Chlamydia[a]			Gonorrhea[a]		
Characteristic	Overall (N = 6,678)	Not treated (n = 1,650)	Treated (n = 5,028)	Overall (N = 2,206)	Not treated (n = 671)	Treated (n = 1,535)
Gender, No. (%)						
Male	1,827 (27.4)	599 (32.8)	1,228 (67.2)	747 (33.9)	363 (48.6)	384 (51.4)
Female	4,845 (72.6)	1,048 (21.6)	3,797 (78.4)[b]	1,459 (66.1)	308 (21.1)	1,151 (78.9)
Age group, No. (%)						
10-19 years	1,829 (27.4)	427 (23.3)	1,402 (76.7)	554 (25.1)	131 (23.6)	423 (76.4)
20-29 years	3,593 (53.8)	861 (24.0)	2,732 (76.0)	1,078 (48.9)	316 (29.3)	762 (70.7)
30-39 years	841 (12.6)	232 (27.6)	609 (72.4)	334 (15.1)	123 (36.8)	211 (63.2)
40-49 years	248 (3.7)	66 (26.6)	182 (73.4)	126 (5.7)	42 (33.3)	84 (66.7)
50-59 years	123 (1.8)	46 (37.4)	77 (62.6)	87 (3.9)	48 (55.2)	39 (44.8)
60-69 years	39 (0.6)	13 (33.3)	26 (66.7)	24 (1.1)	< 11	15 (62.5)
70-79 years	< 11	< 11	0 (0)	< 11	< 11	< 11
≥80 years	0 (0)	0 (0)	0 (0)	< 11	< 11	0 (0)
Race, No. (%)						
Asian	61 (0.9)	19 (31.1)	42 (68.9)	16 (0.7)	< 16	< 16
Hispanic	1,203 (18.0)	280 (23.3)	923 (76.7)	308 (14.0)	99 (32.1)	209 (67.9)
Non-Hispanic Black	1,527 (22.9)	412 (27.0)	1,115 (73.0)	656 (29.7)	225 (34.3)	431 (65.7)
Non-Hispanic White	2,842 (42.6)	658 (23.2)	2,184 (76.8)	877 (39.8)	232 (26.5)	645 (73.5)
Other, unknown, missing	1,045 (15.7)	281 (26.9)	764 (73.1)	349 (15.8)	109 (31.2)	240 (68.8)
Residence, No. (%)[c]						
Urban	4,179 (62.6)	1,041 (24.9)	3,138 (75.1)	1,481 (67.1)	527 (35.6)	954 (64.4)
Suburban	1,159 (17.4)	261 (22.5)	898 (77.5)	430 (19.5)	71 (16.5)	359 (83.5)
Rural	1,325 (19.8)	344 (26.0)	981 (74.0)	289 (13.1)	67 (23.2)	222 (76.8)
Unknown	< 16	< 16	< 16	< 16	< 16	0 (0)
SDI, median (IQR)[d]	57 (33-72)	57 (33-73)	57 (31-72)	57 (36-72)	59 (46-77)	57 (34-70)
Coinfection[e]						
Yes	1,299 (19.5)	304 (23.4)	995 (76.6)	1,278 (57.9)	301 (23.6)	977 (76.4)
No	5,379 (80.6)	1,346 (25.0)	4,033 (75.0)	928 (42.1)	370 (39.9)	558 (60.1)

IQR = interquartile range; SDI = social deprivation index.

Notes: Treatment status was based on administration/prescription of treatment within 30 days after the positive test. American Family Cohort analysis requires cell suppression; therefore, for small cell sizes, we masked actual counts and proportions for cell sizes < 16 (for adult patients) and < 11 (for pediatric patients) but > 1.

[a] Group assignment was based on a positive test, although patients could have also had a diagnosis code for the infection.
[b] Denominator was 5,025 patients because 3 patients were missing their gender identities.
[c] Ascertained from percentage of population for the zip code: urban (> 60% urban), rural (> 60% rural), or suburban (40%-60% urban or rural).
[d] Based on county. Possible values range from 1 to 100, with higher values indicating greater socioeconomic deprivation.
[e] Coinfection with chlamydia and gonorrhea, based on positive test for the index infection (chlamydia or gonorrhea) plus an additional infection of the other type on the same date based on either a diagnosis code or a positive test.

