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A population-based study to compare treatment outcomes among women with urogenital chlamydial infection in Washington State, 1992–2015

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Abstract

Background—United States guidelines recommend azithromycin or doxycycline for chlamydia (CT) treatment. These therapies are similarly efficacious for urogenital infections when outcomes are measured 7–42 days following treatment, though doxycycline may be superior for rectal infections. Some investigators have suggested that persistent rectal infections may lead to autoinfection of the urogenital tract, potentially resulting in higher rates of recurrent infection in azithromycin-treated women.

Methods—We used Washington State surveillance data to identify women aged 14 with urogenital CT (1992–2015) treated with azithromycin or doxycycline. We defined persistent/recurrent CT as a repeat positive CT test 14–180 days after treatment of the initial infection. We used log binomial regression to estimate the adjusted relative risk (aRR) of persistent/recurrent infection associated with treatment with azithromycin versus doxycycline.

Results—From 1992–2015 there were 268,596 reported cases of urogenital CT, including 168,301 (63%) who received azithromycin and 66,432 (25%) who received doxycycline. The risk of persistent/recurrent urogenital CT was 6.7% and 4.7% in azithromycin- and doxycycline-treated cases, respectively ($P < .001$). Adjusting for age, race/ethnicity, year, pregnancy status, jurisdiction reporting, reason for exam, and gonorrhea co-infection, azithromycin-treated cases were significantly more likely to have persistent/recurrent urogenital CT than doxycycline-treated cases (adjusted RR=1.24; 95% confidence interval=1.19–1.30). Adjusting the re-testing window to 21–

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CONFLICT OF INTERESTS

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180 days (aRR=1.24; 95% CI=1.19–1.30) and 28–180 days (aRR=1.25; 95% CI=1.19–1.30) did not alter our primary findings.

Conclusions—Persistent/recurrent urogenital CT may be more common among women treated with azithromycin than doxycycline. The reason for this difference is uncertain and is an important area of future investigation.

Keywords

chlamydia; azithromycin; doxycycline; sexually transmitted disease; surveillance

INTRODUCTION

Chlamydia trachomatis (CT) is the most commonly reported infection in the United States (U.S.) with over 1 million cases reported among women in 2016.¹ The rate of CT among women has increased by 6.2% since 2013, and was 657.3 cases per 100,000 women in 2016.¹ Persistent or recurrent urogenital CT is common following treatment, with an estimated 20% of women experiencing repeat urogenital CT within 12 months after an initial CT diagnosis.² If untreated, urogenital CT can lead to pelvic inflammatory disease, ectopic pregnancy, and tubal factor infertility. Repeat CT infections are associated with an increased risk of these reproductive tract sequelae.³

Recent studies have highlighted the potential importance of rectal CT in women. Rectal CT is common among female STD clinic patients – with prevalence estimates ranging from 3% to 57%⁴ – and is not necessarily associated with reporting anal intercourse.^{5–8} Autoinfection of CT from the vagina to the rectum^{5,6} or from the rectum to the vagina^{9,10} may occur. The latter has been demonstrated in animal models⁹, and in women is likely facilitated by the close proximity of the vagina and anus. If autoinfection does occur, inadequately treated rectal CT could serve as a source of persistent/recurrent urogenital CT in women.

Currently, the Centers for Disease Control and Prevention (CDC) recommends azithromycin (1g orally once) or doxycycline (100mg orally twice daily for 7 days) for the treatment of CT,¹¹ based on evidence that the two therapies are similarly efficacious in the treatment of urogenital CT.¹² However, azithromycin appears to be substantially less effective than doxycycline in the treatment of rectal CT.¹³ Given that 70–89% of women with urogenital CT have concurrent rectal CT^{5,6,14–16} and that azithromycin may not be as effective as doxycycline for rectal CT, if autoinfection from the rectum to the vagina frequently occurs, one would expect that long-term follow-up studies of women with urogenital CT would demonstrate that azithromycin-treated women have a greater risk of persistent/recurrent urogenital CT than doxycycline-treated women. To provide support to this hypothesis, we leveraged Washington State's electronic CT surveillance data to conduct a population-based cohort study of all women with urogenital CT over a 24-year period. Our primary goal was to estimate the risk of persistent/recurrent urogenital CT among women treated with azithromycin compared to doxycycline.

