HHS Public Access

Author manuscript

Public Health. Author manuscript; available in PMC 2019 October 18.

Published in final edited form as:

Public Health. 2017 June ; 147: 101–108. doi:10.1016/j.puhe.2017.02.012.

State-level gonorrhea rates and expedited partner therapy laws: insights from time series analyses

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Abstract

Objective: In this study, we examined state-level monthly gonorrhea morbidity and assessed the potential impact of existing expedited partner therapy (EPT) laws in relation to the time that the laws were enacted.

Study design: Longitudinal study.

Methods: We obtained state-level monthly gonorrhea morbidity (number of cases/100,000 for males, females and total) from the national surveillance data. We used visual examination (of morbidity trends) and an autoregressive time series model in a panel format with intervention (interrupted time series) analysis to assess the impact of state EPT laws based on the months in which the laws were enacted.

Results: For over 84% of the states with EPT laws, the monthly morbidity trends did not show any noticeable decreases on or after the laws were enacted. Although we found statistically significant decreases in gonorrhea morbidity within four of the states with EPT laws (Alaska, Illinois, Minnesota, and Vermont), there were no significant decreases when the decreases in the four states were compared contemporaneously with the decreases in states that do not have the laws.

Conclusion: We found no impact (decrease in gonorrhea morbidity) attributable exclusively to the EPT law(s). However, these results do not imply that the EPT laws themselves were not effective (or failed to reduce gonorrhea morbidity), because the effectiveness of the EPT law is dependent on necessary intermediate events/outcomes, including sexually transmitted infection service providers' awareness and practice, as well as acceptance by patients and their partners.

Keywords

Expedited partner therapy; Law; Gonorrhea; Time series analysis

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Competing interests

None declared.

Ethical approval

No institutional review board (IRB) approval was required because only secondary data were used.

Introduction

Gonorrhea is the second most commonly reported bacterial sexually transmitted infection (STI) in the United States (US).[1] The overall burden of gonorrhea was estimated at over 800,000 new cases in 2008 costing over $162 million (in 2010 US dollars) in direct lifetime medical expenses.[2,3] In women, untreated gonorrhea can cause pelvic inflammatory disease and can develop into more costly and complicated sequelae such as chronic pelvic pain, ectopic pregnancy, and tubal infertility.[4] In men, untreated gonorrhea can cause epididymitis and prostatitis.[4] Thus, the importance of early identification of infected individuals followed by adequate treatment cannot be overstated.

One way to quickly reach and treat potentially infected individuals is the expedited partner therapy (EPT)—a partner management procedure in which medication or prescription is provided to the partner of a patient who tests positive for chlamydia or gonorrhea without previous medical/physical evaluation or prevention counseling of the partner.[5,6] Studies have reported the potential effectiveness of EPT in reducing STIs,[7,8] including randomized controlled trials.[9–11] In addition, EPT is associated with higher percentages of partners treated than other forms of partner notification,[12] and has been shown to be cost-effective under some conditions.[13] Because of its potential effectiveness, EPT has been recommended by the Centers for Disease Control and Prevention (CDC) and other national organizations.[5,14–16] Consequently, just over 50% (n = 26) of the states in the US have enacted laws at different times (mostly within the past decade) that permit EPT for specific STIs (i.e. both chlamydia and gonorrhea or chlamydia only) or non-specific STIs (i.e. ‘the treatment of sexually transmitted disease’).[17,18]

A study of local health departments in high-STI morbidity areas across the country found that partner notification interviews were conducted in <20% of gonorrhea cases with notable variation across geographic regions, suggesting that partner treatment rates in the absence of EPT are low.[19] Effective EPT can potentially reduce transmission by substantially reducing the duration of infectiousness which will eventually reduce the overall burden within the communities or jurisdictions where EPT is practiced. Thus, the objective of this study was to examine state-level gonorrhea morbidity over time and assess the potential impact of existing EPT laws in relation to the time that the laws were enacted (i.e. effective date).