Table 2. Treatment Details for Patients With Chlamydia or Gonorrhea

Treatment measure	Chlamydia[a] (n = 6,678)	Gonorrhea[a] (n = 2,206)	Chlamydia with gonorrhea coinfection[b] (n = 1,299)	Gonorrhea with chlamydia coinfection[b] (n = 1,278)
Treated, No. (%)	5,028 (75.3)	1,535 (69.6)	995 (76.6)	977 (76.5)
Time to treatment[c]				
Within 7 days, No. (%)	4,286 (85.2)	1,296 (84.4)	848 (85.2)	811 (83.0)
Within 8-15 days, No. (%)	551 (11.0)	171 (11.1)	106 (10.7)	118 (12.1)
Within 16-30 days, No. (%)	191 (3.8)	68 (4.4)	41 (4.1)	48 (4.9)
Median (IQR), days	3 (1-6)	3 (1-6)	3 (2-6)	4 (2-6)
Mean (SD), days	4.5 (4.8)	4.6 (5.1)	4.6 (4.9)	4.9 (5.1)
Chlamydia treatment				
Antibiotic regimen, No. (%)[d]				
Amoxicillin	61 (1.2)	NA	< 16	NA
Amoxicillin, azithromycin	22 (0.4)		< 16	
Amoxicillin, doxycycline	< 16		0 (0)	
Amoxicillin, doxycycline, levofloxacin	0 (0)		0 (0)	
Amoxicillin, levofloxacin	< 16		< 16	
Azithromycin	4,220 (83.9)		876 (88.0)	
Azithromycin, doxycycline	49 (1.0)		< 16	
Azithromycin, erythromycin	< 16		0 (0)	
Azithromycin, levofloxacin	< 16		< 16	
Doxycycline	645 (12.8)		88 (8.8)	
Doxycycline, erythromycin	< 16		< 16	
Doxycycline, levofloxacin	< 16		0 (0)	
Erythromycin	< 16		< 16	
Levofloxacin	< 16		0 (0)	
Multiple regimens, No. (%)[e]	83 (1.7)		21 (2.1)	
Recommended treatment of doxycycline, No. (%)				
Any[f]	702 (14.0)		98 (9.8)	
As monotherapy	645 (12.8)		88 (8.8)	
Gonorrhea treatment				
Antibiotic regimen, No. (%)[d]				
Azithromycin	NA	914 (59.5)	NA	647 (66.2)
Azithromycin, cefixime		17 (1.1)		< 16
Azithromycin, cefixime, ceftriaxone		< 16		0 (0)
Azithromycin, ceftriaxone		390 (25.4)		228 (23.3)
Azithromycin, ceftriaxone, gentamicin		< 16		0 (0)
Azithromycin, gemifloxacin		< 16		< 16
Cefixime		< 16		< 16
Cefotaxime		0 (0)		0 (0)
Ceftriaxone		202 (13.2)		92 (9.4)
Ceftriaxone, gentamicin		0 (0)		0 (0)
Gentamicin		< 16		0 (0)
Multiple regimens, No. (%)[e]		412 (26.8)		237 (24.3)
Recommended treatment of ceftriaxone, No. (%)				
Any[g]		594 (38.7)		
As monotherapy		202 (13.2)		

IQR = interquartile range; NA = not applicable.

[a] Group assignment was based on a positive test, although patients could have also had a diagnosis code for the infection.
[b] Coinfection was based on positive test for the index infection (chlamydia or gonorrhea) plus an additional infection of the other type on the same date based on either a diagnosis code or a positive test.
[c] Among patients who were treated.
[d] American Family Cohort analysis requires cell suppression; therefore, for small cell sizes we performed masking of actual counts and proportions for cell sizes < 16 (for adult patients) and < 11 (for pediatric patients) but > 1.
[e] Received more than 1 regimen on the same day.
[f] Any receipt of doxycycline, whether alone or in combination with other antibiotics. Any receipt of doxycycline was required for treatment to be classified as recommended treatment.
[g] Any receipt of ceftriaxone, whether alone or in combination with other antibiotics. Any receipt of ceftriaxone was required for treatment to be classified as recommended treatment.

generally had a longer time to first treatment. Furthermore, among chlamydia cases, adults aged 50-59 years and Non-Hispanic Black patients typically had a longer time to first treatment compared with their peers aged 20-29 years and non-Hispanic White counterparts, respectively.

