

## Temporal Patterns in Chlamydia Repeat Testing in Massachusetts



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**Introduction:** National guidelines recommend test-of-cure for pregnant women and test-of-reinfection for all patients with chlamydia infections in order to interrupt transmission and prevent adverse sequelae for patients, partners, and newborns. Little is known about retesting and positivity rates, and whether they are changing over time, particularly in private sector practices.

**Methods:** Electronic health record data on patients with chlamydia tests were extracted from three independent clinical practice groups serving  $\cong 20\%$  of the Massachusetts population. Records were extracted using the Electronic medical record Support for Public Health platform (esphealth.org). These data were analyzed for temporal trends in annual repeat testing rates by using generalized estimating equations after index positive chlamydia tests between 2010 and 2015 and for differences in intervals to first repeat tests among pregnant females, non-pregnant females, and males. Data extraction and analysis were performed during calendar years 2017 and 2018.

**Results:** An index positive *C. trachomatis* result was identified for 972 pregnant female cases, 10,309 non-pregnant female cases, and 4,973 male cases. Test-of-cure 3–5 weeks after an index positive test occurred in 37% of pregnant females. Test-of-reinfection 8–16 weeks after an index positive test occurred in 39% of pregnant females, 18% of non-pregnant females, and 9% of males. There were no significant increases in test-of-cure or test-of-reinfection rates from 2010 to 2015. Among cases with repeat tests, 16% of pregnant females, 15% of non-pregnant females, and 16% of males had positive results.

**Conclusions:** Chlamydia test-of-cure and test-of-reinfection rates are low, with no evidence of improvement over time. There are substantial opportunities to improve adherence to chlamydia repeat testing recommendations.

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### INTRODUCTION

**C**hlamydia *trachomatis* is the most common nationally reportable sexually transmitted infection in the U.S. and a potential cause of pelvic inflammatory disease, infertility, ectopic pregnancy, and long-term pelvic pain if left untreated.<sup>1,2</sup> Up to 20% of patients fail to clear their infections or become re-infected in the 12 months after treatment of an initial episode.<sup>3–5</sup> Repeat testing is therefore recommended for all patients to interrupt transmission and to prevent adverse sequelae to patients, their partners, and newborns.<sup>1</sup>

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The Centers for Disease Control and Prevention (CDC) periodically release sexually transmitted disease treatment and prevention guidelines. Successive releases between 1998 and 2010 made increasingly stringent repeat testing recommendations for *C. trachomatis* infections (Appendix Table 1). The most recent guidelines from 2015 recommend test-of-cure 3–4 weeks after treatment for pregnant women, and test-of-reinfection approximately 3 months after treatment for all patients (or at the next healthcare visit within the following 12 months).<sup>1</sup> Few studies have investigated adherence to follow-up testing recommendations in the U.S. and whether repeat testing patterns are changing over time. The present study used the Electronic medical record Support for Public Health (ESP, [esphealth.org](http://esphealth.org)) surveillance network to assess repeat testing and positivity patterns over a 6-year period in Massachusetts.<sup>6,7</sup>

## METHODS

### Study Sample

Electronic health record data on *C. trachomatis* infections were extracted from three large multisite, multispecialty ambulatory practice groups in Massachusetts using the ESP surveillance platform. ESP is an open source software package that automatically extracts data from electronic health records, maps them into standardized tables, runs algorithms to detect events of public health interest, and electronically transmits cases or summary data to public health agencies.<sup>6–10</sup> Participating practices included Atrium Health, Cambridge Health Alliance, and the Massachusetts League of Community Health Centers. These three practices collectively serve >1.4 million patients ( $\cong 20\%$  of the Massachusetts population) and are broadly representative of the state.<sup>8</sup>

### Measures

Eligible patients included individuals of all ages with positive genital or extra-genital culture or nucleic acid amplification tests for *C. trachomatis* between January 1, 2010, and December 31, 2015. Both genital and extra-genital infections were included because both serve as reservoirs for persistent transmission within sexual networks. The frequency, timing, and results of all subsequent chlamydia tests within 1–365 days after the index positive test were assessed. If a patient had more than one positive test in a 12-month period, then the first positive result was used as the index infection. A patient could contribute multiple cases to the analysis if they had positive tests >12 months apart.

### Statistical Analysis

The annual frequencies of on-time tests-of-cure in pregnant females at 3–5 weeks and delayed tests-of-cure at 6–7 weeks after an index positive test result were calculated. On-time tests-of-reinfection at 8–16 weeks and late tests-of-reinfection at 17–52 weeks were also assessed. The annual percentage of non-pregnant females and males with early test-of-reinfection at 3–7 weeks, on-time test-of-reinfection at 8–16 weeks, and late test-of-reinfection 17–52 weeks after the index infection were also calculated, along with the frequency of non-recommended early testing

<3 weeks after an index infection and the percentage of repeat tests that were positive.