Methods

Study design

We designed a longitudinal study that examined and compared monthly gonorrhea rates within and across all 50 states and the District of Columbia in the US over specified time periods.

Data

We obtained monthly gonorrhea rates (number of cases/100,000) for male, female, and both sexes (total) from January 1995 to December 2014 (where available) for each state and the District of Columbia, a total of 51 geographic units, from national STI surveillance data. For the purpose of this study, the District of Columbia was considered a state. However, monthly

data were not available for all the states over the entire period. For instance, monthly gonorrhea rates data were not available for California and Arizona before January 2002 and January 2003, respectively. Next, based on the findings from Hodge et al.,[17,18] we summarized and merged state-level information on EPT laws and policies as of December 2014.

Visual examination

In the first part of our analyses, we created charts of the data—monthly morbidity (number of gonorrhea cases/100,000 residents) for all the 51 states. We then included a vertical line representing the time of the intervention (i.e. the month in which EPT law was effective) for the states with the laws. This enabled us to visually examine the changes over time in relation to the changes that occurred at and/or after the law was enacted for the states with the law (experimental group). In addition, it enabled us to visually examine the changes over time for the states that did not have the law (control group). Finally, the charts assisted us in the time series model specification, including when (which month) to apply the expected changes as most changes might be realized sometime after the dates/months in which the EPT laws were enacted.

Although we used data on the burden of gonorrhea, we did not focus our impact analyses on only the states with gonorrhea-specific EPT laws in our analyses. We included all the states that enacted any form of law—explicitly permitting EPT for gonorrhea and chlamydia, for chlamydia only, or for STIs in general terms. First, given the recommendation for presumptive dual treatment of patients with either gonorrhea or chlamydia,[5] there was the potential for spillover impact—EPT for chlamydia resulting in treatments for gonorrhea as well. That was why we included states with EPT laws for chlamydia only as well. Second, there was the potential for EPT for STIs in general to also impact gonorrhea rates. Finally, we separately examined the potential for a relatively higher and/or noticeable impact of the EPT laws for three of the states (Arkansas, Illinois and Louisiana) in which EPT was prohibited prior to the dates/months that their EPT laws were enacted.

Initially, we planned to assess the impact of the EPT laws for a total of 26 states that had some form of the EPT law as of December 2014. However, we could not include California in the experimental group because the monthly gonorrhea morbidity data for California was available from January 2002, although their EPT law was enacted in January 2001. As a result, California was included in the control group. Due to the large number of states, we showed miniature charts for the states in the experimental group only ($n = 25$).

Statistical analyses

Next, we used a panel time series approach to statistically examine the potential impact of the EPT laws on gonorrhea morbidity across the states. Based on the structure of our data, we used an autoregressive time series model in a panel format and applied an intervention (interrupted time series) analysis based on the months in which the EPT laws were enacted. Panel data analyses have several advantages, including higher variability and degrees of freedom while minimizing multi-collinearity concerns.[20–22] In addition, beside examining and testing the difference in the burden of the disease before and after the laws were enacted

within each state, it was equally important to examine and test the changes that occurred in the experimental group with the contemporaneous changes in the control group. This was because if another state that did not have any EPT law showed analogous change(s) in gonorrhea morbidity at or around the same time, then the change(s) in the state with the EPT law cannot be ascribed exclusively to the EPT law. As a result, we used a mixed model approach by exploring both fixed effects (within state) and random effects (within and across states).

We transformed the monthly gonorrhea morbidity data into natural logs. This was done to reduce/stabilize the variance. Also, log transformation allowed easy interpretation of the results. Next, because the panel was unbalanced, we applied the Fisher-type unit root test with a Dickey-Fuller option to determine stationarity of the data.[21,23] It was determined that at least one of the series was stationary. So we analyzed the data in levels—differencing was not required.

