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Rate and Predictors of Repeat Chlamydia trachomatis *Infection Among Men*

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Background: ***Chlamydia trachomatis* (Ct) infection, especially repeat infection, is associated with serious sequelae among women, including pelvic inflammatory disease, ectopic pregnancy, and infertility. There are few reports evaluating repeat infection and predictors among men treated for Ct infection.**

Objective: **To measure the predictors and incidence of repeat Ct infection among men.**

Methods: **Men 15 to 35 years of age were screened for Ct infection in different venues in Baltimore, Denver, and San Francisco using urine-based nucleic acid amplification tests. Men with Ct infection were evaluated for repeat Ct infection from February 2001 until September 2003. Enrolled men had a baseline, 1-month, and 4-month follow-up visit and were tested for Ct infection at each visit. Project staff sought to locate and notify all female sex partners of infected men during the study to provide testing and treatment. We evaluated predictors of repeat Ct infection, time to infection, and incidence of infection.**

Results: **Three hundred fifty-nine men were recruited into the study and 272 (76%) had at least 1 follow-up visit with Ct results. Repeat infection occurred in 13% of men with Ct infection; there was no significant difference in repeat infection by site (Denver 13%, Baltimore 13%, San Francisco 12%). Independent predictors of repeat infection were history of an STD and venue. Incidence of repeat infection was 45.4 infections per 100 person years.**

Conclusion: **Repeat Ct infection is common among men and similar in geographically distinct cities. Incidence of repeat Ct infection support routine rescreening of men within the first 3 months after Ct infection.**

CHLAMYDIA TRACHOMATIS (CT) INFECTION is the most common reportable bacterial sexually transmitted infection (STI) in the United States.[1] Among women, Ct infection is associated with serious consequences such as pelvic inflammatory disease, ectopic pregnancy, and infertility. Recommendations exist for screening, and follow-up rescreening, of women aged <26 years.[1–5] Screening women 15 to 29 years of age for Ct has been found to be cost-effective, and in some cases cost-saving.[6] However, challenges exist to universally and effectively implement these recommendations, in part due to limited resources.

Existing data demonstrate prevalence of Ct infection among men is often high and may vary, depending on the city and venues conducting screening.[7–15] A study of Ct infection in 4 US cities found that 7% of men had Ct infection and in some venues, the infection was as high as 16%.[15] In another study, 9% to 15% of men had Ct infection, depending on the city where testing was conducted.[14] There are no standard screening guidelines for detection of Ct infection in men, however guidelines do exist for programs that currently screen men for Ct on where to most effectively screen.[16]

Men with repeat infection might be considered core STI transmitters and maybe an appropriate target for prevention strategies. Core transmitters of STIs may sustain high infection rates in the population, and may have a higher proportional contribution to the burden of STIs. There are no published studies that evaluate an actively followed cohort of men for repeat Ct infection. Data on the rate and predictors of repeat Ct infection in men can inform potential public health prevention strategies.

Materials and Methods

Study Population

Men 15 to 35 years of age were screened for Ct infection as part of a male Ct screening demonstration project in Baltimore, Denver, and San Francisco.[15] Venues in which screening occurred included adult and juvenile detention, high schools, college, sexually transmitted disease (STD) clinics, adolescent and adult primary care clinics, street outreach, and community-based organizations. In Baltimore, men were screened in adolescent primary care clinics, adult detention, and school clinics; in Denver men were screened in adolescent primary care clinics, adult and juvenile detention, school and STD clinics, Community Based Organizations and

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street outreach; and in San Francisco, men were screened in adolescent and adult primary care clinics, adult and juvenile detention, school and college clinics, Community Based Organizations, and street outreach. Response rates to enrollment were not captured for this study. This study was approved by human subject review committees at each of the sites and at the Centers for Disease Control and Prevention.

Longitudinal Study Enrollment

Men were treated with appropriate therapy for Ct infection,[1] and were enrolled in the longitudinal study that included a baseline, 1-month, and 4-month follow-up visit from February 2001 until September 2003. All men identified with documented Ct infection through the male chlamydia screening demonstration project[15] and able to attend follow-up visits were eligible for the study. At each visit, men were asked demographic, behavioral, and partner information and were tested for Ct infection. Project staff sought to locate and notify all female sex partners of men with Ct infection during the study to provide evaluation, testing and treatment; data on partners were collected in a partner record.

Laboratory Testing

Screening was conducted on first-void urine samples using urine-based nucleic acid amplification tests at a central laboratory in each city; either LCR (Abbott Laboratories, Abbott Park, IL), PCR (Roche Diagnostic Systems, Indianapolis, IN), or SDA (Becton Dickinson Diagnostic Systems, Sparks, MD).

