Impact of an Electronic Medical Record Best Practice Alert on Expedited Partner Therapy for Chlamydia Infection and Reinfection

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Background. Atrius Health implemented a best practice alert (BPA) to encourage clinicians to provide expedited partner therapy (EPT) in October 2014. We assessed (1) the impact of the BPA on EPT provision and chlamydial reinfection and (2) the impact of EPT on testing for chlamydial reinfection and reinfection rates.

Methods. We included patients ≥15 years with ≥1 positive chlamydia test between January 2013 and March 2019. Tests-of-reinfection were defined as chlamydia tests 28–120 days after initial infection, and corresponding positive results were considered evidence of reinfection. We used interrupted time series analyses to identify changes in (1) frequency of EPT, (2) tests-of-reinfection, and (3) reinfections after the BPA was released. Log-binomial regression models, with generalized estimating equation methods, assessed associations between (1) EPT and tests-of-reinfection and (2) EPT and reinfection.

Results. Among 7267 chlamydia infections, EPT was given to 1475 (20%) patients. Expedited partner therapy frequency increased from 15% to 22% of infections between January 2013 and September 2014 (β = 0.003, P = .03). After the BPA was released, EPT frequency declined to 19% of infections by March 2019 (β = −0.004, P = .008). On average, 35% of chlamydia infections received a test-of-reinfection and 7% were reinfected; there were no significant changes in these percentages after BPA implementation. Patients given EPT were more likely to receive tests-of-reinfection (prevalence ratio [PR] 1.09; 95% confidence interval [CI], 1.01–1.16) but without change in reinfections (PR 0.88; 95% CI, 0.66–1.17).

Conclusions. Best practice alerts in electronic medical record systems may not be effective at increasing EPT prescribing and decreasing chlamydial reinfection. However, patients given EPT were more likely to receive a test of chlamydia reinfection.

Keywords. antibacterial agents; chlamydia; electronic health records; expedited partner therapy.

Chlamydia trachomatis is the most common sexually transmitted infection (STI) in the United States with 1 758 668 new infections reported in 2018 [1]. Among women, chlamydia infections are associated with cervicitis, urethritis, and proctitis and, if left untreated, can lead to pelvic inflammatory disease and infertility. Chlamydia infections are associated with urethritis, epididymitis, and proctitis among men. All patients with chlamydia infections are at high risk for reinfection if their sexual partners are not treated [2–4].

The traditional approach to partner treatment includes clinical evaluation of the index patient in a healthcare setting and notification of the sexual partner(s) by either the index patient, the provider, or an agent of the provider, such as the local health department. This approach requires sexual partners to seek medical care to be tested and treated, if infected. However, expedited partner therapy (EPT) allows providers to prescribe antibiotics to partners of patients diagnosed with chlamydia without examining or counseling the partner [5]. Expedited partner therapy is often accomplished by patient-delivered partner therapy, whereby clinicians provide their patients with antibiotics to give to their partners, prescribe extra doses of antibiotics in the index patient’s name intended for partners, or write prescriptions with partners’ names [5].

Randomized controlled trials (RCTs) suggest that EPT can reduce chlamydia and gonorrhea reinfection rates compared with traditional partner notification strategies, although the reductions have been greater for gonorrhea infections than for chlamydia [6–8]. In an RCT in King County, Washington, gonorrhea-infected index patients who received EPT had a 73% reduction in gonorrhea reinfection, whereas reinfections for
patients with chlamydia were reduced by 15% [6]. In another RCT of EPT among women infected with chlamydia, there was a trend towards fewer reinfections among women in the patient-delivered partner treatment arm versus the self-referral arm (12% vs 15%; odds ratio 0.80; 95% confidence interval [CI], 0.62–1.05), but it was not statistically significant [8]. The strong signal for EPT on reducing gonorrhea reinfection compared with the equivocal signal for chlamydia reinfection bespeaks the need for more real-world studies on EPT implementation and its impact on chlamydia reinfections.

A challenge to increasing EPT uptake is provider knowledge and reporting. Only one half of pediatric residents surveyed in California reported ever providing EPT for chlamydia or gonorrhea, and 43% of those who provided EPT used it rarely (<10% of treatments) [9]. In a qualitative study of healthcare providers in Pennsylvania, providers believed EPT was beneficial, but most did not use it or know whether their specific institution allowed them to provide it to patients [10]. In Massachusetts, the state legalized EPT for chlamydia infections in 2010 [11]. However, in 2012, 71% of chlamydia case report forms were missing information on EPT, and on forms in which EPT data were captured, only 18% of chlamydia cases were offered EPT [12].