We then went through a comprehensive exploratory process to determine the autoregressive (the significant lags) determinants of the series. We included categorical variables to determine intercept shifters (instant changes) and slope changes (gradual change). Below is a summarized mathematical representation of our final model.

$$R_{st} = \sum_{i=1}^{p} \beta_i R_{st-i} + \delta_{s*} D_{s*t} + \phi_{s*} T_{s*t} + \varepsilon_{st}$$

Where R was the log of gonorrhea rate (number of cases/100,000 residents) for state s in month t regressed on lags i through p; β was the autoregressive coefficients for each lag i; D was assigned 0 before and 1 after the effective month for all the states with EPT law (experimental group) based on the respective months in which the laws were enacted; * represents the states in the experimental group; D was assigned 0 for the entire period for all the states in the control group; thus, the estimated coefficient associated with D (δ) was the coefficient of the intercept shifter (instant change) for the states in the experimental group; Consequently, δ measured the change in gonorrhea morbidity after the EPT law; T was assigned 0 before the month the law was enacted and was continuous starting at 1 through the end of period after the month the law was enacted for the states that had the law; T was assigned 0 for the entire period for the states without the EPT law (control group). Thus, the associated coefficient (ϕ) measured the change in slope (slope) after the laws went into effect for the states in the experimental group; ε is the error term. Given that there might be delays in the impact of the EPT laws, we explored delayed changes by varying the month of the intervention (the month the laws were enacted) up to 12 ahead, where applicable.

Given that there is substantial heterogeneity among the control states which might confound our results, we assumed that states within each census subregion were similar (or less heterogeneous). Thus, we conducted subregion-specific analyses for all the subregions that had at least one state that had EPT (i.e. New England, Middle Atlantic, East North Central, West North Central, East South Central, West South Central, Mountain and Pacific). See the footnote for Fig. 1 for more details. The South Atlantic subregion was not included because

there were no states with EPT law(s). By this approach, we were comparing each of the states with EPT law(s) with only the states within the same subregion that did not have the laws. As an example, in the East North Central subregion, Wisconsin, Illinois, and Indiana (experimental group) were compared with Ohio and Michigan (control group).

Because the dependent variable in the panel regression analyses was the natural log of gonorrhea morbidity and the instant change variable (D) was categorical, the resulting coefficients (δ) were transformed as $(e^{\delta} - 1)*100$ and interpreted as the relative decrease (in percentages) in gonorrhea morbidity after the intervention.[24]

We used Microsoft Excel, version 2010 (Microsoft Corporation, Redmond, Washington) for data organization and for producing the charts. All the statistical analyses (including panel model identification, estimation, and evaluation) were conducted using STATA version 11.2 (StataCorp LP, College Station, Texas).

Results

Drawing from Hodge et al.'s findings,[17] Fig. 1 depicts a summary of the state EPT law categories that we used as described in the methods. As of December 2014, approximately 51% ($n = 26$) of the states had some form of EPT law for STI(s) and the remaining 49% ($n = 25$) did not have any EPT law. Of the 26 that had some form of EPT law, seven of them (Alaska, Arizona, Maine, Massachusetts, North Dakota, Oregon, and Texas) were laws explicitly permitting EPT for STIs in general terms (i.e. 'the treatment of sexually transmitted disease'[17,18]); three of the 26 states had laws explicitly permitting EPT for chlamydia only (New York, Tennessee, and Vermont); the remaining 16 (Arkansas, California, Connecticut, Hawaii, Idaho, Illinois, Indiana, Iowa, Louisiana, Minnesota, Missouri, Nebraska, New Mexico, Rhode Island, Utah, and Wisconsin) had EPT laws explicitly permitting both gonorrhea and chlamydia (see Fig. 1). Finally, among the 16 states that had EPT laws explicitly permitting both gonorrhea and chlamydia, three of them (Arkansas, Illinois and Louisiana) prohibited EPT before the enactment of the laws (see Fig. 1).