Data Analysis

We defined a repeat Ct infection as any Ct infection among men at the first or second follow-up visit, and these visits had to be at least 21 days from the baseline study visit in which Ct infection was treated. Men who had more than one repeat infection were evaluated only once (at the first follow-up visit with infection detected) in bivariate and multivariable analysis. Variables such as race and ethnicity were collected as 2 separate variables—race and Hispanic/non-Hispanic ethnicity. Condom use was determined by number of sex acts in which condoms were used divided by the total number of sex acts; "always condom" use was defined as 100% condom use with a specific partner. Condom use for new partners was evaluated only among men with new partners during the study, and condom use for baseline partners was evaluated only among men who continued to have sex with baseline partners. Partner information (number and type) during the study was collected from the study participant at follow-up visits. Partner Ct treatment was analyzed using data in the partner record that included partners who were evaluated and interviewed. Female partner race and ethnicity differences from the male participant were evaluated only among men with information on race or ethnicity for all partners during the study. All variables collected at baseline, and selected variables at the follow-up visits were evaluated by bivariate analysis for risk of repeat infection using Epi Info 6.0 and SAS v 9.1 (Cary, NC).

Multivariate analysis was conducted including baseline variables that had a chi-square P value <0.02 in bivariate analysis, or key demographic variables such as age group. A backwards elimination approach was used with a criteria for exclusion based on the Wald chi-square P value being >0.05. Once all the variables in the model were statistically significant at the 0.05 level, all pairwise interactions were evaluated. Variables evaluated in the multivariate model included age group, history of an STD, venue, less than high school education, and baseline symptoms. Incidence of infection was calculated based on number of repeat infections, time to first infection, and total time in the study. Incidence of repeat infection was calculated by the number of infections divided by the total time to first infection or study time. Because time to repeat infection was interval sensored, we used the Turnbull estimator of the cumulative distribution of repeat infection.

TABLE 1. Baseline Demographic Factors and Symptoms and Repeat Chlamydia Infection Among Men, Baltimore, Denver, and San Francisco

	No. Tested (%)	No. Pos. (%)	OR (95% CI)
Overall	272	34 (13)	
Site			
Baltimore	56 (21)	7 (13)	Referent
Denver	140 (52)	18 (13)	1.0 (0.4–2.5)
San Francisco	76 (27)	9 (12)	0.9 (0.4–2.4)
Baseline symptoms: dysuria or discharge			
No	191 (77)	20 (10)	Referent
Yes	56 (23)	12 (21)	2.33 (1.0–5.1)*
Follow-up visits			
First follow-up only	84 (31)	8 (10)	Referent
First follow-up and second follow-up	188 (69)	26 (14)	1.5 (0.6–3.9)
Venue			
STD clinic	117 (44)	12 (10)	Referent
Adult/juvenile detention	19 (7)	5 (26)	3.1 (0.7–11.4)
Community venue	53 (20)	5 (9)	0.9 (0.2–3.0)
School/college clinic	43 (16)	3 (7)	0.7 (0.1–2.6)
Adolescent primary care	31 (12)	8 (26)	3.0 (1.0–9.1)*
Age (yrs)			
15–17	51 (19)	10 (20)	Referent
18–19	63 (23)	6 (10)	0.4 (0.1–1.4)
20–24	97 (36)	11 (11)	0.5 (0.2–1.5)
<24	61 (22)	7 (11)	0.5 (0.2–1.7)
Race/ethnicity			
Non-Hispanic Black	108 (40)	15 (14)	Referent
Hispanic	77 (28)	11 (14)	1.1 (0.4–2.6)
Non-Hispanic White	50 (18)	5 (10)	0.7 (0.2–2.2)
Other	37 (14)	3 (8)	0.6 (0.1–2.2)
Highest grade completed			
At least some high school	248 (92)	25 (10)	Referent
<High school	22 (8)	8 (36)	5.1 (1.9–13.3)*

*P <0.05.

Results

Three hundred fifty-nine men were enrolled in our study from 6 different venues at the 3 different cities. Two hundred seventy-five (76.6%) men had a follow-up visit at which repeat Ct infection was evaluated; 3 men had follow-up visits, but no test results were available; thus, 272 men were included in our final analysis of repeat Ct infection. Men with a follow-up visit were not different from those without a follow-up visit with regard to age, race/ethnicity, symptoms, or history of STDs (data not shown).

Among the 272 men in our analysis of repeat infection, 56 men were from Baltimore, 140 from Denver, and 76 from San Francisco (Table 1). Men were enrolled from a variety of venues including STD clinics (44%), community based venues (20%), schools (16%), adolescent primary care (12%), and detention (7%). The median age of the men enrolled was 21 years (range, 15–30 years). One hundred eight (40%) men enrolled were non-Hispanic black, 77 (28%) Hispanic, 50 (18%) non-Hispanic white,

and 37 (14%) other race/ethnicity. Most men were single (92%). The median number of sex partners in the 60 days before enrollment was 1 (range, 1–8).