Temporal trends in repeat testing and positivity rates were evaluated using binomial regression models with generalized estimating equations accounting for clustering by patient and incorporating an independence working correlation structure.<sup>11</sup> The quasi-likelihood under the independence model criterion was used to select between flexible and linear models.<sup>12</sup> The flexible model included relative risk (RR) estimates for each year versus 2010. The linear model assumed a constant linear RR for each year compared with the preceding year. The model with the smallest quasi-likelihood under the independence model criterion was chosen as the best balance between goodness of fit and overfitting. This activity was reviewed by the Harvard Pilgrim Health Care Institute IRB and deemed exempt because data were collected and analyzed for the purpose of public health surveillance. Data extraction and analysis were performed during calendar years 2017 and 2018.

## RESULTS

Between 2010 and 2015, a total of 15,223 patients had 16,254 positive *C. trachomatis* tests. Of these, 972 (6%) were pregnant females, 10,309 (63%) were non-pregnant females, and 4,973 (31%) were males. The median time to repeat testing was lowest in pregnant females, intermediate in non-pregnant females, and longest in males (Figure 1).

Repeat testing was performed within 1 year in 87% of pregnant female cases but on-time test-of-cure 3–5 weeks after the index infection was only performed in 37% of pregnant females. Likewise, on-time test-of-reinfection was only performed within 8–16 weeks of the index infection in 39% of pregnant female cases (Table 1). There was no change between 2010 and 2015 in the annual percentage of pregnant females receiving a test-of-cure at 3–5 weeks (RR=1.01, 95% CI=0.97, 1.07; Figure 2, linear model). There was a decrease in the annual percentage of pregnant cases with a test-of-reinfection at 8–16 weeks (RR=0.95, 95% CI=0.90, 0.99; Figure 2, linear model).

Repeat testing within 1 year was performed in 68% of non-pregnant female cases and 41% of male cases. Only 18% of non-pregnant females and 9.0% of males had a test-of-reinfection within the recommended time interval of 8–16 weeks. There was no change between 2010 and 2015 in the annual percentage of non-pregnant female cases with a test-of-reinfection at 8–16 weeks (RRs for each year relative to 2010 were nonsignificant except for 2012; Figure 2, flexible model) or in the annual percentage of male cases with a test-of-reinfection at 8–16 weeks (RR=1.02, 95% CI=0.97, 1.08; Figure 2, linear model).

Test-of-cure for pregnant females 3–7 weeks after the index test was positive in 13% of cases. Test-for-reinfection at 3–52 weeks was positive in 16% of pregnant

**Table 1.** Repeat Testing Among Pregnant *Chlamydia trachomatis*–Infected Cases in Three Large Multispecialty Clinical Care Practices in Massachusetts (2010–2015)

Test type and time interval	Pregnant female cases, n (%) <sup>a</sup>
Not retested within 1 y	128 (13.2)
Retested within 1 y	844 (86.8)
Retested early	
Repeat test <3 wks	108 (11.1)
Test-of-cure	
Repeat test 3–5 wks <sup>b</sup>	358 (36.8)
Late repeat test 6–7 wks	114 (11.7)
Test-of-reinfection	
Repeat test 8–16 wks <sup>c</sup>	381 (39.2)
Late repeat test 17 wks–1 y	282 (29.0)
Test-of-cure and test-of-reinfection	
Repeat test 3–5 wks <sup>b</sup> and repeat test 8–16 wks <sup>c</sup>	116 (11.9)
Repeat test 3–7 weeks and repeat test 8 wks–1 y	318 (32.7)
Positive repeat test 3 wks–1 y <sup>d</sup>	130/817 (15.9)

Note: Percentages may not add to 100%, as a case may contribute to multiple categories.

<sup>a</sup>N=972 unless otherwise noted.

<sup>b</sup>Recommended time period for test-of-cure.

<sup>c</sup>Recommended time period for test-of-reinfection.