The miniature charts showing the monthly burden of gonorrhea (males, females, and total) are presented in Fig. 2, panels a through y. As mentioned in the methods, we showed gonorrhea morbidity trends for the states in the final experimental group only ($n = 25$). The remaining charts are available from the lead author. The vertical lines depicting the effective months of the laws represent the earliest month that we believe any change attributable to the laws could be realized. Thus, when the effective date was close to or within the last week of the month, the vertical line was placed in the following month as depicted in Arizona (Fig. 2b), Indiana (Fig. 2h), Louisiana (Fig. 2j), Missouri (Fig. 2n), New York (Fig. 2q), Rhode Island (Fig. 2t), Texas (Fig. 2v), and Wisconsin (Fig. 2y).

Visual examination

Our thorough visual examination of the monthly gonorrhea morbidity showed that periods of change in monthly gonorrhea incidence (increases as well as decreases) were common in states both before and after the EPT laws were enacted. In most states, however, there were

no noticeable decreases in the burden of gonorrhea on or after the laws were enacted. In fact, in some cases, gonorrhea morbidity increased markedly on or after the effective month (see Arizona [Fig. 2b], Maine [Fig. 2k], Massachusetts [Fig. 2l], New York [Fig. 2q], and North Dakota [Fig. 2r]). In Alaska (Fig. 2a) and Minnesota (Fig. 2m), an initial decrease in gonorrhea morbidity was observed sometime around the effective date. However, this initial decrease was followed by an almost equivalent increase in the following months. The rest of the states did not show any visible (and sustained) decrease on or after the respective months in which the laws were enacted. The exception was the trend for Illinois which showed the most graphically apparent sustained decrease in the burden of gonorrhea around the month that the law was enacted. Based on the Illinois data, the EPT law was enacted on the first of January 2010 and the total gonorrhea rate (number of cases/100,000) decreased by approximately 40% within 2 months—from 142 in December of 2009 to 85 in February of 2010 which was also the lowest rate over the entire period (Fig. 2g).

The charts also showed that among the 25 states in the experimental group, the majority (n = 16) revealed marked upward trends—three-fold increases in some cases—in monthly gonorrhea morbidity, which decreased substantially over several months in some cases before the laws were enacted. Essentially, the laws were enacted in the periods of low gonorrhea morbidity. The steep upward trends are depicted by the bold slanted trend lines shown in the charts for Alaska (Fig. 2a), Arizona (Fig. 2b), Hawaii (Fig. 2e), Idaho (Fig. 2f), Iowa (Fig. 2i), Louisiana (Fig. 2j), Maine (Fig. 2k), Massachusetts (Fig. 2l), Minnesota (Fig. 2m), Missouri (Fig. 2n), New Mexico (Fig. 2p), Oregon (Fig. 2s), Rhode Island (Fig. 2t), Texas (Fig. 2v), Utah (Fig. 2w), Vermont (Fig. 2x), and Wisconsin (Fig. 2y). In addition, we observed that the lag time between the peak of the upward trend and the month that the laws were enacted ranged from about 2 months in Alaska (Fig. 2a) to about 6 years in Maine (Fig. 2k) and Rhode Island (Fig. 2t).

Statistical analysis

A summary of the panel time series regression results using total gonorrhea morbidity data is presented in Table 1 (only coefficients with $P < 0.10$ were shown). Although the annual/seasonal lag was significant, we had to drop it in our final model. This was because including the 12-month lag drastically reduced the number of data points after the intervention for most of the states. Consequently, we used the first two autoregressive lags which were statistically significant ($P < 0.01$) and the overall r-squares were not very different—88% with the seasonal lag vs. 86% otherwise. As described in the methods, we explored different times after the laws were enacted in determining the instant changes and slopes. Thus, the months in parenthesis for each state in Table 1 represent the period that we used in the final models.