We sought to increase EPT familiarity and provision within a large multisite healthcare system in Massachusetts. To do so, a best practice alert (BPA) in the practice’s electronic health record (EHR) system was implemented in October 2014. When clinicians prescribe medications to treat chlamydia, the BPA screen (Supplemental Figure 1) is automatically triggered and offers the clinician the option of providing EPT through patient-delivered partner therapy. The BPA did not address gonorrhea because Massachusetts regulations only explicitly permit EPT for chlamydia. We hypothesized that integrating an automated alert into the EHR would increase EPT provision and decrease the frequency of chlamydia reinfections in our population.

METHODS

Setting

Atrius Health serves a well insured population of approximately 720,000 people in eastern Massachusetts. In October 2014, Atrius Health implemented the BPA for EPT for patients diagnosed with chlamydia. When clinicians prescribe medications to treat chlamydia, the BPA screen pops up (Supplemental Figure 1) and offers the clinician the option of providing EPT. The alert links to predefined order sets that facilitate dispensing antibiotics for chlamydia in the clinic or providing a written prescription for patients to pass to their partners. Clinicians also have the option to decline to offer EPT. At the time of publication, the BPA has been continuously in place at Atrius since October 2014.

The EHR data from Atrius, including clinicians’ responses to the BPA, were collected via the Electronic medical record Support for Public Health (ESP) system. The ESP is an open-source public health surveillance platform that uses daily extracts of data from EHR systems to identify and report conditions of public health interest to health departments (esphealth.org). The ESP maps EHR data to common terms, analyzes these data for reportable diseases and updates to existing cases, and automatically submits case reports or aggregate summaries to health departments’ electronic surveillance systems [13–18].

Statistical Methods

The first analysis examined the impact of the BPA on the following: (1) the percentage of chlamydia infections provided EPT by prescription or direct dispensing of medication, (2) the percentage of chlamydia infections with a test for chlamydia reinfection between 28 and 120 days after initial infection, and (3) the percentage of chlamydia infections that were retested and had evidence of reinfection. Evidence of reinfection was defined as a positive chlamydia laboratory result between 28 and 120 days after the initial infection. Data on initial chlamydia infections among patients 15 years of age or older were available from January 1, 2013 through March 31, 2019. Subsequent chlamydia laboratory tests were available through July 30, 2019 to allow for 120 days of follow-up.

We performed an interrupted time series analysis to estimate the effect of the BPA on the percentage of chlamydia infections provided EPT, percentage retested for chlamydia, and percentage with evidence of reinfection among those retested. Segmented linear regression models were used to compare the outcomes between January 2013 and September 2014 (time period before the BPA was implemented) to the outcomes between October 2014 and March 2019 (time period that includes BPA implementation and follow-up). We used an autoregressive form of segmented linear regression and tested for the presence of autocorrelation between months using the Durbin-Watson test.

Each regression model estimated 3 coefficients: (1) the slope, or average monthly change in the outcome before the BPA was introduced; (2) the slope, or average monthly change in the outcome after the BPA was implemented; and (3) the change in slope when the BPA was implemented in October 2014.

The second analysis was a patient-level analysis and assessed whether patients with chlamydia who were given EPT were more or less likely to receive a test for chlamydia reinfection or to have evidence of reinfection compared with patients who were not given EPT. Patients who were ≥15 years of age and had 1 or more positive chlamydia laboratory tests between January 1, 2013 and March 31, 2019 were included in this analysis. Tests-of-reinfection were defined as chlamydia testing between 28 and 120 days after the initial infection, and we considered a positive chlamydia test result during this time period as evidence of reinfection.
Log-binomial regression models were used to estimate prevalence ratios (PRs) and 95% confidence intervals (CI) assessing (1) the association between EPT and test-of-reinfection and (2) the association between EPT and reinfection among patients who were retested for chlamydia. We used generalized estimating equation methods to account for patients who had multiple chlamydia infections between January 1, 2013 and March 31, 2019.