Findings in Context

Similar to a prior study,[11] our study uncovered patient characteristics related to the delivery and documentation of timely recommended treatment for chlamydia and gonorrhea in clinical settings. Consistent with other observational studies,[9-11] our study found that about 30% of patients with chlamydia or gonorrhea did not receive any treatment for their infection. This relatively large population of patients with untreated STIs provides an opportunity for the infection to be transmitted to others.[3] In addition, treatment was sometimes delayed, and the antibiotics clinicians used were commonly not those recommended.[8]

The nonadherence to guidelines we found has several possible explanations. It took a median of approximately 3 days from the date of the positive result from the test (conducted at either the primary care clinic or an off-site laboratory) for treatment to be initiated. This delay could be partly due to the qualitative reporting methods that some independent laboratories use to communicate test results, as those reports need to be read by the clinician, rather than being automatically uploaded into an EHR. It underscores a critical need for affordable point-of-care, rapid diagnostic tests to reduce

Table 3. Fully Adjusted Time Ratios and Differences in Days to Treatment vs Reference Group for Patients With Chlamydia or Gonorrhea

	Chlamydia[a]			Gonorrhea[a]		
Characteristic	**Time ratio (95% CI)[b]**	***P* value**	**Difference, days[c]**	**Time ratio (95% CI)[b]**	***P* value**	**Difference, days[c]**
SDI quintile[d]						
Quintile 1	Ref	…	Ref	Ref	…	Ref
Quintile 2	0.94 (0.79-1.12)	.49	−0.18	0.76 (0.56-1.05)	.10	−0.71
Quintile 3	0.91 (0.77-1.08)	.28	−0.26	0.65 (0.48-0.87)	.00	−1.05
Quintile 4	1.12 (0.92-1.35)	.27	0.35	0.90 (0.64-1.26)	.53	−0.31
Quintile 5	1.02 (0.82-1.27)	.86	0.06	1.03 (0.70-1.53)	.88	0.10
Age group						
10-19 years	0.94 (0.85-1.04)	.21	−0.18	0.90 (0.76-1.08)	.26	−0.29
20-29 years	Ref	…	Ref	Ref	…	Ref
30-39 years	1.06 (0.94-1.21)	.35	0.19	1.09 (0.87-1.37)	.44	0.28
40-49 years	0.87 (0.70-1.10)	.25	−0.38	0.72 (0.50-1.04)	.08	−0.83
50-59 years	1.61 (1.12-2.30)	.01	1.82	1.38 (0.83-2.27)	.21	1.13
60-69 years	1.17 (0.63-2.17)	.62	0.50	0.57 (0.26-1.29)	.18	−1.28
Residence						
Urban	0.96 (0.84-1.09)	.51	−0.13	1.25 (1.02-1.53)	.03	0.74
Rural	1.06 (0.92-1.21)	.45	0.17	1.17 (0.92-1.49)	.19	0.52
Suburban	Ref	…	Ref	Ref	…	Ref
Race						
Asian	0.98 (0.62-1.55)	.92	−0.07	1.48 (0.51-4.33)	.47	1.45
Hispanic	0.98 (0.85-1.14)	.82	−0.05	0.91 (0.68-1.22)	.53	−0.27
Non-Hispanic Black	1.17 (1.04-1.33)	.01	0.52	0.91 (0.74-1.11)	.34	−0.28
White	Ref	…	Ref	Ref	…	Ref
Other, unknown, missing	1.36 (1.20-1.55)	.00	1.09	1.21 (0.97-1.51)	.09	0.63
Sex: female (Ref = male)	0.62 (0.55-0.70)	.00	−1.14	0.38 (0.29-0.48)	.00	−1.87
Coinfection: yes (Ref = no)	1.14 (1.02-1.28)[e]	.02	0.43	0.89 (0.74-1.07)[f]	.21	−0.33

Ref = reference group; SDI = social deprivation index; STI = sexually transmitted infection.

Note: Assuming the median time to treatment of 3 days for chlamydia and 3 days for gonorrhea (Table 2).

[a] Group assignment was based on a positive test, although patients could have also had a diagnosis code for the infection.
[b] The ratio of the time to treatment between the indicated group and the reference group, adjusted for all other variables in this table. Estimated using a multivariate shared frailty parametric Weibull accelerated failure time (AFT) model to account for patients who may have had multiple STIs throughout the study period. Shared frailty models were estimated both with and without the shared frailty component, and the likelihood ratio test of the theta parameter indicated shared frailty effects existed; therefore, all final models accounted for multiple STI patient episodes that could have occurred during the study period.
[c] The increase (in the case of positive values) or decrease (in the case of negative values) in number of days with respect to the median time to treatment of 3 days.
[d] Range is from least deprived (quintile 1: SDI of 0-20) to most deprived (quintile 5: SDI of 81-100).
[e] The time to treatment is based on the relevant antibiotics that would be prescribed for chlamydia, regardless of gonorrhea coinfection.
[f] The time to treatment is based on the relevant antibiotics that would be prescribed for gonorrhea, regardless of chlamydia coinfection.