Based on our regression results, our fixed effects (within states) model showed that only four states had significant instant decreases sometime after the EPT laws were enacted—Alaska (19%, $P < 0.01$), Illinois, (13%, $P < 0.05$) Minnesota (14%, $P < 0.01$), and Vermont (13%, $P < 0.10$) (see Table 1). Our results also showed that two states had significant increases in the slope of gonorrhea morbidity after the laws were enacted—Maine (52%, $P < 0.01$) and North Dakota (38%, $P < 0.01$). When we used the random effects model (within and across

states – the appropriate approach for our study), there were no significant changes in any of the states except for Vermont. However, the result from Vermont was not reliable. This was because Vermont had substantially low rates that were largely between 1 and 20 (cases/100,000) coupled with missing data in some months particularly after the law was enacted (see Fig. 2x). Thus, compared with the changes in gonorrhea morbidity that occurred in the control states around the months that the EPT laws were enacted in the states with EPT laws (experimental group), there were no statistically significant differences. The results were consistent when we repeated the analyses using monthly gonorrhea morbidity data for males only and females only.

When we repeated the analyses for each subregion, our main results did not change. In other words, when we compared the gonorrhea rates within and across states focusing on similar states based on subregion categories, we did not find any statistically significant differences between the states with EPT laws and those within the same subregion that did not have EPT law(s).

Discussion

In this study, we examined state-level monthly gonorrhea morbidity and assessed the potential impact of existing EPT laws in relation to the time that the laws were enacted. Based on the data and comprehensive analyses, we found significant decreases (ranging from 13% to 19%, $P < 0.10$) within four of the states with EPT laws around the months that the laws were enacted (Alaska, Illinois, Minnesota, and Vermont). On the contrary, we found significant upward trends in gonorrhea morbidity in two states that had the laws (Maine and North Dakota). However, when the changes within the four states were compared with the contemporaneous changes in the states that did not have the laws, the changes were no longer statistically significant. Together with the upward trend we found for two other states on or after the EPT laws were enacted, our results suggest that the decreases that we found within the four states cannot be ascribed exclusively to the enactment of the EPT laws.

To our knowledge, this is the first study that assessed the impact of the EPT laws at the state level. Thus, comparison with results from previous studies is not possible. Within Illinois, our results showed a smaller decrease in gonorrhea morbidity when compared with the magnitude of the decrease found by Staras et al.[25] – 13% vs. 21%. However, Staras et al. used a different set of states in their control group and their objective was to assess the impact of a September 2009 alcohol excise tax on gonorrhea morbidity.[25] Although Staras et al., did not discuss the EPT law as a potential confounding event, they acknowledged other events that might have resulted in the decrease in gonorrhea morbidity around that time. We found that the lowest gonorrhea morbidity over the entire period was in February 2010 which was the same month that the Illinois STI reporting system switched to the electronic platform.[25] Based on the confluence of events around the time of the decrease in gonorrhea morbidity, it is difficult to ascribe the decrease found within Illinois exclusively to the EPT law (or any other/combination of events) without additional and more specific analyses.

In most of the states with the EPT laws, we observed periods of steep increases in gonorrhea morbidity followed by a period of sustained low morbidity before the laws were enacted.

Thus, in those states, the laws were enacted in the periods of low morbidity. However, the length of the periods of steep increases, the magnitude of the increases, and the lag time between the peak of the increase and the month that the laws were enacted varied widely across states. It is conceivable that during the period of the increases, EPT laws were considered as part of the efforts to control/slow the trend. However, due to the lengthy legislative processes including the prevailing political atmosphere, the laws were enacted several months after the upward trends had subsided.