The log-binomial regression models were adjusted for covariates of interest that were associated with the primary exposure, EPT, and the outcome of interest, either test-of-reinfection or reinfection. Covariate-exposure and covariate-outcome associations were defined by Wald $\chi^2 P < .10$. Covariates assessed for possible inclusion included the following: sex; race/ethnicity; chlamydia symptoms; pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) prevention; chlamydia, gonorrhea, syphilis, and HIV tests during the past 2 years; HIV or gonorrhea infection at the time of chlamydia diagnosis. Age (in years) on the date of positive chlamydia test was categorized as 15–24, 25–34, 35–44, and ≥45. Race/ethnicity was categorized as Non-Hispanic White, Non-Hispanic Black, Hispanic, Non-Hispanic Other. The “Other” race/ethnicity category included Asian, American Indian, Native America, Alaskan Native, and races recorded as other or unknown. Chlamydia symptoms were defined by at least 1 diagnosis code for fever, urethral discharge, urethritis, vaginitis, cervicitis, vaginal leukorrhea, or abdominal pain recorded up to 14 days before or 30 days after a positive chlamydia test. The complete list of International Classification of Diseases, Ninth Revision (ICD-9) and ICD-10 codes for chlamydia symptoms are in Supplemental Table 1. Pre-exposure prophylaxis use was measured during the 2 years before the positive chlamydia test and defined as 2 or more prescriptions for emtricitabine/tenofovir disoproxil fumarate 2 or more months apart while HIV status was negative. The total number of chlamydia, gonorrhea, syphilis, and HIV tests and chlamydia, gonorrhea, and syphilis diagnoses during the 2 years before each positive chlamydia laboratory test were counted for each patient. Data on STI tests and diagnoses were available from January 1, 2011 for all patients. Age, sex, race/ethnicity, chlamydia symptoms, PrEP, previous bacterial STI tests, previous chlamydia diagnoses, and evidence of HIV or gonorrhea coinfection were included in the model assessing the association between EPT and test-of-reinfection. The model assessing the association between EPT and reinfection among retested patients was adjusted for age, sex, race/ethnicity, and PrEP.

The final analyses assessed whether there were differences in test-of-reinfection and evidence of reinfection by type of EPT received, ie, prescription for EPT or medications to give directly to partners, and by sex. Log-binomial regression models with generalized estimating equation methods were used to estimate PRs and 95% CIs. Each model was adjusted for covariates associated with both the exposure and outcome; the specific covariates are provided in Supplemental Tables 4–6. All data analyses were conducted with SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Between January 2013 and March 2019 there were 7267 laboratory-confirmed chlamydia infections among 6751 unique patients (Table 1, Supplemental Table 2). Of these, 1475 (20.3%) were provided EPT, 1363 (92.4%) patients with an infection were given a prescription for partners, and 112 (7.6%) were provided medication for partners. Two thirds of all chlamydia infections were among patients 15 to 24 years of age (62.6%). Approximately half of infections were in non-Hispanic whites (50.2%) and 23.8% were in non-Hispanic blacks. Most infections were among females, but a higher percentage of infections that received EPT were female (80.8% vs 63.3% of infections not receiving EPT). Pregnancy was also more common among chlamydia infections that received EPT (7.0% vs 2.9% of infections not receiving EPT). Approximately one quarter of chlamydia infections had concurrent coding for symptoms compatible with chlamydia, and tests in the 2 years before chlamydia infection were common (28.9% with 1 chlamydia test in the preceding 2 years, 27.4% with ≥2 chlamydia tests in the preceding 2 years). Most chlamydial infections were genital; however, 1.4% were rectal and 0.2% were pharyngeal. Gonorrhea and HIV coinfections and PrEP use were less common among infections that received EPT (1.0%, 0.1%, 1.3%, respectively, vs 2.5%, 0.9%, 2.0%, respectively, among infections not receiving EPT).

Before the BPA release, EPT prescription frequency increased from 15.3% of chlamydia infections in January 2013 to 22.3% of chlamydia infections in September 2014 ($\beta = 0.003, P = .03$) (Figure 1). The estimated percentage of chlamydia infections provided EPT increased slightly to 23.3% when the BPA was implemented in October 2014 ($\beta = 0.01, P = .64$). Thereafter, there was a decrease in EPT frequency, and by March 2019 only 18.7% of chlamydia infections were provided EPT ($\beta = -0.004, P = .008$).