MATERIALS AND METHODS

Study design and population

We used chlamydia surveillance data to create a population-based retrospective cohort of all women in Washington State (WA) aged 14 years who tested positive for urogenital CT between January 1, 1992 and December 31, 2015.

Data collection and measures

All data for this study were obtained from WA Department of Health (DOH)'s electronic STD surveillance database (PHIMS-STD), which includes data from laboratories, medical providers (via case report forms), and partner services interviews. WA laws require laboratories and medical providers to report all CT cases to local health authorities, who subsequently provide case report and interview data to WA DOH via PHIMS-STD. PHIMS-STD is a person-based system which allows the identification of repeat infections. Users must search for an existing person in PHIMS-STD prior to entering a new case. WA DOH uses Registry PlusTM LinkPlus software, a probabilistic record linkage program, to identify duplicate patients. The start date for this study reflects the year when surveillance data become available electronically.

Demographic information, date of diagnosis and treatment, treatment provided, anatomic site of infection, pregnancy status, and gonorrhea co-infection were obtained from PHIMS-STD. Case report data recorded in PHIMS-STD also include information on reason for exam, which includes three fixed response options: symptoms, routine exam (no symptoms), and exposed to infection. In WA, field services staff routinely contact medical providers if a case report form is not submitted or if treatment information on the case report form is incomplete.

We defined urogenital CT as a positive lab-confirmed chlamydia test where the case report form indicated the anatomic site of infection as the cervix, urethra, urine, or vagina. Surveillance data do not include information on the method of CT testing (i.e., culture or nucleic acid amplification test [NAAT]). However, NAAT testing for chlamydia became widespread in WA in the mid to late 1990s.

Definition of treatment and outcome

This analysis only includes women who received azithromycin or doxycycline, per the case report data. We assumed that women who were treated with azithromycin or doxycycline received the regimen consistent with the CDC treatment guidelines;¹¹ we excluded women from the analysis if there was evidence that a woman received a dose that was inconsistent with the CDC guidelines (e.g., 2g azithromycin).

We defined our primary outcome, persistent/recurrent urogenital CT, as the first positive urogenital CT test in the surveillance data that occurred 14–180 days after treatment for the initial infection. Because surveillance data only include information on positive CT tests, women without a repeat positive urogenital CT test within 14–180 days include women who

were not re-tested for CT during that period and women who were re-tested for CT during that period but re-tested negative.

Statistical analysis

We used chi-square tests to compare characteristics of women who received azithromycin versus doxycycline. For our primary analysis, we used chi-square tests to compare the proportion of women with persistent/recurrent urogenital CT 14–180 days after treatment who were treated with azithromycin versus doxycycline. We used log binomial regression models with robust variances to estimate the unadjusted and adjusted relative risk (aRR) and corresponding 95% confidence intervals (CI) of persistent/recurrent infection associated with treatment with azithromycin versus doxycycline. We adjusting for the following factors: age (continuous), race/ethnicity, year of diagnosis (continuous), gonorrhea co-infection, pregnancy status, reason for exam (including a category for missing), and county where the case was reported. We also report the association between each confounder and persistent/recurrent urogenital CT. Because a repeat positive CT NAAT test within 21 days of treatment may be a false positive due to the presence of non-viable organisms¹⁷, in a sensitivity analysis we repeated these analyses using two alternative outcome windows (21–180 days and 28–180 days after treatment).

We conducted three secondary analyses. First, to more closely align this analysis with previous studies comparing the two therapies in the treatment of urogenital CT¹², we stratified the re-testing window (i.e., the number of days from the date of treatment to the date of the repeat positive test) into four categories: 14–30 days, 30–60 days, 61–90 days, and 91–180 days. Second, to reduce the possible effect of antibiotic treatment for gonorrhea co-infection on our results, we excluded women with gonorrhea co-infection from the multivariate model. Third, to examine if reported exposure to CT was similar for women treated with azithromycin or doxycycline during the time between treatment of the initial infection and the repeat positive test, we compared the distribution of reasons for receiving the repeat CT test among women with a positive repeat CT test 14–180 days after treatment.