All men were treated for Ct infection at the baseline visit; 193 (71%) were treated with azithromycin, 23 (8%) with doxycycline, and the remaining were treated with an unknown regimen. Overall, 56 (21%) men with information available had symptoms of discharge or dysuria at the first visit that men were tested.

Most men had 2 follow-up visits (69%), and the visits ranged from 21 to 323 days (median 83 days). First follow-up visits ranged from 21 to 215 days (median 33 days) and second follow-up visits ranged from 27 to 323 days from the first follow-up (median 91 days). Twelve percent of men had symptoms at either the first or second follow-up visit.

Overall, the repeat infection rate for men with at least 1 follow-up visit 21 days from the baseline visit was 13% (Baltimore 13%, Denver 13%, San Francisco 12%) (Table 1). The median time to infection from the baseline visit was 52 days with a range of 22 to 296 days. Among the men with repeat infection detected and who had 2 follow-up visits, most men (76%) had infection detected at the first visit, and the remaining (23%) had infection detected at the second follow-up visit. Among men negative for infection at the first follow-up, 4% had repeat infection at the second follow-up visit. Three men had repeat infection more than 1 time.

The 272 men evaluated for repeat Ct infection identified 660 partners during the study, and 338 (51%) of these partners had data in the partner record. Men reported a median of 2 partners during the study (range, 0–9). There were 160 (58.8%) men with information regarding treatment for all baseline partners. All baseline partners were treated for Ct infection for 51 (32%) of these men; most of these men had 1 partner. There was no significant difference in repeat Ct infection among men with all baseline partners located and treated compared with men without all baseline partners located and treated.

In a bivariate analysis evaluating baseline characteristics of the men, history of STD, less than high school education, baseline symptoms of dysuria/discharge, and venue were significantly associated with repeat Ct infection ($P < 0.05$) (Tables 1 and 2). The multivariable model evaluating baseline characteristics and repeat infection demonstrated that venue (AOR 3.2 for adolescent primary care vs. STD clinic, 95% CI 1.1–8.8, and AOR 3.3 for adult and juvenile detention vs. STD clinic, 95% CI 1.0–10.9) and history of STD (AOR 2.6, 95% CI 1.2–5.7) were independently associated with repeat Ct infection.

TABLE 2. Baseline Sexual Behavior and Repeat Chlamydia Infection, Baltimore, Denver, and San Francisco

	No. Tested	No. Pos. (%)	OR (95% CI)
History of STD (any)			
No	204	20 (10)	Referent
Yes	67	14 (21)	2.4 (1.1–5.1)*
History of CT			
No	238	27 (11)	Referent
Yes	34	7 (21)	1.2 (0.5–3.3)
No. sex partners last 60 d			
0	13	0	
1	136	15 (11)	Referent
2	76	14 (18)	1.8 (0.7–4.2)
>2	46	5 (11)	0.9 (0.3–3.0)
Condom use with baseline partners			
Never	72	9 (13)	Referent
Sometimes	147	21 (14)	1.2 (0.5–2.9)
Always	38	4 (11)	0.8 (0.2–3.2)

*$P < 0.05$.

TABLE 3. Partner(s) Characteristics During Study and Repeat Chlamydia Infection, Baltimore, Denver, and San Francisco

Behavioral/Partner Characteristics	No. Tested	No. Pos. (%)	OR (95% CI)
No. partners during study			
0	5	0	
1	95	9 (9)	Referent
2	67	10 (15)	1.7 (0.6–4.8)
>2	105	15 (14)	1.7 (0.6–5.0)
New partner during study			
Yes	119	18 (15)	Referent
No	153	16 (11)	0.7 (0.3–1.4)
Total new partners during study			
1	61	11 (18)	Referent
2	30	4 (13)	0.7 (0.2–2.7)
3–5	28	3 (11)	0.6 (0.1–2.4)
Condom use with baseline partners at last sex during study			
Always	47	9 (19)	Referent
Less than always	99	13 (13)	0.6 (0.2–1.9)
Condom use with new partners at last sex during study			
Always	71	5 (7)	Referent
Less than always	44	10 (23)	3.8 (1.1–15.5)*

*$P < 0.05$.

Among the behavioral variables evaluated during the study, less than always condom use with a new partner was the only factor associated with repeat infection (OR 3.8, 95% CI 1.1–15.5) (Table 3) Information reported by the participant, including age and race and ethnicity differences of the partner, was not significantly associated with repeat Ct infection.