turnaround time and facilitate effective management of these STIs.[31-33] Incomplete or inaccurate documentation in EHRs resulting from medical coding errors[34] and/or a lack of system interoperability[35,36] can further contribute to a large number of cases of STIs going untreated. Finally, nonadherence to treatment guidelines appeared to vary by patient race and ethnicity. Non-Hispanic Black individuals may experience more socioeconomic disadvantages. Research indicates that Black people living in urban areas tend to have lower educational levels and higher unemployment rates, and tend to live in poorer neighborhoods compared with their White counterparts,[37,38] which can affect their access to health resources.[39] Further, these individuals may live in areas with high levels of social deprivation, possibly leading to longer times to first treatment for an STI.[40-42]

We found that azithromycin was the most frequently prescribed antibiotic for both chlamydia and gonorrhea. This finding confirms that azithromycin remains a widely chosen first-line treatment available to and used by primary care clinicians, despite some studies reporting that it is less efficacious than doxycycline in treating genital and rectal chlamydia infections.[43,44] Furthermore, azithromycin monotherapy for gonorrhea is not recommended by the CDC because of regimen resistance and adverse effects.[45] Our findings, together with findings of higher rates of use of recommended regimens in sexually transmitted disease clinics reported in other studies,[10,46-48] suggest that additional education and training may be needed for primary care clinicians to improve adherence.

Clinicians' preferences for treatments that do not adhere to CDC guidelines may be driven by several clinical considerations that could affect treatment outcomes. For chlamydia, a single-dose of azithromycin is preferred over a 7-day course of doxycycline because of concerns about patient adherence to a week of medication and the resulting need for follow-up.[49,50] For gonorrhea, a preference for a nonrecommended therapeutic regimen—orally administered azithromycin alone—might be due to patient fear of needles.[51] This could make it more attractive than recommended treatments that involve intramuscular injections, such as ceftriaxone, or gentamicin alongside oral azithromycin. An alternate oral regimen—a single dose of cefixime—is also recommended for treating uncomplicated gonorrhea, but its limited efficacy could be a concern.[52] Other factors affecting treatment choices include clinicians' education and experience,[20] patients' allergies, resource availability,[53] and delays in adopting updated guidelines in clinical practice.[54] Greater adherence to CDC guidelines for STI treatment could lead to changes in clinical practices, ultimately improving treatment rate disparities and shortening time to first treatment.[55] Future efforts are needed to develop and integrate a safe, effective, and standardized approach in outpatient settings to improve the outcomes of STI management.

Limitations

The study has several limitations. The analysis was conducted for all participating clinicians throughout the entire study period. Clinician information was missing for more than 50% of chlamydia and gonorrhea cases; therefore, we were unable to investigate clinician-level characteristics associated with treatment. Annual patterns of treatment, especially during the COVID-19 pandemic, were not examined. Drug allergies, pregnancy, and reasons for testing were not included in the model because of a lack of data. Future work with linked or alternate databases could be leveraged to examine their confounding effects on antibiotic-prescribing patterns.[56] Information regarding the test-ordering process was also not available in the database. Furthermore, we did not have access to patients' health records for services received outside the PRIME registry network because of a lack of system interoperability; this could potentially lead to underestimation of treatment rates. We did not include other STIs, such as syphilis or HIV, in the analysis. We also did not conduct any sensitivity or specificity analyses to evaluate the impact of medical coding errors on study results. With respect to STI test results, we were unable to determine whether the date of the test referred to the date on which the test result was ready at the testing facility, or the date on which the test result was available to the clinician and patient for review. We were also unable to determine the date on which a test was ordered or how patients received their results.

Conclusions

This study characterized guideline adherence and clinical practices for chlamydia and gonorrhea treatment in US primary care. Given the importance of timely treatment for these STIs to curb the spread of infection, there remains substantial opportunity to improve treatment rates across all patient groups, with particular attention directed to those in vulnerable populations. Additional incentives may be needed to promote adherence to clinical practice guidelines and thereby ensure timely treatment and selection of the appropriate antibiotic regimen. More efficient and standardized management approaches could be considered to improve the quality of care and address health inequities.

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Key words: chlamydia; gonorrhea; primary care; antibiotics; guideline adherence; nonadherence; clinical practice patterns; treatment delay; sexually transmitted disease; practice-based research; minority groups; vulnerable populations

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Supplemental materials

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