All analyses were performed using Stata statistical software, version 13.1 (StataCorp, College Station, TX). Tests were performed at a significance level of 0.05. Study procedures and analyses were approved by the University of Washington Human Subjects Division.

RESULTS

Between January 1, 1992 and December 31, 2015, there were 299,256 CT cases among women aged 14 years in WA, of which 268,595 (89.7%) were urogenital CT cases (representing 201,536 unique women). Of urogenital CT cases, we excluded 22,898 (8.5%) from this analysis because of missing treatment information (n=14,969), receipt of a treatment other than azithromycin or doxycycline (n=5,345), receipt of both azithromycin and doxycycline (n=2,554), or receipt of a non-recommended regimen for uncomplicated CT (n=30). Among urogenital cases who received either azithromycin (n=176,279; 65.6%) or doxycycline (n=69,422; 25.8%), we further excluded 10,965 (4.6%) cases because of missing treatment date (n=6,764) or a repeat test earlier than 14 days after treatment (n=4,201); these were not proportionately different between cases who received

azithromycin or doxycycline. The final analytic sample included 168,301 urogenital CT cases treated with azithromycin and 66,432 urogenital CT cases treated with doxycycline.

Three-quarters of women with urogenital CT were <25 years old, approximately half were White, non-Hispanic, and one-third were diagnosed in 2011–2015 (Table 1). Compared to women treated with azithromycin, women treated with doxycycline were more likely to be White, non-Hispanic, to be symptomatic, and to have been diagnosed prior to 2006.

Of 234,733 women treated with azithromycin or doxycycline, 14,382 (6.1%) had persistent/recurrent urogenital CT within 14–180 days after treatment, including 11,242 (6.7%) women treated with azithromycin and 3,140 (4.7%) treated with doxycycline ($P<0.001$) (Table 2). Of 14,382 women with persistent/recurrent urogenital CT 14–180 days after treatment, approximately 9% ($N=1,230$) were re-tested within 30 days of treatment and 72% ($N=10,308$) were re-tested after 60 days. The difference in the percentage of women with persistent/recurrent urogenital CT for azithromycin versus doxycycline ranged from 0.2 percentage points for women re-tested within 30 days to 0.8 percentage points for women re-tested 91–180 days after treatment (Table 2).

In unadjusted analyses, women treated with azithromycin were 41% more likely to have persistent/recurrent urogenital CT compared to women treated with doxycycline ($RR=1.41$, 95% $CI=1.36–1.47$). Adjusting for age, race/ethnicity, year of diagnosis, pregnancy status, gonorrhea co-infection, reason for initial CT test, and county where the case was reported, treatment with azithromycin was associated with a 24% higher risk of persistent/recurrent CT ($aRR=1.24$, 95% $CI=1.19–1.30$) (Table 3). Adjusting the re-testing window to 21–180 days and 28–180 days did not alter our primary findings (21–180 days: $aRR=1.24$; 95% $CI=1.19–1.30$ and 28–180 days: $aRR=1.25$; 95% $CI=1.19–1.30$). Similarly, excluding women co-infected with gonorrhea from the study population did not modify our results ($aRR=1.24$; 95% $CI=1.18–1.29$).

Among all women with an initial urogenital CT test, those aged 14–17 had the highest risk (9.1%) of persistent/recurrent urogenital CT, and each one-year increase in age was associated with a 6% lower risk of persistent/recurrent urogenital CT ($aRR=0.94$; 95% $CI=0.93–0.94$) (Table 3). Other factors significantly associated with an increased risk of persistent/recurrent urogenital CT were being non-White, having concurrent gonorrhea, having a symptomatic infection, and year of diagnosis (Table 3).