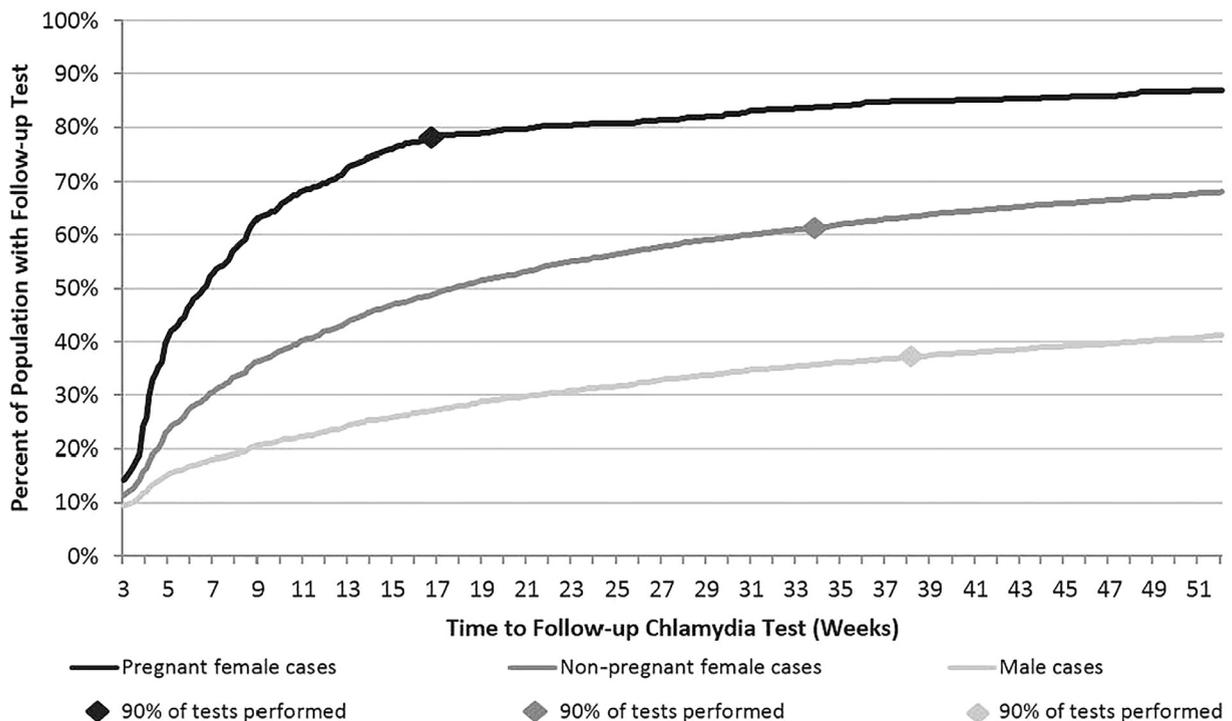
<sup>d</sup>Percentage calculated among the subset of patients with a repeat test within 3 weeks to 1 year.

female cases, 15% of non-pregnant female cases, and 16% of male cases (Tables 1 and 2). There was a significant decrease in the percentage of pregnant cases with positive repeat tests from 2010 to 2015 (RR=0.81, 95% CI=0.74, 0.89; linear model). There was no significant change in the percentage of positive repeat tests amongst non-pregnant female cases (RR=0.97, 95% CI=0.93, 1.00; linear model) or male cases (RR=0.95, 95% CI=0.89, 1.01; linear model).

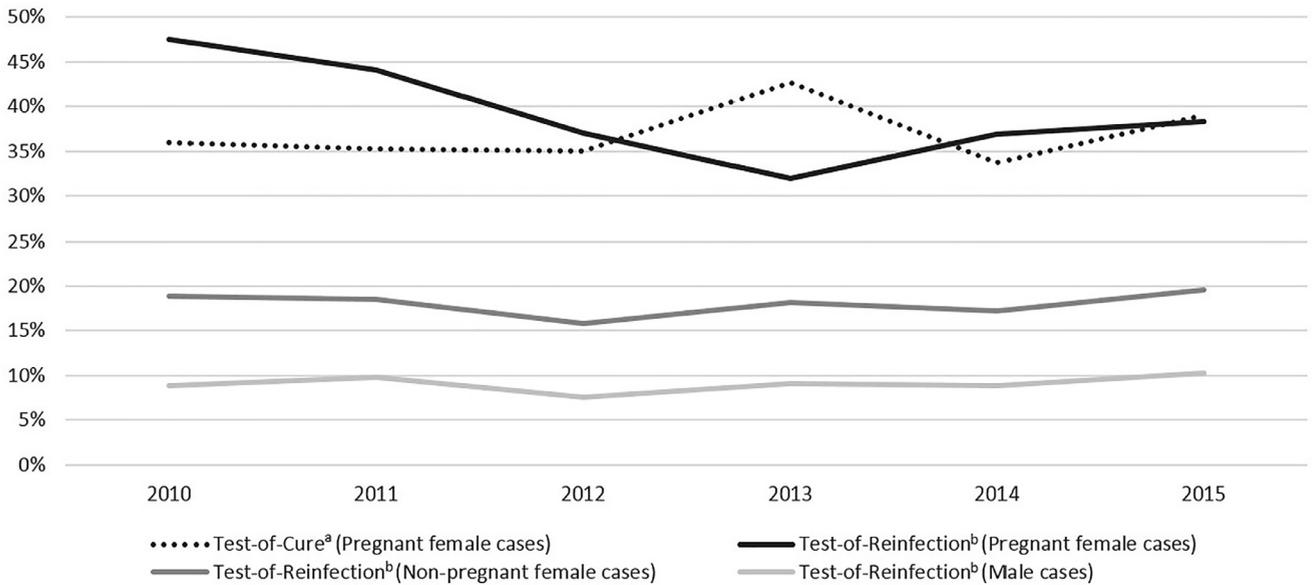
Early repeat testing at <3 weeks occurred in 9.3% of cases: 11% of pregnant female cases, 10% of non-pregnant female cases, and 8.5% of male cases. Repeat tests performed at <3 weeks were positive in 26% of cases.