Limitations

Our study has some limitations largely associated with the surveillance data that we used. In general, the surveillance data depend largely on medical providers testing and reporting practices.[1] Thus, given that our study was a state-level analyses that compared changes in gonorrhea morbidity within and across states, it is conceivable that the disparate data collection patterns might bias our results. However, it is difficult to know the magnitude of these biases. On the other hand, to the extent that these reporting systems and practices are specific to individual states, the inconsistencies might not be as much of a limitation as one would expect when focusing on trends.[1] Consequently, changes in reporting systems might make the interpretation of result in such analyses quite challenging, as was found for Illinois. Finally, we did not consider the possibility that EPT laws in one state might affect gonorrhea morbidity in the neighboring states.

It is important to note that there is a cascade of necessary intermediate events/outcomes between the enactment of the EPT law and the final expected outcome (decreased morbidity). The potential for EPT laws to cause notable reductions in gonorrhea or chlamydia morbidity at the population level likely depends on achieving high compliance to the following intermediate outcomes:

- STI service providers are aware of the law and practice it—offer the medication to their clients (infected persons);[26]
- Clients (infected persons) understand the benefits of EPT and accept the offer to deliver the medication to their sex partners;[10]
- Clients find and offer the medication to their partners on time;[10] and
- The partners accept the medication and use them to treat their infections successfully.[10]

Due to lack of data, we do not have state-wide measures on any of the intermediate outcomes listed above. Analyses of data on interviewed gonorrhea cases from select sites in the US found that EPT laws and policies were associated with higher reports of receipt of EPT.[6] However, Cramer et al. noted that the proportion of patients who received EPT in the jurisdictions with laws permitting EPT for gonorrhea were relatively low—less than 14%.[6]

Conclusion

In this study, we examined monthly gonorrhea morbidity data from all the states in the US to assess the potential impact of existing EPT laws. Based on our comprehensive analyses, we

did not find any visual or statistical evidence that the states with laws permitting EPT for gonorrhea (and/or STIs) had any favorable impact on gonorrhea morbidity. However, our finding should not be construed as a measure of inadequacy, or failure of the EPT law itself. This is because EPT has to be practiced effectively at different levels and for a relatively large proportion of identified gonorrhea cases for it to result in a measurable final outcome (decreased morbidity). This suggests that activities to increase awareness of EPT and its laws and policies among providers and patients should be part of major STI control and prevention efforts. Second, our study examined gonorrhea trends at a relatively large scale (state level) which might not show impacts at particular service venues or smaller geographic units with specific STI services. Thus, more studies are needed to assess the intermediate outcomes of the EPT laws. In addition, more localized evaluation studies (such as in neighborhoods, cities, within sub-populations or sexual networks) are needed to better assess the effectiveness (or the lack thereof) of the EPT laws.

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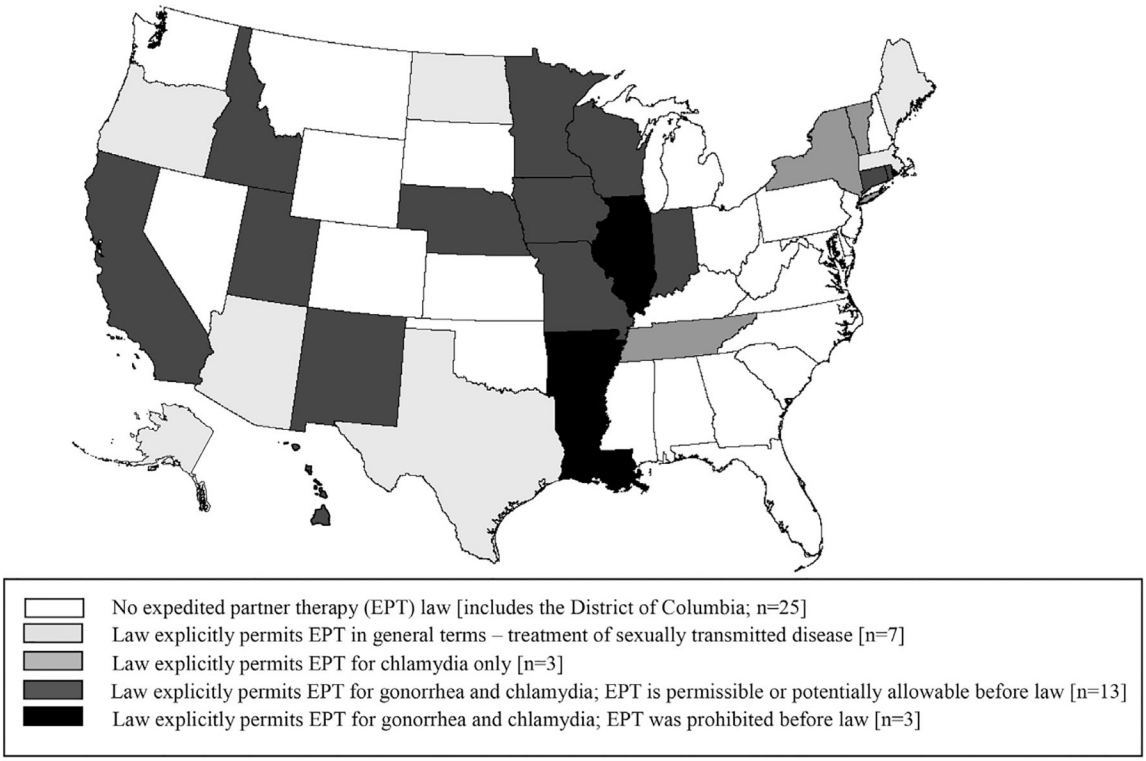