On average, 35.0% of chlamydia infections had a corresponding test-of-reinfection between January 2013 and September 2014 ($\beta = -0.0008, P = .67$). This declined to 30.4% when the BPA was implemented in October 2014 ($\beta = -0.04, P = .13$). There was no change in the percentage of chlamydia infections with a test-of-reinfection between October 2014 and March 2019 ($\beta = 0.003, P = .17$) (Figure 2).

Before the BPA was implemented, 7.2% of chlamydia diagnoses with a test-of-reinfection had evidence of reinfection ($\beta = 0.0002, P = .94$). Immediately after the BPA was introduced in October 2014, the percentage of patients with
The estimated average percentage of infections with evidence of reinfection between October 2014 and March 2019 was 12.1% ($\beta = 0.0001$, $P = .95$) (Figure 3). The patient-level analysis assessed whether EPT was associated with tests-of-reinfection and evidence of reinfection. Approximately 41.2% of patients who received EPT and 33.8% of patients who were not provided EPT received a test-of-reinfection, respectively (Supplemental Table 3). After adjusting for demographic and clinical characteristics, patients who received EPT were more likely to receive a test-of-reinfection (PR 1.09; 95% CI, 1.01–1.16). Among patients who received a test-of-reinfection, the percentage with evidence of reinfection was 9.0% among patients given EPT versus 11.2% among patients without a prescription or medication for EPT. However, after adjusting for demographic and clinical characteristics, there was no difference in chlamydia reinfections among patients who did and did not receive EPT (PR 0.88; 95% CI, 0.66–1.17). When we stratified these analyses by sex, females who received EPT were more likely to receive a test-of-reinfection compared to those who did not receive EPT (PR 1.09; 95% CI, 1.01–1.17) (Supplemental Table 4). Among males, those who received EPT were more likely to receive a test-of-reinfection, but the results were not statistically significant (PR 1.18; 95% CI, 0.97–1.43) (Supplemental Table 5). There were no differences in chlamydia reinfections among those who did and did not receive EPT when stratified by sex.
also had similar rates of reinfection compared to patients who received a prescription (PR 1.15; 95% CI, 0.49–2.68).

**DISCUSSION**

Increasing the use of EPT has been identified as a key strategy to protect patients from the possible adverse consequences of gonorrhea and chlamydia reinfection and to decrease the population burden of these conditions by interrupting transmission in sexual networks [5, 19, 20]. However, there is a pressing need to identify effective strategies for EPT implementation. We hypothesized that integrating an automated alert into the EHR to facilitate prescribing EPT within providers’ natural workflows would increase EPT provision and decrease the frequency of reinfections in our population. Instead, we found that although EPT provision rates were rising before we instituted the BPA, there was no significant improvement in EPT provision after introduction of the BPA and, in fact, EPT prescribing rates declined. Similarly, there were no changes in testing for chlamydia reinfections or frequency of reinfections after the BPA was released.

We found that patients provided EPT were more likely to receive a test-of-reinfection within recommended time frames than those who were not given EPT. These results were also consistent when we stratified by patient sex. Whether this reflects an effect of the BPA, indicates that providers who prescribe EPT are more compliant with repeat testing recommendations, or signifies that patients given EPT are considered high risk and followed more closely is unclear. We also found that more than 90% of the chlamydia infections provided EPT were given a prescription for sexual partners rather than medications. We did not identify an association between the mechanism of EPT (provision of prescriptions versus medications for partners) and the frequency of tests-of-reinfection or evidence of reinfection.

Our findings of no significant improvement in EPT provision after introduction of the BPA may be due to limited educational efforts to support the BPA. Before the BPA was implemented at Atrius, a specialty lecture on STI treatment in primary care was given, and EPT was addressed during the lecture. The lecture was not mandatory for providers, but continuing medical education credits were provided to incentivize attendance. A
clinical standards committee, which includes several active providers, also reviewed the BPA before it was implemented. It is possible that this lecture and review led to the increase in EPT provision before the BPA was implemented. After instituting the BPA, the Massachusetts Department of Public Health provided several educational presentations during the follow-up period of our analysis, and EPT and the BPA were discussed during these too. Providers who attended the Department of Public Health presentations were also asked to complete surveys about EPT and the BPA. Overall, 95% of survey respondents had seen the BPA and 86% agreed that it reminded them to offer EPT to their patients. However, only 37 of the more than 750 providers at Atrius attended at least 1 of these presentations and responded to the survey. Therefore, the information provided in the BPA was likely the only additional information on EPT most providers received after it was implemented.