The incidence of repeat infection was 45.41 per 100 person years. The time to repeat infection was a median of 52 days (range, 22–296 days). Using a cumulative incidence curve, repeat infection occurred relatively constantly from 21 to 45 days, and then decreased between 45 and 150 days (Fig. 1).

Discussion

This longitudinal study of repeat Ct infection in a geographically diverse sample of men in the United States found 13% had repeat chlamydia infection, similar to what has been found among women.[17] Incidence of repeat infection was 45.41 per 100 person years, and highest within the 45 days after first infection.

Independent baseline factors associated with increased risk of repeat Ct infection included history of an STD, and specific venues (adolescent primary care, juvenile and adult detention). Some of the commonly found factors associated with repeat Ct infection among men in other studies, including sex with multiple partners, acquisition of a new partner, or young age were not associated with repeat infection in our study.[13,18,19] Men who used a condom consistently with new partners at last sex during the study had a significantly reduced risk of repeat infection. It is important to note that most men in our study had few partners and risk associated with increasing partners or new partners may be better evaluated in

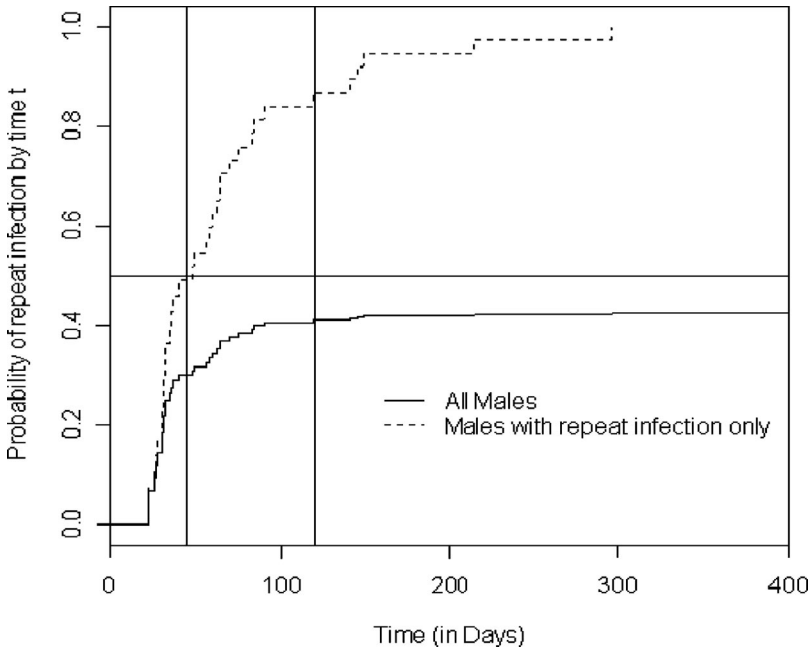

Fig. 1. Incidence of repeat Ct infection in days among men, Turnbull Survival Curve.

settings in which men have multiple partners and a wide social network. Also, we were not able to evaluate treatment of new partners during the study as many new partners were not identified for treatment.

The incidence of repeat infection of 45.41 infections per 100 person-year was higher than what has been reported in other studies.[20] Infection occurred most commonly within the first 45 days after initial Ct infection, which suggests most repeat infections could be captured with rescreening at 3 months. It is unclear why infection occurs early; this could be because infection persists, repeat infection occurs from an untreated partner, or other reasons.

Our study was subject to limitations. Our evaluation included only men electing to enroll in a longitudinal study, and as such, our population may not be representative all men with Ct infection. We had limited sample size and may have not had adequate power to detect significant predictors of repeat Ct infection. Our analysis was dependent on the time frame of the scheduled follow-up of our assessment (1 and 4 months), which could have biased the evaluation of time to repeat Ct infection. Finally, we could not exclude the possibility that repeat infection represented treatment failure, persistent infection, or failure to complete therapy before sexual contact; although, our 21 day window to measure repeat Ct infection was designed to decrease the probability of including persistent infection. Information on partner treatment was incomplete in our study so we could not verify partner treatment for all partners of men with Ct.

Ct infection may cause symptoms and possibly morbidity in men, and can result in transmission to female partners. Screening men should be considered to reduce the risk of transmission to female partners and rescreening should be considered early. The high rate of reinfection found early (within the first 100 days) could limit the public health impact of screening; mathematical modeling may help address such concerns.

Men with repeat Ct infection may be considered core STI transmitters and are an appropriate target for prevention strategies. Based on clear evidence from our study that repeat infections are common and usually occur within the first 45 days, standard policies on rescreening of men within the first 3 months after a Ct infection should be implemented.

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