Fig. 1 –.

Map of the United States showing the EPT status for all 51 states (including the District of Columbia) as of December 2014. Note: Alaska and Hawaii were not drawn to scale. Subregions included: New England—Maine, New Hampshire, Massachusetts, Vermont, Rhode Island, and Connecticut. Middle Atlantic—New York, New Jersey, and Pennsylvania. East North Central—Ohio, Michigan, Indiana, Illinois, and Wisconsin. West North Central —Minnesota, Iowa, Missouri, Kansas, Nebraska, South Dakota, and North Dakota. South Atlantic—Delaware, Maryland, District of Columbia, West Virginia, Virginia, North Carolina, South Carolina, Georgia, and Florida. East South Central—Kentucky, Tennessee, Alabama, and Mississippi. West South Central—Arkansas, Louisiana, Oklahoma, and Texas. Mountain—Montana, Idaho, Wyoming, Colorado, Utah, Nevada, Arizona, and New Mexico. Pacific—Washington, Oregon, Hawaii and Alaska, California.

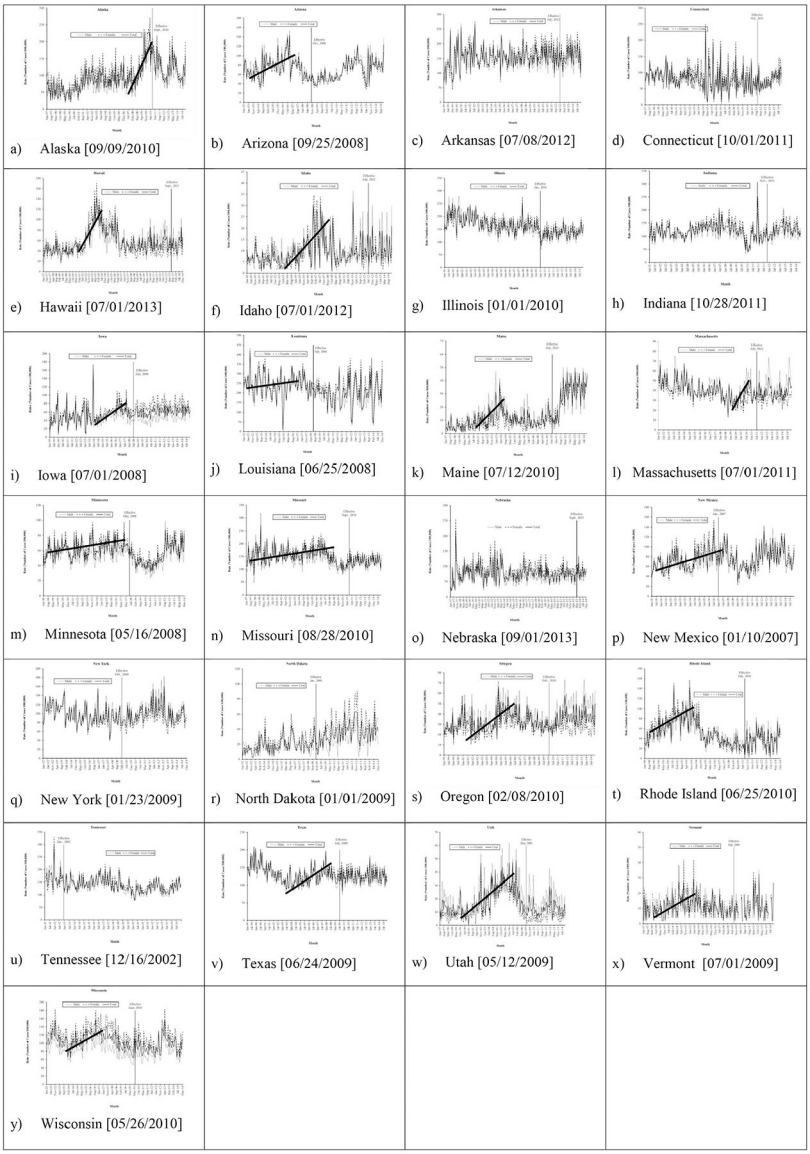

Fig. 2 –.

Charts of monthly gonorrhea rates (number of cases/100,000) by gender and total from January 1995 to December 2014 (where available) for states with all the available forms of expedited partner therapy (EPT) laws and their respective effective dates as of December 2014. Notes: We omitted California, Hawaii, and Nebraska because the effective dates were outside the dates for which monthly data was available. Dates in square brackets represent the effective dates of the EPT law. Vertical lines represent