In the future, providing more EPT training and soliciting feedback from providers may increase the impact the BPA has on EPT provision and chlamydial reinfections. Other clinical practices have reported positive changes associated with BPAs including higher rates of recognition of pediatric hypertension and higher screening rates for hepatitis C [21, 22]. Both of these initiatives were accompanied by educational materials and included feedback sessions to elicit suggestions and encourage acceptance by frontline staff. Soliciting feedback from providers about the medical or social complexity of patients who have positive chlamydia results and the frequency of alerts may help overcome alert fatigue associated with BPAs as well [23].

Increasing EPT provision and reducing chlamydial reinfections in our setting may also have been limited due to cultural and logistical challenges that the BPA could not address. The stigma associated with STI creates reluctance among patients and providers to discuss sexual health and sexual partners [24]. Providers may be hesitant to offer EPT because they want to meet partners and provide counseling or have concerns over liability [25], particularly among clinicians treating men who have sex with men. The 2015 Sexually Transmitted Disease Treatment Guidelines recommend against routinely using EPT for men who have sex with men due to the risk of missing HIV infection if patients’ partners are not evaluated [19]. There are
additional challenges for patients who receive a prescription for EPT, rather than antibiotics to give directly to their partners. Potential embarrassment [26], pharmacists’ refusal to fill prescriptions without patient identifiers [27], and out-of-pocket expenses when a partner does not have insurance or when an index patient’s insurance does not cover multiple doses of treatment [28] may preclude the prescription from being filled. Even when cost barriers are removed, less than half of EPT prescriptions are filled [29].

Several limitations should be considered when interpreting this study. First, this is an observational study and there may be residual or unknown confounders biasing the results, particularly when assessing chlamydial reinfections. For example, we did not account for site of infection in the log-binomial model due to small numbers of extragenital infections. Recent data suggest that undiagnosed extragenital infections (eg, concurrent rectal infections in women) are incompletely treated by single-dose azithromycin (which was standard of care at the time this study was done), and this may account for some of the EPT failures we observed [30, 31]. Other potential confounders such as the number of sexual partners for each index patient, which could affect risk for reinfection, were not available.

Second, only 35% of our study population received a test-of-reinfection within the recommended time frame. Small sample size in our analyses examining chlamydial reinfections among patients who were retested may have prevented us from seeing statistically significant effects. Third, these data were derived from a single healthcare system. Therefore, patients could have been provided EPT or received testing for chlamydia reinfections at other facilities. In addition, chlamydia infections, EPT provision, and retesting within this 1 facility may not be representative of other healthcare systems in Massachusetts or other jurisdictions. We also did not account for the clinical settings in which patients received care for chlamydia and were not able to determine whether there were significant changes in EPT provision in certain settings such as pediatric care, obstetrics/gynecology, or primary care practices, after the BPA was implemented.

Figure 3. Effect of the electronic best practice alert (BPA) on chlamydia reinfections between 28 and 120 days after diagnosis, Atrius Health, January 1, 2013 through March 31, 2019. The open circles represent the observed percentages of chlamydia diagnoses that had a test and evidence of reinfection 28 to 120 days after initial infection. The solid black line represents the linear trend before the BPA was implemented, and the dotted black line represents the linear trend after implementation.

Slope before BPA: $\beta = 0.0002$, $P = .94$
Level change: $\beta = 0.04$, $P = .14$
Slope after BPA: $\beta = 0.0001$, $P = .95$
Despite these limitations, we believe this study from a large healthcare system in eastern Massachusetts provides data on the implementation and effectiveness of a BPA for EPT in a real-world setting. We observed that 1 in 5 chlamydia infections were provided EPT, and this was done predominantly via prescription rather than direct provision of medication to deliver to partners. The study also demonstrates how data from EHRs may assist health departments overcome current challenges in measuring how often and to which patients EPT is provided in their jurisdiction.

CONCLUSIONS

Expedited partner therapy provision declined after introducing a BPA to facilitate EPT prescribing for patients with positive chlamydia tests. Best practice alerts by themselves may not be effective at sustaining awareness of EPT. Regular provider trainings related to EPT, in conjunction with the BPA, may increase EPT provision among clinicians. However, patients given EPT were more likely to receive a test-of-reinfection, but there were no differences in chlamydial reinfections.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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