## DISCUSSION

Guidelines advocate chlamydia test-of-cure for all pregnant women to protect their newborns and test-of-reinfection for all patients to protect the reproductive health of patients and their partners and to mitigate ongoing transmission within sexual networks.<sup>13,14</sup> Tests-of-cure and tests-of-reinfection within recommended timeframes were low and static from 2010 to 2015 among a diverse population of patients in Massachusetts. Only one third of pregnant patients received a test-of-cure within 3–5 weeks and less than 40% received a test-of-reinfection at 8–16 weeks. Only when extending the



**Figure 1.** Cumulative incidence curve for time to first follow-up chlamydia test by gender and pregnancy status in three large multispecialty clinical care practices in Massachusetts (2010–2015).



**Figure 2.** Percent of *Chlamydia trachomatis* cases retested within recommended time period by year in three large multispecialty clinical care practices in Massachusetts (2010–2015).

<sup>a</sup>Test-of-cure includes repeat tests occurring 3–5 weeks after the index positive test, regardless of whether a test-of-reinfection occurs.

<sup>b</sup>Test-of-reinfection includes repeat test occurring 8–16 weeks after the index positive test. For pregnant women, tests are included regardless of whether a test-of-cure occurred.

surveillance window to 1 year did the percentage of pregnant females receiving a repeat test reach 87%. Similarly, only 18% of non-pregnant female cases and 9% of male cases received a test-of-reinfection at 8–16 weeks. There were no improvements over time.

**Limitations**

This study has several limitations. Study estimates of repeat positivity may be unduly low if repeat tests were performed outside the practice group that performed the index positive test because ESP only links patients within

a single practice group. Conversely, estimates of repeat positivity rates may have been inflated if patients with persistent symptoms or additional high-risk exposures preferentially returned for repeat testing. Pregnancy status may have been misclassified for some patients without electronic health record indicators of pregnancy (estimated delivery date, actual delivery date, diagnosis codes for pregnancy and delivery) and it is possible that patients’ providers did not know of their patient’s pregnancy status at the time of the index positive test. Finally, these results may not be representative of the

**Table 2.** Repeat Testing Among Non-pregnant *Chlamydia trachomatis*–Infected Cases in Three Large Multispecialty Clinical Care Practices in Massachusetts (2010–2015)

Test type and time interval	Non-pregnant female cases, <sup>a</sup> n (%)	Male cases, <sup>b</sup> n (%)
Not retested within 1 y	3,285 (31.9)	2,923 (58.8)
Retested within 1 y	7,024 (68.1)	2,050 (41.2)
Retested early		
Repeat test <3 wks	978 (9.5)	424 (8.5)
Test-of-reinfection		
Early repeat test 3–7 wks	2,573 (25.0)	570 (11.5)
Repeat test 8–16 wks <sup>c</sup>	1,841 (17.9)	449 (9.0)
Late repeat test 17 wks–1 y	2,245 (21.8)	783 (15.7)
Positive repeat test 3 wks–1 y <sup>d</sup>	974/6,659 (14.6)	293/1,802 (16.3)

Note: Percentages may not add to 100%, as a case may contribute to multiple categories.

<sup>a</sup>N=10,309 unless otherwise noted.

<sup>b</sup>N=4,973 unless otherwise noted.

<sup>c</sup>Recommended time period for test-of-reinfection.

<sup>d</sup>Percentage calculated among the subset of patients with a repeat test within 3 weeks to 1 year.

state population as a whole, as the study was limited to patients receiving care with participating clinical partners.

## CONCLUSIONS

There is considerable under-testing-for-cure in pregnant females and for reinfection in all patients during recommended time periods. These findings are consistent with reports from other jurisdictions.<sup>15–21</sup> Notwithstanding pilot projects demonstrating potential interventions to increase repeat chlamydia testing,<sup>22–26</sup> substantial work still needs to be done to translate guideline recommendations into routine practice.

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## SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at <https://doi.org/10.1016/j.amepre.2018.10.006>.

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