Table 4 describes the reason for receiving a repeat CT test, among the 14,382 women with a repeat positive urogenital CT test 14–180 days after treatment. Compared to women treated with azithromycin, women initially treated with doxycycline were more likely to receive a repeat CT because of symptoms and less likely to receive a repeat CT test as part of a routine exam. However, a similar proportion of women initially treated with azithromycin or doxycycline received a repeat test because they had been exposed to CT (11.1% vs 10.5%, respectively).

DISCUSSION

In this population-based study of 234,733 women with urogenital CT, we found that 6.1% of women had persistent/recurrent urogenital CT within six months of treatment and this risk was higher for women treated with azithromycin (6.7%) compared to doxycycline (4.7%). The relative risk of persistent/recurrent urogenital CT was significantly higher for women treated with azithromycin vs. doxycycline (RR=1.41; 95% CI: 1.36–1.47) and remained elevated (aRR=1.24; 95% CI 1.19–1.30) after adjustment for several confounding factors. This finding did not appreciably change when we altered the repeat testing window from 14–180 days to 21–180 or 28–180 days. Although there are a number of possible explanations for our findings, we believe that this study lends support to the hypothesis that undiagnosed and inadequately treated rectal CT may be a source of persistent/recurrent urogenital CT in women.

Our findings are in the range of those from several randomized, controlled trials (RCT) comparing azithromycin and doxycycline in the treatment of urogenital CT. In RCTs that included women with follow-up testing within one to six weeks after treatment, the percentage of individuals with persistent/recurrent urogenital CT ranged from 0.0% to 11.8% for those treated with azithromycin and 0.0% to 12.5% for those treated with doxycycline.^{18–29} A meta-analysis of these RCTs found a pooled fixed effects efficacy difference for women (efficacy for doxycycline minus efficacy for azithromycin) of 0.5 (95% CI: –4.9 to 5.8).¹² However, the most recent RCT on this topic, which employed a 28-day follow-up period, found that the absolute risk of treatment failure was 1.9 percentage points higher in women treated with azithromycin compared to doxycycline.³⁰ Despite the methodologic differences between our study and the RCTs –differences in study design (retrospective cohort versus RCT), follow-up method (passive versus active), and follow-up time (six months versus one to six weeks) – we similarly observed a 2.0 percentage point difference in favor of doxycycline and found that the proportion of women with persistent/recurrent urogenital CT (6.7% for azithromycin and 4.7% for doxycycline) is within the range reported in previous studies.

Although our study does not directly assess whether the rectum is a source of persistent/recurrent urogenital CT among women, these findings add support to the hypothesis that prevalent and inadequately treated rectal CT may lead to subsequent autoinfection from the rectum to the urogenital tract. Because rectal CT screening among women is not routine in WA, we do not have data on how many women in this study had concurrent rectal CT. However, an estimated 70–89% of women with urogenital CT have concurrent rectal CT^{5,6,14–16}; thus a substantial portion of these women may have also had undiagnosed rectal CT. If azithromycin-treated women were less likely to clear their rectal infection than doxycycline-treated women¹³, and autoinfection from the rectum to the vagina did occur, this may explain the increased risk of persistent/recurrent urogenital CT that we observed. Notably, it is possible that autoinfection from the rectum to the urogenital tract, if it does occur, may take several weeks. Tests-of-cure performed in the first few weeks after therapy may be too early to detect recurrent infection due to autoinoculation. Our study somewhat supports this hypothesis, as the absolute difference in the percentage of women with persistent/recurrent infection (azithromycin minus doxycycline) increased from 0.2

percentage points in the first 30 days after treatment to 1.8 percentage points after 30 days treatment.