the earliest month in which the impact of the EPT law can be realized. For effective dates on or after the 23rd of the month, the vertical lines are placed in the following month. Bold slanted lines represent trend lines for selected periods.

Table 1 –

Summary panel regression results: dependent variable is the log of total gonorrhea rate in month t.

Variables	Fixed effects model	Random effects model
Autoregressive (R_t)	**β [95% CI]**	**β [95% CI]**
Gonorrhea rate, month t-1 (R_{t-1})	0.2264 [0.2054 to 0.2473]***	0.4720 [0.4532 to 0.4908]***
Gonorrhea rate, month t-2 (R_{t-2})	0.2318 [0.2054 to 0.2473]***	0.4737 [0.4549 to 0.4924]***
State-specific instant change (D)[a]	**δ [95% CI]**	**δ [95% CI]**
Alaska (January 2011 to December 2014)	−0.2064 [−0.3514 to −0.0614]***	NS
Illinois (February 2010 to December 2014)	−0.1345 [−0.2671 to −0.0018]**	NS
Minnesota (January 2009 to December 2014)	−0.1500 [−0.2632 to −0.0369]***	NS
Vermont (July 2009 to December 2014)	−0.1445 [−0.2914 to 0.0025]*	−0.2304 [−0.3778 to −0.0830]*
State-specific slope/change overtime (T)[a]	**ϕ [95% CI]**	**ϕ [95% CI]**
Maine (July 2010 to December 2014)	0.5181 [0.3761 to 0.6600]***	NS
North Dakota (January 2009 to December 2014)	0.3820 [0.2539 to 0.5101]***	NS

*** $P < 0.01$;

** $P < 0.05$;

* $P < 0.10$; only coefficients with $P < 0.10$ were shown.

CI, confidence interval; NS, not significant.

[a] The months in parenthesis represent the period we used in the final models.