There are also a number of alternative explanations for why women treated with azithromycin had a higher risk of persistent/recurrent urogenital CT in this study. First, it is possible that women treated with azithromycin were more likely to be re-exposed to CT compared to those treated with doxycycline. However, in our study, at least among women who re-tested CT positive, the proportion for whom re-exposure was documented as the reason for the repeat CT test was similar (11%) for women treated with azithromycin or doxycycline. This suggests a non-differential risk of re-exposure by therapy received, though this is only known or suspected re-exposure. Second, women who were treated with azithromycin may have been more likely to re-test for CT within six months of treatment, which may have increased CT case-finding in that group. In 2002, CDC modified CT screening guidelines to suggest that clinicians “consider” rescreening patients following treatment, and the 2010 guidelines firmly recommend rescreening. This change in guidelines occurred during a period of increasing azithromycin use in WA; thus, it is possible that azithromycin-treated women were more often re-tested than those treated with doxycycline. Unfortunately, we have no information on the proportion of women who re-tested within six months of treatment or if this proportion differs by therapy received. However, in our multivariate model we did include year of diagnosis to account for this secular trend. Fourth and similarly, azithromycin use in WA State increased concurrently with an increase in the use of NAAT testing for chlamydia. Thus, the higher risk of persistent/recurrent urogenital CT we observed among azithromycin-treated women may be due to the use of a more sensitive test among the azithromycin-treated cases. Surveillance data do not include information on the type of test (culture vs. NAAT) that was used, but, as stated above, our multivariate models were adjusted for year of diagnosis, which does address this secular trend. Fifth, there may be factors specific to the therapies – such as peak drug levels of duration above the minimum inhibitory concentration – that influenced the results. Finally, azithromycin may in fact be less effective than doxycycline to treat urogenital CT and may be influenced by other (often unmeasured) factors such as the microbiome.¹⁰

This study has several strengths. This is a population-based study of over 230,000 women with urogenital CT and efforts by field services staff to document treatment for CT cases resulted in <6% of cases with incomplete treatment information. There are also many key limitations. First, these are surveillance data and there was no active follow-up of women in this cohort. Thus, this study likely underestimates the true proportion of women with persistent/recurrent CT. Second, women without a repeat positive test includes women who re-tested negative for CT within six months of treatment and those who did not re-test at all. Differential re-testing by therapy may have influenced our findings, though the extent of this is unknown. Third, we cannot eliminate the possibility that our findings may be due to confounding. Our multivariate model included several possible confounding factors, but there may be other factors, particularly risk for re-exposure, that were unavailable in surveillance data. Fourth, we cannot distinguish between persistent or recurrent infection. It is likely that many of the persistent/recurrent infections we observed were the result of re-infections. This may have influenced our findings if women treated with azithromycin were more likely to be re-infected compared to women treated with doxycycline. Fifth, as

described above, azithromycin use increased in WA concurrently with an increase in NAAT testing and a change in the rescreening guidelines. We addressed this by including year of initial CT diagnosis in our multivariate model, but this secular trend is still key a confounder. Sixth, although we excluded only 8.5% of CT cases from this analysis due to missing treatment information, one-half of those cases occurred prior to 2000; thus, there was differential exclusion by year. Seventh, data on symptomatic cases are from the “reason for exam” field in the case report form and may not completely capture all true symptomatic cases. Finally, WA State surveillance data do not include information on bacterial vaginosis (BV) diagnosis or metronidazole use. This may be an important unmeasured confounder in this analysis, as BV may contribute to CT acquisition.

In conclusion, we found that women with urogenital CT treated with azithromycin were more likely to have persistent/recurrent urogenital CT within 6 months compared to those treated with doxycycline. This finding is consistent with our underlying hypothesis that use of a drug that inadequately treats rectal infections would lead to a higher risk of persistent or recurrent urogenital CT, and supports a growing body of literature suggesting that undiagnosed rectal CT infection may play a role in women’s reproductive health. However, the importance of rectal CT as a contributor to persistent/recurrent urogenital CT among women remains uncertain. We still do not know how long rectal CT persists, how often positive NAAT tests for rectal specimens represent true infections, and if and how often women auto inoculate infections from the rectum to the urogenital tract. We also do not have definitive data regarding the relative efficacy of doxycycline and azithromycin in the treatment of rectal CT. Answers to these outstanding questions and others may influence CT screening and treatment guidelines for women.

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SUMMARY

Among 234,733 women with urogenital chlamydia in Washington State 1992–2015, persistent/recurrent urogenital CT was more common among women treated with azithromycin compared to doxycycline (6.7% vs 4.7%; $P<0.001$).

Table 1

Characteristics of women receiving azithromycin or doxycycline for urogenital chlamydial infection (at the time of diagnosis), Washington State 1992 – 2015 (N=234,733)

	Total N = 234,733	Azithromycin N = 168,301	Doxycycline N = 66,432	
Characteristic	N (%)	N (%)	N (%)	P-value
Age (years)				<0.001
14–17	41,202 (18)	28,706 (17)	12,496 (19)	
18–24	134,648 (57)	96,343 (57)	38,305 (58)	
25–29	33,646 (14)	25,064 (15)	8,582 (13)	
30–34	13,721 (6)	10,083 (6)	3,638 (5)	
35	11,516 (5)	8,105 (5)	3,411 (5)	
Race/ethnicity				<0.001
White, NH	115,539 (49)	78,171 (46)	37,368 (56)	
Black, NH	23,509 (10)	16,983 (10)	6,526 (10)	
Hispanic	35,220 (15)	27,146 (16)	8,074 (12)	
Other or multi-race, NH	26,786 (11)	20,784 (12)	6,002 (9)	
Unknown, NH	33,679 (14)	25,217 (15)	8,462 (13)	
Concurrent gonorrhea	8,014 (3)	5,478 (3)	2,536 (4)	
Pregnant				<0.001
Yes	7,983 (3)	7,292 (4)	691 (1)	
No	37,603 (16)	28,488 (17)	9,115 (14)	
Unknown	189,147 (81)	132,521 (79)	56,626 (85)	
Reason for Exam				<0.001
Symptomatic	74,791 (32)	49,985 (30)	24,806 (37)	
Routine exam (no symptoms)	113,670 (48)	88,036 (52)	25,634 (39)	
Exposed to infection	17,230 (7)	13,277 (8)	3,953 (6)	
Missing	29,042 (12)	17,003 (10)	12,039 (18)	
Jurisdiction reporting				<0.001
Pierce County	42,333 (18)	31,484 (19)	10,849 (16)	
King County	57,698 (25)	42,734 (25)	14,964 (23)	
Spokane County	17,347 (7)	12,017 (7)	5,330 (8)	
Yakima County	15,647 (7)	10,555 (6)	5,092 (8)	
North Sound	24,428 (10)	17,429 (10)	6,999 (11)	
Eastern WA *	32,448 (14)	23,005 (14)	9,443 (14)	
Western WA **	44,832 (19)	31,077 (18)	13,755 (21)	
Year of Diagnosis				<0.001
1992–1995	21,356 (9)	2,853 (2)	18,503 (28)	
1996–2000	29,790 (13)	16,230 (10)	13,560 (20)	
2001–2005	41,616 (18)	27,360 (16)	14,256 (21)	
2006–2010	63,154 (27)	50,373 (30)	12,781 (19)	
2011–2015	78,817 (34)	71,485 (42)	7,332 (11)	

NH, non-Hispanic

*
Excludes Yakima and Spokane

**
Excludes King, Pierce, North Sound

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Table 2

Number and percent of women re-testing positive for urogenital chlamydia, by number of days since treatment and therapy received, N=234,733

	Total N=234,733	Azithromycin N=168,301	Doxycycline N=66,432
Repeat positive window*	N (%)	N (%)	N (%)
Overall (14–180 days) **	14,382 (6.1)	11,242 (6.7)	3,140 (4.7)
14–30 days	1,230 (0.5)	951 (0.6)	279 (0.4)
31–60 days	2,844 (1.2)	2,264 (1.4)	580 (0.9)
61–90 days	3,088 (1.3)	2,468 (1.5)	620 (0.9)
91–180 days	7,220 (3.1)	5,559 (3.3)	1,661 (2.5)
No repeat positive test within 180 days	220,351 (93.9)	157,059 (93.3)	63,292 (95.3)

* Number of days between treatment and repeat positive test

** P<0.001 for overall comparison of azithromycin vs. doxycycline

Table 3

Risk of persistent/recurrent urogenital CT 14–180 days after treatment, by treatment received and other characteristics at the time of initial diagnosis, N=234,733

	Persistent/recurrent infection n/N (%) [*]	Adjusted Relative Risk (95% CI) ^{**}
Characteristic at time of initial diagnosis	N (%)	
Treatment received		
Azithromycin	11,242/168,301 (6.7)	1.24 (1.19 – 1.30)[†]
Doxycycline	3,140/66,432 (4.7)	<i>Referent</i>
Age (years) [‡]		0.94 (0.93 – 0.94)
14–17	3,739/41,202 (9.1)	--
18–24	8,402/134,648 (6.2)	--
25–29	1,439/33,646 (4.3)	--
30–34	455/13,721 (3.3)	--
35	347/11,516 (3.0)	--
Race/ethnicity		
White, NH	6,264/115,539 (5.4)	<i>Referent</i>
Black, NH	1,838/23,509 (7.8)	1.28 (1.22 – 1.36)
Hispanic	2,406/35,220 (6.8)	1.23 (1.17 – 1.29)
Other or multi-race, NH	1,813/26,786 (6.8)	1.20 (1.14 – 1.26)
Unknown, NH	2,061/33,679 (6.1)	1.06 (1.01 – 1.11)
Concurrent gonorrhea		
Yes	630/8,014 (7.9)	1.19 (1.10 – 1.29)
No	13,752/226,719 (6.1)	<i>Referent</i>
Pregnant		
Yes	508/7,983 (6.4)	1.01 (0.92 – 1.11)
No	2,366/37,603 (6.3)	<i>Referent</i>
Unknown	11,508/189,147 (6.1)	1.07 (1.02 – 1.12)
Reason for Exam		
Symptomatic	5,337/74,791 (7.1)	1.33 (1.28 – 1.37)
Routine exam (no symptoms)	6,455/113,670 (5.7)	<i>Referent</i>
Exposed to infection	1,031/17,230 (6.0)	1.10 (1.03 – 1.17)
Missing	1,559/29,042 (5.4)	1.04 (0.98 – 1.10)
Jurisdiction reporting		
Pierce County	2,676/42,333 (6.3)	0.90 (0.86 – 0.95)
King County	3,960/57,698 (6.9)	<i>Referent</i>
Spokane County	1,043/17,347	0.88 (0.82 – 0.94)
Yakima County	1,093/15,647 (7.0)	1.01 (0.95 – 1.08)
North Sound	1,296/24,428 (5.3)	0.79 (0.74 – 0.84)
Eastern WA	1,751/32,448 (5.4)	0.79 (0.74 – 0.83)
Western WA	2,563/44,832 (5.7)	0.85 (0.81 – 0.90)

	Persistent/recurrent infection n/N (%) [*]	Adjusted Relative Risk (95% CI) ^{**}
Characteristic at time of initial diagnosis	N (%)	
Year of Diagnosis [‡]		1.02 (1.02 – 1.03)
1992–1995	767/21,356 (3.6)	--
1996–2000	1,550/29,790 (5.2)	--
2001–2005	2,527/41,616 (6.1)	--
2006–2010	4,310/63,154 (6.8)	--
2011–2015	5,228/78,817 (6.6)	--

^{*} n/N = number with a persistent/recurrent infection divided by the total number in that subgroup

^{**} Bold denotes statistical significance

[‡] unadjusted relative risk=1.41 (1.36 – 1.47)

[‡] Age and year included as continuous variables in multivariate model. They are presented as categories in this table to show the number and percent with persistent/recurrent infection within each sub-group

Table 4

Reason for receiving repeat CT test among women with a repeat positive CT test 14–180 days after treatment, by treatment received for the initial infection, N=14,382

	Total N = 14,382	Azithromycin N = 11,242	Doxycycline N = 3,140
Reason for Repeat Test	N (%)	N (%)	N (%)
Symptoms	5,132 (35.7)	3,755 (33.4)	1,379 (43.9)
Routine Exam (no symptoms)	5,924 (41.2)	4,865 (43.3)	1,059 (33.7)
Exposed to infection	1,582 (11.0)	1,251 (11.1)	331 (10.5)
Missing	1,742 (12.1)	1,371 (12.2)	371 (11.8)